MINISTRY OF HEALTH OF UKRAINE

BOGOMOLETS NATIONAL MEDICAL UNIVERSITY

DERMATOLOGY VENEREOLOGY

(Second edition, revised and expanded)

Edited by Corresponding Member
of the National Academy of Medical Sciences of Ukraine,
Professor V.I. Stepanenko

Recommended By the Academic Council of the Higher Educational Institution of the National Medical University named after O.O. Bohomolets, Ministry of Health of Ukraine, as a textbook for higher medical education seekers at higher education institutions of Ukraine

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The second edition of the textbook (the first edition was released in 2013) was prepared by the staff of the Department of Dermatology and Venereology with the course in Cosmetology of the National Medical University named after O.O. Bohomolets and leading dermatovenereologists from similar departments of higher education institutions of Ukraine, under the general editorship of Corresponding Member of the NAMS of Ukraine, Professor V.I. Stepanenko.

The textbook presents modern views on the etiology and pathogenesis of skin diseases and their appendages, as well as infections transmitted mainly by sexual contact. It includes the clinical picture and course of several dermatoses and infections, primarily transmitted through sexual contact, and presents the latest methods of diagnosis, treatment, and prevention of these conditions.

The textbook is compiled in accordance with the Law of Ukraine «On Higher Education» (2014), the Higher Education Standard for the specialties «Medicine», «Pediatrics», and «Dentistry», which defines the volume of theoretical knowledge, skills, and other competencies required to achieve the learning outcomes, in line with the educational activity concept and educational programs for these specialties based on relevant sectoral standards.

The textbook includes compulsory topics based on the thematic plan for lectures and practical sessions. It also includes several other sections of dermatology and venereology, the knowledge of which is essential for differential diagnosis of nosological forms of skin pathology. In addition, the textbook features topics from elective courses «Medical Cosmetology» and «Skin Neoplasms». The text includes illustrative material based on clinical observations by the co-authors of the textbook, including staff from the Department of Dermatology and Venereology with the Cosmetology course of the N.M.U. named after O.O. Bohomolets, as well as some exclusive illustrations from the museum of waxworks of this department. The «Medical Cosmetology» section presents illustrative materials from clinical observations by the co-authors from the relevant department at Odessa National Medical University.

For students of higher medical education institutions in Ukraine, interns, and practicing doctors.

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PREFACE TO THE SECOND (REVISED AND EXPANDED) EDITION

Since the first edition of this textbook was published in 2013 and recommended by the Ministry of Health of Ukraine as a textbook for students of higher medical educational institutions of the IV accreditation level, several methodological changes have taken place at the legislative level concerning higher education in Ukraine. Taking this into account, the second edition of the textbook has been prepared in accordance with the Law of Ukraine «On Higher Education» (2014) and the Higher Education Standard for the specialties «Medicine,» «Pediatrics,» and «Dentistry.» These standards define the scope of theoretical knowledge, skills, competencies, and other learning outcomes in line with the concept of educational activities and programs based on relevant industry standards.

During the preparation of this second edition, advances in dermatovenerology in recent years were taken into account. Several sections related to skin diseases and sexually transmitted infections have been revised and expanded, particularly in light of updated diagnostic and treatment protocols.

Dermatovenerology is a branch of clinical medicine that includes dermatology (from the Greek words derma – skin and logos – study) – the science of skin structure, function, and diseases – and venereology (Venus, the Roman goddess of love) – the science of venereal diseases. The unification of these fields was based on the fact that some venereal diseases present with skin rashes.

In recent decades, the term «venereal diseases» has been replaced with «sexually transmitted infections» (STIs) due to the significant increase in diseases where the pathogen is primarily transmitted sexually. Currently, there are approximately 2,000 known dermatological conditions, along with more than 20 diseases primarily transmitted through sexual contact.

This textbook presents modern perspectives on the etiology, pathogenesis, clinical presentation, course, and classification of skin diseases, as well as sexually transmitted infections. It also describes available and novel diagnostic methods, differential diagnostic criteria, contemporary treatment approaches, and preventive measures.

Studying the fundamentals of dermatovenerology in the fourth year of medical and dental faculties at higher educational institutions in Ukraine is an essential component of medical training. This field is closely connected to internal

medicine, infectious diseases, urology, obstetrics, and gynecology. Pediatric dermatovenerology, in turn, is closely linked with neonatology and pediatrics.

As an independent clinical discipline, dermatovenerology is divided into general and specialized sections. Its study involves acquiring knowledge about the etiology, pathogenesis, and clinical manifestations of various dermatological disorders, as well as mastering modern diagnostic and treatment approaches and implementing preventive measures. Medical students must develop the ability to identify and correctly diagnose different dermatoses and sexually transmitted infections, communicate with patients in a professional and ethical manner, and ensure appropriate patient care.

Mastering the curriculum outlined in this textbook should help medical students develop both clinical and preventive thinking. It emphasizes the medical and social significance of dermatovenerology and the rationale for implementing specific preventive measures.

The goal of this textbook is to ensure compliance with the requirements of the Law of Ukraine «On Higher Education» (2014), particularly by providing up-to-date theoretical knowledge and assisting medical students in acquiring practical skills. The textbook is designed to encourage independent study of each topic and lecture material through self-directed learning and practical sessions.

The material is presented at a professional level, integrating interdisciplinary elements. Given the vast number of dermatological conditions and sexually transmitted infections, this textbook helps consolidate theoretical knowledge and assess students' professional reasoning through self-assessment questions and practical applications of previously acquired skills.

Finally, I would like to express my deep gratitude for the technical assistance in preparing this second revised and expanded edition to V.M. Serebrova, a staff member of the Department of Dermatology and Venereology with a Course in Cosmetology at Bogomolets National Medical University; O.O. Kupriyanova, director of the «KIM» publishing house in Kyiv; and V.V. Bobrova, an employee of this publishing house.

We invite users of this textbook to submit their comments and suggestions regarding its content to the Department of Dermatology and Venereology with a Course in Cosmetology at Bogomolets National Medical University at the following address 01601, Kyiv, Taras Shevchenko Boulevard, 13.

Corresponding Member
of the National Academy of Medical Sciences of Ukraine,
Professor V.I. Stepanenko

ANNOTATION
TO THE TEXTBOOK «DERMATOLOGY, VENEREOLOGY»
(Second Edition, Revised and Expanded)

The second edition of this textbook (the first was published in 2013) was prepared by the staff of the Department of Dermatology and Venereology with a Course in Cosmetology at Bogomolets National Medical University and leading dermatovenerologists from similar departments of higher education institutions in Ukraine, under the general editorship of Corresponding Member of the National Academy of Medical Sciences of Ukraine, Professor V.I. Stepanenko.

The textbook has been compiled in accordance with the Law of Ukraine «On Higher Education» (2014) and the Higher Education Standard for the specialties «Medicine,» «Pediatrics,» and «Dentistry.» These standards define the theoretical knowledge, skills, and competencies required to achieve specified learning outcomes in accordance with the educational programs for these specialties, based on relevant industry standards. The textbook includes mandatory topics according to the thematic plan of lectures and practical sessions. Additionally, it covers other sections of dermatology and venereology essential for the differential diagnosis of dermatological conditions. Furthermore, elective courses on Medical Cosmetology and Skin Neoplasms are also included.

This second edition takes into account recent advancements in dermatovenerology. Several sections on skin diseases and sexually transmitted infections (STIs) have been revised and expanded, reflecting updates in diagnostic and treatment protocols.

From a modern perspective, the textbook presents views on the etiology and pathogenesis of skin diseases and its appendages, as well as STIs. It describes the clinical manifestations and progression of various dermatoses and sexually transmitted infections in contemporary conditions. Additionally, it covers the latest diagnostic methods, treatments, and preventive measures. The textbook includes illustrative materials based on clinical observations by its co-authors, particularly the staff of the Department of Dermatology and Venereology with a Course in Cosmetology at Bogomolets National Medical University. Some illustrations feature exclusive teaching exhibits from the department's moulage museum. In the section «Medical Cosmetology,» illustrative material of clinical observations by the co-authors of this section, staff members of the specialized department of the Odessa National Medical University, is presented.

This publication enables medical students to navigate the diverse clinical presentations of skin diseases and STIs, perform differential diagnoses, prescribe appropriate treatment using modern pharmaceuticals, and provide patients with recommendations to prevent the occurrence and recurrence of specific inflammatory conditions, as well as to curb their further spread.

The authors of the textbook considered current teaching standards, incorporating an innovative approach to independent student learning. Special attention was given to transitioning to European educational principles and assessment of theoretical knowledge, skills, and practical competencies. This work is based on many years of teaching experience in this discipline at medical faculties of higher education institutions in Ukraine.

The textbook is intended for medical students, interns, and practicing physicians in higher education institutions of Ukraine.

V.I. Stepanenko

1 TOPIC

Introduction to Dermatovenerology

Dermatovenerology is a clinical medical science to study objective and subjective features of a variety of clinical manifestations of human skin and mucous membrane lesions in their unity and interaction with internal organs and systems, as well as environment in general.

TRAINING AND EDUCATIONAL PURPOSES

- To analyze the stages of formation of dermatovenerology as an individual clinical science
- To define the main achievements of global and domestic dermatovenerology

TO KNOW:

- the value and place of dermatovenerology in residency training;
- definition of dermatological pathology as a medical-psychological problem;
- the general description of historical development of dermatovenerology (the role of works by Hippocrates, Cornelius Celsus, Avicenna, Mercurialis, Whelan, etc.);
- data on formation and development of various foreign schools of scientific dermatovenerology in the XIX–XX centuries (French and German schools of dermatology, their founders and prominent representatives – Jean Alibert, F. Gebre, K. Gibert, M. Kaposi, etc.);
- the contribution of the founders of Russian school of dermatovenerology – Polotebnov A.V., Tarnowski V.M., Pospelov A.I. and others in development of dermatovenerology;
- significant contribution of Ukrainian school of dermatovenerology (Stukovenkov M.I., Nikolsky P.V., Zelenev I.F. and others) in global dermatology.

TO BE ABLE TO:

- distinguish the main phases of development of dermatology and venereology;
- evaluate evolutionary breakthroughs of global and domestic science towards development of diagnostic methods and pathogenic therapeutic regimens of dermatovenerologic patients;
- manage basic deontological principles of dermatologist.

Dermatology: Stages of Development

Dermatology is the science to study skin. Dermatology studies skin structure and functions in normal condition and upon incurrence of any skin problems from different points of view: anatomical, physiological, clinical, biochemical, histochemical, immunological and others.

Dermatology is closely related to other areas of clinical medicine: venereal diseases, infectious diseases, medical diseases, pediatrics, endocrinology, neuropathology, psychiatry, etc. At present, the fact that skin is a body linked to the whole organism with circulatory, lymphatic, endocrine and nervous systems is considered an axiom. In addition, skin is an important part of the immune system. Respectively, visceral diseases affect skin condition to any extent. As the outer body covering, skin is affected by a variety of harmful environmental factors that can manifest itself in a barely noticeable to severe form.

As science, dermatology originated in XVIII century. Though, a number of skin diseases are known to mankind since ancient times. Development of dermatology is closely linked to advancement of natural science and social systems, which allows studying the history of dermatology in stages.

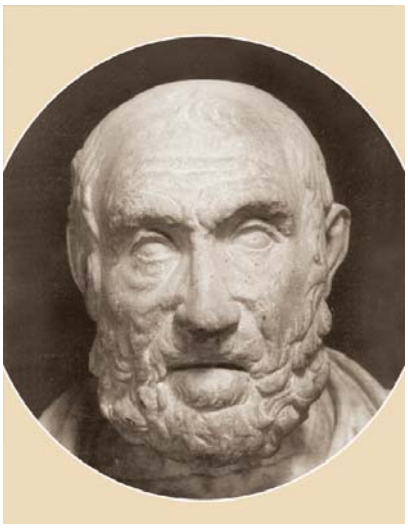
The first phase refers to the time of primitive society and formation of the slave- owning system. Definitely, primitive man paid attention to various skin lesions, responded to itching caused by different pathological processes and noticed that some plants helped to reduce, while others just increased irritation. From generation to generation, people accumulated observations over the course of various skin diseases and means to treat them.

With the advent of writing, the accumulated experience made its appearance in medical treatises. The first data on skin diseases is recorded in ancient China, India, Egypt and Greece. In particular, a doctor known as Goang-Tee systematized medical knowledge of that time in China in 2637 BCE. The diseases described in his treatise involved some cases of dermatopathy: mange, furuncle, carbuncle, erysipelas, impetigo, ichthyosis, eczema, leprosy, alopecia, vitiligo, and others. The work also reported on methods of treatment of these diseases.

Ancient Indian medical treatises (2000–700 years. BCE) described numerous skin diseases, as well as over seven hundred of different plants used to treat them.

Egyptian papyrus dated by 1700 BCE contains a list of drugs for various diseases, including scabies, as well as a large number of recommendations on hygienic skin care. Dated by 1500 BCE, so-called books of Moses describe leprosy *(lepra)*, loss of skin pigment *(vitiligo)* and hair loss *(alopecia)*.

In ancient Greece and Rome, people also studied dermatology. The greatest of Greek physicians of the time, Hippocrates (460–370 yrs. BCE), is the founder of scientific medicine. He summarized and systematized known data on skin



Hippocrates
(460-370 years. BCE)



Aulus Cornelius Celsus
(25 BCE – 50 CE)

diseases, described leprosy, scabs, alopecia, herpes and other dermatoses (more than 40 clinical entities). Hippocrates was the first to focus on the link of skin diseases with changes of internal organs and influence of environmental factors. In his view, human skin diseases associated with some pathology of internal organs were predetermined by the «spoiled juices» of the body (humoral theory). In ancient Rome, science in general, including medicine, reached a higher level. Descriptions of some skin diseases become more detailed, while new dermatological terms appear; some of them are used to date.

The 1st century BCE allocates an outstanding physician, Aulus Cornelius Celsus, who left a detailed description of many skin diseases, including furunculus, carbuncles, barber's rash, psoriasis, erysipelas. In treatment of eczema and similar lesions, Celsus advised to use lead and sulfur ointment. His successor, Galen (2nd century BCE), attempted to study skin structure. He proposed a classification of skin diseases based on their location: diseases of head, arms, legs and other body parts.

In the following century of Great Migration, general science, including medicine, is falling into decay. The second stage in the development of medicine, particularly dermatology, belongs to the period of Middle Ages. Instead of slave-owning system, European countries welcome feudalism. The center of medical research is moving to the East: to Arab countries. On the border of the X–XI centuries CE, the world received the most famous work of the outstanding scientist and physician, Abu Ali Ibn Sina, better known as Avicenna. His «Canon of Medicine» was the first paper to successfully encyclopedize and summarize the medical knowledge of the time. Avicenna devoted considerable attention to the study of skin diseases. He described pemphigus, leishmaniasis, and hives; knew how to differentiate leprosy from

elephantiasis, pruritus of scabies; addressed the issues of cosmetology.

In the second half of the XVI century, Europe welcomed the third stage in the development of medicine, particularly dermatology. This period is associated with the decay of feudal society, which is replaced by capitalist socio-economic system. There comes development of natural sciences, physics, chemistry, medical science, especially anatomy and physiology. During this period, the first books of skin diseases appear. The work of an Italian scientist Jerome Merkurialis (1572) was considered most popular paper of the time. Girolamo Mercuriale provided all previously described skin conditions, but failed to classify them.



Avicenna (Abu Ali Hussain Ibn Abdallah Ibn Sina) (980-1037 yrs.)

As an independent scientific medical discipline, dermatology was allocated in the second half of the XVIII century. Morphological direction comes to the fore. This fact involves the need to organize and unify the description, as well as interpret manifestations of skin diseases: morphological elements of the rash. There appears a set of textbooks, particularly a book by an Austrian doctor, Plenk (1772), in which he attempts to classify skin diseases basing on morphological characters; a textbook by a French doctor, Lorrie (1777), in which he described the anatomy and physiology of skin and tried to identify the etiology and pathogenesis of some skin diseases; a textbook by an English doctor, Wheellen (1798), who succeeded to classify skin diseases by primary morphological features.



Jerome Merkurialis (Girolamo Mercuriale) (1530-1606 yrs.)

In the early nineteenth century, first dermatological schools are formed. Establishment of dermatology as a separate field of clinical medicine is completed. Formed in 1801 in Paris and based on the Saint-Louis Hospital, French Dermatovenereological School was the first institution for patients with skin diseases. Jean-Louis Aliber (1768–1837 yrs.) is justly considered the school's founder. He introduced the terms of «dermatitis», «syphilide»



Jean-Louis Alibert
(1768-1837 yrs.)



Ferdinand von Hebra
(1816-1880 yrs.)

and «ichthyosis». Talented students and followers of Aliber, particularly Biett (1781–1840 yrs.), Cazenave (1795–1877 yrs.), Gibert (1796–1866 yrs.), Vidal (1825–1893 yrs.), Bazin (1807–1878 yrs.), Hardy (1811–1893 yrs.) are also to be noted. The concept based on the fact that the main cause of skin diseases is presented by humoral factors, so-called dyscrasia and diathesis, is typical for French dermatological school.

Vienna (German) Dermatologic School was formed in the 40s of the XIX century. Ferdinand von Hebra (1816–1880 yrs.) is considered the school's founder. F.Hebra believed that postmortem skin studies were of biggest importance in the study of skin diseases. He created an appropriate classification of dermatoses. Considering the majority of skin diseases as local processes mainly caused by external factors, Hebra reduced the value of domestic factors in the etiology of dermatoses to a minimum.

Divergent views on the nature of skin diseases caused long controversy between the French and Viennese dermatological schools, which ended only in the early twentieth century.

Among talented members of the Vienna (and hence German) dermatological school of the nineteenth century, the following scientists are to be noted: Simon (described *Demodex folliculorum*), Kaposi (investigated idiopathic hemorrhagic sarcoma, known as Kaposi's sarcoma), Neumann (identified vegetating pemphigus), Auspitz (determined a triad of symptoms characteristic of psoriasis), Koebner (established the phenomenon of isomorphic reaction in psoriasis).

In other countries, development of dermatology was based on views and attitudes of the French or Vienna dermatological schools and featured no significantly independent, original peculiarities

In 1863, the establishment of the Charter of the Universities facilitated evolution of academical medical science, including scientific dermatology.

In 1863, the academic specialized clinic of dermatology was formed on the basis of the Kiev Military Hospital. Goretskiy L.K., the assistant professor of the Department of Special Treatment of the Kiev University of St. Vladimir, became a head of the clinic and curator of the skin disease course. Headed by Goretskiy L.K., the institution was virtually the first clinic of dermatology. Headed by Professor Gyubbenet Kh.Y., syphilitic clinic was a part of surgical clinic. In 1864, associate professor Goretskiy L.K. gave a course of lectures in skin diseases to medical students. Students of the 9th and 10th semesters attended classes twice a week. Since 1873, Goretskiy L.K. was asked to teach not only the course of skin diseases, but also give lectures on syphilis. He was able to properly combine theoretical and practical training of students. At the end of the 60ies of the XIX century.

In 1884, the readership course of skin and syphilitic diseases was redeveloped into a separate department. Within the period from 1884 to 1897, Professor Stukovenkov M.I. became the first head of the department. He is justly considered the founder of the Ukrainian (Kiev) School of Dermatology. The school created by Stukovenkov M.I. stood for a patient's comprehensive examination, rather than just studying of visible manifestations of a skin disease. Thus, the members were to reveal the inner connection of dermatoses with the general body condition, as well as detect the causes of the lesions. Stukovenkov M.I. devoted special attention to studying of nervous system of patients with skin diseases. He first acquainted physicians with foliaceous pemphigus, mycosis fungoides, rhinoscleroma and idiopathic Kaposi's sarcoma in his publications. His original researches of treatment of syphilis with mercurial preparations are of particular significance. Stukovenkov M.I. provided the world's first scientific proof of therapeutic doses of mercury drugs in treatment of syphilis infection.

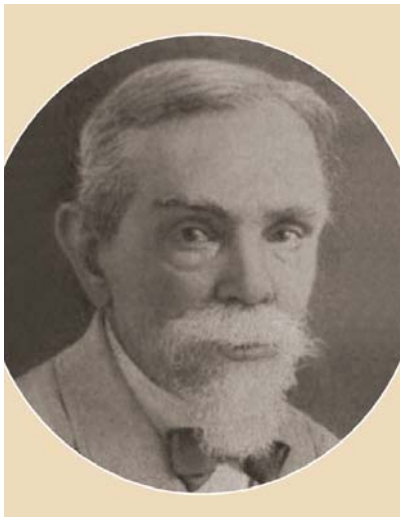


Ludwig Kazimirovich Goretsky
(1826-1885 yrs.)

The best representatives of the national school of dermatovenerologists established by Stukovenkov M.I. became well known scientists and headed the specialized departments of medical faculties in some universities, in particular Nikolsky P.V. (Warsaw, Rostov-on-Don), Borovsky V.K. (Kiev), Zelenev I.F. (Kharkiv), and others. Professor Nikolsky P.V. became world famous thanks to the fact he was the first to describe the symptom of exfoliation in pemphigus verus, which entered into the world diagnostic practice under his name. In turn, Nikolsky P.V. established



Stukovenkov M.I.
(1842-1897 yrs.)



Nikolsky P.V.
(1858-1940 yrs.)

a scientific school that created future professors Glukhenky T.T., Kozhevnikov P.V., Lavrov A.P., Shiryaev F.I., etc.

Within the period from 1898 to 1916, professor Tomaszewski S.P. replaced Stukovenkov M.I. as a head of the university department. He lobbied for women's higher medical education and became one of the organizers of the Kiev Medical Women's Institute, founded in 1916. In 1900, Tomaszewski S.P. established the Scientific Association of Dermatology and Venereology of Kiev.

In the future, chairholders and employees of the science department of the University of Kiev kept with the best traditions to enrich national and global Dermatovenereology with their scientific achievements. So, Professor Terebinsky V.I. studied the histopathology of skin and ichthyosis, worked on the clinical diagnosis of syphilis; Professor Borovsky V.K. improved treatment and prevention of syphilis, Professor Tyzhnenko A.M. actively prepared scientific and pedagogical staff, researched skin cancer, red and tubercular lupus, hyperkeratosis. Associate professor Bogdanovich S.N. was a talented clinician and gifted diagnostician of skin diseases. He developed and introduced the expurgatory mode of treatment of skin allergic diseases into clinical practice, worked out diagnostics of skin tumors. Scientific and practical developments and achievements of Professor Kuznets M.M. (studied the histological changes in skin aging, malnutrition, vitamin deficiency) and Professor Kartamyshev A.I. (introduced additional diagnostic test for the diagnosis of pemphigus – to determine the level of chloride in the urine, actively prepared scientific and pedagogical staff, created a tutorial «Skin and Venereal Diseases», which has been repeatedly published and republished in Ukrainian and Chinese) are also especially noteworthy.

Professor Pototsky I.I. is considered an opinion leader in medical-scientific schools of Ukraine. His works are devoted to a deep research of the role of



Zelenev I.F.
(1860-1918 yrs.)

nervous system in development of some chronic dermatoses, respiratory function of skin, skin lesions in leukemia, as well as improvement of treatment of syphilis. His methods of zonal ultraviolet skin irradiation in psoriasis and oxygen therapy in a number of dermatoses are well known. He trained a large group of talented scientists, most of whom were heads of departments of dermatology in various medical schools or heads of departments in professional research institutes, in particular Kolyadenko V.G. (Kiev), Lyashenko I.N. (Vinnitsa), Levkovsky N.M. (Kiev), Tsirkunov L.P. (Kiev), Khasabov L.M. (Rostov-on-Don), Grebennikov V.A. (Rostov-on-Don), Rodin A.Y. (Simferopol), Karagezyan M.A. (Krasnodar), Tseraidis G.S. (Kharkiv) and others. Professors Karysheva K.O., Kalantaevskaya K.A., Glukhenky B.T., Kalyuzhnaya L.D. are also well-known representatives of the school of Dermatovenereology of Kiev.

The dermatological school of Kharkov is considered a strong Ukrainian institution. Since 1876, associate Professor Kuznetsov A.K. lectured the course of skin diseases, while Professor of surgery Zarubin I.K. lectured a course of syphilology to students of the medicine faculty of Kharkov. An independent chair of skin and venereal diseases was founded in Kharkov in 1885. Until 1897, this department was headed by Professor Brunev O.Y. From 1897 to 1911, the position was given to Professor Zelenev I.F., the founder and editor of the «Journal of Skin and Venereal Diseases», published from 1901 to 1918 in Kharkov. Renowned scientists that headed the Department of Skin and Venereal Diseases at the Kharkov Medical Institute included Professor Sobolev L.A., Professor Popov I.S. (developed a microtest- tissue method to research mushrooms, described new clinical forms of pyodermas). In addition, Popov I.S. prepared a number of talented scientists and organizers of dermatovenereological field, among which professors Zadorozhny B.Y. (conducted fundamental research of psoriasis and several other severe dermatoses) and Pyatikop A.I. are to be mentioned.

An important role in development of the Ukrainian School of Dermatovenereology belongs to the first Ukrainian Scientific Research Institute of Dermatovenerology, established in 1924 in Kharkov. This institute was headed by famous dermatovenereologists: professors Fedorovsky A.N., Krichevsky A.M., Pyatikop A.I., Mavrov I.I.

From 1961 to 1976, Professor Torsuev N.A., the Head of the Department of Skin and Venereal Diseases of the Medical Institute of Donetsk was considered

an outstanding representative of the Ukrainian dermatological school. He implemented systematization of occupational skin diseases. A comprehensive study of leprosy conducted by Torsuev N.A. received worldwide recognition.

Venerology: Stages of Development

Venereology is the science of sexually transmitted diseases (diseases transmitted primarily through sexual contact). These infectious diseases feature specific pathogens. Therefore, venereology studies the epidemiology, pathogenesis, clinical manifestations, diagnosis, treatment and prevention of related infections.

The data about sexually transmitted diseases (diseases transmitted mainly through sex) came down to us from ancient times. However, until the 30s of the XIX century the understanding of these diseases was fairly simplistic.

The first stage in development of venereology dates back to ancient times and continued until the end of the XV century. Historical monuments of Egyptian medicine, particularly the Ebers Papyrus (1700 BC. E.), report about inflammation of the urinary canal (urethra). Hippocrates (V century BC) provided a sufficiently detailed clinical picture of inflammation of the urethra. He also described a «white discharge» from the vagina. Later, Galen (II century AD) proposed qualifying relevant lesions as gonorrhea(*γονοζ* – seed, *ρεω* – flow). Arabic physician Abu-Bakr-Rhazes (IX century BC) proposed to treat urethritis with lead solution syringing. By the end of the XV century, scientists accumulated numerous observations of these diseases, in particular diagnosed their infectiousness and transmission, as well as and identified the means of prevention.

The second phase of the development of venereology belongs to the end of the XV century, when Europe faced a pandemic of a previously unknown disease, which was first called «*lues*» (punishment). In the future, the disease received the names of some saints (St. Jorgen's disease), as well as that of the countries it came from (Spanish, French, German, Polish disease). Later, the disease was called «syphilis.»

Until now, the issue of origin of syphilis remains debatable. Some scientists believe syphilis existed in Europe, Asia and the Middle East since ancient times. Proponents of this hypothesis point out that excavations of Neolithic burials at various places of Eurasia revealed bones of people with signs of past specific syphilitic gummatous osteomyelitis and gummatous osteoperiostitis. In addition, to prove this hypothesis they reference to the ancient Chinese, Indian and Egyptian treatises that provide descriptions of diseases in the genital area, anus, mouth and nose, as well as bones, which can be considered as manifestations of syphilis. We also know that Hippocrates (V c. BC. E.), Celsus (I c. BC. E.) and Galen (II c. BC. E.) described condylomatous rash on the genitals in combination with diseases of the larynx and bone, which are also

possible manifestations of syphilis. In his treatises (X–XI centuries, BC. E.), Avicenna described diseases similar to the clinical manifestations of syphilis.

Ex another hypothesis by some modern scholars, syphilis first appeared in Africa. They suggest that pathogens of tropical treponematoses, including frambesia, carate, bejel, as well as and the causative agent of syphilis represent different versions of once common primary treponema. The early Neolithic age is considered the period when the disease of human treponematosis emerged. In addition, there is further evidence for this hypothesis: there is observed some morphological and biological identity of Treponema pallidum (the causative agent of syphilis) and treponemes that cause tropical treponematosis with a similar clinical course of these infections and cross-immunity.

However, the hypothesis of American origin of syphilis features the greatest number of adherents. It is indicated that the disease was brought to Europe by the sailors from the expedition of Christopher Columbus, after the discovery of America. Sailors were infected from the natives of Haiti, where the disease was known long before the arrival of Europeans. It is important to note that authoritative domestic epidemiologist Gromashevskiy L.V. also supported the hypothesis of an American origin of syphilis and suggested that the disease arose as a result of sexual spirochetosis of South American llamas and moved to the local people as a result of bestiality. In further, the locals infected the sailors of Columbus. The first data on the disease appeared in Spain (1494), then – in Italy, and with time – in other countries of Europe and Asia.

In 1530, Italian physician, philosopher and poet Girolamo Fracastoro named the disease as syphilis, after shepherd Syphilus (from *sys* – pig, *philos* – friend), the hero of the poem «Syphilis, or the Gallic disease.» The essence of the disease remained unknown. Some doctors referred formerly known gonorrhea to syphilis. With the progress in microbiology, a number of pathogens of sexually transmitted diseases were identified. This marked the beginning of the third stage in development of venereology. In 1836, Donne A. first discovered trichomonads in a woman's vagina. Nearly a century after that, they were considered harmless inhabitants of the vagina. Though, in 1870 Kharkov scientist Lazarevich I. wrote that the presence of trichomonads in vagina is accompanied by inflammatory manifestations and foamy discharge. In 1879, German scientist Neisser A. discovered the causative agent of gonorrhoeae – gonococcus. In 1905, Schaudinn F. and Hoffmann E. found a specific causative agent of syphilis – Treponema Pallidum.

In later years, it was found that the so-called abacterial urethrides can be caused by viral, chlamydia, mycoplasma and ureaplasma infections. Implementation of methods of serodiagnosis was a significant event in the development of syphilology. In 1906, *Wassermann*, *Neisser*, *Bruck* suggested a complement fixation test, which gradually improved. In the future, specific reactions for serological diagnosis of syphilis were proposed: treponema

pallidum immobilization test (R. Nelsen, M. Mayer, 1949), immunofluorescence test (Weller, Coons, 1954). At the present stage, the method of diagnosis of syphilis using enzyme multiplied immunoassay is applied.

To speed up the diagnosis of syphilis, flocculation tests by Kahn, Sachs-Witebsky and indicative rapid test method of microreaction on glass were offered. In parallel, considerable attention was paid to the further study of the causative agent of syphilis, its ultra structure and interaction with cells of the patient, variability of L-forms of Treponema pallidum; the possibility of persistence of Treponema in poly-membranous phagosomes of cells was established (Ovchinnikov N.M., Delektorsky V.V., 1965).

Throughout the history of syphilology, researchers focused on a comprehensive study of clinical manifestations of the disease.

Fundamental studies of Ricord Ph., Fournier A., Tarnowski V.M., Grigoriev P.S., Astvatsaturov K.S. and many other scientists refined various features of manifestations of syphilis infection and improved quality of the disease clinical diagnosis. In recent decades, the study of clinical picture of syphilis by scientists from research institutes of dermatovenerology, centers and departments of dermatology in several countries, including the Ukraine, revealed some features of syphilis symptoms (oligosymptomatic forms, prolonged latent time of infection after introduction of infection, etc.). Syphilologists always focused on the problem of innate and latent syphilis.

Doctors paid special attention to treatment of syphilis. At the end of the XV – beginning of the XVI century, right after Europe faced pandemic syphilis, the studies of methods and treatments that have been used in medicine at that time (diuretic, laxative, diaphoretic drugs, bleeding, etc.) were started, but they failed to be efficient.

As evidenced by numerous domestic and foreign medical chronicles, mercurial were one of the oldest antiluetic therapeutic agents. Since the end of the XV century, rubbing mercury ointment was the most common method of syphilis treatment used in Europe...

In 1894, the founder of the Ukrainian (Kiev) Research School of Dermatovenereologists Prof. Stukovenkov M.I. was the first in the world to scientifically prove the methods of treating syphilis with mercurials and clearly defined therapeutic daily doses through a proposed protein-based methodology for identification of mercury in biological fluids.

In 1909, an entirely new approach to treatment of syphilis appeared. German physician and researcher P. Ehrlich proposed to treat the disease with a triad arsenic drug – Salvarsan. In 1912, an improved product based on arsenic was synthesized – *Neosalvarsan*. Given a sufficiently high therapeutic effect, Neosalvarsan was used in syphilological practice for decades.

In 1921, Levaditi K. and Sazerac Z. offered to introduce bismuth compounds into syphilological practice. Biiochinolum, Bismoverolum, Pentabismolum

were often used for intramuscular administration. From the 30ies of the XX century, the treatment of syphilis widely used iodine drugs (potassium iodide, sodium iodide, Lugol's solution). Iodine was administered orally mainly in advanced syphilis, as well as for trial treatment with diagnostic purpose to differentiate syphilitic inflammations in visceral organs from those non-specific.

With the 40ies of the XX century, a new era in treatment of syphilis began, after introduction of penicillin in medical practice. In terms of antibacterial effect, this antibiotic exceeded all known at the time antiluetic medicines. Until the 60ies of the XX century, the method of syphilis treatment included the use of intermittent scheme (combined prescription of penicillin antibiotics and bismuth drugs). Later, a continuous (permanent) scheme of treatment with penicillin group of drugs and no bismuth drugs was used.

Basic modern medicines for etiotropic treatment of syphilis are presented by penicillin and its repository drugs. Tetracyclines, macrolides and cephalosporins are reserve drugs of etiotropic treatment of this infection.

In recent decades, methods of treatment of chlamydia, mycoplasma, ureaplasma, herpes and other urogenital infections are developed and improved. Studies are still in progress.

Development of Venereology is closely related to the control of infections that are primarily transmitted through sexual contact. Practical and scientific solution to the problem was significantly contributed by Stukovenkov M.I., Zabolotny D.K., Mechnikov I.I., Tarnowski V.G., Tomaszewski S.P., Zelenev I.F., Rakhmanov V.A., Grigoriev P.S., Tyzhnenko A.M., Torsuev N.A., Pototski I.I., Turanov N.M., Ovchinnikov N.M., Porudominsky I.M., Ilyin I.I., Mavrov I.I. and others.

GENERAL ISSUES ON DERMATOLOGY AND VENEREOLOGY

- Morphology, physiology and pathomorphology of skin and its appendages
- Introduction to Dermatology and Venereology
- Principles of Treatment applied in Dermatology and Venereology

Morphology, physiology and pathomorphology of skin and its appendages

Introduction to Dermatology and venereology

Principles of Treatment applied in Dermatology and Venereology

2 TOPIC

TRAINING AND EDUCATIONAL PURPOSES

- To explain physiological and morphological characteristics of skin, its appendages and mucous membranes in normal functioning of the body and in various disease states;
- To disclose the concept of «rash» and its role in setting appropriate dermatologic diagnosis;
- To know basic common and special methods of examination and principles of treatment applied in Dermatology and Venereology.

2.1 Morphology, Physiology and Pathomorphology of Skin, its Appendages and Oral Mucosa

TO KNOW:

- The anatomy of skin, its appendages and oral mucosa;
- Histological structure of skin, its appendages and oral mucosa;
- The nature of functional properties of skin, their age and sex characteristics;
- The function of cells, tissues, organs and physiological systems in health and in various disease states;
- Histopathological changes in the skin and its appendages and oral mucosa of mouth in health or in various pathological conditions.

TO BE ABLE TO:

- Distinguish between the structure of different layers of epidermis, dermis, subcutaneous fat and oral mucosa;
- Distinguish between the histological structures of skin appendages;
- Recognize different types of histopathological skin changes.

Skin (*cutis*) covers the entire surface of the body and transfers to the mucous membrane in the areas of natural openings i.e. mouth, nose, urinary tract and anus. The total area of the skin is 1.5 m^2. There are many folds, depressions, elevations on the surface of the skin. The skin is striated with furrows of different texture, which divide the surface into a number of fields, mostly triangular or diamond-shaped. Rough skin furrows include facial wrinkles, folds of the palms, scrotal folds and furrows on the extensor surfaces of the joints.

The color of the skin is defined as flesh-colored. It includes colors of all tissues that compose the skin and mainly depends on the color of blood in the capillary vessels and skin pigment. Healthy skin is dull in appearance.

Morphology of skin and its appendages

The skin consists of three layers i.e. the epidermis, dermis and subcutaneous tissue (hypodermis). These layers differ in embryonic origin: the epidermis is derived from ectoderm, while dermis and hypodermis – from mesoderm.

Important anatomical constituents of skin include its appendages, which consist of sweat, sebaceous glands, hair and nails.

Epidermis. Histologically epidermis (*epidermis*) is presented by keratinized stratified squamous epithelium. There are five layers of cells separated from the dermis by basement membrane. Directly on the membrane there is a layer of cylindrical cells located palisade and perpendicular to it. This layer is called the basal or primary (*stratum basale*), as well as malpighian (*germinal*), as this is the place, where mitotic cell division that ensures epidermis regeneration takes place.

Above the basal layer there is a ribbed layer (*stratum spinosum*) containing several rows of polygonal cells that are becoming flatter progressively as they are approaching the next layer.

Granular layer (*stratum granulosum*) is represented by one or two (sometimes four) rows of elongated spindle-shaped cells located along the surface of the skin. The cell nuclei are poor in chromatin and therefore are bright. The protoplasm contains keratohyalin grains, keratin precursor protein grains and grains of main keroid of skin and its appendages.

These layers of the epidermis are sometimes combined under the name of Malpighian layer.

Translucent layer (*stratum lucidum*) is located above the granular layer and consists of one or two rows of flat non-nuclear cells. Protoplasm of these cells contains a protein eleidin, which is an intermedium in the formation of keratin.

Horny layer (*stratum corneum*) is the most superficial layer of the epidermis consisting of flat thin horny plates that lie on the top of each other in several rows. Horny plates are completely dead cells that have lost their nuclei. Keratinization is achieved by substituting the protoplasm with keratin protein. The thickness of the horny layer in different parts of the skin varies greatly. Maximum thickness of the horny layer is on the palms and planta. On the surface of this layer, horny plates are

less dense and exfoliate gradually. Their gradual exfoliation occurs constantly and is called physiological desquamation.

The epidermis enters dermis with more or less developed processes called dermal ridges. Derma enters the space between the crests of the epidermis with projections, which are called dermal papillae.

Dermis. Under the epidermis there is the second layer of the skin called the actual skin or dermis (*derma*). It is rich for connective tissue fibers, which form bundles interwoven in different directions. There are rather few cells in the connective tissue of the dermis (fibroblasts, fibroclasts, melanocytes, macrophages, mast cells, mesenchymal cells).

There are three types of connective tissue fibers, which include collagen, elastic and argentophilic fibers. The gaps between fiber bundles are filled with the main amorphous substance, which plays an important role in metabolism and in the protective functions of the skin.

Argentophilic fibers form the basement membrane at the boundary between the epidermis and dermis, cover sebaceous and sweat glands, hair follicles and skin muscles with fine reticulum. By weaving in different directions, collagen and elastic fibers continuously distribute in the dermis, thereby dividing dermis into two layers – papillary and reticular.

Papillary dermis is located immediately below the epidermis. The bundles of connective tissue fibers in the papillary layer are quite thin and interweave in different directions. Many bundles are perpendicular to the skin surface and enter the papillae.

Reticular layer of the dermis consists of thicker fiber bundles, which when combined, form a dense reticulum. Much of these bundles are parallel to the skin surface. Such structure of the dermis ensures its great strength and elasticity.

The thickness of dermis in different areas of the skin varies from 0.5 to 4 mm. Dermis with no clear boundaries moves into the subcutaneous fat layer (hypodermis).

Hypodermis. The subcutaneous fat layer (subcutaneous adipose tissue, hypodermis) (*hypoderma*) also consists of bundles of interwoven connective tissue fibers. These bundles are the continuation of connective tissue bundles of the dermis; they are loose and form glomerular reticulum (*retinaculum cutis*). The nests of these reticulum contain fat lobules i.e. accumulation of fat cells. Subcutaneous fat layer plays an important role in fat metabolism being one of the most important depots of fat in the body. The thickness of hypodermis in different parts of the body is not the same, thus it is more significant in the abdomen, thighs and buttocks.

Dermis and hypodermis are scattered with different cells, which in various stages of differentiation, are divided into connective tissue cells and white blood cells.

Dermis and hypodermis include skin glands, hair, as well as blood vessels, nerves and muscles.

Blood and lymphatic vessels in the skin. The skin has a well-developed system of blood vessels. Blood vessels in the skin can make up to 1/5 of the total human body blood mass. In the process of circulation in the body, that is regulated by central nervous system, the skin acts as one of the major depots.

Arterial trunks penetrate into the subcutaneous fat layers from deeper located tissues. Here, they give branches that feed the hypodermis and at the border of dermis form arterial plexus, which is called deep dermal spider veins. From deep dermal spider veins there are vessels that rise up into the dermis. From these vessels and deep dermal spider veins there are arterial branches feeding dermis, sweat and sebaceous glands, hair, muscles and nerves. On the border of the papillary and reticular layers there is the second arterial plexus called superficial skin spider vein. Therefrom arteriole goes into every single papilla. Terminal arterial branches are divided into skin capillaries, which gradually merge with each other and give rise to the skin veins. Venous skin vessels run parallel to the blood vessels.

The lymphatic system of the skin begins with intercellular gaps of epidermis and numerous lymph slots of dermis. Lymphatic vessels are located along blood vessels. Lymphatic vessels, like blood vessels, form superficial and deep spider veins. Skin blood vessels can quickly change their clearance, which means that they can expand or narrow reflectory under the influence of stimulation of nerve endings, which can be caused by the action of heat, cold, mechanical action (friction, hit) and chemicals. Reflectory expansion or narrowing of blood vessels can also occur due to a variety of neuropsychiatric emotions i.e. joy, fear, anger etc.

Nervous system of the skin. Nerves form the main plexus in the subcutaneous layer, wherefrom numerous trunks, which give rise to new plexus, go to derma. Particularly dense plexus is formed in the papillary layer. Nerve fibers extending therefrom, give rise to numerous nerve endings in the connective tissue and in the epidermis, thus making the skin sensitive. In the subcutaneous fat layer there are Pacinian and Ruffini's corpuscles; in the papillary dermis there are Meissner's, Golgi-Mazzoni's corpuscles and Krause's bulbs and in the epidermis there are Merkel's menisci.

In addition to the sensory nerves there are secretory glands and nerve plexuses in the skin, which are located along the vessels.

Pacinian corpuscle (Lamellar corpuscles) is a complex encapsulated nerve receptor. It consists of the processes of altered cells of ciliated epithelium with sensory cilia, which are in contact with cell membrane of nerve process end. Cytosomes are separated from contact zone by the capsule consisting of several longitudinally oriented glial cells. Sensory cells cilia are located between external and internal capsule, thus contacting with the inner surface of outer capsule.

Pacinian corpuscle acts as:

- mechanoreceptor (due to a change of curvature of the outer surface of the capsule, mechanical effect is transmitted to the sensory cells cilia that generate nerve impulses);
- chemoreceptor (via sulcate channel that is present in the area of corpuscle pole different substances penetrate into the space between the inner and outer capsules, thus inducing nerve impulses);
- baroreceptor (change of blood pressure in the network of blood capillaries in the space between the inner and outer capsule alters the state of the sensory cells, thus inducing nerve impulses).

Pacinian corpuscles have a large receptive field, i.e. represent a rough sensitivity.

Meissner's corpuscle (tactile corpuscles) is a receptor, which is an encapsulated nerve ending present in the skin dermis, most often on the tips of fingers, soles, nipples, eyelids, lips and genitals. It is round. In its center there is a gyrate basket of myelin fiber, which passes through the transverse oval cells resembling Schwann's cells of nervous membrane. From the outside the corpuscle is covered with a connective tissue capsule.

Meissner's and Pacinian corpuscles belong to receptors that are rapidly adapting, i.e. they fix the skin pressure force.

Ruffini's corpuscle is a spindle-shaped receptor containing the inner bulb with a dense network of branched nerve cells and supportive lamellocytes. From the outside the corpuscle is covered with a connective tissue capsule consisting of several layers of flattened fibroblasts. Between the inner bulb and the capsule there is a capsule space filled with liquid. Ruffini's corpuscles are skin stretching receptors that are slow to adapt. There is an assumption that they are also heat thermoreceptors.

Golgi-Mazzoni's corpuscles are thick myelin fibers, «wrapped» around groups of collagen tendinous fibers and surrounded by a connective tissue capsule. Likewise Ruffini's corpuscles, they react to the tension, but their sensitivity threshold is higher.

Tactile Merkel's meniscus (disk) is a set of Merkel's cell with nerve ending. Tactile Merkel's cells are round or elongated cells, which are located among the epithelial cells and are larger than the latter. These cells are connected to the epithelial cells by desmosomes and form a contact with reticulated branched nerve endings.

Merkel's menisci are slow to adapt (to fix the duration of touch) and have small receptive fields, i.e. fine sensitivity.

Krause's bulbs are encapsulated nerve endings, which are composed of terminal branches of sensitive nerve fiber, inner glial bulb and outer connective tissue capsule. They are located in the connective tissue of mucous membranes and in the dermis, mainly on the hairless areas. They are considered to be cold thermoreceptors.

Hair. Hair *(pili)* is divided into: 1) long (head hair, beards, mustaches, armpits hair, hair in the area of external genital organs); 2) setaceous (eyebrows, eyelashes, hair in nose nostrils, in the external ear canal); 3) vellus (in all areas of the skin except for the so-called hair-free sites, in particular on the palms, soles, vermilion zone, nipples, breasts, labia, balanus and the inner layer of the foreskin).

The hair consists of the area freely located over the skin i.e. the hair shaft *(scapus)* and the area hidden in the skin i.e. the hair root *(radix)*. The root ends with extended part, which includes hair follicle, wherefrom the hair grows. From the connective tissue of the dermis the hair follicle is penetrated by dermal papilla, which contains blood vessels that feed the follicle.

The hair shaft consists of three layers: the medulla, cortex and cuticle.

The medulla is a hair marrow and consists of keratinized polygonal cells. There is no hair marrow in vellus.

The cortex is composed of extended cells with elongated nucleus or its fragments. These cells contain pigment melanin that defines the color of the hair. In gray hair pigment is absent, while silver color is achieved by air bubbles that appear in the cortex.

The cuticle is the outer layer of the hair represented by plane dead cells, which are arranged in a single layer leaning on one another like shingles.

Hair root is located in the hair follicle *(folliculus pili)*, which opens as a small hole in the skin *(ostium)*. At the boundary of the inner and middle thirds of the hair the hair follicle is entered by excretory duct of sebaceous gland.

Hair follicle is composed of connective tissue and epithelial parts. Starting from the confluence of sebaceous glands duct the connective tissue part is the most developed in the lower part of the root. Epithelial portion of the hair follicle represents an invagination of the epidermis. From the skin to the mouth of the excretory ducts of sebaceous glands (so called hair funnel – *infundibulum*) one may clearly see all the layers of the epidermis. Then, horny layer disappears, and funnel epithelium goes into outer root sheath epithelium, which is composed of cells similar to the cells of the basal and spinous layers. From the mouth of sebaceous glands duct and lower between the inner sheath and the hair cuticle there is the inner root sheath. There are three layers of inner root sheath: the inner – the inner root sheath cuticle (one row of dead skin cells), medium – Huxley's layer (one to three rows of semi-dead cells with pyknotic nuclei or completely devoid of them) and external – a layer of Henle (one row of dead skin cells). In the course of desquamation, the cells of all three layers mix with sebum near the mouth of the sebaceous gland.

All elements of the component parts of the hair and of the inner root sheath directed to the hair follicle have the cores and at the follicle they blend into the germinal zone of increased cell division, wherefrom the hair grows.

Hair life span is from several months to 4 years.

Skin muscles. Hair is associated with muscular system *(musculi arrectores pilorum)*, which consists of a strip-smooth muscles, one end of which is attached

via short tendon to the reticular layer of the dermis, and the other end – to the outer root sheath of hair just below the confluence of sebaceous glands duct. When contracting, muscles raise hair (the effect of the so-called «goose bumps») and, thus squeezing the sebaceous gland, induce the release of their secret.

Striated muscles are present only in the face skin *(musculi faciales)*. They are called mimic, as their contraction makes face movable and expressive and displays changes in mental state of a person.

Sebaceous glands. Sebaceous glands *(glandulae sebaceae)* are alveolar glands. They are predominantly open in hair follicles. A small number of sebaceous glands open directly on the surface of the skin i.e. on the balanus, the foreskin, on the labia lips, nipples and lips.

By secretion type, sebaceous glands are holocrine, which means that secretion is associated with destruction of adenocytes. In secretory regions, adenocytes are arranged in several rows. External cells make up a germ layer where mitosis takes place and deeper rows' cells accumulating fat droplets are formed. Cell maturation is accompanied by filling of the cell with large drops of fat, by pyknotic changes in the nucleus, which disappears with time, thus resulting in the destruction of the whole cell. Cell fragments, mixed with fat, fill in the gland and secrete via ducts to the skin surface.

Sweat glands. In terms of structure**,** sweat glands *(glandulae sudoriferae)* are simple tubular glands, which consist of a long ductless and secretory region, twisted into a ball, located deep in the reticular dermis at the border with subcutaneous fat layer. Terminal sections are lined with cuboidal epithelium, followed by a series of longitudinally arranged contractile cells (myoepithelial cells) which lie on the basement membrane. Duct in the dermis is straight and is lined with two rows of cells, and within the epidermis, it is corkscrew and is an extension of the intercellular spaces of the epidermis.

By the type of secretion sweat glands are divided into eccrine (merocrine), in which secretion occurs without destruction of adenocytes, and apocrine, where secretion is accompanied by destruction of the apical parts of adenocytes. Apocrine glands are bigger than eccrine ones, have less tightly curled ball and tend to appear in the hair funnel.

Eccrine glands are evenly arranged across the whole surface of the skin (to exclude vermilion zone, balanus and the inner layer of foreskin). They secrete lubrication for horny layer, are involved in thermoregulation and in the selection of products of nitrogen metabolism.

Apocrine glands are found primarily in the armpit, around the anus, on pubis and abdomen skin, below omphalus and on the labia lips. They develop at puberty. The secret of apocrine sweat gland has a specific smell and contains sex attractants (pheromones).

Nails. Nails *(unguis)* are dense horny quadrate plates located on the back surface of distal phalanges of fingers and toes. They lie on the so-called nail bed.

Their purpose is to protect terminal phalanges from damage. The front edge of the nail plate is free, and its rear and side edges are surrounded by skin fold and go deep into it. The upper part of the skin fold comes over the nail plate, thus nail folds (rear and side) are formed. The nail has its body *(corpus unguis)* and the root *(radix unguis)*. Nail root is the posterior part of the nail plate, which lies deep in the folds of skin at the back of the rear nail fold. Only a small part of the root of nail protrudes from nail fold in the form of white semilunar area (lunula – *lunula unguis*). It is better seen on the thumbnails. The lunula is covered with thin horn rim i.e. nail skin *(eponychion*), which is a continuation of the rear nail fold. Nail root is located on the back of the nail bed, which is called matrix *(matrix)*. Matrix is a place where the nail plate is formed. It consists of epithelial cells in character resembling the cells of basal and spinous layers of epidermis. Spinous layer contains onychoblasts i.e. cells that form the nail and which turn into horny nail plates. Nail plate itself corresponds to translucent and horny layers of the epidermis. Nails grow slower than the hair. In an average, fingernails grow by 1 mm per week, while feet nails by 0.25 mm per week.

Skin Functions

The state of the skin depends on a number of functions it performs, namely protective, immune, melanin-forming, thermoregulatory, secretory, excretory, metabolic, receptor, sorption, respiratory, repository etc.

Protective function of the skin. Skin is a barrier on the way of various environmental agents that affect the body i.e. mechanical, physical, chemical and biological.

Mechanical impact is prevented by epithelium density, the elasticity of fibrous structures of the dermis and shock-absorbing properties of subcutaneous fat layer. The reduction of any of these components can cause sharp weakening of protective properties of the skin. For example, atrophy of intercellular processes in spinous layer of the epidermis, which is typical of acantholytic pemphigus, results in an extreme vulnerability of epidermis.

The presence of natural sebum (sebaceous matter) on the surface protects skin against drying out and the impact of a number of chemical substances. Only the impact of depleting (strong acids, alkalis and some keratolytics) and fat-soluble substances can weaken protective features of the horny layer.

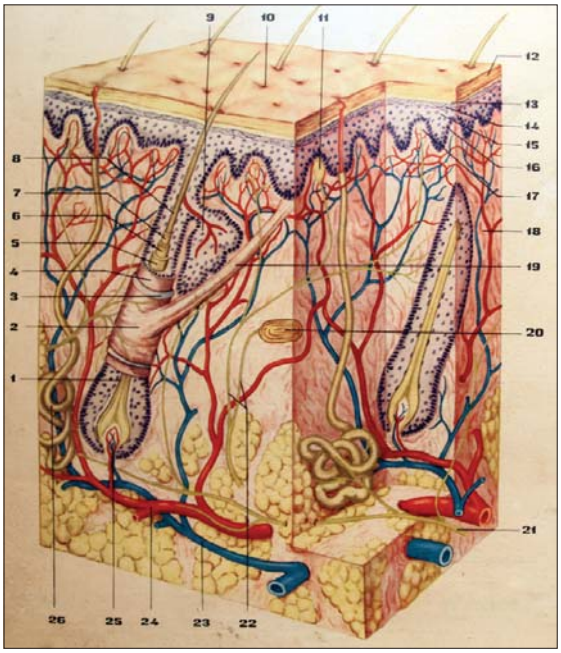
Undamaged epidermis is a poor conductor of electric current. When moistening and reducing fat body substances, skin resistance to electric current greatly decreases.

The protective function of the skin as concerns light is expressed in the action of pigment (melanin) skin system.

Immune function of the skin. The skin plays an important role in the immune system. The main elements of the immune system of the skin are keratinocytes, Langerhans' cells, epidermal T-lymphocytes. Keratinocytes favor the maturation of

T-lymphocytes by impacting thereon with deoxyribonucleotidyl transferase enzyme (DRNT). The majority of human skin T-lymphocytes is in the dermis, usually around the post-capillary venules and skin appendages. They are able to recognize exogenous and endogenous antigens only after their presentation by Langerhans' cells, which are antigen presenting cells. T-cells recognize antigen only in a single structure of MHC (*Major Histocompatibility Complex*). To be recognized by T-helper lymphocytes (CD4 +) antigen should be presented in conjunction with II class MHC (HLA-DR, DP, DQ), whereas the majority of T-suppressor cells (CD8 +) recognize antigen in association with I class MHC molecules (HLA- A, B, C). In the course of immune response to exogenous or endogenous antigens Langerhans's cells involved in antigen presentation are exposed to phenotypic and functional changes, leave the epidermis and enter the lymphatic vessels of the dermis, and then migrate to lymph nodes paracortex. At this stage, Langerhans' cells represent a complex antigen i.e. MHC T-cell antigen receptor on the surface of helper or suppressor. Antigen-specific T-cell response involves the formation of T-lymphocytes blast forms, which return to the skin regions containing the antigen.

Immune disorders play a pathogenic role in various diseases of the skin, including bullous dermatosis, allergodermatosis, psoriasis, T-cell malignant lymphoma of the skin.



Healthy skin and intact mucous membranes are a barrier for most microorganisms, except for those who have a special penetration device. Previously such protective function of the skin has been explained only by mechanical factors i.e. the presence of horny layer, water-lipid mantle, high elasticity and the existence of polyunsaturated fatty acids. Today, however, there is information on the immunological activity of basic structures of the skin that ensure immune response of epidermis,

Fig. 2.1. Human skin structure:
1 – hair cuticle; 2 – connective tissue layer; 3 – vitreous membrane; 4 – outer coat; 5 – layer of Henle; 6 – Huxley's layer; 7 – cuticle; 8 – hair shaft; 9 – sebaceous gland; 10 – sweat gland duct; 11 – Meissner's corpuscle; 12 – horny layer; 13 – translucent layer; 14 – granular layer; 15 – spinous layer; 16 – basal layer; 17 – papillary layer; 18 – reticular layer; 19 – muscle lifting the hair; 20 – Pacinian corpuscle; 21 – motor nerve; 22 – sensory nerves; 23 – veins; 24 – artery; 25 – hair follicle papilla; 26 – sweat-gland.

dermis and subcutaneous fat. One had proved anatomical, molecular and functional similarity of epidermal keratinocytes with epithelial cells of the thymus. Keratinocytes produce epidermal thymocyte activating factor (ETAF), interleukins-1, 2 (T-cell growth factors), interleukin 3 (mast cells proliferation and degranulation factor), natural killers activating factor (NKAF) and epidermal factor of granulocytes activity. Besides these, keratinocytes produce a number of non-specific mediators, biologically active factors that are involved in immune and inflammatory reactions of the skin. Amongst them the most studied are fatty acid metabolites (prostaglandins, leukotrienes, fat hydroxides) and plasminogen activator and inhibitor.

Keratinocytes induce maturation of T-cells by the action of deoxynucleotidyl transferase enzyme (DRNT). Epithelial cells are able to induce the expression of this enzyme, as well as the secretion of thymopoietin in T-lymphocyte differentiation.

The similarity of keratinocytes with epithelial cells of the thymus is confirmed by common heterogenic antigens detected in the basal cells of epidermis and thymus hormone epithelium. Common morphological features of these bodies have been established in the cultivation of thymus epithelium. It was found that thymus cells, when cultured, turn into typical epidermis keratinocytes. In thymus corpuscle (Hassall's corpuscles) receptors there has been revealed an antigen characteristic for the basal layer cells of epidermis.

In dermis immunological activity is conditioned by the presence of lymphocytes around post-capillary venules of the superficial vascular plexus and skin appendages. Immunomorphological methods have found that T-lymphocytes represent 90% of all cells of the skin and are located mainly in the epidermis and papillary dermis. B-lymphocytes are located in the reticular dermis. Endothelial cells of post-capillary venules of the upper vascular plexus and macrophage system play one of the major roles in the development and formation of skin immune responses.

Macrophage system is presented in the dermis and subcutaneous fat by fibroblasts, phagocytic macrophages (histiocytes) and dendritic cells. Morphologically, differentiated histiocyte is a dendritic cell with lots of microvilli. Macrophage system of the skin also includes mast cells involved in migration of T-lymphocytes, in antigen-antibody reactions based on immediate hypersensitivity type. The implementation of immune processes in the skin also involves participation of blood cells migrating into the skin (monocytes, eosinophils, neutrophils, basophils) and performing various immunological functions, one of the basic of which is the interaction of T-lymphocytes with nonspecific protection factors.

Immune function is also given to dendritic epidermocytes representing a modified variant of tissue macrophages population. Likewise mast cells and macrophages, these cells do not have immunological specificity, but when activated by antigens or cytokines, they exhibit physiological activity by secreting biologically active substances.

Melanotic skin system. Melanin (Greek μελας – black) is a class of organic compounds found in plants, animals, protozoa and bacteria, where they mainly play the role of pigments. Chemically, these compounds are derivatives of amino acid tyrosine. The most common in humans are:

- eumelanin – brown-black polymer of dihydroxyindole, dihydroxyindolerodizonic acids and their reduced forms;
- pheomelanin – red-brown polymer of benzothiazine responsible for red hair and freckles.

The synthesis of melanin in the skin i.e. melanogenesis is stimulated by ultraviolet radiation impact on the DNA. Photochemical properties of melanin make it a good photoprotector. It absorbs harmful ultraviolet radiation and converts it into energy in a safe amount of heat in a process known as ultrafast internal conversion. Due to this property melanin absorbs 99.9% of UV light and keeps free radicals at a minimum, thus preventing DNA damage.

Melanogenesis occurs in melanocytes i.e. specialized dendritic cells. During embryonic development melanocytes precursors arise from the neural crest and actively migrate to the peripheral zones. As it has already been noted epidermis basal layer cells contain melanin pigment grains. These grains are also present in melanin pigment cells of papillary dermis and they are called melanoblasts. The number of pigment grains in the cells of the basal layer of epidermis and of melanoblasts in dermis in diverse people differs quite significantly. The more pigment inclusions, the darker the color of the skin. In people with dark skin, Asians and Afro-Americans, pigment inclusions are found in the cells of spinous and granular layers.

Thermoregulatory role of the skin. Thermoregulatory processes in the human body are controlled by central nervous system. The skin is involved in this process via nervous apparatus, blood vessels and sweat glands. Moreover, horny and especially subcutaneous fat layer are bad heat conductors both from external and internal environments. The release of heat in the body results from a number of metabolic processes, such as oxidation, muscle activity etc.

The heat is emitted to the environment via blood vessels and sweat glands.

Blood vessels in the skin react quickly to changes in ambient temperature. When ambient temperature rises, skin blood vessels extend, thereby increasing the amount of blood per time unit flowing through their lumen. This leads to an increase in skin heat emission to the environment. When the temperature goes down, the reverse phenomenon is observed. This process is done by reflex.

The body emits heat to the environment in one of the following ways: radiation, emission, convection and evaporation.

Radiation is a way the surface of the human body emits heat to the environment in the form of infrared rays (λ = 5-20 μm). The amount of heat the body radiates to the environment is proportional to the surface of radiation area and to the difference between the mean values of skin and environment

temperature. The surface radiation area is the total surface area of body parts that contact the air. At 20°C ambient temperature and 40-40% of relative humidity an adult body radiates nearly 40-40% of the total emitted heat. Elimination of heat by radiation increases with a decrease in ambient temperature and decreases with its increase. Under constant ambient temperature, body radiation increases with increase in skin temperature and decreases when it is down. If the average temperature of skin surface and environment are aligned, elimination of heat by radiation becomes impossible. It is possible to reduce elimination of heat by radiation via reduction of the surface of radiation area («winding oneself into a ball»). If the ambient temperature is higher than the average temperature of the skin, the human body is warmed up via absorption of infrared rays emitted by surrounding objects.

Emission is a way to eliminate heat when human body contacts with other physical bodies. The amount of heat eliminated by the body to the environment in this way is proportional to the difference between average temperatures of contacting bodies, to the area of contacting surfaces, to the time of heat contact and thermal conductivity of the body in contact. Dry air and adipose tissue are characterized by low thermal conductivity and, thus are considered to be thermal insulators. The use of clothing made of fabrics containing many small stationary bubbles of air between the fibers (e.g. wool fabric) enables the human body to reduce heat dissipation. Wet, water-vapor saturated air and water are characterized by high thermal conductivity. Therefore, human's staying in a high humidity environment at low temperature is accompanied by increased body heat loss. Wet clothes also lose its insulating properties.

Convection is a way the body eliminates heat by means of transferring heat via moving particles of air or water. To dissipate heat by means of convection body surface shall be airflowed at a temperature that is lower than the temperature of the skin. At that, air layer contacting with the skin warms up, decreases its density, rises and is replaced by cooler, denser air. At 20°C air temperature and 40% relative humidity adult body dissipates into the environment nearly 25% of heat by means of emission and convection (basic convection). By increasing the speed of the air flow (wind, ventilation) heat emission increases significantly as well (forced convection). The heat loss via emission, convection and radiation, which are collectively referred to as «dry» heat loss, becomes ineffective when aligning average temperatures of the body surface and the environment.

Evaporation is a way the body dissipates heat to the environment by its evaporation via sweat or evaporation of moisture from the skin and respiratory tract mucous membranes of («wet» heat loss). A man is constantly experiencing the process of sweating via skin sweat glands («perceivable» or glandular loss of water) and moistening via respiratory tract mucous membranes («unperceivable» loss of water). At that, "perceivable" loss of water impacts the total amount of heat that is given off via evaporation more dramatically than the «unperceivable» one.

Secretory skin function. Sweating is the process of sweating carried out reflexively by sweat glands. Receptors responsible for sweating reflexes are located in the skin, mucous membranes and muscles. The centers of sweating are located in the cerebral cortex of the brain, the hypothalamus, medulla and spinal cord.

The composition and volume of sweat liquid can vary within wide limits, depending on the environmental conditions. On average, at room temperature, the human body releases 400-600 ml of sweat per day. In hot weather, and as a result of heavy physical work, sweating may amount to 12 liters per day. The sweat consists of mineral metabolism products i.e. sulfuric compounds, phosphates, potassium chloride, calcium, calcium salts and protein metabolism products, which include urea, lactic acid, uric acid, ammonia and some amino acids. Also sweat contains volatile fatty acids. Sweat reaction is acidic: pH 3.8-6.2, which contributes to the bactericidal action of the skin.

Sweating plays an important role in thermoregulation of the body, water-salt metabolism and, partially, in separation of metabolic products from the body.

Skin sebaceous excretions. Sebum is the grease of the horny layer of epidermis. It softens the friction between skin folds, prevents the formation of cracks and protects skin from maceration. Sebum is a complex mixture of various lipids, comprising glycerides (40%), free fatty acids (16%), wax and cholesterol esters (25%), squalene (12%) and cholesterol. Sebum triglycerides are decomposed by bacteria to free fatty acids. Some of them form volatile fatty acids, which give the skin a certain smell. Sebum itself is odorless.

On the skin surface fat is a part of the so-called protective mantle – the layer formed by the skin glands secret, its microflora and exfoliated horny scales. Due to the presence of acidic medium on the skin surface (pH 4-5.5), it is also called «acid mantle.»

Sebum performs several functions. It prevents water loss and drying of the skin and protects it from damage by acidic or alkaline medium, thus preventing the penetration of bacteria.

It is believed that sebaceous glands of the skin secrete from 100 to 300 g of secretion per week. Most fat is released on the wings of the nose, the chin and ears. The function of the sebaceous glands is under the direct influence of neuroendocrine system.

Metabolic function of the skin. The skin is involved in the general metabolism of the body – water, mineral, nitrogen, carbohydrate, vitamins. The skin accumulates and releases water, fat, glycogen and salts.

The skin takes special place in water exchange process, as it is the second after muscles reservoir that collects water introduced into the body. Water content in the skin is 62-71%, but in the subcutaneous fat it is much smaller – up to 10%. In children's skin there is much more water than in the adults' skin, and its volume decrease with the age. Mineral components in the skin make 1% of its weight. The skin holds not only water but also sodium chloride (kitchen salt), and at some acute skin diseases its content increases to dangerous levels.

In mineral metabolism an important role is played by potassium and calcium, potassium and sodium ratios, which vary depending on the diet.

Nitrogen metabolism of the skin is mainly caused by proteins. Of the proteins, the skin is rich for collagen (which makes up to 98% of all the proteins of the skin and is in the dermis) and keratin (found in the horny layer of epidermis, hair and nails).

Carbohydrate metabolism in the skin is characterized mainly by the content of glucose. For a healthy person the norm is 50-70 mg%. The amount of glucose in the skin is not equal to its content in the blood. ***Receptor function of the skin.*** The skin, being the peripheral unit of skin analyzer, is a large receptor field that perceives a number of sensations from outside and transmits them to the central nervous system.

There are the following types of skin sensitivity:

- tactile (sense of touch and pressure);
- pain;
- temperature (feeling of cold and heat).

Sense of touch (pressure) is perceived by tactile corpuscles, the number of which varies on different parts of the skin. The sense of deep pressure is perceived by Pacinian corpuscles.

Pain is perceived mostly by free nerve endings located in the epidermis and dermis.

Temperature sensation, perception of heat and cold, is of great importance for the reflexive processes that regulate body temperature. It is assumed that thermal stimuli are perceived by Ruffini's corpuscles, while cold is perceived by terminal Krause's bulbs. There are much more cold points on the entire surface of the skin than the heat once.

Suction (absorption) function. Water and dissolved salts are not absorbed by the skin as translucent and horny layers of the epidermis contain lipids preventing the penetration of water into the skin. However, water-soluble substances can be absorbed through the hair follicles and sweat gland ducts. Alternately, fat-soluble substances are easily absorbed through the epidermis.

Respiratory function of the skin involves the exchange of gases i.e., the uptake of an oxygen and the emission of carbon dioxide and water vapor.

The skin plays small role in the exchange of gases: nearly 1/180 of the oxygen penetrates into the body through the skin and from 1/90 to 1/65 of carbon dioxide is released via lungs. Via sweat glands skin releases up to 800 g of water vapor per day, thus surpassing the lungs for more than twice.

Gas exchange of the skin is qualitatively identical to pulmonary gas exchange and is limited to the diffusion between blood capillaries of the skin and the surrounding atmospheric air.

Repository function. At room temperature, most of the skin blood vessels are in semi-contracted state, which means that the rate of blood flow in the capillaries is negligible. With increasing temperature, dilated blood vessels of the dermis can hold

up to 1 liter of blood (reposition of the blood), and their proliferation may lead to significant changes in the circulatory system.

Morphology of oral mucosa

Oral cavity *(cavitas oris)* is the initial unit of the digestive tract. In front and on the sides, it is limited by lips and cheeks, on the top – by hard and soft palate, at the bottom – by the mouth bed. With mouth lips closed, the mouth has fissure shape, while with mouth lips open – it has round shape.

Oral cavity consists of two sections: front or vestibule of mouth *(vestibulum oris)*, and rear – oral cavity itself *(cavitas oris propria)*. In front and on the sides, vestibule of the mouth is limited by lips and cheeks, from behind and inside – by teeth and mucous membrane upper and lower jaws alveolar processes. Oral cavity is connected with pharyngeal cavity via pharynx.

Vestibule and oral cavity itself are covered with mucous membrane.

Oral mucosa *(tunica mucosa oris)* consists of three layers – epithelial, proper mucous plate *(lamina propria)* and submucous layer.

Epithelial layer. Oral mucosa is covered with stratified squamous epithelium. Its structure is not the same in different parts of the oral cavity. The epithelium on the lips, cheeks, soft palate and mouth bed is normally not coarsen and consists of basal and spinous layers, while on the hard palate and gingiva, it is exposed to keratinization. Thus, besides the aforementioned layers, it has granular and horny layers. It is believed that epithelium keratinization is the result of its response to the influence of the stimulus, especially mechanical.

Between basal layer cells there are individual leucocytes. Through the epithelium, gingival sulcus epithelium in particular, they can penetrate to the oral cavity, and, thus, appear in the oral fluid. In some parts of the epithelium one may find melanocytes i.e. the cells that make melanin. At the border of the epithelial layer and the lamina propria there is a basal membrane consisting of fibrous structures.

Proper mucous plate *(lamina mucosa propria)*, which contains a layer of epithelium, consists of a dense connective tissue. On the border with the epithelium, it forms numerous processes, namely papillae that protrude into the epithelial layer at different depths. The connective tissue is represented by fibrous structures i.e. collagen and reticular fibers and cellular elements i.e. fibroblasts, mast and plasma cells and segmented leukocytes. Proper mucous plate of cheeks and lips is the richest for cellular elements.

Macrophages that perform protective function phagocytize bacteria and dead cells. They are actively involved in inflammation and immune reactions. Labrocytes (mast cells), which are characterized by the ability to produce biologically active substances i.e. heparin and histamine, ensure microcirculation and vascular permeability. Labrocytes are involved in delayed type of hypersensitivity reactions.

Proper mucous plate smoothly goes to submucosa *(tunica submucosa*) formed by loose connective tissue. It has small vessels and minor salivary glands. The intensity of submucosa determines the mobility of tunica mucosa of the mouth.

Physiology of oral mucosa

Due to anatomical and histological features, mucosa performs a number of functions, which include protective, plastic, sensory and suction.

Protective function. This function is ensured by a number of mucosa properties. Microorganisms and their metabolic products together with the scales of epithelium are removed from the mucosal surface. An important role in the protective function is played by leucocytes that penetrate into the oral cavity through the epithelium of tooth-gingival attachment (gingival sulcus). Normally, 1 ml of saliva contains 4 000 leukocytes. In case of diseases of mucous membranes of the mouth (gingivitis, stomatitis) the number of white blood cells in the oral fluid increases dramatically.

Plastic function. This function is ensured by high mitotic activity of the epithelium, which, as some people believe, is by 3-4 times higher than mitotic activity of skin cells. This accounts for high regenerative capacity of oral mucosa, which is often exposed to some kind of damage.

Sensory function. This function is carried out due to the presence of cold, heat, pain, taste, touch receptors. Oral mucosa serves as a reflexogenic zone of glands and gastrointestinal tract muscles. It has been found out that stimulation of taste receptors alters the function of the digestive tract, affects the composition of blood and cardiovascular system. Changes in the level of sensitivity occur not only by increasing or decreasing the sensitivity threshold, but, as conducted studies showed, through the mobilization or demobilization of functional receptors.

Suction function. Oral mucosa has the ability to absorb a number of organic and inorganic compounds, including drugs and toxic substances. It has been defined that the level of suction can be changed. Tanning agents reduce the intake of substances, while the impact of physical factors (electrophoresis, ultrasound, phonophoresis) increases it.

Major skin pathological changes

A significant number of skin diseases are of an inflammatory character. Clinically the inflammatory process is divided into acute and chronic. Such division of inflammatory processes, which is based on their duration, is rather arbitrary and mainly has clinical significance. They believe that pathologic feature of the process transition into chronic type is the proliferation of connective tissue in the area of inflammation, which in average takes place in two months after the beginning of inflammatory process.

Inflammation is a reflex reaction of the body that occurs under the influence of various pathogenic stimuli. Inflammation is mostly a local manifestation of the general reaction of the body. Due to the impact of the pathogenic agent, which excites the nervous system, there appears a complex of pathological phenomena i.e. local

damage to the tissues and organs, breach of circulatory and metabolic processes therein. These processes are interdependent and interconditioned and reflect reactive properties of the body the latter had acquired in the course of evolution.

From the pathologic point of view, inflammation is the result of interaction between damaging agent and the body. The combination of these interactions can vary dramatically, yet in the microscopic picture of inflammation they always single out the following changes: alteration – manifestations of tissue damage (degeneration and necrosis of tissue elements), exudation – changes in the blood vessels (emergence of liquid and formed elements from vessels) and proliferation – multiplication of tissue elements.

Peculiar pathological processes occur in the epidermis, which is related to anatomical features of its structure.

There are three main types of inflammatory changes in the epithelium.

The first type of serous inflammation of the epithelium is ***intracellular edema***, granular degeneration of cells *(alteratio cavitatis),* which is characterized by the appearance of malpighian layer of vacuoles in the cytoplasm of cells, which are located near or around the nucleus, and, thus push it to the periphery. The nucleus is deformed and often has all signs of degeneration and pyknosis. The increasing of intracellular edema can lead to the complete disintegration of epithelial cells. Less commonly, the vacuoles are localized in the nucleus of cells. This phenomenon is called vacuolar (hydropic) degeneration. The nucleus swells, chromatin disappears. The nucleus is transformed into a round vial filled with a liquid, where sometimes nucleolus floats.

The second type of serous inflammation is ***intercellular edema*** of the epidermis *(status spongioides)*, which is characterized by the fact that the exudate separates individual epithelial cells and stretches intercellular bridges. The progression of the process leads to the rupture of intercellular bridges, loss of intercellular communication and the beginning of formation of epithelial vesicle.

The third type of inflammation of the epithelium is ***ballooning degeneration*** *(degeneratio balloon),* which is a necrobiotic process. In addition to the most profound changes in the epithelial cells, intercellular bridges are destroyed. The cells lose their mutual connection and take the form of spherical formations freely floating in the intercellular spaces.

Inflammatory skin diseases are mainly accompanied by the combination of intra- and intercellular serous edema of the epidermis.

Besides serous inflammatory phenomena, there is a number of other pathological processes that can develop in the epidermis. They include as follows:

acanthosis, which is characterized by increased proliferation of spinous layer cells, that results in elongation and expansion of epithelial ridges;

acantholysis**,** in which atrophy of intercellular epithelial bridges takes place, a strong connection between epithelial cells is disrupted and the cells easily shift to one another, which leads to the detachment of more or less significant layers of the

epithelium. For the first time, acantholysis phenomena have been described in pemphigus by Nikolskyi P.V.;

hyaline degeneration of cells, which is characterized by the appearance of dense homogeneous translucent vitreous substance in the cells that is called the hyaline;

hyperkeratosis as a thickening of the horny layer;

granulosis as a thickening of the granular layer of the epidermis;

parakeratosis**,** wherein stained nuclei are found in the cells of the horny layer; granular layer is absent;

epidermis atrophy**,** which is observed in a number of skin diseases. The number of epidermis layers is reduced to a minimum, the cells decrease in volume. Atrophy may extend to the entire epidermis, when there is also an atrophy of epidermis ridges i.e. smoothing of the border between the epidermis and dermis or, of their individual layers.

2.2 Introduction to Dermatovenereology. General Issues of Etiology and Pathogenesis of Dermatoses

In the course of the disease most of the changes in the body is a manifestation of its dynamic response to the influence of pathogenic agent. The state of the organism, in its turn, is closely associated with social conditions of existence, social conditions of life and work of a man, which is the basis to define the disease as a social phenomenon.

Etiology studies the causes of diseases. These causes may be of exogenous and endogenous nature. The term «pathogenesis» refers to the mechanism of occurrence and development of the disease and the ways of its spreading throughout the organism.

Exogenous and endogenous factors of skin diseases occurrence

Exogenous factors of dermatoses (i.e., skin diseases) include those which affect body and skin from outside. There are physical factors (mechanical, thermal, impact of radiant energy), chemical and biological (viruses, bacteria, fungi and fungous organisms, algae sometimes, some arthropods, plants, etc.).

Endogenous factors are very diverse, to include the impact of almost all organs and systems on the skin.

Thus, endocrine disorders as an etiological factor in the occurrence of skin diseases are diverse and have a variety of clinical manifestations, to include the disorder in the anatomical structures, alteration of skin glands function, appearance of autonomic and vasomotor symptoms, disorders of pigment etc.

The disorder in lymph, blood circulation and blood diseases give rise to elephantiasis, acrocyanosis, rosacea, leukemia skin manifestations etc.

Autointoxication caused by the absorption of abnormal food from gastrointestinal tract, the disorder in excretory capacity of kidneys and other organs also leads to a number of diseases (urticaria, pruritus etc.).

Many chemicals and nutrients that enter the body can lead to a number of toxic erythema and itching dermatoses.

Microorganisms, which originally are localized in internal organs or blood, could also cause a number of diseases, such as septic erythema, secondary skin actinomycosis etc.

The clinical picture of skin and sexually transmitted diseases is a compound complex of symptoms consisting of various manifestations. First of all, these manifestations include those that are localized on the skin and visible mucous membranes. We differentiate between subjective and objective symptoms. The subjective symptoms are those that are felt by the patient and for the most part directly touch the skin. Objective symptoms include changes that the doctor notes to the patient during checkup or other physical examination of the skin.

It is important to remember that dermatoses are often accompanied by symptoms relating to the whole organism. These include fever, anemia, weakness and unstable mental status. However, skin diseases may occur due to the diseases

of individual organs or systems, in particular lesions of the gastrointestinal tract, nervous and endocrine systems, blood formation organs, blood and lymph vessels.

Subjective and objective symptoms of skin diseases

Subjective symptoms. Subjective symptoms of skin diseases largely depend on the individual peculiarities of the patient. Some of them react vigorously and vividly on relatively minor manifestations of the disease, while others are quietly even to rather pronounce manifestations of dermatosis. An example is the itching sensation. This feeling deprives some patients of sleep and disrupts their overall health, while others do not perceive itching as discomfort and almost do not notice it.

Subjective symptoms are different in character and strength, depending on personal feelings of the patient. Such feelings mostly include different sensory disturbances in the form of hyperesthesia (itching, burning and pain), hypo-and anesthesia, paresthesia (formication, contraction and numbness). These symptoms are felt by the patient, and only some of them can be marked by a doctor: disorder of skin sensitivity and itching sensation, which the doctor can notice from skin excoriations (scratching) available on the patient's skin.

Objective symptoms. To study objective symptoms in the patients, one should study the condition of the entire skin, wherefore you should use visual impressions and tangential sensations. The study of the entire condition of the skin includes the study of its color, luster, turgor, dryness or humidity, temperature reaction and local changes. When studying local changes of the skin it is very important to know the elements of skin rashes that cause skin lesion.

Diagnostic stages

To correctly build the diagnostic process it is necessary to know its three stages – morphological, clinical and ethiopathogenetic.

Morphological stage concludes with the establishment of preliminary diagnosis. It can be made analytically or synthetically. The first type of morphological stage is more typical for Viennese dermatological school. In this case, first of all, you should determine all the morphological elements of the patient, i.e. make tests. First determine whether the element rises above the level of the skin, whether it has a cavity, how the element's regression goes on – disappears without a trace, leaves crust, flakes, scars etc.

Further analysis is performed as follows. If the element is not raised above the surface of the skin, it's a macule (the only primary element, not protruding above the skin). In that case, you need to determine the nature of this macule (see below). If the element is raised above the surface of the skin, it is necessary to conduct a survey for the presence or absence of a cavity therein, and then analyze primary cavitary and non-cavitary elements. Besides examination, the nature of the morphological element is also established on the basis of palpation, vitropression, scraping etc.

Synthetic type of the morphological stage of diagnostics is more characteristic for dermatologists sticking to French school teaching foundations. In this case they first estimate the entire rash, determine the interdependence of individual elements, their prevalence, localization, grouping, mono-or polymorphism. Thus, for example, in Gibert's disease (pityriasis rosea) oval rash elements are located along Langer's lines on the chest skin and the overall picture resembles a Christmas tree, while in psoriasis the lesions are often localized on the scalp, elbows and knees and lower back. This allows us to make a preliminary diagnosis and then proceed to the analysis of the nature of individual rash elements and use additional methods of examination.

After completion of the morphological stage and establishing a preliminary diagnosis, one proceeds to the *clinical stage* of diagnostics. At this stage, first of all they associate the results of morphological analysis with disease anamnesis, and then use additional studies (vitropression, Brocq scraping, determination of dermographism etc.). In this case, they eliminate the diseases of those that have been suspected, when setting preliminary diagnosis, starting from the least possible. This stage ends up with the establishment of clinical diagnosis, which, e.g., can be eczema, psoriasis.

The top stage of diagnostics is *ethiopathogenetic*, which ends up with the establishment of final diagnosis. At this stage, they define the form of nosologic unity of the disease, its etiologic and pathogenetic nature with all the features typical of the body of a particular patient. At this stage of diagnostics they define the presence of concomitant diseases and their relationship with dermatosis, thus making it possible to assign a rational combination therapy.

Morphological elements of rash on the skin and mucous membranes

Rash or efflorescence *(eruptio, efflorescentia)* are clinical and morphological changes in the skin (exanthema) and mucous membranes (enanthema) that develop under the influence of various endogenous and exogenous factors and are a major symptom of skin and a variety of infectious diseases. The peculiarities of morphological elements of the rash, their color, shape, texture, location and other attributes coupled with the general properties of the skin (e.g. color, elasticity, secretory activity) are critical to the diagnostics of skin diseases.

Any skin rashes consist of certain morphological elements that make up the alphabet of dermatology. It is impossible to describe any skin changes without proper knowledge of this alphabet.

There are primary and secondary rash elements. Primary elements are those that arise as a direct consequence of pathological process in the skin. Secondary elements develop from the primary as a result of their spontaneous evolution or arising in the course of treatment. One should consider the relativity of division of efflorescence into primary and secondary elements. This is related to the fact that, in

certain circumstances, primary elements can act as secondary i.e. be a consequence of the evolution of an element, and secondary elements, in some diseases, may be characterized as primary efflorescence. Below, to characterize individual elements we will give examples of how primary elements act as secondary and vice versa.

Primary morphological rash elements

Primary morphological rash elements are divided into non-cavitary (a spot, papule, tubercle, nodule, blister) and cavitary (vesicle, bulla, pustule).

A spot *(macula)* is an element having no relief, but with changed color of skin. Spots are divided into vascular, pigmented and hemorrhagic.

Vascular macules can be inflammatory and non-inflammatory. Inflammatory vascular spots are characterized by temporary dilation of blood vessels in the dermis. When pressing the affected area of the skin, blood vessels fall down and intensity of macules color becomes lesser or a macule disappears at all, but when stopped pressing, the color of the macule restores. The color of inflammatory macules ranges from bright red to bluish-red. When self-resolved, inflammatory macules may be covered with scales, leave secondary pigment changes in skin color for a long period of time or disappear without a trace.

By the size, inflammatory macules are divided into *roseola* (up to 2 cm in diameter) and *erythema* – of a larger diameter.

Non-inflammatory vascular macules are associated with improper development of blood vessels in the skin. They are divided into congenital (e.g., vascular nevi – *naevi vasculosi*) and those acquired as a result of persistent expansion of surface vessels (e.g. telangiectasia – *teleangiectasiae*).

Pigmented macules may have high (hyperpigmentation), low (hypopigmentation) content of pigment or have not it at all (depigmentation). They can be congenital and acquired. The examples of congenital hyperpigmented spots are pigmented nevi (*naevi pigmentosi*), of acquired hyperpigmented macules – freckles (*ephelides*), of congenital depigmented macules – albinism (*albinismus*) and of acquired depigmented macules – *vitiligo*.

Hemorrhagic macules appear due to bleeding into the skin when blood vessels are injured or permeability of their walls is increased. When pressing on such macules, their color remains almost unchanged. The coloring gradually changes from red to blue, green and yellow (due to the formation of degradation products of hemoglobin). As a rule, such macules disappear completely in 1-2 weeks.

By the size, hemorrhagic macules are divided into petechiae (*petechiae*) – punctate hemorrhage, purpura (*purpura*) – up to 2 cm and ecchymosis (*ecchymosis*) – of a larger size. Separately, they distinguish linear hemorrhage (vibex, pl. v*ibices*) and extensive bruising *(sugylatio)*.

There are also *macules arising from the introduction of foreign substances into the skin* (such as tattoos).

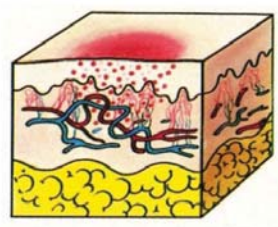


Fig. 2.2. Schematic representation of inflammatory macule *(macula inflammatoria)*.

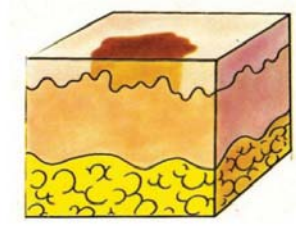


Fig. 2.3. Schematic representation of hyperpigmented macule *(macula hyperchromica)*.

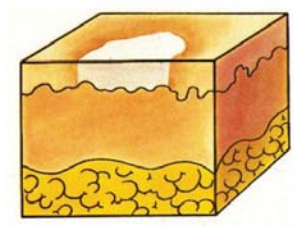


Fig. 2.4. Schematic representation of depigmented macule *(macula achromica)*.

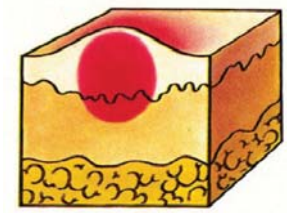


Fig. 2.5. Schematic representation of papula *(papula)*.

Papule is primary non-cavitary morphological element, which is characterized by changes in the skin surface, often its color, texture and usually disappears without a trace. According to the depth of occurrence there are epidermal papules, located within the epidermis (flat warts); dermal, which are located in the papillary dermis (*papular syphilides*) and epidermodermal (papules of psoriasis, lichen planus, atopic dermatitis). Papules can be inflammatory or non-inflammatory. The latter are formed as a result of acanthosis-type sprawl of epidermis (warts), papillomatosis-type sprawl of dermis (papillomas) or concentration of metabolic products in the skin (xanthoma). Inflammatory papules are much more common in psoriasis, secondary syphilis, lichen planus, eczema etc. At that, in the epidermis one may observe acanthosis, granulosis, hyperkeratosis, parakeratosis, while in the papillary dermis – a concentration of cellular infiltrate. Depending on the size, papules can be miliary (1-3 mm in diameter), lenticular (0.4-0.9 cm in diameter) and nummular (1-3 cm in diameter). In some dermatoses there occurs a peripheral growth of papules and their merge, which leads to the formation of larger elements – *plaques* (e.g. in psoriasis). Papules can be round, oval, polygonal in line, flat, semi-circular, conical (with pikes) in shape and thick, densely elastic, pasty and soft by consistency. Sometimes a vesication appears on the surface of papules. Such elements are called papulo-vesicles.

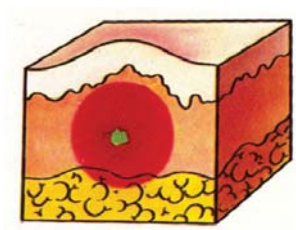


Fig. 2.6. Schematic representation tubercle *(tuberculum)*.

Tubercle (*tuberculum*) is a primary non-cavitary infiltrate morphological element that occurs in the reticular dermis and is characterized by small size (0.5 to 1 cm in diameter), change in color of the skin, its topography and texture and leaves behind a lasting trace in the form of scar or scar atrophy.

There are inflammatory and non-inflammatory tubercles. The first are formed mainly in the reticular dermis due to the formation of infectious granuloma. Clinically, they are quite similar to papules. The main difference is that tubercles usually tend to ulcerate and leave behind scars. Tubercle may also expand omitting ulcer stage with the transition into scar atrophy of the skin. Inflammatory tubercles are observed in leprosy, skin tuberculosis, leishmaniasis and tertiary syphilis. Non-inflammatory tubercles are benign growths of the dermis (fibroids, leiomyoma).

Nodule *(nodus)* is a primary non-cavitary infiltrate morphological element occurring deep in the dermis and hypodermis and having big sizes (from 2 to 10 cm and over in diameter). To the extent the pathologic process is in progress, in most cases nodule undergo ulceration followed by scarring. They distinguish inflammatory nodule, such as syphiloma, boils and non-inflammatory nodes that result from benign deposition of fat in the skin (lipomas) or malignant proliferative processes (lymphoma). Sometimes nodule can completely resolve (e.g. boils at a formative stage), group in calcium salts or fibrous tissue (syphiloma in the areas of the joints).

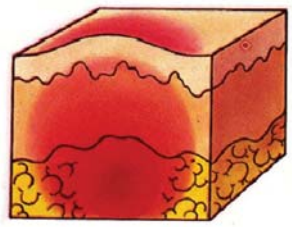


Fig. 2.7. Schematic representation of a nodule *(nodus)*.

Vesicle *(vesicula)* is a primary cavitary morphological element to 0.5 cm in diameter, which has a bottom, a tegmentum and a cavity filled with serous or sero-hemorrhagic matter. Vesications are found in the epidermis (intraepidermaly) or under it (subepidermaly). They can occur on the background of unmodified skin (with dyshydrosis) or on an erythematous background (cold sores). They are often formed due to spongiosis (eczema, atopic dermatitis) or ballooning degeneration (in simple and herpes zoster). The opening of vesications causes the formation of multiple oozing erosions, which eventually are epithelized and leave no permanent change in the skin. There are unicameral (eczema) or multicameral (with herpes) vesications.

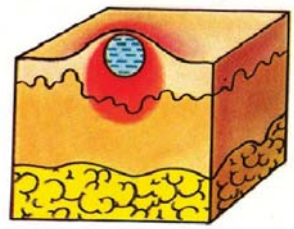


Fig. 2.8. Schematic representation of vesicle *(vesicula)*.

Bulla *(bulla)* is a primary cavitary morphological element consisting of a bottom, a tegmentum and a cavity filled with serous or sero-hemorrhagic matter. The tegmentum can be hard or loose, thick or thin. The bulla differs from vesication by much larger size – from 0.5 to a few centimeters in diameter. The elements can be found both on intact skin and on inflamed one.

Bulla may appear as a result of acantholysis and be placed intraepidermaly (in acantholytic pemphigus), or as a result of swelling of the skin that leads to the

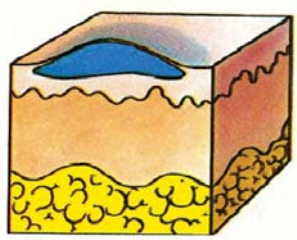


Fig. 2.9. Schematic representation of bulla *(bulla)*.

detachment of epidermis from dermis and be placed subepidermaly (simple contact dermatitis). In places of open bulla there appear erosive surfaces, which eventually are epithelized and leave no permanent change in the skin.

Pustule *(pustula)* is a primary cavitary morphological element filled with purulent matter. According to the location on the skin they distinguish superficial and deep, follicular (usually staphylococcal) and non-follicular (usually streptococcal) pustules. Superficial follicular pustules are formed at the mouths of the follicle or cover up to two thirds of its length, which means that they are located in the epidermis or papillary dermis. They have a conical shape, often permeated with hair in the central part where one may see yellowish purulent matter. Their diameter is about 1-5 mm. At pustules regression, a purulent matter may shrivel into a yellowish-brown crust, which then disappears. At the site of follicular surface pustules there are no any persistent skin changes; only temporary hypo-or hyperpigmentation is possible. Superficial follicular pustules are observed in ostiofolliculitis, folliculitis and sycosis usual. Deep follicular pustules (deep folliculitis) cover the entire hair follicle and are located within the entire dermis and often hypodermis.

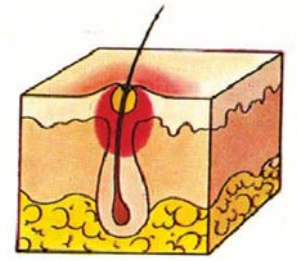


Fig. 2.10. Schematic representation of superficial follicular pustule *(ostiofolliculit)*.

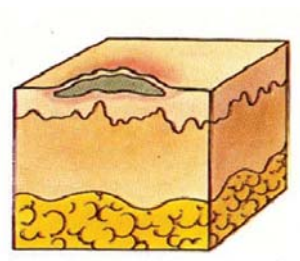


Fig. 2.11. Schematic representation of superficial non-follicular pustule *(impetigo streptogenes)*.

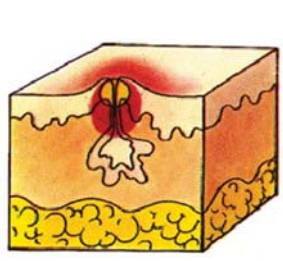


Fig. 2.12. Schematic representation of a blackhead *(acne)*.

Superficial non-follicular pustules – phlyctenule *(phlyctaena)* have a tegemntum, the bottom and a cavity filled with cloudy matter, surrounded by hyperemia aureole. They are located in the epidermis and outwardly look like pustule with a noticeable content. Observed in impetigo. At pustule regression, the exudate shrinks in crust, after the rejection of which there remains temporary de-or hyperpigmentation. Deep non-follicular pustules – ecthymas *(ectyma)* form ulcers with purulent bottom, which are observed in chronic ulcerative pyoderma etc. They remain scars. Ecthyma that is covered with a layered crust resembling snails shell is called rupia *(rupia)*. The pustules can appear around the excretory ducts of sebaceous glands (acne vulgaris), and since sebaceous glands open into the hair follicle, they are also of follicular nature (blackhead – *acne*). Deeper pustules that are formed around excretory ducts of apocrine sweat glands, in spiradenitis, open via fistulous tract and leave behind scars.

Blister *(urtica)* is a primary non-cavitary exudative morphological element, resulting from the limited acute inflammatory edema in the papillary dermis and

differing by ephemeral nature (exists from few minutes to several hours, disappears without a trace). Usually, blister occurs as an immediate, sometimes delayed allergic reaction to the endogenous or exogenous stimuli. It is observed with insect bites, hives, drug reaction and Dьhring dermatitis. Clinically, blister is a thick elevated element of round or irregular shapes, pink in color, sometimes with a whitish tinge in the center accompanied by itching and burning. It leaves no any (even temporary) secondary changes on the skin.

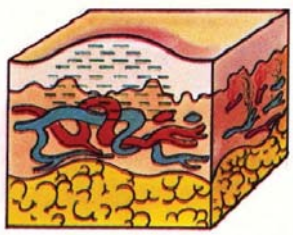


Fig. 2.13. Schematic representation of blister *(urtica)*.

Secondary morphological rash elements

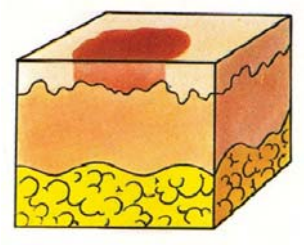


Fig. 2.14. Schematic representation of hyperpigmentation *(hyperpigmentatio)*.

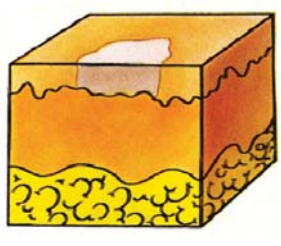


Fig. 2.15. Schematic representation of hypopigmentation *(hypopigmentatio)*.

Secondary morphological rash elements include secondary spot, a crack, excoriation, erosion, ulcer, a scale, scar, tripe, lichenification, vegetation.

Secondary hypo-hyperpigmentation *(hypo-seu hyperpigmentatio secundaria)* is a change of color in the place of primary (papules, pustules etc.) or secondary (erosions, excoriations) elements. For example, in places of former papules in psoriasis there are often depigmentation areas that exactly match the contours of former primary elements (psoriatic pseudoleukoderma), while in regression of planus papules, usually, there is a hyperpigmentation persisting for several weeks and even months.

A crack is a secondary morphological element representing a linear breach of skin integrity caused by weakening of skin elasticity. Cracks are divided into superficial *(fissura)* (which are located within the epidermis; epitelize and regress without a trace, e.g., in mycosis, neurodermatitis etc.) and deep *(rhagas, pl. rhagades)* localized within the epidermis and dermis, often bleeding with formation of hemorrhagic crusts, regressing to the formation of a linear scar, e.g. in congenital syphilis).

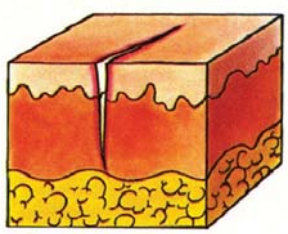


Fig. 2.16. Schematic representation of deep cracks *(rhagas)*.

Excoriation *(excoriatio)* ***or scratching*** is manifested by breach of skin integrity caused by mechanical damage resulting from injuries and scratching.

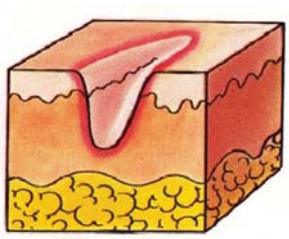


Fig. 2.17. Schematic representation of excoriation *(excoriatio)*.

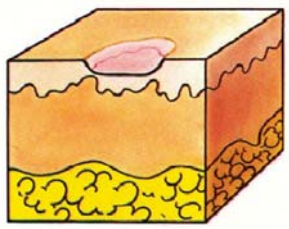


Fig. 2.18. Schematic representation of erosion *(erosio)*.

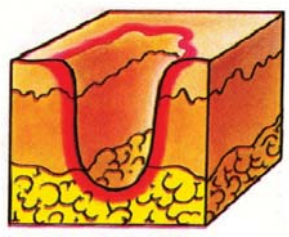


Fig. 2.19. Schematic representation of ulcer *(ulcus)*.

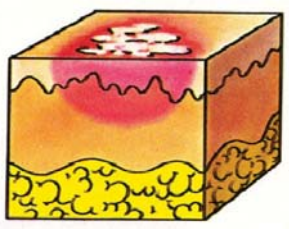


Fig. 2.20. Schematic representation of scale *(squama)*.

Excoriations are most often linear or match the contours of the damaged primary rash element. Depending on the depth of damage to the skin, excoriation may regress without a trace or with a scar, hypo-or hyperpigmentation. Excoriations are objective evidences of itching in patients.

Erosion *(erosio)* occurs at the opening of superficial primary cavitary morphological elements or oozing lesion of inflammatory papules and represents a breach of skin or mucous membranes integrity within the epidermis (epithelium). Erosions appear on the places of vesicles, blisters or superficial pustules and have the same shape and dimensions as primary elements. Sometimes erosion may occur on papular rash, especially when it is localized in the folds, on mucous membranes (erosive syphilides papular, erosive and ulcerative lichen planus). Regression of erosion occurs by epithelialization and ends up with complete disappearance with possible temporary hyperpigmentation.

Ulcer *(ulcus)* is a profound breach of the integrity of the skin within the connective tissue layer of the dermis, and sometimes hypodermis and underlying tissues. It occurs at the opening of tubercles, nodules or deep pustules. The ulcer has the bottom and edges, which can be benign (tuberculosis) or firm (skin cancer). The bottom may be smooth (syphilitic chancre) or uneven (chronic ulcerative pyoderma) covered with a variety of discharge, necrotic plaque or granulation. The edges can be undermined, steep and soucer-shaped. Ulcers always remain scars.

Scale *(squama)* represents horny plates, which, when rejected, result in desquamation *(desquamatio)*. Physiological desquamation occurs constantly and generally is unnoticed. In pathological processes (hyperkeratosis, parakeratosis) desquamation becomes much more pronounced. Depending on the size of scales, desquamation is divided into furfuraceous (scales are small, soft, as if powdering the skin), lamellar (large scales) and gross lamellar (layered rejection of horny layer). Furfuraceous desquamation is observed in pityriasis versicolor, rubrofitii; lamellar – in psoriasis, while gross lamellar – with erythroderma. The scales are loosely held, easily removable (in psoriasis) or sit tight and are separated with difficulty (in lupus).

White scales are typical of psoriasis, yellow – of seborrhea, dark – of some types of ichthyosis. In some cases, the scales are soaked with exudate, thus forming scale crusts (in exudative psoriasis).

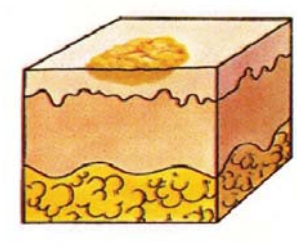


Fig. 2.21. Schematic representation of serous crust *(crusta serosa)*.

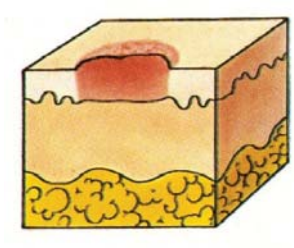


Fig. 2.22. Schematic representation of hemorrhagic crust *(crusta haemorragica)*.

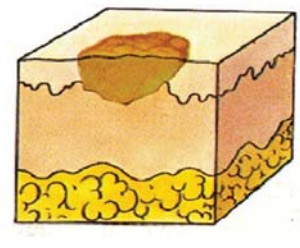


Fig. 2.23. Schematic representation of purulent crust *(crusta purulenta)*.

Crust *(crusta)* occurs when the contents of vesications, blisters, pustules dries out. Depending on the type of fluid, crusts may be serous, hemorrhagic, purulent or mixed. The shape of crusts is often wrong, although its contours match with the contours of primary rash.

Scar *(cicatrix)* arises in the healing of ulcers, deep pustules, cracks and excoriations. It is a newly formed coarse-fibered connective tissue (collagen fibers). In terms of elation to the surface of the skin, scars can be superficial and deep, atrophic or hypertrophic. There are no skin appendages (hair, sweat and sebaceous glands) in the scars; epidermis is smooth and translucent. The color of fresh scars is red, then it becomes pigmented and finally – white.

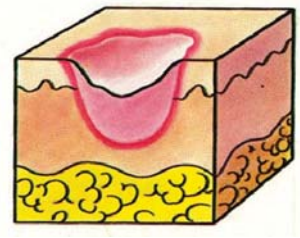


Fig. 2.24. Schematic representation of a scar *(cicatrix)*.

Cicatrical atrophy *(atrophia cicatricans)* is a quantitative and qualitative reduction of all layers of the skin that occurs with resorption of deep dermal infiltrate without prior ulceration. In this case, the skin is thinned, devoid of normal pattern, often impressed if to compare to the surrounding intact areas, and looks like tissue paper, which is particularly noticeable in the side of compression. Similar changes are observed with lupus, scleroderma etc.

Lichenification *(lichenificatio,* or *lichenisation – lichenisatio)* is characterized by increased skin pattern, thickening and densification of skin due to papular infiltration and hyperkeratosis. In lichenification the skin resembles shagreen skin. Such changes are often formed in chronic itching dermatoses, which appear in the form of papular efflorescence (atopic dermatitis, neurodermatitis, chronic eczema).

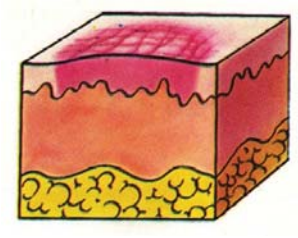


Fig. 2.25. Schematic representation of lichenification *(lichenificatio)*.

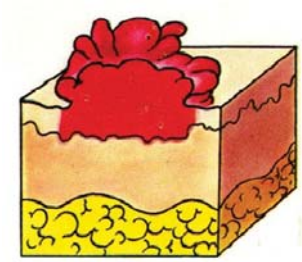


Fig. 2.26. Schematic representation of vegetation *(vegetatio)*.

Vegetation *(vegetatio)* is characterized by the growth of the papillary dermis, has a villous surface resembling a cauliflower or a cock's comb. Vegetation often appears at the bottom of erosive ulcers (wet vegetation) at vegetating pemphigus, on the surface of primary papular rash (dry vegetation) at genital warts.

Determination of morphological rash elements properties

Having established the type of rash elements, you should determine their properties such as color, shape, configuration, consistency, borders, interrelation, placement, location, monomorphism or polymorphism.

The color is described by conventional terms, and it is important to identify the shades of color, which is of great diagnostic value.

The boundaries of rash elements can be clear and fuzzy.

Configuration of rash elements can be round, oval or polyhedral (polygonal).

The consistency of rash elements can be soft or dense.

Interrelation of morphological elements is characterized by their isolation (focal position) or fusion (diffuse location).

There are grouped, systematic or random, symmetric or asymmetric types of placement of rash elements.

Grouped rash is a rash placed in a limited area in the form of certain right or wrong groups. Right groups of elements resemble geometric shapes – a circle, half circle and oval, for example in secondary recurrent syphilis. Wrong groups are those groups of rash elements, which are placed randomly on the site, not making regular geometric shapes. For example, these can be Cuspal syphilides.

Ordered rash is located on the nerve trunks, blood vessels, such as the placement of vesications in herpes zoster.

Disorderly arrangement of rash is characterized by the absence of any patterns in the distribution of elements as in secondary syphilis.

Symmetrical placement of rash is defined by its presence on the left and right parts of the body. It has a diagnostic value, e.g., in determining true eczema.

The localization of rash can be typical (favorite) and atypical (negative).

In a typical localization, rash in whatsoever disease, is observed in definite areas of the skin. For example, in psoriasis, these areas are extensor surfaces of elbows and knees. With atypical localization, rash is found in those areas where, in whatsoever dermatoses, it usually does not occur. For example, in scabies and conventional acne, rash is absent on the palms and soles.

Rash is also divided into monomorphic and polymorphic.

Rash monomorphism is characterized by the presence of primary morphological elements of the same kind. An example is the rash of lichen planus.

Polymorphic rash consists of various elements – either only primary (true polymorphism), or primary and secondary, which are derivatives from primary ones (false or evolutionary polymorphism).

2.3 The Patient's Examination Practice Applied in Dermatovenereology

Examination of the patient in the dermatology clinic is held under the general plan, but has a number of features.

When questioning the patient they establish the time of presence of this or that rash, draw initial picture of the development of the disease, study the clinical course of the disease – whether there were any remissions or relapses, learn about other previous diseases, about the nature and circumstances of the patient's working and living conditions, as well as previous treatment.

Having collected the anamnesis and clarified all the patient's complaints, the latter should be offered to show the areas that disturb him the most. One should examine the entire skin and visible mucous membranes. General examination of the patient often allows setting a correct diagnosis based on such symptoms of the skin to which the patient may or may not pay enough attention. At that, it is very important to spare the feelings of shame of the patients, especially women, do not force them to undress completely, but gradually open individual areas of the skin. Quite often, even at such examination of the lesion and of the entire skin it is possible to set the diagnosis, having dully assessed the existing skin and visible mucous changes.

Pay attention to the color of the skin, which in some cases allows establishing the presence of lesions of gastrointestinal tract, cardiovascular and respiratory systems and blood system. This helps to identify the presence of comorbidities, determine the etiology of the disease and thereby clarify the dermatological diagnosis.

In some cases there is a need to apply a number of additional studies (both, special physical examinations and laboratory and instrumental checks).

The diagnostics of skin and venereal diseases (diseases, primarily, transmitted via sexual contact) is an important step in diagnostic and treatment work of a doctor, as establishment of correct diagnosis is the key to a successful choice of tactics to further manage the patient. In most cases skin diseases assume the appearance of a variety of visceral disorders on its surface, which represent one of the features specific to a particular common disease. Many infectious diseases are accompanied by skin symptoms that allow setting correct diagnosis.

Common and special examination procedures in Dermatology and Venereology

In Dermatology and Venereology they use both common and special examination procedures (vitropression, determination of dermographism, dermoscopy etc.). For example, a general study of the morphology of blood helps to diagnose dermatoses, which are based on organic or functional disorders of hematopoiesis; the definition of ESR and sigma ESR allows you setting the activity of the inflammatory process and clarifying the diagnosis.

Diascopy (vitropression). *Vitropression* (from Greek *δια* – through and *πκπρny* – I see) is a pressing on the affected area of the skin using diascope

(special transparent plastic plate) or a glass slide (vitropression). With this method it is possible to determine the nature of macule element (vascular, hemorrhagic or pigmented): thereat, vascular spots disappear, while hemorrhagic and pigment macules remain. Vitropression is also used to diagnose lupus: when pressing, tubercles change their color to yellow (the phenomenon of «apple jelly»).

Determination of dermographism. Dermographism (from Greek $\delta\varepsilon\rho\mu\alpha$ – skin and $\gamma\rho\alpha\varphi\omega$ – I write) is a vasomotor response to mechanical stroked stimuli that are used to evaluate the tone of the autonomic nervous system based on cutaneous autonomic reflexes.

White dermographism arises in 8-20 seconds after stroked irritation with sharp object in the form of white stripes, which stay from 1 to 10 minutes. Boosted white dermographism witnesses of increased excitability of skin vasoconstrictors, which receive sympathetic innervation, and of the sympathetic tonus of skin vessels. Particularly clear white dermographism is detected on the hips. The sympathicotonia of skin vessels is obvious from a symptom called «white macules», which is similar to white dermographism that occurs when you press on the skin for about 3 seconds, provided that such symptom lasts longer than 2-3 seconds. White dermographism is usually observed in atopic dermatitis.

Red dermographism arises in 5-11 seconds (after stroked irritation of skin) as a red band, which stays from 1.5 min. to 2 hours. Usually, red dermographism is a normal phenomenon. To conclude on the predominance of parasympathetic excitability, only a very diffuse or too long (persistent) dermographism is of relative importance.

More convincing for such a conclusion is an *elevated dermographism* that appears in 1-2 minutes after stroked irritation in the form of edematous skin swelling (in urticaria and other allergodermatoses).

Skin biopsy. A *biopsy* (from Greek $\beta\iota o\zeta$ – life and $o\psi\eta$ – look) is a method of tissue sampling (biopsy) for pathologic study. Histology of biopsy is the support to clinical diagnosis. Therefore, material forwarded to pathological examination should be accompanied by a detailed description of the clinical disease and in severe cases, by the results of differential diagnostics. A biopsy is a small surgery and should be performed in compliance with aseptic and antiseptic requirements, and with the use of anesthesia.

A biopsy is divided into excisional (by excision of the fragment of tissue) and puncture (by puncturing with special tool). The advantage of puncture biopsy is minor injuries, though sometimes it is contraindicated as it may cause activation of processes in tumors. The quantity of material which can be obtained by this method is minimal.

Excisional biopsy can be traditional and electrosurgical. The latter, despite the absence of bleeding after a diagnostic intervention, has the disadvantage that marginal zones obtained by biopsy are exposed to coagulation at quite large depth and, therefore they become unsuitable for research.

The traditional excisional biopsy is performed with intrusion into the biopsy sample of affected and apparently healthy skin. Biopsy sample should include the subcutaneous fat layer. It would be reasonable to sample the material from several affected areas of the skin.

The procedure involves the following steps. Having treated the surgical field, they excise affected skin area together with apparently unchanged skin area, conduct hemostasis and put 2-3 stitches. The biopsy sample is then placed in a normal (10% neutral formaldehyde solution) or exclusive (Fleming's, Chabot's liquids etc.) retainer. The resulting material can be stored up to 4 months.

If you suspect nevus malignancy, the biopsy should be performed in oncology centers Only.

Dermoscopy. *Dermoscopy* (from Greek – *δερμα* – skin and *σκοποσ* – I see) is a non-invasive diagnostic method for visual evaluation of skin lesions by means of a special device called dermatoscope (epiflourescence microscope), allowing more thoroughly to study the surface of the skin and subepidermal structures. This diagnostic tool allows identifying morphological structures that are invisible to the naked eye, thus providing new details of clinical and morphological characteristics of skin lesions. The method involves the study of the skin or hair with a special camera equipped with a magnifying lens that is connected to computer. To test the skin and hair one should use lenses with different magnification. The resulting information is transmitted to a computer and processed via special software. Thus, the process resembles a simple scanning of skin and hair. The patient's skin can be checked on the subject of its:

- type;
- elasticity;
- humidity;
- relief;
- availability and depth of vascular lesions;
- pore size;
- pigmentation;
- sensitivity;
- depth of wrinkles.

The study is conducted with due account for age parameters, since with the increase of age moisture, elasticity and fatness of the skin may change. As concerns hair, one can measure its thickness, size of pores; determine type of scalp and condition of hair shafts.

The diagnostics allows thoroughly and clearly determining the condition of the skin using scientific methods of measurement and choosing professional beauty treatments and products for home care with due account for individual needs of the skin and hair. Application of dermatoscope allows recording primary skin changes in the computer's memory, observing the dynamics of treatment effect, discussing the results with the patient and in obscure diagnostic cases, consulting with other professionals using recorded data.

Determination of psoriatic phenomena. *Psoriatic phenomena* (Auspitz's triology) are almost constant symptoms in progressive and stationary stages of psoriasis. As a result of scraping psoriatic elements (papules, plaques), desquamation increases and scales become white resembling a drop of grinded stearin (the phenomenon of «stearic spot»). When keeping scraping up to the granular layers of epidermis, scales fall down, thus revealing a pink wet film (the phenomenon of «terminal» or «psoriatic» films). If to continue scraping (to the papillary dermis), tiny drops of blood will appear on the surface of the film. Their number depends on the number of capillaries within the papillae damaged during scraping (the phenomenon of «pinpoint bleeding» or «bloody dew»).

Baltzer's Iodine Test. *Iodine test* is an indicator of latent desquamation and is used to diagnose tinea versicolor. The macules are greased with 2-5% alcoholic solution of iodine. Due to loosening of horny layer, the solution is better absorbed within rash area, thus making the spot intensely colored than the surrounding healthy skin. If you have no iodine solution, you may use any aniline dyes. With leukoderma that remains after tinea versicolor, Baltzer's test is negative, especially in persons, who were exposed to UV radiation. This test is also positive in Fox's impetigo.

Skin examination under Wood's lamp. The technique is based on the ability of hair affected by *Microsporum* fungus, to give a bright green fluorescence when exposed to a short part of ultraviolet rays. The source of the latter is a portable specially designed mercury-quartz lamp. In order to restrain the long-wave radiation they use Wood's filter i.e. a glass impregnated with nickel salts. This method allows identifying head hair or smooth skin affected by fungi basing on their characteristic glow. Luminescence of lesions can be weak or disappear, and its color may change after the application of a 5% solution of iodine or ointments. In such cases it is advisable to wash your hair with soap and repeat procedure in 3-4 days. Reliability of the results of this method should be confirmed by the microscopy taken from hair lesions. In favus, one may observe a much darker glow resembling malachite. Skin areas affected by blastomycosis glow with pink-orange, in vitiligo one may see bright white areas dramatically pigmented on the perimeter. Lupus erythematosus, when localized on the red border of lips , gives snow-white glow in hyperkeratosis, whitish – in atrophy and blue – in acute process. Microsporia gives bright green glow, *lichen versicolor* (on the head) – a brick red and erythrasma – coral-red, which is more pronounced on the periphery.

Microscopic diagnostics of pathogenic fungi. To investigate smooth skin mycosis (trichophytosis, microsporia, tinea pedis, keratomycosis, candidiasis) you should take scales from peripheral lesion by scraping with scalpel. With patients suffering from feet, hands dyshydrosis, use scissors or razor blade to cut vesication tegmentum or desquamated epithelium fimbriae, and apply test material to glass slide. In dermatomycosis the material is taken from damaged long hair and vellus using epilation forceps, sometimes sharp side of scalpel, if hair is broken off at the level of the skin («black spots»). To investigate infiltrative-purulent processes, you

need to take hair floating in pus from the periphery using Volkmann's spoon and carry it over into a Petri dish or watch glass. Use the dissecting needle to catch the affected hair and carry it over to a glass slide.

Crush the affected hair, nail plate, thick horn mass and scales on a slide using heated scalpel and then add 2 drops of 10% solution of alkali (NaOH). For clarification purposes, the drug is heated in a spirit-fire, without boiling, until white ring appears on the periphery and then, by pressing a little bit, is covered with cover glass. The affected nail plates, thick horn mass or biopsy material is better investigated by Chernohubov's method of enrichment. The material is treated for 20-30 minutes in 20% alkali solution with a double boiling. For microscopy, use sludge remaining after centrifugation.

The drug is then examined under conventional or phase-contrast microscope, first at low and then at high magnification using a concave mirror, covered diaphragm or lowered condenser.

When studying scales, horny masses and nails physician assistant can only point whether he has or has not found mycelium or other agent of mycosis («mycelium found», «groups of budding cells found»)

Determination of Nikolsky's symptoms. *Nikolsky's Symptom* is one of the leading factors of diagnosing acantholytic pemphigus. There are three types of symptoms – marginal, interbulla, remote. The presence of any of them is of prognostic value.

Marginal symptom – the epidermis exfoliates as a result of loss of communication between the cells of spinous epidermis layer when pulling the bits of bulla tegmentum.

Interbulla symptom – the epidermis exfoliates between bulla when mechanically impacting the apparently intact skin.

Remote symptom – the epidermis exfoliates when mechanically impacting apparently intact skin distant from the lesions.

Study of smears for acantholytic cells. First cytological method of diagnostics of bullous dermatoses was proposed by A Tzank. This method is indispensable in the differential diagnostics of acantholytic pemphigus, pemphigoid and dermatosis herpetiformis (Duhring disease).

Using a piece of gum (eraser) sterilized by boiling, one lightly presses on the bottom surface of fresh bubble. The material is carried over to the fat-free, sterile glass slide, fixed for 1 min. in methanol and dried at room temperature and Gimsa stained (for 20-25 minutes by azure-eosin). The preparation is examined under a microscope at 10x40.

Acantholytic cells are degenerative dystrophic cells found in horny layer of the epidermis. They are smaller than normal epithelial cells, round, with large nucleus, occupying nearly the entire cell and intensely stained (hyperchromic). Two or more lighter nucleoli can be seen inside the nucleus. Cytoplasm is visible on the periphery in the form of the rim. It is abruptly basophilic and light blue – closer to the core.

Jadassohn's skin test. *Jadassohn's test* is performed to confirm the diagnosis of dermatosis herpetiformis. If the result of the first test is doubtful, you need to gradually perform three stages of Jadassohn's test, if necessary.

First stage. On the area free of rashes, apply 1 cm^2 of 50% ointment of potassium iodide to be placed under compress. To control the test, Vaseline compress is applied to the symmetric part of the skin. If test is positive, in 24 hours after application of potassium iodide there appears rash accompanied by itching.

Second stage. Potassium iodide compress is applied to the area of the skin where there is already a rash. If test is positive, previous eruptions become brighter, itching enhances greatly.

Third stage. Throughout the day, 2-3 times, the patient is administered 1 tablespoon of 3% aqueous solution of potassium iodide. If test is positive, new rash appears on any part of the skin accompanied by intense itching.

Sampling of genitourinary discharge for tests. Study of scrapings and discharge from genitourinary organs are mostly performed with inflammatory lesions (gonorrhea, trichomoniasis, chlamydiosis etc.). Test material shall be taken by a doctor. First, using a cotton swab moistened with isotonic sodium chloride solution wipe the external genitalia. With men, if pus does not freely flow, easily push on the back of the urethra squeezing a drop of discharge on a glass slide and evenly smear it with another glass. If there is no discharge, the material is sampled with a loop or blunt Volkmann's spoon after 5-8 hours of refrain from urination. Materials (scraping) for immunofluorescence studies are taken by Volkmann's spoon of smallest diameter in 15-20 minutes after urination, which prevents contamination of scraping with mucus and microflora secretions.

In women they usually study discharge from the cervix, vagina and urethra. Before taking tests it is prohibited to conduct any hygiene throughout the day. Cusco's mirror is introduced into the vagina. Using sterile loop, material is first taken from cervical canal, then from vagina and urethra. Cervical scrapings are informative provided that they are taken in the middle of menstrual-ovulatory cycle (not earlier than five days after the period and not later than five days prior to them). The material is taken by blunt Volkmann's spoon or special disposable instruments. In microbial cervical erosion, scrapings can also be taken from cervix.

Treponema pallidum dark-field study. This study is performed to confirm the diagnosis of primary seronegative syphilis. The technique is used in a dark field with the application of paraboloidal condenser or cardioid condensers and electric light.

The surface of chancre is twice-washed with isotonic sodium chloride solution, then a lotion with saline solution is periodically applied for 12-24 hours. Clean chancre surface is gently stroked with bacteriological loop until the serum, which is then carried over to a thin glass slide, mixed with a drop of warm saline, covered with watch glass and investigated under microscope.

If the chancre is complicated by secondary infection or phimosis, you should puncture regional lymph node. This is done by a 5 ml syringe. The node is captured with fingers, the needle is introduced into one of node poles and then the needle is gradually withdrawn and tissue juice is sucked with syringe. A drop of the resulting tissue juice is mixed with a drop of warm isotonic sodium chloride solution and investigated under microscope.

Treponema pallidum in the dark field looks like thin a little bit sparkling spirals with 8-12 uniform curls. Their movements can be translational (forward and backward), pendulous, around their axis, flexuous and are characterized by slowness and regularity.

2.4 Principles of Treatment Applied in Dermatology and Venereology

The main task of treatment of patients with skin and venereal diseases is to eliminate the causes and favoring events that cause disease, and to increase the resistance of the patients' organisms. You should take into account the results of diagnostics, pharmacological properties of medications and dosage forms. Also it is necessary to take into account the etiology and pathogenesis of the disease, comorbidities, complications, tolerance of drugs and their effectiveness in the case of previous treatment. Accordingly, there is causal therapy that tackles the cause (agent) of the disease, pathogenetic therapy that is aimed at eliminating some of the pathogenesis, especially if etiology of the disease has not been established, and symptomatic therapy that is aimed at eliminating symptoms that the patient are most concerned about. It is also important to take into account the patient's psychological response to the disease it has.

There is general and local treatment of dermatoses and venereal diseases (diseases transmitted primarily through sexual contact).

General Treatment

General therapy involves systematic use of drugs (oral or parenteral) with their delivery to the lesions via blood. This treatment is used for disseminated, extensive skin lesions, infections and parasitic dermatoses, as well as diseases transmitted primarily through sexual contact.

Antibacterial agents. Antibacterial agents are substances that selectively suppress the activity of microorganisms. Under the selective effect one should understand the action only on microorganisms, maintaining the viability of the host cells and the effect on not all, but on some genera and species of microorganisms. For example, fusidic acid has a high activity against staphylococci, but has no effect on Pseudomonas aeruginosa.

Traditionally, antibiotics are divided into natural (actually antibiotics, such as penicillin), semi-synthetic (natural molecules modified products, such as Amoxicillin or Cefazolin) and synthetic (e.g. sulpha drugs, nitrofurans). At the present stage, this division has lost its relevance, because a number of natural antibiotics is produced by synthesis (chloramphenicol or laevomycetin), and certain drugs that are called antibiotics (fluoroquinolones) are actually synthetic compounds.

You should distinguish between antibiotics and antiseptics, which do not selectively impact on microorganisms and are used for their destruction in living tissues, and disinfectants intended for non-selective killing of microorganisms outside live organism (for care items, etc.).

Antibiotics are the most numerous group of remedies. All antibiotics, despite the differences in chemical structure and mechanism of action, are united by a number of unique qualities.

Antifungal agents (antimycotics). As fungal diseases (mycoses) are infectious diseases the main way of their treatment is causal treatment that assumes application of antifungal agents (antimycotics). Elimination of the pathogen leads to the

disappearance of all symptoms. Despite the large number of existing antimycotics, their application in treatment is characterized by a number of common principles, which are listed in Table. 2.1.

By chemical composition antifungal agents can be divided into the following main groups:

Azole derivatives:

- Imidazole derivatives (Ketoconazole, Clotrimazole, Econazole, Miconazole, Bifonazole);
- Triazole derivatives of (Fluconazole, Itraconazole, Terconazole).
- Allylamines derivatives (Naftifine, Terbinafine)
- Antifungal antibiotics (Nystatin, Griseofulvin, Amphotericin B, Natamycin)
- Miristamin derivatives (Miramistin)
- Karbamotioat derivatives (Tolciclate, Tolnaftate)
- Undecylenic acid derivatives (Mikoseptin)
- 5-fluorocytosine (Flucytosine)
- Morpholine (Amorpholine)

Table 2.1
General principles of causal treatment of mycoses (by Yu.V. Sergeev and A.Yu. Sergeev)

General principles		*Compliance means*
Efficiency	Drug's compliance with infection etiology	Knowledge of infection etiology: • attribution of causative agent to the species • drug sensitivity test Knowledge of the drug spectrum of action and its indication
	Drug's compliance with the form of disease	Knowledge of drug pharmakokinetics: • rational way of administration • drug's distribution in the lesion • time for effective concentration
Safety	Prevention of severe side and toxic effects	Knowledge of drug's side and toxic effects: • comparison of the benefits and risks of treatment • determination of contraindications • selection of appropriate dose Treatment control: • regular examination • corrective treatment
	Prevention of undesired drug-drug interaction	Knowledge of interaction and compatibility of drugs: • exclusion of non-compatible drugs • correction of a dose and prescription regimen

Of course, not all of the groups of drugs are equally well used at present. Specific indications for the use of different groups of antifungal agents are considered in the description of individual clinical forms of fungal infections.

Antihistamines. Antihistamines include drugs that prevent the interaction of histamine with histamine receptors (antihistamines) and inhibit the release of histamine from tissues that are involved in the biosynthesis and deposition of histamine and mast cells (by stabilizing their membrane). In dermatology the usage of antihistamines prevails.

The mechanism of action of antihistamines is based on competition with histamine for histamine receptors, which are of two types – H1 and H2. H2-receptors are found in the stomach and their blockade inhibits production of hydrochloric acid and pepsin by parietal cells. The term «antihistamine agents» is often referred to H1-receptor blockers, which are in the walls of blood vessels. Their blockade attenuates histamine-induced hypotension, smooth muscle spasms, reduces capillary permeability, eliminates the risk of histamine edema, prevents the development and facilitates the course of allergic manifestations. Antihistamines are divided into three generations (Table 2.3).

First generation includes so-called sedating antihistamines, which also blockade cholinergic muscarinic and serotonin receptors. They have a marked sedative effect, which limits their prescription if you need to do works requiring sustained attention, rapid and coordinated mental and physical reactions. *Second generation of antihistamines* differs by the absence of sedative properties due to selective effect on H1-receptors. Due to the ability to block potassium channels they may affect the cardiac rhythm.

Third generation is represented by active metabolites of the first and second generation of medications. They selectively affect H_1-receptors and are almost free of cardiotoxic and sedative effects.

Glucocorticosteroids. Glucocorticoid hormones (GCS) are one of the most common groups of drugs that are used to treat a variety of inflammatory dermatoses. Local administration of glucocorticoid drugs with strong positive impact on different components of pathogenesis of diverse dermatoses allows directly affecting the lesions of damaged tissue and thus arrest inflammation process in the skin without the use of systemic treatment. On the other hand, even local hormone therapy requires relative caution due to possible development of adverse effects and resistance to conventional therapeutic agents.

The success of treatment with topical GCS (local, topical) is largely determined by correct choice of the preparation and adequate use of its dosage forms in each individual case. Ever-increasing incomings of new drugs to the pharmaceutical market, makes the choice of corticosteroid agents for the practitioner rather difficult, thus requiring constant updating of its knowledge.

Today topical corticosteroids by their strength are divided into four classes (Table 2.3).

Table 2.2
Antihistamine agents' generations

Antihistamines		
I generation	**II generation**	**III generation**
Diphenhydramine (Dimedrolum, Benadryl, Allergin)	Acrivastine (Sempreks)	Cetirizine (Tsetrin, Zyrtec)
Clemastine (Tavegil)	Astemizole (Gismanal)	Fexohenadine (Telfast)
Doxylamine (Dekaprin, Donormil)	Dimetinden (Phenistil)	Desloratadine (Aerius)
Diphenylpyraline	Oxatomide (Tinset)	
Bromodiphenhydramine	Terphenadine (Bronal, Histadin)	
Dimenhydrinate (Dedalon, Dramamine)	Azelastine (Allergodil)	
Chloropyramine (Suprastin)	Levocabastine (Histimet)	
Pyrilamine	Mizolastine	
Antazoline	Loratadine (Claritin)	
Mepyramine	Epinastine (Alezion)	
Brompheniramine	Ebastin (Kestine)	
Chlorpheniramine	Bamipin (Soventol)	
Dexchlorpheniramine		
Pheniramine (Avil)		
Mebhydrolin (Diazolinum)		
Kviphenadin (Fenkarol)		
Sekviphenadin (Bikarphenum)		
Promethazine (Phenergan, Diprazinum, Pipolphen)		
Trimeprazine (Terale n)		
Oxomemazin		
Alimemazin		
Cyclizine		
Hydroxyzine (Atarax)		
Meclizine (Bonine)		
Cyproheptadine (Peritol)		

Table 2.3
Division of topical glucocorticoids by their strength

Strength	International pharmaceutical name	Invented name
Weak	Hydrocortisone acetate 0,1%, 0,25%, 1%, 5%	Hydrocortizone (ointment and cream)
Moderate	Prednisolone 0,25%	Prednisolonum 0,25%
	Clobetazone butyrate 0,1%	Emoveyt
	Mazipredone hydrochloride 0,25%	Deperzolone
	Triamcinolone acetonide 0,1%	Phtorocortum.Tricortum. Polcortolon
	Flumetasone pivalate 0,02%	Lorinden. Locacoten
	Fluocinolone acetonide 0,025%	Flucinar.Sinalar. Sinaflanum
	Fluocortolon 0,025%	Ultralan
	Prednicarbate 0,25%	Prednitop
Strong	Betamethasonedipropionate 0,1%	Diproderm
	Betamethasone valerate 0,1%	CelestodermV. Betnoveytiun
	Hydrocortisone butyrate 0,1%	Laticort. Locoid
	Mometasone 0,1%	Elocom. Moleskine. Elozone. Momederm
	Methylprednisolone aceponate 0,1%	Advantan
	Halomethazone monohydrate 0,005%	Sicorten
	Budesonide 0,025%	Apulein
	Dexamethasone 0,025%	Esperson
	Flucazone propionate 0,05%	Cutivate
Very strong	Clobetazole propionate 0,1%	Dermovate. Delor. Clovate
	Halcinonide 0,1%	Halciderm

Hydrocortisone acetate preparations belonging to the first generation and due to having the mildest action are not used in dermatological practice today. More often they use topical PSL medications, which belong to the second generation and produce a moderate effect. The third generation is represented by numerous mainly halogenated topical corticosteroids, which have moderate, strong or very strong anti-inflammatory properties due to poor percutaneous adsorption. During prolonged use of topical corticosteroids it is necessary to consider some features of the mechanism of action of halogenated steroids, which can lead to adverse

events. Side effects can be divided into local, i.e. arising in the area of application, and systemic i.e. arising as a result of penetration of drug into systemic circulation.

Local side effects include skin atrophy, striae (atrophic scars), telangiectasia, perioral dermatitis, steroid acne, hypertrichosis, activation of viral, fungal or bacterial infections, impaired trophic skin, delayed recovery, congestive hyperemia (rosacea-like dermatitis), hemorrhagic purpura, reactive dermatitis (transient burning sensation, itching, or tingling), withdrawal state (maculopapular rash in the area of application), achromatosis, development of photosensitivity, colloidal pseudomilium, local ischemia, etc.

Systemic effects may occur only at very long-term use of topical corticosteroids in large areas of the skin. Systemic absorption of corticosteroids may suppress the hypothalamic-pituitary-adrenal system. This suppression causes reduction in generation of endogenous corticosteroids and may lead to the breach in metabolism of carbohydrates and unstable blood pressure. Prolonged suppression may result in the atrophy of adrenal cortex and Cushing's syndrome. In children, adrenocortical insufficiency leads to slower growth. However, the therapeutic effect of topical steroids, if properly selected and used, is much stronger than the impact of side effects.

Recently created topical corticosteroids of fourth generation are the best in application as they successfully combine all the positive features of their predecessors, which means that they have high activity comparable with the potency of fluorinated corticosteroids and minimal adverse effects typical of hydrocortisone acetate. The fourth generation of topical steroids includes strong GCS, which do not contain fluorine atom in their structure.

The mechanism of action of topical corticosteroids is based on their interaction with steroid receptors of skin cells resulting in inhibition of the inflammatory response due to vasodilator effect, inhibition of proliferation of epidermal cells, inhibition of the release of inflammatory mediators from eosinophils and neutrophils, inhibition of hyaluronidase activity, stabilization of lysosomal membranes of epidermal cells and the impact on connective tissue (inhibition of mitotic activity of fibroblasts, reduction of production of acid mucopolysaccharides, basophilic regeneration of collagen and elastic fibers).

Topical corticosteroids have anti-inflammatory, antipruritic, anti-proliferative and immunosuppressive properties that determine their use in dermatological practice. Most often, these medications are prescribed in simple and allergic dermatitis, toxicodermatoses, insect bites and various forms of erythema, psoriasis, eczema, neurodermatitis, discoid lupus erythematosis, urticaria, strofulyuse, atopic dermatitis, pemphigus erythematosus, seborrheic dermatitis, lichen planus, cheilitis, Dьhring's dermatosis, hypertrophic and keloid scars, Alopecia areata.

In some cases, to treat acute inflammatory reactions topical corticosteroids may temporarily be used in combination with other drugs for pyoderma, mycosis, herpes zoster, preulcerous eczematous process.

Topical corticosteroids can penetrate into the skin in two ways – directly through epidermis or through open hair follicles, sebaceous and sweat glands. Transepidermal penetration is the main way for topical GCS to penetrate into the skin. However, you should use medications with caution in areas of significant hair distribution, as penetration via hair follicles accelerates penetration of steroids into the microcirculatory bed.

Penetration of corticosteroids through skin depends on six main factors, which include the place of application of the drug, the patient's age, the properties of active ingredients, the basics of the drug, its method of application, stage of disease (skin condition).

General rules for the application of topical corticosteroids:

1. Before using external GCS you should accurately set the diagnosis and define the stage of inflammatory process.
2. It is recommended to start the treatment with weak drugs (to exclude hyperkeratotic forms of dermatoses). If there is no effect after 2-3 weeks of treatment, you should switch to a more powerful drug, and after the effect, you may return to weaker corticosteroids.
3. The medication is applied to clean skin with a thin layer 1-2 times a day (depending on the properties of GCS), do not massage the skin and rub the drug.
4. In chronic processes it is advisable to use the ointment, while in acute – creams and emulsions (sometimes lotion and spray).
5. It is advised to treat scalp with lotion, gel or emulsion.
6. In case of secondary infection of the lesions you should use a combination of drugs with antimicrobial agents, while in hyperkeratotic processes – with keratolytic agents.
7. Less potent corticosteroids should be used on thin skin areas (face, folds), as well as in children and elderly people.
8. During pregnancy it is not recommended to use corticosteroids for long period of time and on large areas of the skin.
9. You should take into account all the environmental factors (temperature, humidity) that contribute to a more rapid absorption of the drug.
10. It is not recommended to use drug under occlusive dressing, except for some forms of hypertrophic dermatoses. Tightly compressing clothes and children's swaddling may serve as occlusal factor and increase the permeability of the skin.
11. You should pay attention to the properties of active components and the basis that itself can cause local inflammation.

Local treatment

Local treatment of dermatoses and STD involves the use of external resources that directly affect the lesion.

Lotions. Lotions are prescribed for acute inflammatory processes in the skin, which are accompanied by the formation of erosive and moist areas (eczema, dermatitis), burning, itching, as well as the presence of bruised and bleeding sites in the skin.

The therapeutic effect of lotions is based on the effect of cold wet and, therefore, cold (icy) medicinal solutions (potassium permanganate in the ratio of 1: 2000, 3.2% of boric acid solution and Furacilin solution in a ratio of 1:10,000 etc.) are required.

Wet-to-dry dressings. The action of wet-to-dry dressings is based on the action of moist heat, and are applied in a number of diseases (eczema, neurodermatitis etc.) that are characterized by the development of limited cutaneous lesions with marked infiltration and oozing. Apply 10-15 layers folded gauze soaked in a drug solution and then squeezed on the affected skin. On top of gauze, put somewhat larger compress paper (without wool) and tape it up. Wet-to-dry dressings should be changed after 4-6 hours to the extent of their drying. Pustular skin diseases and acute generalized inflammation are considered to be contraindications to the use of wet-to-dry dressings.

Compress dressing *(hot compress)*. Application of compress bandages is based on the prolonged action of moist heat. They are used as an aid contributing to the resorption of limited infiltration of the skin, subcutaneous fat and muscles in chronic diseases of the joints and ligaments and in a number of limited inflammation processes.

Contraindications include the breach of the integrity of skin, pustular skin diseases (impetigo, ulcer pyoderma, abrasions etc.) and acute inflammation accompanied by weeping.

A nurse prepares a bandage, gauze, compress paper, cotton wool, medical sterile tray, tweezers and all the necessary substances that are used in compress (leaden water, 5% solution of alcohol, camphor oil). These substances must be of room temperature, except for oil which is preheated to 38-39°C.

Compress dressing should be changed twice a day.

Complications with compress dressings include possible appearance of maceration of the skin, dermatitis, pruritus, pustular skin diseases. However, these phenomena rapidly disappear (with the exception of pustular disease).

Salve dressings. Salve dressings are used to get deeper penetration of the drug contained in ointments or pastes inside the skin, as well as with hygienic purpose (protection of clothes and the surrounding healthy skin from penetration of applied drugs thereon). Under dressings they often apply paste or ointment.

Pastes. A paste is a mixture of equal parts of fat base and powdered substances. They are added with various medicines (naphthalene, ichthyol, tar acids etc.). Pastes have a drying effect and are applied to surface inflammations (eczema, neurodermatitis, dermatitis etc.).

Ointment. Unlike pastes, ointments are less dense in consistency because they contain fatter base. Ointments are widely used with flakes, peels, cracks, chronic inflammatory processes etc.

Apply paste or ointment using a spatula and stripe-smear it on the lesion making light movements of spatula. On the surface area of lubricated site, put sterile gauze and tape it up (no more than 2-3 rounds of roll gauze). In case of massive crusts, the ointment is covered with compress paper, which is tightly fixed with a bandage (ointment compress dressing). This promotes more rapid loosening and rejection of crusts. In parasitic diseases that affect large areas of skin (scabies etc.), an ointment, previously applied on palm, is rubbed into the skin. Some potent substances (Naftalan oil, tar, ihtiola) are sometimes used in pure form, without any basis. Thus, using a gauze or a cotton swab apply these substances only within the lesion. Usually lubrication of lesions with a paste or ointment is applied 1-2 times a day, and with clean tar ihtiola – once in 1-2 days. Contraindications to the use of ointment dressings are acute inflammation of the skin accompanied by oozing. Frequent use of ointments or their misuse (rubbing instead of light lubrication, etc.) can worsen the disease. In case of skin irritation i.e. redness, swelling, itching or pain, the procedure should be stopped.

The paste should not be applied to those areas of the body that are densely covered with hairs.

Talcum. Talcum is used with acute inflammatory processes that are not accompanied by oozing, and in the folds of the skin with chafing. Talcum applied to the skin absorbs moisture from the skin and increases surface evaporation by many times. This increases skin heat emission and, thus causes anti-inflammatory effect.

Creams. Creams are a dosage form consisting of fat mixed with water. Skin cooling creams are used in chronic inflammation.

Shacked-up mixtures *(«magma»).* Shacked-up mixtures that contain powdered substances (usually zinc) in oil or boric-alcohol solution are used for dermatitis, erythroderma, eczema etc. These mixtures dry quickly and requiring no bandaging. Before use, they are shaken and, then using a cotton or gauze, are applied to the affected area of the skin followed by talc or zinc oxide sprinkle. It is not allowed to apply these mixtures with abundant oozing, excessive dryness of skin lesions and localization of lesions on hairy areas.

Plaster. Plaster is a sticky ointment base with thick consistency covered with impermeable matter that may contain active drug substance. Plaster containing no drugs is used to fix dressings on the skin and in the treatment of venous ulcers.

Plaster containing drugs (mercury, salicylic acid, urea etc.) has an intensive deep tissue effect and is used for boils, onychomycosis, warts and bounded hyperkeratosis. Contraindications to the use of plaster are eczema, dermatitis and taxidermy. Before applying plaster the skin is thoroughly degreased with alcohol or medical gasoline; the hair should be shaved off. To fix the bandage, apply usual plaster. It is cut into strips of desired length and then applied so that the central part of the cut strip was pressed against the adhesive bandage, and ends – against degreased skin. If plaster badly sticks to the skin, it should be slightly warmed up.

As concerns complications, the application of plaster may cause dermatitis.

1. Which layer of European people epidermis contains melanocytes?

A. Translucent
B. Spinous
C. Basal
D. Horny
E. Granular

2. Sweat glands can be:

A. Eccrine
B. Border
C. Apocrine
D. Glomerular
E. All answers are correct

3. Which nerve receptors in the skin are responsible for the sensation of cold?

A. Krause's bulbs
B. Ruffini's corpuscles
C. Meissner's corpuscles
D. Pacinian corpuscles
E. Merkel's corpuscles

4. Which pathomorphological process in the skin causes appearance of bulla?

A. Parakeratosis
B. Acanthosis
C. Acantholysis
D. Hyperkeratosis
E. Spongiosis

5. What histopathological changes underlie the concept of «hyperkeratosis»?

A. Irregular proliferation of dermal papilla
B. Intensive growth of the granular layer of the epidermis
C. Thickening of horny layer of epidermis due to the enhanced keratinization and delayed rejection of horny scales
D. None of the aforesaid
E. Intensive growth of spinous layer of epidermis

6. What types of morphological elements constitute monomorphic rash?

A. One type of primary elements
B. One primary and several secondary types of elements
C. Several types of primary elements
D. Several types of secondary elements
E. Elements accompanied by skin defects

7. Clinically, a crust differs from the scale by the fact that it is:

A. Transparent
B. Microscopic
C. Thick and non-transparent
D. Appears as a result of evolution of hemorrhagic macules
E. Appears as a result of evolution of a nodule

8. Erosion is the second morphological elements that:

A. Epithelizes without traces
B. Remains scars
C. Appears as a result of evolution of pigmented macules
D. Appears as a result of scratching
E. Appears exclusively on the physiological lines of skin tension

9. What technique allows distinguishing between vascular inflammatory macules and other types of spots?

A. Angioscopy
B. Vitropression
C. Scratch test
D. Scraping
E. Brocq test

10. What diagnostic technique allows studying functional state of neurovascular system?

A. Diascopy
B. Angioscopy
C. Determination of dermographism nature
D. Luminescent diagnostics
E. Vitropression

Task 1. Pathomorphological examination of biopsy material taken from affected skin cells of a patient has revealed a change in the spinous layer of epidermis and the absence of intercellular connections**.**

a) What kind of histopathological processes is this?
- **A**. Parakeratosis
- **B**. Acanthosis
- **C**. Hyperkeratosis
- **D**. Spongiosis
- **E**. Acantholysis

b) What morphological element of rash appears thereby?

Task 2. An individual papilla of skin biopsy material contains a structural element, which is an encapsulated nerve receptor and consists of the processes of modified cells of ciliary epithelium with sensitive cilia that are in contact with cell membrane of the nerve end of process. Body cells are separated from contact zone by capsule consisting of several longitudinally oriented glial cells. The cilia of sensitive cells are located between outer and inner capsule, thus contacting with inner surface of outer capsule.

a) What kind of nerve receptors is that?
- **A.** Krause's bulbs
- **B.** Ruffini's corpuscles
- **C.** Meissner's corpuscles
- **D.** Pacinian corpuscles
- **E.** Merkel's corpuscles

b) What function the receptors perform?

Task 3. The patient's skin has a redness of a palm size, which disappears when applying diascopy.

a) What kind of element is that?
- **A**. Telangiectasia
- **B**. Roseola
- **C**. Petechia
- **D**. Chloasma
- **E**. Erythema

b) How the described element is resolved?

Task 4. The patient's skin of upper and lower extremities is covered with numerous non-cavitary (infiltrated) rash elements with clear-cut boundaries of a coin size covered with scales.

a) What kind of elements is that?
- **A**. Vesication
- **B**. Tubercle
- **C**. Nodule
- **D**. Bulla
- **E**. Papulle

b) Outline the stages of evolution of described rash element.

Task 5. The examination of the patient has revealed that skin is covered with translucent polygonal papules of various sizes with impression in the middle. Koebner's phenomenon is observed on the postoperative scar. The diagnosis is lichen planus.

a) What stage of diagnostics is that?
- **A**. Morphological
- **B**. Functional
- **C**. Clinical
- **D**. Anamnestic
- **E**. Ethiopathogenetic

b) The setting of which diagnosis is finished with this type of diagnostic process?

Answers to the quiz of the first level of complexity
1 – **C**; 2 – **E**; 3 – **A**; 4 –**C**; 5 – **C**; 6 – **A**; 7 – **C**; 8 – **A**; 9 – **B**; 10 – **C**
Answers to the quiz of the second and third levels of complexity
1a – **E**; 2a – **D**; 3a – **E**; 4a – **E**; 5a – **C**

3 TOPIC

Ectoparasite Infections

Ectoparasite Infestions – skin diseases caused by human and animal parasites. There are two groups of ectoparasite infections, these are diseases caused by the penetration of the parasites into the skin (scabies, demodecosis), and diseases caused by parasites bites (lice infestation) and insect stings.

TRAINING AND EDUCATIONAL PURPOSES

- To determine the ways and possible conditions of ectoparasites infection of the patients
- To explain general course and clinics of scabies
- To determine the clinical varieties of pediculosis
- To generalize the clinics of typical demodecosis manifestations
- To generalize the principles of therapy and prevention of skin infestation

3.1 Scabies

Scabies is a parasitic contagious skin infestation caused by the itch mite *Sarcoptes scabies.*

TO KNOW:

- etiological, pathogenetic and epidemiological features of scabies;
- clinical forms of scabies and peculiarities of disease course;
- diagnostic criteria of skin manifestation during scabies and its complications;
- notion of acarophobia and its manifestations which may arise due to post-scabies itch development;
- methods and principles of treatment, prophylaxis and clinical examination of scabies patients.

TO BE ABLE TO:

- correctly collect anamnesis of scabies patients;
- run laboratory diagnostics (traditional, express-diagnostics, by alkaline skin preparation method) in order detect itch mite;
- make a differential diagnostics in comparison with dermatoses which have similar clinical presentation picture;
- prescribe rational treatment for scabies patient and to correctly prescribe medicines for eternal therapy taking into account the patient's age;
- recommend the necessary preventive measures of scabies.

Etiology. Human scabies is caused by the itch mite *Sarcoptes scabiei* of *Sarcoptidae* family. The size of the male mite is 0.2 mm in length, 0.14-0.19 mm in width. Female is somewhat larger, it is 0.4-0.45 mm in length and 0.25-0.35 mm in width. Under the microscope itch mite is like turtle. After fertilization the male dies, and female burrows into the epilayer of the epidermis, where makes tunnels in parallel with the surface of the skin, in which it lays eggs. A mite can be removed from the itch tunnel with an injection needle or by means of thin sections of stratum corneum in the places of itch tunnels made by the female. For the period from one and a half to two months of its life, the female lays up to 50 eggs, of which three or four days later the mite larvae hatch. After two weeks, the mites become mature.

Epidemiology. Annually up to 300 million cases of scabies morbidity are registered in the world. Fluctuation of scabies morbidity is of sinuous character with rise and fall rates periods in 15-30 years. Mainly, morbidity rate increase is caused by the worsening of sanitary conditions, poverty, migrations, economic crisis, natural disasters, population crowding, especially during the wars. It is observed the parallelism of increase of scabies cases and diseases transmitted predominantly through sexual contact. The source of infection is ill person. The main way of disease transmission is family and domestic. The infection occurs through the direct contact with the sick person, through bed sheets, clothing, gloves, socks and other items that he used. The children often become infected through shared toys in the kindergarten.

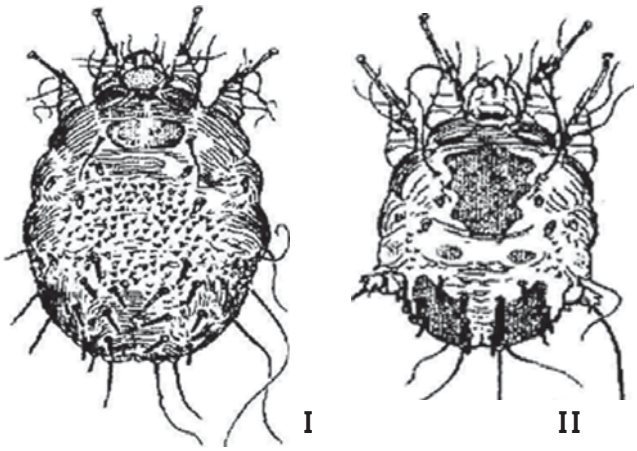


Fig. 3.1. Schematic representation of the itch mite:
I – female, II – male.

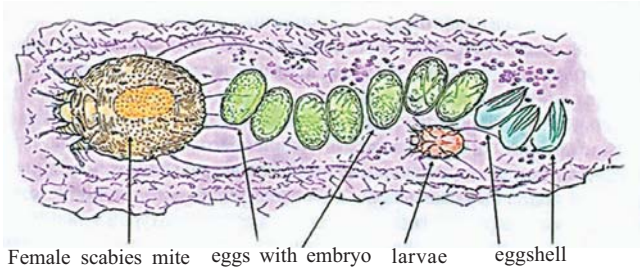


Fig. 3.2. Schematic representation of itch tunnel
in epidermis of the human skin.

Clinical picture. The clinic of scabies is based on the peculiarities of agent parasitizing, skin reaction and topical distribution of itch mites on the host. The incubatory period at the introduction of infection by the female is virtually absent, as it immediately borrows into the epilayer of the epidermis and starts to gnaw through tunnel and lay

eggs, that is, there is the main clinical symptom of the disease. At the introduction of infection by larvae one can talk about the incubation period, which corresponds to the period of larva transformation into the mature female (approximately two weeks). The clinical symptoms of the scabies are itching, which increases in the evening time, the presence of borrows, polymorphism of skin (papulovesicles, papules, scratches, bloody crust), characteristic localization of the rash.

The first subjective sign of the disease is intense itching in the places of borrows made by the female. The itching becomes worse in the evening and at night, that is due to the biological female characteristics, *(period of agent activity, salivation and substances present in the excrements; irritation of the nerve endings at movement of the itch)*, tunneling mainly at night, and the development of organism sensitization to parasites and their waste products. Itch can be localized and generalized. Its intensity varies with different people and depends upon the number of rashes and distribution process.

On the place of the female penetration into the skin a small papulovesicle (rarely papule) appears, which has infiltrative basis. At the distance of 2-7 mm from this element another papulovesicle appears (that is the exit site of the female onto the skin surface), these are so called conjugated freckles. Between the papulovesicles one can see itch tunnels, which have the form of thin strips of grey color, either straight or curved in the form of S letter. By means of light palpation one can find the tunnel relief, this is symptom Cezary. In the result of scratching there appear excoriations or small erosions with bloody crusts.

Typical places of scabies localization are areas of the hands between the fingers, flexor surface of the brachium and elbow joints, the front and rear edges of axillary cavities, lateral surface of the chest and abdomen, nipples areola breast of women, navel area, buttocks and inter-gluteal folds, internal surface of the femora and external genitalia, these are areas with thin stratum corneum. The symptom of Hardy-Gorchakov helps in the diagnostics; this is the presence of pustules (impetigo, rarely ecthyma) and purulent crusts on elbows. The eruptions in view of impetigenous elements, papulovesicles, crusts in the area of inter-gluteal fold skin with the transition to the lumbus, were called the triangle symptom or the rhomb of Michaelis. Scabies, as a rule, is not localized on the skin of the head, neck, back, axillary cavities, palms and plantae (except for children and persons with mental disabilities), that is an



Fig. 3.3. Scabies.

important feature for the differential diagnostics with some other dermatoses. Clinical presentations of scabies on hand skin can be absent or slightly observable as to neat people and persons working with mineral oils, fuel oil (drivers, fitters, turners and others), turf and asphalt.

The peculiarities of clinical presentation of scabies nowadays are light itching and inconsiderable in number eruptions during continuous course. There can be urticarial elements, the absence of rash on the hands due to frequent contact with detergent agents, pastes, chemicals and others.

Scabies is often complicated by the secondary pyococcus infection in the results of the scratching (impetigo, ecthyma, folliculitis, boils), and by microbial eczema, especially in the area of breasts as for women. At eczematization there appears rash, which is typical to eczema; on the erythematous ground there appear small vesicles, oozing lesion, excoriations, and crusts. Eczematization, as a rule, develops as a result of irrational therapy or intolerance to some local agents (of brilliant green, benzyl benzoate, furacilin and others), less frequently as a result of sensitization of mite waste products.

Morbid anatomy. Histologically borrows look like tunnels in the horny layer of epidermis. Cephalic reminds a funnel and slightly opens outwards and the cavity is visualized in the caudal section of the borrow, where the female is situated. Small vasodilatations with a little cellular infiltration around them take place in papillary dermis. Sometimes acanthosis and spongiosis are observed in the epidermis.

Diagnostics. The diagnosis is based on the characteristic clinical picture of the disease and the identification of scabies mite in the laboratory research. With the traditional method the material for the study is obtained by means of the needle from the papulovesicles, located in the end of the borrow, or by means of superficial slice of the epidermis with a razor in the location of borrow. After putting



Fig. 3.4. Scabies.



Fig. 3.5. Scabies. Symptom Hardy-Gorchakov.

the obtained material on a glass slide in a drop of 10-20% of alkali solution, the specimen is examined at law magnification under a light microscope.

Differential diagnostics. Most frequently it is necessary to differentiate scabies from skin prurigo, wherein intense itching and papular elements are observed as well. In contrast to scabies, in indicated disease itching worries patient both in the daytime and at night, and more often it takes priority of rash. The popular elements are not conjugated, are located randomly and can appear on face skin, the itch borrows are absent. Indirect evidence in favor of scabies can be itching and similar rash of family members of the patient.

Scabies affection of the penis skin, especially in the form of ecthyma, can be crucial for the suspected syphilitic solid chancre or popular rash, specific to the secondary period of syphilis. The presence of specific carnification at the heart of syphilitic solid chancre, the revealing of pale treponemes in serum of chancre or in lymph node aspirates, as well as the absence of scabies signs on other parts of the body and positive serological reactions allow diagnosing syphilis.

One type of neglected stage of scabies is so-called Norwegian scabies, which is observed in persons with mental illness and in patients suffering from syringomyelia, multiple sclerosis, leprosy. The skin at this time is covered with thick, as bark, crusts of dark green colour, resembling shell. Under the crusts after their removal on erythematous background a lot of white dots can be seen these are scabies mites.

Treatment. In order to kill off the scabies mites, local antiparasitic agents, disintegrating the cornel layer of epidermis and killing parasites, are applied. Appropriate antiparasitic agents as ointments, solutions and sprays are necessary to rub in all skin integuments, except for face and scalp, for adults. As infants and young children can have scabies manifestations on the face, scalp plantae and palms, accordingly, the indicated parts of the body subject to treatment with antiparasitic agents as well.

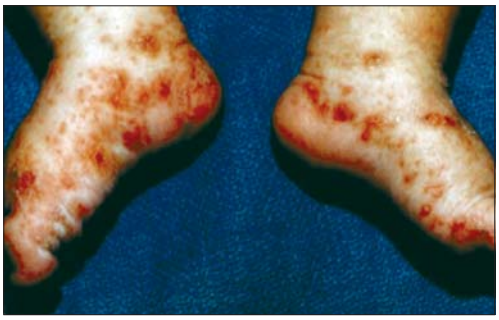


Fig. 3.6. Scabies in nursing infant.



Fig. 3.7. Scabies complicated by pyoderma.

For scabies treatment benzyl benzoate is used. This method differs from the others in such a way that along with high efficiency, there is no unpleasant smell that allows the patient to be at work, in public transport etc. Benzyl benzoate (benzyl-benzene carboxylate in form of 20% suspension in soap solution: 20 g of benzyl benzoate, 2 g of green soap and 78 ml of water) is rubbed in with a cotton swab after that the patient puts on clean clothes and change linen. Infrictions are repeated during the period of two days more without washing. In three days after end of treatment the patient takes a shower and changes clothing. Nowadays, 25% benzyl benzoate cream is used more often than suspension.

The application of the above methods of therapy of scabies, taking into account the toxicity of antiparasitic medicines, is often accompanied by skin irritation (contact dermatitis). In this case, the patients are recommended desensitizing agents and antihistamines, zinc oxide powders, indifferent water magmas, steroid creams and ointments. In case of bacillosis overlay, antibiotics both oraly and topically are used temporarily, and lesion focuses are salved with aniline dyes and 2% salicyl alcohol, as well. If scabies is accompanied by eczema, then 24 hours before the antiscabious therapy, the affected area must be salved with one of the topic corticosteroids. The patients with constant itching after the treatment for a long time are recommended mitigatory and local anti-itching therapy.

Prophylaxis and antiepidemic measures for scabies patients are carried out accounting the epidemiology of disease. Early diagnostics and active case detections are of great importance here. Control of curability is executed in three days after the ending of therapy, and then in every ten days during a month and a half. The effectiveness of therapy mostly depends on thoroughness of sanitary and preventive measures.



Fig. 3.8. Scabies manifestations in the area of glans.



Fig. 3.9. Scabious ecthyma.

3.2 Demodecosis

Demodecosis is a parasitic skin disease caused by the mites-Demodex, these are *Demodex folliculorum* and *Demodex brevis.* Most of researchers consider that mites-Demodex live in the skin of healthy people, and only under certain conditions they reveal their pathogenic features.

Aetiopathogenesis. The mites-*Demodex folliculorum* and *Demodex brevis* of *Demodecidae* family. They are in the follicles and sebaceous glands of the face mainly, as well as of the ear and auditory canals, palpebrae, breasts and genitals. There are two species of Demodex, which parasitize on human body; these are *Demodex folliculorum* and *Demodex brevis*. Both species of the mites are very small in size (0.2–0.3 mm), with fusiform body, short legs and piercing-sucking mouthparts. The mites-Demodex causes illness under the common name demodecosis. More frequently these are people of young or middle age who suffer from a disease, especially in the presence of oily seborrhea. Factors contributing to the development of the disease are gastrointestinal and hormonal disorders, autonomic nervous disorders, menopause, dysmenorrhoea, and work in conditions of sharp change in temperature.

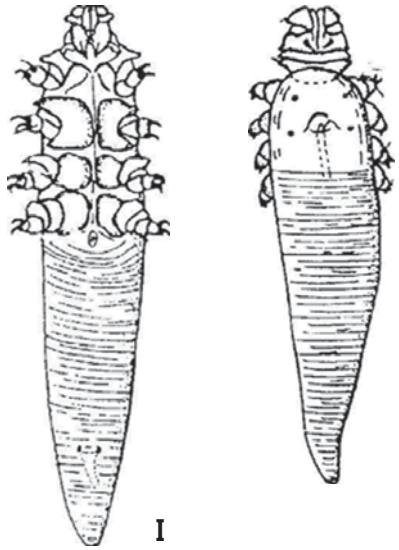


Fig. 3.10. Schematic presentation of the mite *Demodex folliculorum:* I – female, II – male.

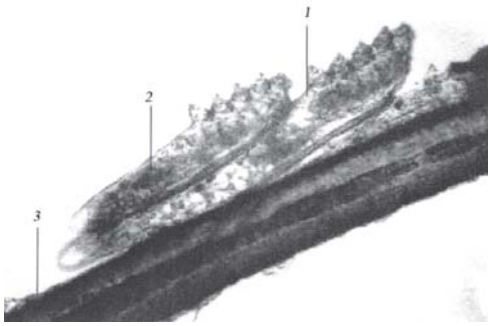


Fig. 3.11. Female and male of the mites-*Demodex folliculorum* in the hair follicle ostium of the eye lash hair:
1 – female, 2 – male, 3 – hair shaft.
Microscopy, 20X magnification.

Clinical picture. It predominantly involves the facial region (cheeks, forehead, and chin). There appear erythematous spots, telangiectasia, focal or fuse infiltration, peeling, as well as follicular papules of pink or red color, papulovesicles, papulopustules or separate macropustules. All these morphological manifestations of the demodecosis are accompanied by a number of subjective sensations, such as itching from minor to insufferable; sensation of skin heat and tightening; reduction of its elasticity and softness; sense of "screwing" something into the skin and "pins and needles" on its surface.

Nowadays there are several classifications of clinical forms of demodecosis. In particular, one defines erythematous-squamous, papular, pustular, rosacea-like, combined and oligosymptomatic forms. With erythematous-squamous form of demodecosis peeling secondary to skin redness is observed in the affected

areas. Disease, as a rule, occurs in spring and summer time. Its clinical symptoms exist up to two months, and then they gradually disappear or manifest less intensively. The relapse of disease occurs again in spring of the next year.

Papular form is the most prevalent form of demodecosis. Except the face, the other areas of the skin can also be affected, such as ears, neck, back and abdomen. The main features of this clinical form are popular or papulovesicular rash, always follicular. The sizes of the papules range from 0.5 to 2 mm in diameter. The color of the papules can be of different intensity from pink to intense red. Silver squamosa or microvesicles appear on the surface of some papules, which can transform into micropustules.

With the pustular form of demodecosis, the clinical picture resembles follicle, acne, rosacea-like or combined form of lesion, but with pustular rash dominating.

Clinical manifestations of rosacea-like form of demodecosis look like manifestations of true rosacea. The peculiarities of this form are stable erythema on face, mainly in the area of nose, as well as the presence of telangiectasia with periodic presentation of flare. An important differential diagnostic criterion of rosacea-like form of demodecosis, as distinct from true rosacea, is the discovery of a large number of the mites-*Demodex* in the lesion areas during the laboratory research. With this clinical form of demodecosis the postulation can be due to parasitizing and activity of the mites-*Demodex*, or the result of action of associated impetiginous bacterial population.

With combined form of demodecosis the rash elements appear which are characteristic for all other clinical forms. The combined form appears in the setting of any other clinical form of demodecosis, but it can develop also as independent form from the beginning of the sickness.

Oligosymptomatic form of demodecosis is characterized by the presence of erythematous spots, small follicular peeling, isolated small papulovesicles and vesicle-pustules.

Depending on the extension of inflammatory process the following forms of demodecosis are recommended to define: limited form with localization of the rash, mainly in the folds of the face skin and near the angles of the eyes; diffusive form which

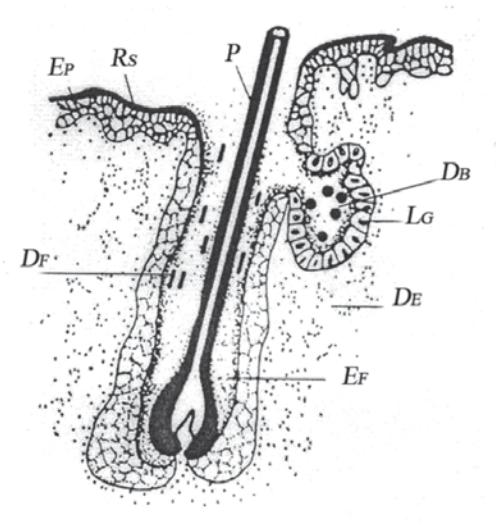


Fig. 3.12. Scheme of mites-*Demodex folliculorum* and mites-*Demodex brevis* localization in the hair follicle:
Df – mite-*Demodex folliculorum,* **Db** – mite-*Demodex brevis,* **De** – derma, **Ef** – follicle epithelium, **Ep** – epidermis, **Lg** – sebaceous gland, **Rs** – corneal layer of skin, **P** – hair.

affects the entire skin of the face; extensive form in which the inflammatory process extends beyond the face.

At the present stage it is also recommended to define the primary and secondary forms of demodecosis. The criterion of such dividing is that the primary demodecosis appears on the unchanged skin in appearance; and the secondary demodecosis is the complication of the principal disease, such as rosacea, perioral dermatitis and some other ones.

Diagnostics. The diagnostics of the demodecosis is in microscopic study of pathological material taken from the lesions with aim of detection of the mites-*Demodex*.

A variety of clinical forms of demodecosis defines specific material sampling for study for the presence of the mites-*Demodex*. With erythematous form of inflammatory process the material is taken from different areas of skin lesion by superficial scraping of squamosa. With papular, pustular and combined forms of demodecosis a puncture is made by means of scalpel and the content of pustules or sebaceous glands is received by extracting. It is also recommended to use comedone extractor or cyclodialysis spoon for extracting of follicle content. The obtained material is transferred onto the glass plate, treated with 20% solution of potassium hydroxide (kerosene, glycerol), covered with a cover slide, and examined under the microscope at low and high magnification in 10-20 minutes.

The laboratory diagnostics of demodecosis of the eyes is also based on the detection of the mites-*Demodex* in the content of hair follicles of the eye lashes or scrapings from the eyelid margins. Epilated 4-6 eyelashes from each eyelid are placed onto the glass plate, applied with 1-2 drops of clear liquid (water, plant or mineral oils, glycerin) onto them, and then covered with cover slide.



Fig. 3.13. Demodecosis.

It should be noted that up to the present moment there is no generally accepted methodology of collection of samples to determine the number of the mites-*Demodex* in a limited area of affected skin. Besides, the point of significance of identified number of the mites-*Demodex* for setting nosological diagnosis "demodecosis" remains to be debating.

Individual researchers recommend defining the number of the mites-*Demodex* in the affected skin area of 1 cm^2. In this case the detection of the mites-*Demodex* in an amount of more than 5 mites per 1 sm^2 is considered a diagnostic criterion for setting diagnosis

"demodecosis". A lower concentration of these parasites is regarded as carriage, which does not require antiparasitic therapy for the patient to be conducted.

At the same time, the other researchers to determine the diagnosis "demadecosis" offer to take into account the number of the mites-*Demodex (D. folliculorum, D. brevis)* in the structure of one hair follicle in the area of affected face skin, that methodologically is performed by means of histological examination. The detection of the mites-*Demodex* in an amount of 10 mites and more in the structure of one hair follicle is offered to regard as diagnostically significant for setting diagnosis "demodecosis". Herewith, during the quantitication both mature species of the parasites (imago) and the presence of the eggs, larvae and nymphs must be accounted.

Demodecosis should be differentiated from rosacea, acne vulgaris, seborrheic dermatitis, perioral dermatitis, bacterial folliculitis.

Treatment.

Taking into account the proven significance of a number of endogenous factors in the pathogenesis of demodecosis, it is recommended to hold a comprehensive examination of these patients with aim of defining foci of chronic infection, pathology of gastrointestinal tract, liver, pancreas, as well as endocrine and immune disorders.

Treatment of demodecosis requires a complex therapy with accounting of the stage of inflammatory process and presence of associated pathology.

In case of acute facial oedema and oozing lesion antihistamines and dehydration agents, as well as topical anti-inflammatory therapy are prescribed. The presence of pustular elements of rash requires prescription of one of the tetracycline antibiotics, in particular, doxycycline or macrolides (azithromycin) and others. After the elimination of oozing lesion and fresh pustular rash the patients are prescribed with topical antiparasitic therapy.

For the treatment metronidazole (oral) is used as well. Antiparasitic topical therapy can be conducted with use of 20% suspension of benzyl benzoate, 33% sulfur ointment.

The medicines of pyrethroid group, which are synthetic analogues of natural pyrethrins, known for their insecticidal and acricide action, are also used. Concerning appropriate medicines with synthetic pyrethroid-permethrin, it should be noted that the permethrin concentration of the preparation "Spregal" (spray) is higher in comparison with analogues. Besides, the preparation formula of "Spregal" consists of piperonyl butoxide, which contributes to prolongation and strengthening of permethrin action.

During the treatment the diet and avoiding of hot and spicy food is important. To normalize the metabolic processes the treatment of the revealed pathology of other organs and systems is recommended.

Prophylaxis. In order to prevent exacerbation of demodecosis prolonged sun exposure and excessive use of cosmetics should be avoided.

3.3 Pediculosis

Pediculosis *(pediculus)* is an infestation of the skin and hair, caused by the parasites of three kinds, these are head lice *(Pediculus capitis)*, body lice *(Pediculus corporis)* and pubic or crab lice *(Pediculus pubis)*.

Head lice *(Pediculus capitis)* are spread through direct head-to-head contact or due to sharing hair combs, hats and others. The size of the male is 2-3 mm, the female is 2.4-4 mm, and both are of grey color with black dots on the belly edges. Inhabiting the scalp, the female lays eggs (nits) of grayish-white color with 0.75-0.8 mm in length, which are attached to the hair with help of chitinous membranes. In neglected cases the lice can infest the eyebrows, mustache and beard. The nits are attached to the hair and can be seen as white spot formations.

Clinical picture. Due to bites of the lice, there occurs intense pruritus (itching), which causes the appearance of excoriations, covered with hemorrhagic crusts. Often due to pyococcus infection in lesions there appear sycoses, follicles, and impetigo vulgaris. Abscesses and eczematous foci may develop. In complication of the pediculosis with pyoderma, the hair in the affected areas is glued in form of thick bundles, so called mats, at the same time, the regional lymph nodes can increase and become painful. In the back of the head, especially of the girls and women with long hair, there appears grainy pyodermia *(impetigo granulata).*

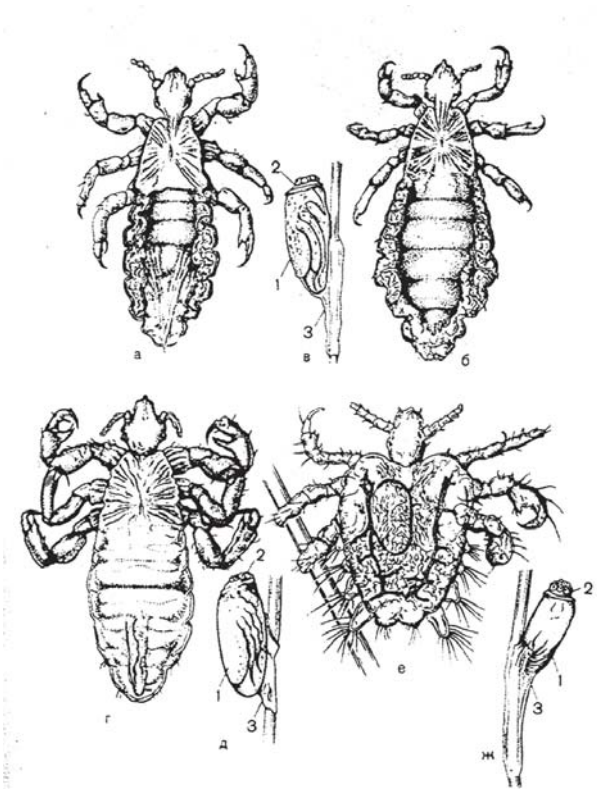


Fig. 3.14. Schematic presentation of the human lice:
a – head louse, male; *b* – female; *c* – nit (egg) of the head louse;
d – body louse, male; e – nit of the body louse;
f – pubic louse; *g* – nit of the pubic louse;
h – egg; 2 – tectorium; 3 – adhesive.

Diagnostics. To diagnose infestation, the scalp should be examined for the presence of the living parasites and nits.

Treatment. For the treatment of scalp pediculosis, 10% water-soap emulsions of benzyl benzoate and such shampoos as Pedilin, Nittiform are used, for treating the skin and hair of the head for 10-15 minutes, thereafter they are washed with hot water and soap. The use of Para-Plus spray is effective. The preparation is sprayed onto the scalp skin and the entire length of the hair; herewith the tip of the spray should be at a distance of 3 cm from the hair. After spraying the preparation it is necessary to wait for 10 minutes. During the exposure one should not cover a head with a towel or scarf. After use of preparation "Para-Plus" it is

necessary to thoroughly wash a head with a shampoo. The dead nits, remained on the hair, should be combed out. All textile products, which the patient contacted with, such as towels, pillows, hats and others, must be treated with the preparation "Para-Plus" to prevent the secondary infestation. In case of dermatitis or eczematization inflammations are eliminated with neutral lotions, which contain corticosteroids.

Body lice *(Pediculus corporis, seu vestimenti)* are rare nowadays on the territory of Ukraine; mainly people without a permanent residence have them. They are somewhat larger than head ones, with size 3-5 mm in length, of white color, without black spots on the abdomen. Lifetime of the parasites is 30-45 days; they well tolerate cold and can starve for several days, die immediately in boiling. Body lice carry saprotyphus and relapsing fever. Lice live and lay eggs in the folds of the clothes, especially in areas adjacent to the neck, shoulders and lower back.

Clinical picture. The lice bites cause intense itching; sometimes the eruption in form of urticarial elements can appear. In result of itching in the areas of lice parasitizing the scratches covered with bloody crusts appear, which are often complicated by the secondary pyococcus infections (impetigo, follicles, boils, abscesses), eczema. During long-term parasitic process the skin thickens and become dry (lichenification).

Diagnostics. To diagnose pediculosis, the dressing should be examined for the presence of the lice and the clinical picture should be appropriate.

Treatment. Treatment involves clothing disinfection (such as ironing, boiling, use of the spray "A-PAR", "Para-Plus" etc.) and the following shower of the patient.

Pubic or crab lice *(Pediculus pubis),* differ from the head and body lice by a smaller size (male is 1 mm, female is 1.5 mm) and round form (look like crabs). The places of parasitizing are mainly area of pubis, perineum, scrotum and anus. In case of people with excessive pilosis, the pubic lice can migrate to the chest, in the axillary cavities, on the beard and eyebrows. There, they are attached to the skin by means of craw-like formations. With their curved legs the parasites cling to the lower parts of the neighboring hairs. The pubic lice do not affect scalp. Small nits are found on the hair. Pubic lice are visible to the naked eye as greyish-brown spots with size of a pin's head near the base of the hair.

Pubic lice infestation occurs, mainly, through sexual contacts, but as an exception, it can occur during visiting public bathes or through the bedding. From time to time in pubic lice, the phenomena of eczematization appear on the skin (especially on the thighs) in the result of scratching and use of irritating solutions and ointments.

Clinical picture. Pubic lice cause intense itching with their bites, which is the reason of excoriation and bloody crusts appearance. Blue spots *(maculae*

cocruleae) with a diameter up to 1 cm of round or oval form appear in view of the line in the places of lice bites on skin of the abdomen, inner thighs and sides of the chest. The appearance of the spots is the result of the mixing of the patient's blood and lice saliva when biting. The blue spots do not disappear during diascopy, which is a significant sign in differential diagnostics from roseolous syphilides and saprotyphus.

Diagnostics. Pediculosis is determined on the basis of the presence of the parasites and nits, as well as blue spots, in the places of the bites on the skin of the abdomen, inner thighs and sides of the chest.

Treatment. Treatment of pubic pediculosis is in the removing of the hair from the affected areas and rubbing of the 33% sulfuric ointment, or 25% emulsion (cream) of benzyl benzoate during the following 3-4 days, after that the patient should take a shower with a soap and change clothes. Last time the sprays containing permethrin are successfully used for the treatment of the pubic pediculosis.

1. What agent causes scabies?

A. *Pediculus corporis*
B. *Sarcoptes scabiei*
C. *Demodex folliculorum*
D. *Pediculus capitis*
E. *Pityrosporum orbiculare*

2. What is incubation period for scabies?

A. 1–3 days
B. 3 months
C. 7–14 days
D. 2 months
E. 1 month

3. What is the character of eruptions in case of scabies?

A. Asymmetric-monomorphic
B. Asymmetric-polymorphic
C. Symmetric-monomorphic
D. Symmetric-polymorphic
E. Diffuse

4. Which of the following symptoms is uncharacteristic for scabies?

A. Sezary symptom
B. The triangle symptom or the rhomb of Michaelis
C. Hardy's symptom (Hardy-Gorchakov symptom)
D. Typical Hebra's borrow
E. Auspitz' symptom

5. What is not clinically typical for scabies?

A. Monomorphic character of rash
B. Presence of papulovesicular elements
C. Presence of itching borrows
D. Specific localization of rash (for adults and children)
E. Itching (in the evening, at night)

6. Rash elements in case of demodecosis are localized on?

A. Extensor surface of extremities
B. Flexor surface of extremities
C. Lumbus
D. Palms, plantae
E. Face

7. Which forms (stages) of disease are uncharacteristic for demodecosis?

A. *Rosacea erythematosis*
B. *Rosacea papulosa*
C. *Rosacea bullosa*
D. *Rosacea pustolosa*
E. *Rosacea hypertrophtica*

8. Scalp pediculosis is diagnosed on the following signs, except:

A. Excoriation
B. Itching
C. Eczematization
D. Secondary pyoderma
E. Presence of bullous elements

9. To treat pediculosis one uses:

A. Emulsion of benzyl benzoate
B. Celestoderm
C. Elocom
D. Herpevirum
E. Nizoral

10. To treat scabies all following preparations are used, except:

A. Benzyl benzoate
B. Solutions of sodium thiosulfate and hydrochloric acid
C. Common sulfur ointment
D. Permethrin
E. Aciclovir

Task 1. A man, who attended a medical appointment with a three-year-old son, is complaining that they both have skin itching which becomes worse at night. *Status localis*: there are eruptions in form of conjugated papulovesicles, a lot of crusts of the brown color and excoriations on the skin of the flexor surface of extremities, body, in the area of lumbus, on abdomen, but child also on the skin of the palms, plantae, face and the hair part of the head.

a) What diagnosis will you set?
- **A**. Scabies
- **B**. Allergic dermatitis
- **C**. Neurodermatitis
- **D**. Psoriasis
- **E**. Eczema

b) Call the methods of treatment and preventive measures of scabies for adults and children.

Task 2. A woman at the age of 35 is complaining of intense itching in the area of pubis and inguinal folds. She caught an illness a few days ago after work travel. *Status localis:* there are multiple scratches and hemorrhagic spots on the skin of abdomen (below), inner thighs.

a) Which diagnosis should be suspected?
- **A**. Scabies
- **B**. Pediculosis
- **C**. Eczema
- **D**. Epidermophytosis
- **E**. Dermatitis

b) Give the grounds for diagnosis.

Task 3. A teenager at the age of 13 has multiple conjugated papulovesicles, borrows, excoriations on the anterolateral surface of the trunk, in the lumbar area, on the buttocks, arms and in the area of radiocarpal joints. *Status localis*: skin itching at night. In view of the data of clinical and laboratory study, "scabies" is diagnosed.

a) Choose acaricide means for patient's treatment:
- **A**. 2% boric acid solution
- **B**. Aniline dyes
- **C**. 0.5% tannin solution
- **D**. 20% benzyl benzoate solution
- **E**. 6% hydrochloric acid solution

b) Call the specific clinical manifestations of scabies.

Task 4. A patient at the age of 50 is complaining about the eruption on the skin of nasolabial triangle and forehead, burning sensation and little itching in the rash areas. *Status localis:* there are papulopustular eruptions associated with erythema on the skin of nasolabial triangle and forehead. In the result of laboratory study the mite-*Demodex folliculorum* has been detected in the scrapings of rash elements.

a) Set the clinical diagnosis:
- **A**. Demodecosis
- **B**. Seborrheic dermatitis
- **C**. Erythema centrifugum
- **D**. Dermatitis
- **E**. Psoriasis

b) Conduct the differentiate diagnostics of the given disease.

Task 5. A patient at the age of 50 was admitted in gastroenterological department with gastritis and biliary dyskinesia. She was prescribed with adequate treatment. The patient was directed to the gastroenterologist for the consultation and treatment by the dermatologist, who set the diagnosis "scabies" to the patient after clinical and laboratory study.

a) Which laboratory study was executed to confirm the diagnosis?
- **A**. Identification of acantholytic cells
- **B**. Identification of *Sarcoptes scabiei*
- **C**. Identification of pathological fungi
- **D**. Identification of *Demodex folliculorum*
- **E**. Identification of *Pediculus vestimenta*

b) How is the laboratory diagnostics of demodecosis performed?

Answers to the quiz of the first level of complexity
1 – **B**; 2 – **C**; 3 – **D**; 4 – **E**; 5 – **A**; 6 – **E**; 7 – **C**; 8 – **E**; 9 – **A**; 10 – **E**

Answers to the quiz of the second and third levels of complexity
1a – **A**; 2a – **B**; 3a – **D**; 4a – **A**; 5a – **D**

4 TOPIC

Bacterial skin infections – pyoderma

Bacterial skin infections or pyodermae are a group of diseases, caused by microorganisms inducing purulent inflammation of skin.

TRAINING AND EDUCATIONAL PURPOSES

- To determine the ways and possible conditions of infection by pyogenic flora
- To generalize classification and general characteristics of pyogenic lesions of skin and mucous membranes
- To explain the role of different factors promoting its development
- To determine the general course and clinic of pyoderma
- To distinguish peculiarities of pyogenic lesions of mucous membranes
- To distinguish characteristic clinical peculiarities of staphyloderma
- To classify typical manifestations of streptoderma
- To define the principles of therapy and prophylaxis of pyogenic lesions

TO KNOW:

- modern views on etiology and pathogenesis of different clinical types of pyoderma;
- factors promoting developments and progression of pyoderma;
- principle of classification of impetiginous lesions of skin and its appendages;
- symptomatology of the main clinical types of pyoderma;
- the main approaches to the general and local treatment of pyoderma;
- the peculiarities of preventive measures of impetiginous lesions of the skin and its appendages.

TO BE ABLE TO:

- correctly collect anamnesis and carry out examination of the patient with pyoderma;
- run diagnostic tests and use additional examination methods, which confirm the diagnosis;
- make a differential diagnostics with the diseases with the similar clinical presentation picture;
- make a plan of recommendations for treatment and prophylaxis of pyoderma patients.

Epidemiology, etiology, pathogenesis of pyoderma

Epidemiology. In economically developed countries the patients with pyoderma compose 1/3 of patients, suffering from infectious diseases. The morbidity rate in children is higher than in adults, it composes 25-60% of the total number of cases of dermatoses. Pyoderma is the most common among the worker of such industries as metalworking, metal mining, coal mining, timber manufacturing, transportation, and various branches of agriculture as well.

Etiology. Most frequently the agents of pyoderma are staphylococcus and streptococcus. Different types of pustular skin diseases can occur initially as separate nosologic entities or as a complication of other dermatoses (scabies, eczema, atopic dermatitis etc.).

Staphylococci under the microscope have got rather correct round shape (their accumulations are often similar to a bunch of grapes) with a diameter of about 0.8-0.9 microns. The most virulent is Staphylococcus aureus. Staphylococci are also presented in form of spherical formations, joining in long chains. The diameter of one coccus varies from 0.5 to1 micron. Pycocci occur on the skin in the form of avirulent microorganisms in 90-92% of healthy people, and it is possible to detect their pathogenic forms only in 8-10% of population. Saprophytes can acquire pathogenicity under certain conditions and their virulence can increase under the action of alkaline reaction of the skin or in case of joining of other agents, such as fungi.

In case of Gram-stained pus smear, both staphylococci and streptococci are well stained in blue that means they are Gram-positive. The toxins, released by pyococcy, are highly toxic and are capable to lyse erythrocytes, leukocytes.

Pathonesis. Virulence of pyococci plays an important role in the occurrence of pyoderma. A number of factors, such as the acid reaction of the horny layer of epidermis, sebaceous glands, enzymatic activity of the skin etc., counteract the increased virulence of staphylococci and streptococci. A number of exogenous and endogenous factors contribute to the development of pustular lesions of skin. The most frequent exogenous factors include the excessive skin contamination with gasoline, oil, dust particles (coal, cement and other), micro injuries (insect bites, excoriations, needlesticks and other), maceration of horny layer (long dish-washing, doing laundry), hypothermia and hyperthermia.

The endogenous factors, contributing to the development of pyoderma, are low-calorie food, hypovitaminosis, chronic debilitating diseases, intoxications (alcoholism, narcomania), physical and nervous strains, diabetes, immunodeficiency etc.

There is no innate immunity against the pyococcus infections, but unstable infectious immunity can appear in the course of pyoderma, the intensity of which varies in wide range. The frequent for pustular diseases are the allergic reactions appearing in the result of sensitization to metabolic products of their agents, whereof the positive intracutaneous tests with the corresponding allergens (vaccines) indirectly testify.

The character of pyoderma development in clinical respect depends on the place of influence of agent. Staphylococci more often affect hair follicles, whereas streptococci mainly parasitize on the smooth skin. Favorite localization of panaritium, for example, is periungual walls, of ectymas is shins, furuncles and carbuncles are more common on the buttocks, lower back etc.

Besides pyococci, the pustular skin lesions can be caused also by collibacillus, proteus vulgaris, fungi, pseudomonas aeruginosa, pneumococci etc.

Depending on the agent, pyodermae are divided into staphylococcus, streptococcus and mixed; depending on the deepness of lesion they can be superficial and deep, on the character of the course they are acute and chronic, on the origin they are primary and secondary.

Staphylococcal skin infections

Staphylodermae are characterized by the development of inflammatory process, mainly in the area of appendages location, such as cutaneous and hair follicles, sebaceous and sweat glands. As a rule, a hair or opening of sebaceous gland is in the center of pustules. Much less frequently, staphylococci cause the lesions of the surface layers the smooth skin that is mainly observed in children. Newborns and infants have got the connection of epidermis with derma insufficiently developed due to the weakness of the basal membrane and dermal papillae smoothness that is why during the staphylococci penetration, the morphological elements such as bubbles and phlyctenas develop.

The following forms of staphylodermae are distinguished; these are surface – ostiofolliculitis and deep – folliculitis, furuncle, carbuncle, hydradenitis, sycosis, vesicle-pustulosis in children, neonatal impetigo, multiple abscesses of children (pseudofurunculosis), exfoliative dermatitis, and neonatal bullous impetigo.

Ostiofolliculitis is characterized by the appearance of small pustule with the size of grain of millet or pinhead, of greenish-yellow or milky-white colour, of spherical shape, surrounded by acute inflammatory hyperemic circle. A pustule is localized in hair follicle and pierced with unaltered hair in the center. The accumulation of pustules is observed in a small area of skin; they do not increase due to peripheral enlargement and do not merge. The process is most often localized on the skin of face, neck, forearms, lower legs, hips. The patients feel little itching. The pustules shrivel forming greyish-yellow crusts in 4-8 days. After crusts falling, insignificant pigmentation remains on the skin, which soon disappears. Ostiofolliculitis appear under the influence of minor skin irritations such as shaving, friction, maceration due to excessive sweating.

In some cases, certain ostiofolliculitis can grow at periphery or deathward, becoming deep folliculitis, furuncles and carbuncles. Growing at periphery ostiofolliculitis eventually reaches the size of a pea, especially in children and scabies patients with wrists lesion. These ostiofolliculitis are called ***Bockhart's impetigo.***

The diagnosis of ostiofolliculitis is set in presence of small tight conical pustules, in their center pierced with a hair and surrounded by hyperemic circle.

Hystologically, a small cavity, bounded above by the horny layer, and bounded below by the callous cells of epidermis, is located in the ostium of the hair follicle. The cavity is filled by the conglomerate mass of polymorphonuclear leukocytes, some lymphocytes, and staphylococci as well. An edema appears around the hair follicle in the derma and capillaries broaden, around which perivascular infiltrate from lymphoid and polymorphonuclear cells is observed.

For the treatment of ostiofolliculitis, the pustule is pierced with a sterile needle, the tectum and pus is removed, the affected areas are anointed by the 1–2% alcohol solutions of aniline dyes (methylene blue, brilliant green, Castellani liquid). After that the skin is wiped with 2% salicylic or boric spirits and sprinkled with 5-10% of boric powder. With large crusts the affected surface is salved with antibiotic ointments (Fusiderm, Bactroban, Altargo, neomycin, tetracycline, and erythromycin). The topical application of Zineryt lotion (erythromycin zinc complex), OXI, Ugrinum lotions, and Diacneal cream is also effective.

Profound folliculitis *(folliculitis profunda)* is a purulent inflammation of the entire hair follicle and the adjacent adipose tissue, arising in the result of pathogenic staphylococci penetration in the depth of follicle. Initially a painful red papule (nud) of size from a pea to a cherry appears on the skin around the ostium of hair follicle. A hair is located in the center of a papule. In a few days, the papules tauten, becoming a follicular pustule of conic form with base induration. A pustule dries out after some time forming the crust, in some cases connective tissue necrosis and intense suppuration can occur. A pustule in the center ulcerates gathering to matter of greenish-yellow or white colour. Profound folliculitis remains pigmented scar. The reasons for the appearance of profound folliculitis are the same as for ostiofolliculitis.

Hystologically, in profound folliculitis there is infiltrate consisting of neutrophils and lymphocytes around the hair follicle. A hair follicle melts itself, and a cavity filled with matter, forms in its place.

The treatment of folliculitis is the same as of ostiofolliculitis.



Fig. 4.1. Ostiofolliculitis.

Furuncle *(furunculus)* is acute purulonecrotic inflammation of hair follicle and its surrounding connective tissue, caused by pathogenic staphylococci. A furuncle develops in the presence of low immunological reactivity of organism. The contributing factors in furuncle appearing are the cutaneous

injuries, scratching of allegrodermatosis, catarrhal and infectious diseases, vitamin deficiencies, hypothermia and other. A typical localization of furuncle is the areas of friction between skin and clothes, such as neck, lower back and buttocks.

The symptoms of furuncle develop gradually. In the majority cases, the process develops in the setting of ostiofolliculitis, which spreading depthward, leads to the formation of the node of acute inflammatory character. During the period of 5 to 7 days the furuncle becomes soft in the center, the fluctuation appears. The infiltrate ulcerates discharging matter prolifically. In the center of the burst there appears necrotic tissue of green colour (necrotic core). After its separation there is a deep crater-like ulcer. The ulcer bottom is covered with granulations, gradually discharging from the matter, thus the ulcer cicatrizes.

The development of the furuncle is accompanied by the pains and burning sensation, and sometimes high temperature.

In the case of relapses of furuncle several times in different places they say about the chronic furunculosis. The development of furunculosis is promoted by the dysfunction of internal organs and nerve system, depletion of immunological reactivity, anemia, diabetes, infectious diseases, hypo and avitaminosis, the presence of chronic foci of infection, the use of corticosteroids and other. In children the furunculosis develops with gastro-intestinal disorders, hypotrophy, and rickets.

The typical clinical picture is a massive infiltration, conical shape, redness, pain, the presence of a hair and necrotic core in the center enables quite easy to set a diagnosis of furuncle.

Hystologically, a massive infiltration, consisting of polymorphonuclear leukocytes, lymphocytes, fibroblasts and a small number of plasma cells, forms in derma and subcutaneous fat. Collagen and elastic fibers break down completely with hair follicle. In the focus of lesion, a massive argentophil grid appears which forms the membrane, impeding penetration of infection from the focus into the patient organism.

In the treatment the skin around the furuncle is disinfected with alcohol or ether, after that a hair is pulled out gently from the center of infiltrate with a sterile forceps, pure ichthyol is put on the furuncle, covering it with a thin layer of cotton wool. The procedure is repeated twice a day, until in the center of the follicle the opening forms, on which the gauze folded in several times and moistened with hypertonic solution of sodium chloride is put. After discharge of the core, the ointment with antimicrobial effect and stimulating tissue regeneration is



Fig. 4.2. Furuncle.

applied, such as (Fusiderm, Bactroban, Altargo), and skin around the furuncle is wiped with 2% boric and salicylic spirits.

In the case of multiple furuncles, furuncles in the area of face, hairy part of the head, as well as chronic relapsing furunculosis, antibiotic therapy should be applied in order to prevent the occurrence of septicophlebitis of cerebral vessels and general sepsis. Currently, it is recommended to use the broad spectrum antibiotics from the group of cephalosporins, tetracyclines, macrolides etc. in adequate doses during 7 to 10 days with an obligatory determination of pyococcus sensitivity to antibiotics. In severe cases the antibiotics are administrated parenterally. Concurrently antihistamines, such as suprastin, cetrine, claritine, aerius etc. are prescribed.

Carbuncle *(carbunculus)* represents a severe inflammatory process, covering several hair follicles, sebaceous glands and subcutaneous fat. As a rule, a carbuncle develops in the result of dissemination of purulent process with numerous profound folliculitis or in conjugating of close furuncles that leads to extensive skin necrosis. Carbuncle is caused by the pathogenic stains of staphylococci.

Endogenous factors first of all play an important role in the development of carbuncles.

The general condition of the carbuncle patient is usually compromised, there is high temperature, headache etc.

Carbuncles are most often localized on the skin of hindhead, back, lumbus, i.e. in the places of friction and irritation of the skin and its frequent pollution.

At the beginning of the process there are several openings on the skin surface above infiltrate, and infiltrate is surrounded by edema. After the cores separation and intense discharging of matter, mixed with blood, necrotic mass of green colour can be seen on the infiltration site. After purification of the openings from the necrotic masses, there appear deep ulcers, sometimes reaching up to fasciae or muscles. In the result of filling the ulcers with granulations, their cicatrization occurs, and the process ends with formation of retracted stellar scars.

In advanced age, as well as with exhaustion, neuropsychic defatigation and diabetes, the course of the disease acquires malignancy, neuralgic pains and deliration appear and sepsis and erysipelatous inflammation can occur.

Hystologically, in carbuncle there is deep necrosis of all layers of derma and subcutaneous fat. Around the necrotic area there is a massive infiltrate, consisting of neutrophils and a small number of lymphocytes.



Fig. 4.3. Carbuncle.

Carbuncle treatment requires an obligatory use of antibiotics and other systemic drugs, so as in treatment of severe forms of furuncle and chronic furunculosis. A topical treatment is the same as in furuncle.

Hydratenitis is a purulent inflammation of apocrine sweat glands, located in axillary cavities, on labia majora, mammillae, anal area. It is caused predominantly by staphylococcus aureus. The contributing factor of development of hydratenitis is excessive sweating in axillary folds and perineum, consumption as a result of hypotrophy, infectious, nervous and endocrine diseases. From the external factors, the significant are excessive contamination of skin, microtraumas and cuts resulting from shaving hair in the axillary cavities.

Hydratenitis in children is observed only in senior age, when apocrine sweat glands attain full growth and begin to function (period of puberty).

Hydratenitis develops gradually. At the beginning the feeling of discomfort and insignificant soreness appear at the sites of localization of apocrine glands. The skin is not changed, and in palpation it is possible to detect small indurated formations. Later the skin at the affected sites becomes red, painful pea-sized nodes begin to extrude, which rapidly increasing reach the size of pigeon egg. Sometimes separate nodes can merge. In one to two days the nodes acquire soft consistency and are perforated with formation of openings, from which a large amount of matter is discharged. Gradually, the abscess cavity is filled with granulations, and the process ends with formation of retracted scar.

Maturation of hydratenitis is accompanied by high temperature, severe pains and general weakness. Disease can become chronic, when new nodes are developing one by one. The relapses are especially frequent in people with heavily pronounced sweating, insufficiently observing hygiene. The relapses occur mainly in summer in hot period.



Fig. 4.4. Hydratenitis.

Hystologically, the pathological process in hydratenitis develops in the deep layers of the skin around the body and excretory ducts of apocrine gland, where there is an infiltrate from neutrophilic leukocytes and purulent fusion of sweat gland. The profound destructive changes of vessels occur in the center of necrosis.

The disease is so typical by localization and clinical picture, that the diagnosis is set without much difficulty.

The treatment does not differ from the similar treatment of

numerous furuncle, furunculosis and carbuncle; it includes timely application of antibiotics, immunomodulators, local and symptomatic agents.

Sycosis *(sycosis vulgaris, sycosis simplex, sycosis staphylogenes)* is a chronic staphylococcal skin lesion of face in the area of beard and mustache. Sycosis is observed almost exclusively in men. It can rather rare affect also internal surface of nose, eyebrows and pubic area. It is characterized by chronic course, relapsing eruptions of ostiofollicular pustules on the indicated areas of the skin. Contributing factors in the development of sycosis are integrity violation of epidermis, chronic rhinitis, nervous and endocrine diseases, in the first place, hypofunction of testes.

The development of sycosis begins with the appearance on the skin in the area of beard and mustache of small pustules the size of a millet grain, placed in the follicle ostium. In a few days, the purulent process affects the entire hair follicle (profound folliculitis). Gradually the skin of the affected site infiltrates, gets bluish discoloration, is covered with mixed crusts, swells. The site of the lesion focus enlarges peripherally due to the formation of new folliculitis. When pressing on the infiltrate, droplets of yellow green pus are discharged from the extended hair follicles.

After dropout of crusts, at the sites of lesions small erosions and ulcers appear, from which seropurulent liquid is released.

The general state of health of sycosis patients is not altered, sometimes the patients can complain about light itching, burning sensation and insignificant sickliness. Prolong course of the disease and its localization on the open skin area sometimes leads to oppression of mental state of patients.

Sycosis is rather easy to diagnose on basis of typical localization of lesion areas, chronic course, and presence of infiltrate with follicular pustules. Parasitic sycosis (profound barber's rash) differs by more severe course; the pathogenic fungi are detected during laboratory testing.

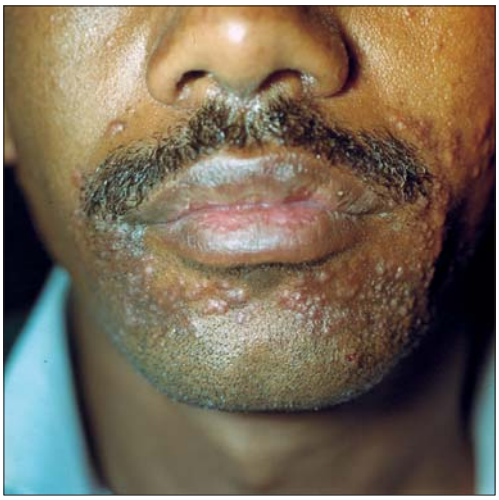


Fig. 4.5. Sycosis staphylococcal.



Fig. 4.6. Sycosis staphylococcal in pubic region.

Hystologically, in the area of hair follicle, the abscesses appear, filled with matter, the infiltrate consists of polymorphonuclear leukocytes and fibroblasts, a small number of lymphocytes and plasma cells. The edema, degeneration of hair follicle and surrounding connective tissue is observed in epidermis and derma.

In the acute period of sycosis development the broad spectrum antibiotics are administrated, including tetracyclines or macrolides (azithromycin, doxycyclinum, tetracyclinum etc.).

The topical therapy of sycosis should be started with removal of all crusts from the surface under purulent process, by softening them with plant oil, then the lotions of 1% solution of resorcinol, 0.1% solution of rivanol or furacilin are put on. The affected hairs are tweezed, and the surrounding tissues are wiped daily with 70% ethyl alcohol. Later, the antibiotic and corticosteroid ointments are applied (Fusiderm, Oxycortum, Betaderm, Bactroban, Flucinar N).

Vesiculopustulosis in children is a widespread purulent disease, which appears in the first years of life. In the ostium of the sweat glands numerous pustules appear, filled with white yellow matter, the size of a pin head to a small pea, they do not merge with each other and are surrounded by bright edematous circle. Vesiculopustulosis is localized at the sites of the greatest sweating and skin maceration. Premature infants of asthenic constitution mainly suffer from disease.

Diagnosis is set on grounds of typical clinical presentation and process localization. The disease should be differentiated from scabies, in which the papulovesicles are paired.

Epidemic neonatal pemphigus *(pemphigus neonatorum epidemicus)* is a cute infectious disease, differentiating from other pyodermae by very high contagiousness. Often the infection is transmitted to children from the adults (especially from medical personnel), suffering from pyodermae or quinsy, or through household articles. Sometimes, there are epidemic outbreaks of neonatal pemphius in maternity hospitals or day nursery.

The disease appears in 7-10 days after the birth. In the setting of erythematous patches, the blisters the size of pea are forming, filled with serous contents, they are rapidly increasing in the periphery, reaching the size of nut and becoming less stressed. The content changes from serous into purulent.

The blisters can be placed over the entire the skin cover, especially often on the abdomen near the umbilicus, on the buttocks, hips, back, chest and extremities. They rather quickly go into wet erosions, on the periphery of which the remains of blisters i.e. scraps of epidermis overhang. Drying up, the erosions do not leave crusts and regress with the formation of pink-brown pigment spots without scars.

The general condition of the patients is not altered; the disease mostly lasts 4 to 5 weeks. The process in weakened children can rapidly spread, covering new skin areas by autoinoculation (infection transmission from affected skin areas to the health). Children condition significantly worsens, the temperature rises up to 38–39°C, dyspeptic phenomena join. As concerns blood there are leucocytosis,

eosinophilia, increased ESR. In some cases the disease can be complicated by conjunctivitis, otitis and even sepsis that sometimes lead to the death of a child.

Exfoliative dermatitis *(dermatitis exfoliativa)* presents especially severe form of epidemic neonatal pemphigus. The disease begins with prodromes, such as nausea and temperature rise. Bright erythema appears in the folds of skin, around the mouth, umbilicus, anus and genitalia. In the setting of erythema there appear rather big tense blisters, which rapidly erode. In exfoliative dermatitis the positive Nikolsky's sign is observed, i.e. in case of friction of skin at the visible-healthy sites, it flakes off, forming the erosions; when pulling the scraps of blister with the tweezers, the epidermis exfoliates on the surrounding skin areas (the presence of acantholysis). The disease is accompanied by high temperature, dyspeptic phenomena. For several days, the process affects the entire skin cover, and sepsis develops, often with fatal outcome.

The diagnosis of epidemic neonatal pemphigus is set on the basis of appearance in children on erythematous acute inflammatory background of stressed blisters, which rapidly erode. The disease is necessary to differentiate mainly from syphilitic neonatal pemphigus and congenital epidermolysis bullosa. Both of these diseases are already observed at childbirth, when epidemic neonatal pemphigus develops only on the 7^{th} to 10^{th} day after the birth. In case of syphilitic pemphigus, the blisters affect the skin of palms and feet, which is not observed in case of epidemic pemphigus. In case of congenital syphilis in children it is possible to observe at one time syphilitic rhinitis, diffuse popular infiltration of Hochsinger, osteochondritis, and in the process of microscopy of blisters content in the dark field of view there are a large number of causative agents of syphilis such as pale treponems, classic serological reactions of blood, treponemal immobilization test and fluorescent antibody test are strong positive. Congenital epidermolysis bullosa is characterized by intrauterine appearance of blisters, which occur most frequently at the sites of birth injuries, such as hairy part of the head, buttocks, upper and lower extremities.

The treatment of epidemic neonatal pemphigus involves high-priority administration of antibiotic therapy in order to prevent complications and development of sepsis.

Multiple abscesses in children *(abscessus multiplex infantum),* or ***pseudofurunculosis***, is observed in neonates and infants. The disease begins with the appearance of superficial pustules in the ostium of sweat glands (periporihis). The agent is staphylococcus aureus, which penetrates in the depth of the sweat gland and causes the forming of deep indurated painful nodules. The skin over the nodules is not altered at the beginning, but soon it acquires reddish-brown color. The nodules the size of a pea to a nut soon suppurate and dense yellowish-green matter is discharged onto the surface of the skin. The nodules are very similar to furuncles, but they have not got core in the center (hence the name pseudofurunculosis) and are not connected with pilosebaceous apparatus. Multiple nodules are located on the trunk, hairy part of the head, buttocks, lower and upper extremities. After discharge of a matter, the process ends with cicatrization.

The course of the disease is rather soft, often relapses, is accompanied by high temperature, leukocytosis, increased ESR, and can be complicated with phlegmon, septicemia.

In the pathogenesis of multiple abscesses appearance a significant role is played by unhygienic maintenance of children, increased sweating, malnutrition, the presence of dyspepsia and enteritis, rickets, tuberculosis and other infectious diseases.

The diagnosis is set on grounds of appearance in children of persistent recurrent abscesses not connected with hair follicles and sebaceous glands.

Hystologically, the appearance of purulent abscesses, connected with sweat glands and their ducts, are observed in derma and subcutaneous fat.

The treatment includes the administration of antibiotic injections. Topically, unmixed ichthyol is applied at the affected sites or the abscess is pierced with a sterile needle after skin disinfection with the following anointment by alcoholic solutions of aniline dyes. After ulceration the antibiotic ointments are applied at these sites.

Bullous impetigo *(impetigo bullosa)* is referred by one authors to streptoderma, and the others to the pyoderma, caused by staphylococci (benign form of staphyloderma). Clinically, the disease is characterized by the appearance of blisters or phlyctenas the size of a pea to a pigeon's egg, filled with serous nebulous liquid or matter. The elements are not stressed; they are surrounded with hyperemic circle, and quickly erode. The erosions with wet surfaces can enlarge at periphery; they are surrounded with the scraps of epidermis. Bullous impetigo is localized on the trunk, back of the hands, less often on the feet and lower legs. The course of the disease is benign; the general state of the children is satisfactory. The treatment consists of anointment of erosions with the alcoholic solutions of aniline dyes and antibiotic ointments.

Streptococcal infections of skin – streptoderma

Streptoderma are caused by streptococci, which unlike staphylococci, do not affect pilosebaceous apparatus and sweat glands and do not infect derma and subcutaneous fat with the following development of necrosis. Streptococci mainly cover the smooth skin, and the diseases caused by them are of superficial character and in majority of cases manifest as elements in the form of blisters or phlyctenas, filled with clear or slightly nebulous contents. Most frequently, streptodermae are observed in women and children due to the fact that their skin is more delicate.

The following forms of streptodermae are distinguished, these are streptococcal impetigo, streptococcal intertrigo, syphiloid papular impetigo, superficial panaritium, perleche, lichen simplex, ecthyma vulgaris, and superficial chronic diffuse streptoderma.

Streptococcal impetigo *(impetigo streptogenes)* is caused by streptococcus and localized mainly on the face, extremities, sometimes on the trunk. In the pathogenesis of streptococcal impetigo the skin injuries are of certain importance, as well as its unhygienic conditions, metabolic disorder, reduced immunological reactivity. Impetigo is especially common in children.



Fig. 4.7. Streptococcal impetigo.

The blisters or phlyctenas with the size of a pea to a nut, not stressed and filled with serous or slightly nebulous liquid appear on the hyperemic, lightly swollen skin, and rapidly increase in size. There is a hyperemic circle on the periphery of phlyctenas. Phlyctenas quickly erode (during the period of several hours) and are covered with thin straw-yellow crust. After the falling of crust away, the pink spot remains and after some time it disappears without any trace. A patient suffers from itching, which sometimes can become intense. In some cases regional lymphadenitis can develop. Phlyctenas are located independently, but sometimes they can merge due to peripheral growth, forming arcs, rings, garlands (ring-shaped impetigo). Streptococcal impetigo has benign course and it ends in full recovery after 7-8 days.

Intertriginous streptoderma, or ***streptococcal inertrigo*** *(intertrigo streptogenes)* is mostly observed in children, especially overfed children, with excessive sweating and gastrointestinal disorders. In the pathogenesis of the disease the dermatoses, accompanied by itching, and diabetes are also important. Intertriginous streptoderma is localized in the skin folds, such as inguinal-scrotal, gluteal, in axillary cavities, behind the ears, under the breasts in women, and in the folds of the abdomen in obese people. This disease is characterized by the appearance of erosive wet surface of bright pink colour, strictly bounded from the adjacent skin and surrounded by epidermal collarette. In the depth of the folds the bleeding folds appear. Subjectively, the patients notice itching and burning sensation. It is possible to notice at the close skin sites the pustules at different stages of development. The disease has long-term course.

Syphiloid papulose impetigo *(impetigo papulata syphiloides)* develops predominantly in infants and is localized on the buttocks, posterior surface of femora and lower legs. On the hyperemic surface the phlyctenas appear, at the base of which there is papulous infiltrate. Phlyctenas erode very quickly, leaving erosive papules. Clinically the disease is analogous to papulo-erosive syphilide. For differential diagnostics it is necessary to carry out the analysis of erosion discharge for the presence of treponema pallidum, and serological study of the patient as well.

Hystologically, in all forms of streptococcal impetigo there is formation of cavity under the horny layer of epidermis. The cavity is filled with serous exudate with some amount of neutrophilic leukocytes and separate epithelial cells. Spongiosis occurs in

the spinous layer of epidermis. Vascular distention with perivascular infiltrate, consisting of neutrophils and lymphocytes, occurs in derma.

Superficial panaritium, is predominantly observed in adults. The phlyctenas appears on the hands around the nail plates, which contain at the beginning serous, and then nebulous purulent discharge. The disease is associated with injuries of the fingers, burrs, which create favorable conditions for the penetration of streptococci. The affected phalanx of a finger swells and hurts.

After breaking of phlyctena there appears erosion, covering the nail wall like horseshoe. The process can lead to the rejection of nail plate. Sometimes there are lymphangitis, general uneasiness and fever.

Angular impetigo *(angulus infectiosus)* is characterized by the appearance of linear phlyctenas at the corners of the mouth, which quickly erode, and the cracks appear on their place, which are especially painful when the mouth is opened. The disease can be localized in the corners of the eyes, in the places of adhesion of ear conches. On the skin around the crack of the angle of mouth there appear melichrous crusts, and maceration of epidermis on the edges of the cracks. The contributing factors to the perleches development are frequent lips licking, dental prostheses wearing, i.e. maceration of the corners of the mouth sites with saliva. The patients complain about itch, pain while eating.

Angular impetigo should be differentiated with yeast affection of the corners of mouth, in case of which the process is not so vivid and there are no crusts. It must be taken into account the possibility of affection of the corners of mouth with erosive syphilitic papules, which certainly are based on tight elastic infiltrate; eruptions of syphilides are observed on the other parts of the body, as well as positive serological reactions.



Fig. 4.8. Superficial panaritium.



Fig. 4.9. Angular impetigo.

The treatment of different forms of impetigo, and angular impetigo is generally external. In the case of presence of crusts the ointments with disinfectants or antibiotics are applied.

On the erosive wet surfaces the lotions with disinfectants (0,25% solution of silver nitrate, 2% solution of resorcinol etc.) are applied. The healthy skin around the lesion foci is regularly wiped with the 2% salicyl alcohol in order to prevent autoinoculation of infection. At the same time, it is necessary to treat the diseases, which cause the appearance of streptoderma, and eliminate the promoting factors.

Ecthyma vulgaris *(ecthyma vulgare)* refers to profound pyodermae, caused by streptococcus, though there are a number of publications, which indicate that ecthyma can be of staphylococcal etiology as well. Micro injuries and excoriations contribute to the penetration of the agents from the external environment. Nervous and mental stresses, diseases of liver and blood (anemia, leucosis), diabetes, thrombophlebitis, vasculitis, vitamin deficiency etc. are of certain importance in the pathogenesis of the disease is played.

The disease develops gradually, beginning from the appearance on the skin of usual phlyctena the size of pea to a nut, filled with serous contents, which later acquire mattery hemorrhagic character. Phlyctena is located in the setting of erythematous infiltrate, its contents dry up very quickly in the crust of yellowish-brown colour, which has got multi-layer characteristic. Under the skin, there is deep tissue necrosis, covering not only derma, but subcutaneous fat as well. The crust drops off in several days, and the ulcer with soft uneven congested hyperemic edges and bleeding bottom, covered with dingy pultaceous detritus. After two-three weeks the ulcer is slowly cicatrizing. The scar is surrounded by the zone of hyperpigmentation.

There are, as a rule, several ecthymae, and they are most frequently localized on the skin of the lower legs, buttocks, femoris, lumbus, less often they are on the upper extremities. Ecthymae can recur, causing lymphangites and lymphadenites, phlebitis, deep necroses.

In the severe course of the disease so-called *ecthyma terebrans* can appear. Most frequently it occurs in undernourished children, suffering from anemia or rackets. Some authors consider blue pus bacillus to be the agent of ecthyma terebrans. In this case infiltrate and ulcerative defect spread depthward. The disease begins with the appearance on the skin of the buttocks, lower extremities, hairy part of the head of blisters, rapidly evolving into pustules and deeply ulcering. Such ecthymae



Fig. 4.10. Streptococcal scrotal ecthyma.

cause severe pains. Ecthymae terebrans have got malignant course, are complicated by sepsis, and can be fatal.

Ecthyma vulgaris most frequently should be differentiated with syphilitic ecthyma, which has not got acute inflammatory nature. There are no impetiginous multiple small elements near ecthyma, and the syphilides (especially papulous) can be detected at the other sites of the body. The final diagnosis is defined by the positive serological reactions. In case of scabies, complicated by ecthyma, military-papular rash appears on the other typical areas of skin, the borrows are typical; the patient complains about strong itching, especially at night.

Hystologically, in derma and subcutaneous fat there is necrosis of tissue. The focus is surrounded with indurated infiltrate, consisting of neutrophilous leukocytes and lymphocytes. Edema and vasodilatation appear around the infiltrate.

On the initial stages of the development of ecthyma vulgaris, the phlyctenae are pierced with a needle for removing their contents, the crusts are softened with application of 2% salicyl ointment. In case of formed ecthyma or ecthyma terebrans, antibiotic therapy in accordance with the results of antibiogram, A vitamins and B group vitamins, and disinfecting ointments for topical treatment are put on. The skin around erythema is wiped with 2% salicyl alcohol.

Superficial chronic diffuse streptoderma *(streptodermia chronica diffusa superficialis)* is a chronic streptococcal disease, which is characterized by diffuse lesion of significant sites of skin covering. Most frequently it affects the lower extremities, the process can be also localized on the opistheners. The affected areas have got largely-scalloped lines, sharply bordered from the surrounding healthy skin by the rim of exfoliative epidermis. The skin of the affected areas is sharply hyperemic, of congestive bluish colour, slightly infiltrative, the surface is eroded in the form of wet disk-like sites. The erosions are covered with many thin lamellate crusty scales of yellowish or greenish colour. After removal of the crusts the surface wets with the release of dense serous or serous-yellow exudate. The process spreads over the periphery. With time, staphylococcal infection joins to streptococcal, though there is no lesion of hair follicle and sebaceous gland. The skin of the entire lower leg can be affected on the lower extremities. In the process of development, the lesion area is epithelialized and covered with large lamellate scales. Superficial chronic diffuse streptoderma is often complicated with eczematization, especially on separate skin areas, where against the background of bright red erythema there appear military papules, microvesicles, small erosions with release of the drops of serous fluid.

In the pathogenesis of the disease development a significant role belongs to congested phenomena in the lower extremities, varicose symptom complex, i.e. prolonged disturbed circulation, development of tissue hypoxia and derangement of metabolic processes in skin.

The disease has got a chronic course, with often relapses, especially around non-healing wounds and trophic ulcers.

Superficial chronic diffuse streptoderma should be differentiated with eczema, when the erythema is bright red, the foci are without distinct borders, oozing lesion is punctate, there are no crusty scales, and the process has got symmetric character.

Hystologically, in the erosion places there are no horny and granular layers. At the sites of epidermis continuity there are parakeratosis, spongiosis, intensively pronounced acanthosis. Vascular distention with perivascular infiltrate, predominantly lymphocytic occurs in derma.



Fig. 4.11. Superficial diffuse streptoderma.

In case of acute course of superficial chronic diffuse streptoderma antibiotic therapy in accordance with the results of antibiogram is put on. For topical treatment the lotions of disinfecting and astringent solutions(5% tannic or 2% boric acid, 1% solution of resorcinol, 0,25% solution of silver nitrate) are applied. At the same time, it is necessary to carry out curative interventions, aiming at the elimination of factors contributing to disease development.

Strepto-staphylococcal skin infections – mixed pyoderma

Mixed pyoderma combine a number of chronic skin diseases of pyogenic nature, mainly polymicrobial one. Their main etiological cause is combined streptococcal and staphylococcal flora. Possible is the participation in the genesis of these diseases other microorganisms as well, such as collibacillus or blue pus bacillus, Proteus vulgaris etc..

In the pathogenesis of mixed pyoderma the essential role belongs first of all to sharp decrease of immunological reactivity of organism and the appearance of sensitization to byproducts of pyoderma agents, especially in children with allergic dermatitis, malnutrition, vitamin deficiency, metabolic disorders, endocrine dysfunctions etc..

Mixed pyoderma include impetigo vulgaris, chronic ulcerative vegetating pyoderma, chancriform pyoderma and botryomycoma.

Impetigo vulgaris *(impetigo vulgaris)* is preceded by the prodromes, such as high temperature and itching at the sites of the following rash appearance.

The disease appears at the beginning as streptococcal impetigo with the appearance at erythematous and slightly infiltrated background of phlyctenas, the contents of which due to overlay of staphylococcal infection get muddy quickly,

become mattery and acquire yellowish-grey or greenish colouring. The matter dries up into the form of melichrous crust. After the crust drops out, the erosion appears, surrounded with delaminated horny masses of epidermis. Subjectively, the process is accompanied by light itching.

Impetigo vulgaris is mainly localized on the skin of face at the sites of natural orifices, such as nostrils, mouth, palpebral fissures, in women it can sometimes be localized on the hairy part of the head as well. The process seldom causes inflammation of regional lymph nodes.

The evolution of disease lasts 10 to 14 days, after that a temporary hyper pigmentation remains on the skin at the lesion sites. The possible are the lesions of mucous membranes of nostrils.

The treatment is predominantly topical and includes the application of 1-2% boric-tar ointment or naphthalani unguentum. The healthy skin areas are regularly wiped around the foci with 1% salicylic alcohol. Ointments with antibiotics are applied (mupirocin).

Chronic ulcerative pyoderma *(pyodermia chronica ulcerosa)* gradually transforms into ulcerative vegetating form. It is caused by the mixed strepto-staphylococcal infection. For the development of chronic ulcerative pyoderma the essential is, on the one hand, the reducing of pathogenicity of the disease agents and immunological response of the organism, and on the other hand, the weakening of the resistance of the microorganism, that leads to prolonged soft course of the disease. Its manifestations are localized exceptionally on the lower legs, and very seldom on the lower part of femora. In the setting of slightly edematous areas of hyperemia the phlyctenas appear, rapidly covered with thick crusts, beneath which the ulcers with callous undermined edges occur. After the dropping of the crusts off, the bottom of the ulcers becomes naked, it is covered with necrotic masses and soft grey granulations with significant amount of purulent and serous-purulent discharge. The process spreads over periphery, covering large sites of the skin. Around the ulcers there are pustular multiple small erosions. There is painfulness at palpation.



Fig. 4.12. Chronic ulcerative vegetating pyoderma of lower leg.

Chronic ulcerative vegetating pyoderma *(pyodermia chronica ulcero-vegetans)* is characterized by the appearance over the ulcer periphery of vegetations, which are verrucous growths, which can appear over the entire surface of the lesion. The bottom of the ulcers is bleeding. Vegetations can

enlarge along the periphery as well; in this case the process acquires serpiginous character. When pressing at the sites of lesion, the drops of dense matter are released from small fistular openings. The disease lasts for months or years and ends with formation of uneven hyperpigmented scars with small islets of unaltered skin.

It is necessary to distinguish chronic ulcerative vegetating pyoderma from serpiginous nodular syphilide and verrucous form of skin tuberculosis that requires additional examination of the patient.

When there are ulcerative purulent processes, the antibiotic therapy is appointed. In case of intense mattery discharges, the lotions with 2% solution of rivanol, solution of microcide (at a dilution 1:1) are appointed, and in the period of remission 2% gentian violet ointment.

Pyoderma, of the type of ecthyma vulgaris, sometimes is located independently on the genital organs, resembling syphilitic chancre, hence the name of the disease of chancriform pyoderma *(pyodermia shancriformis)*. It is very seldom, that chancriform pyoderma is localized on the face, lips and eyelids. The disease is caused by staphylococcus aureus. The disease is typical for untidy persons, who do not look after hygiene of the body, as well as the subjects with the presence of narrow preputial ring, when smegma accumulation causes maceration of the skin of the penis with further suppuration.

Clinically, chancriform pyoderma manifests as the appearance of clearly limited superficial ulcer of round to oval form with overlapped edges, located on the inflammatory infiltrate the size up to 2 cm. The bottom of the ulcer is fleshy red, sometimes covered with necrotic masses or purulent releases. It is painful at palpation. As a rule, with chancriform pyoderma there is regional lymphadenitis the size from kernel of a cherry to a nut, painful on palpation. The disease lasts from one to three months and ends with the cicatrization.

In all cases chancriform pyoderma should be differentiated with syphilitic solid chancre. In solid chancre the subjective sensations (pain, burning, itching) are absent, the infiltrate is of dense-elastic, but not soft consistency, does not overlap ulcer, the acute inflammatory phenomena are absent. As a rule, there are no purulent discharges. Regional lymphadenitis is also painless on palpation, of dense-elastic consistency. In some cases the clinical picture of chancriform pyoderma reminds syphilitic solid chancre so much, that the diagnosis is possible to be set only on grounds of the results of multiple tests for Treponema pallidum and data of serological reactions.



Fig. 4.13. Chancriform pyoderma.

For the treatment of chancriform pyoderma the bathes with a weak

solution of potassium permanganate, lotions with a physiological solution of sodium chloride or 2% solution of boric acid are applied to the full cicatrization. At the stage of differentiation with syphilitic solid chancre no antibiotics should be applied both topical, and for general therapy.

The group of chronic mixed pyoderma includes also pyogenic granuloma or ***botryomycoma*** *(botriomycoma)*, which is benign fungiform tumor-like growth, caused by Staphylococcus aureus. Botrycoms is most frequently localized on the skin of vermilion border, nose, ears, on the fingers and toes. Its appearance is preceded by the injuries, cuts, pricks, by means of which pyococci penetrate into the skin. Clinically, botryomycoma manifests as small-lobular tumor on the peduncle the size of a pea to a hazelnut, of round form and soft consistency. Botryomycoma has got intense red colouring and a large number of vessels, which are easily injured and bleed. Botryomycoma with time can be partially necrotized or form an ulcer with discharge of insignificant amount of seropurulent liquid.

Botryomycoma can exist without treatment for a long time, not disappearing by itself. The treatment consists in surgical (or with electrocoagulation) removal of the tumor. Sometimes botryomycoma can recur, so it is recommended to remove not only tumor itself, but its base as well, at the same time applying antibiotic therapy up to the absolute regress of the disease.

Pyoallergids are secondary allergic diseases, which are caused by the sensitization of patient organism to pyococci and their byproducts in the presence of purulent skin diseases with chronic course. Pyoallergids are most frequently observed in case of streptococcal infections (superficial chronic diffuse streptoderma, intertriginous streptoderma and other).

Pyoallergids appear mainly at the sites remote from the focus of pyoderma and are symmetrically located. Clinically, they most frequently remind eczematous reaction, as the small miliary papules and microvesicles appear on the bright red background which has not got clear boundaries, and is covered with fine scales. In the result of itch the scratches (excoriations), covered with small hemorrhagic crusts, appear on the surface of pyoallergids. And dense blisters can appear in palpation on the palms and plantae.

The treatment of pyoallergids is analogous to that conducted in case of allergic skin diseases.

Prophylaxis of pyodermae. Preventive measures are essential in treatment of purulent diseases. Physically healthy and weather-beaten people even in adverse conditions seldom suffer from pyodermae, which attack in general people, who are colds-prone, suffering from gastrointestinal disorders, increased sweating, alcohol abuse.

Patients with furunculosis, hidradenitis, ecthyma, multiple abscesses, strepto-staphylodermae should exclude from their diet food rich in carbohydrates (honey, chocolate, sweets, white bread etc.)

Personal hygiene of the skin is important for the prophylaxis of pyoderma. The preventive measures, aimed at the preventing of pyodermae spread, include the timely detection and medicamental sanation of people suffering from chronic nasal staphylococcal carriage. This type of nasal infection is directly connected with the risk of appearance of pyodermae and pyoseptic complications in dermatological and surgical practice. Both patients and medical staff can be the carriers of Staphylococcus aureus, as well as the personnel of child care centers and other categories of persons. To eliminate staphylococcal carriage (eradication of staphylococci), the nasal ointments with antibiotics are applied, the ointment of mupirocin, in particular, by smearing of each nasal opening twice a day during 5 to 7 days.

Children with pustular skin diseases in children's groups must be immediately isolated and treated up to moment of disappearance of all clinical manifestations of disease. The staff of nurseries and kindergartens, suffering from anginas, herpetic eruptions, acute respiratory diseases of the upper airway, as well as pyodermae, must not be allowed to work.

1. There are the following types of staphylococcal pyodermae, except:

A. Ostiofolliculitis
B. Carbuncle
C. Neonatal pemphigus
D. Hydratenitis
E. Hard chancre

2. Staphylococci most frequently affect:

A. Hair follicle
B. Smooth skin
C. Nails
D. Vermillion border skin
E. Skin of the palms and plantae

3. The diagnosis of ostiofolliculitis is set in case of:

A. Presence of small superficial stressed cone-shaped pustules, pierced with a hair in the centre
B. Presence of purulent necrotic inflammation of hair follicle and surrounding connective tissue
C. Presence of small pustules, not connected with a hair
D. Presence of nodule with central necrotic core
E. Presence of phlyctenae

4. Vesicle-pustulosis of children is an inflammatory disease, which appears:

A. In the pinafore stage of existence
B. Not until 12th year of life
C. is congenital
D. at the age from 2 to 6
E. at the age of 7

5. Multiple abscesses (pseudofurunculosis) are observed in:

A. Infants and children at early age
B. Children at the age of 6 to 10
C. persons of ripe years
D. Teenagers
E. Persons of advanced years

6. Ecthyma vulgaris is:

A. Profound streptococcal infection
B. Infectious process involving pilosebaceous apparatus
C. Inflammatory process of sweat glands
D. Inflammatory superficial staphylococcal process
E. Superficial streptococcal infection

7. In epidemic neonatal pemphigus the blisters are located:

A. Exclusively on the hands
B. Exclusively on the legs
C. Over the surface of the body
D. Exclusively on the hairy part of the head
E. Exclusively on the skin of buttocks

8. Children with pustular skin diseases in maternity hospitals and children's groups:

A. can be treated without isolation
B. should be isolated immediately and treated up to the moment of disappearance of all rash elements
C. should be isolated immediately and wait for self-healing
D. should be isolated for the first two weeks
E. should be isolated for the first six days

9. In ecthyma vulgaris:

A. Deep tissue necrosis covers not only derma, but subcutaneous fat as well
B. Deep tissue necrosis covers only derma
C. Necrosis is absent
D. Purulent infiltration is located only in epidermis
E. Process evolves without trace

10. Pathological process in profound folliculate regresses with the formation:

A. Cicatrix
B. Hemorrhagic spots
C. Eschar
D. Passes without trace
E. Lichenification

Answers to the quiz of the first level of complexity
1 – **E**; 2 – **A**; 3 – **A**; 4 – **A**; 5 – **A**; 6 – **A**; 7 – **C**; 8 –**B**; 9 – **A**; 10 – **A**

Answers to the quiz of the second and third levels of complexity
1a – **A**; 2a – **C**; 3a – **A** ; 4a – **B**; 5a – **A**

Task 1. A father led a boy at the age of 5 to visit a doctor with complaints of rash on the face, which appeared six days ago. *Physical examination*: there are several blisters on the face skin the diameter of 0,5-1,5 cm with thin flabby tectum, filled with muddy serous exudate, they are placed on hyperemic, infiltrated base. At the same time, erosions with release of serous-purulent liquid and thick crusts of melichrous colour are observed in the lesion foci.

a) Set clinical diagnosis:
- **A**. Impetigo vulgaris
- **B**. Infantile eczema
- **C**. Simple vesicular herpes
- **D**. Contact dermatitis
- **E**. Candidasis

b) Make the scheme of examination and treatment.

Task 2. An infant of 1 month is under hospital treatment with the diagnosis of enteritis. A pediatrician called dermatologist for consultation concerning rash on the back and buttocks, the temperature is 38 °C. *Physical examination*: there are multiple solid knits on the skin of the napex, back and buttock, ranging in size from a pea to a hazelnut of rich red color, from some knits dense matter of yellowish-green colour is discharged.

a) Set a preliminary diagnosis:
- **A**. Hidratenitis
- **B**. Furunculosis
- **C**. Multiple abscesses (pseudofurunculosis)
- **D**. Pemphigus vegetans
- **E**. Cutaneous tuberculosis

b) Perform differential diagnostics and make treatment schedule.

Task 3. A mother led to outpatient attendance a child of two years with complaints of eruption on the skin of the face. *Physical examination*: on the face skin in the area of mouth there are phlyctenae with the diameter ranging from 1 to 3 cm with muddy contents, over the periphery of which the narrow bright red strip of inflamed skin, erosions, and crusts of yellow color is observed.

a) Set a preliminary diagnosis:
- **A**. Streptococcal impetigo
- **B**. Acne vulgaris
- **C**. Eczema of face
- **D**. Dermatitis
- **E**. Herpes zoster

b) Make the scheme of examination and etiopathogenetic treatment schedule.

Task 4. An infant of 7 days is in nursery with eruption on the skin of trunk, upper and lower extremities. The temperature is 37,5 °C. *Physical examination*: on the skin of the trunk, upper and lower extremities (except palms and plantae), buttocks there are blisters with the diameter of 1,0–1,5 cm with muddy contents and flabby tectum. The skin in the areas of blisters location is not infiltrated, slightly hyperemic.

a) Set a preliminary diagnosis:
- **A**. Varicella
- **B**. Epidemic pemphigus
- **C**. Herpetic infection
- **D**. Pemphigus syphiliticus
- **E**. Infantile eczema

b) Offer the tactic of examination and treatment scheme.

Task 5. A patient at the age of 26 complains of the presence of eruption on the skin of face, itch, burning sensation, pain in the indicated area. He is suffering for year and a half. *Physical examination*: on the skin of face in the area of chin there are infiltrated foci of bright red color, covered with pusteles and crusts with multiple erosions. Submandibular lymph nodes are slightly enlarged, freely movable, and not glomerate with surrounding tissue.

a) Set a preliminary diagnosis:
- **A**. Coccogenic sycosis
- **B**. Parasitic sycosis
- **C**. Eczema
- **D**. Contact dermatitis
- **E**. Acne vulgaris

b) Perform differential diagnostics.

5 TOPIC Psoriasis

Psoriasis *(psoriasis vulgaris)* is a genetically determined chronic autoimmune polysystemic disease of multifactor nature, characterized by the benign epidermal hyperproliferation, papulosquamous eruptions, staging, often severe clinical course and involvement of musculoskeletal system and internal organs in pathological process with corresponding morphological and functional changes.

TRAINING AND EDUCATIONAL PURPOSES

- To highlight the current medical judgments of psoriasis etiopathogenesis
- To identify the factors contributing to the development of the disease
- To determine classification characteristics of this dermatosis
- To determine its typical clinical manifestations
- To understand differential diagnostics of psoriasis
- To understand general principles of medical and preventive measures at this disease
- Define the principles of medical examination of psoriasis patients

TO KNOW:

- modern views on etiology and pathogenesis of psoriasis;
- risk factors of disease development and progression;
- clinical manifestation, evolution of rash, the stages of clinical course;
- diagnostic phenomena of psoriasis;
- clinical types and principles of classification of psoriasis;
- systemic signs of disease;
- features of differential diagnostics of psoriasis;
- histopathological signs of psoriasis;
- treatment algorithm and indications concerning medical-labour expert commission.

TO BE ABLE TO:

- correctly make examination and collect anamnesis of psoriasis patient;
- set clinical diagnosis and define disease severity index;
- run diagnostic tests and use additional examination methods, which confirm the diagnosis;
- make a differential diagnostics of psoriasis with the diseases with the similar clinical presentation picture;
- make a plan of recommendations for treatment and prevention of relapses for psoriasis patients.

Historical data. In ancient Greece the terms *«alphos», «lepra» or «psora»* were used to indicate psoriasis. Cornelius Celsus (30–40 A.D.) was the first who described the clinic of psoriasis in the book *«De medicina».* The term *«psoriasis»* was firstly applied by the Roman doctor Claudius Galen to designate eyelids and eye corners lesions with scaling and the scrotal skin lesions with itching and excoriations. Only at the beginning of the XIX century Robert Willan distinguished two diseases, namely: *«lepra graecorum»,* or discoid psoriasis (lesion in form of round spots), and *«lepra psora»* – figured psoriasis. In 1841 Ferdinand Hebra combined these two forms into one – *«psoriasis»,* having indicated, that the presence of various forms of the rash in the course of psoriasis gave no grounds for distinguishing them as separate diseases.

Epidemiology. Around 2-3% of the world population suffers from psoriasis. The disease is spread across all geographical latitudes among people of different nationalities and races. Although it often appears between the ages of 10 and 25 years, there are the cases of psoriasis occurrence both at the age of 4 to 7 months and at the age of 80 years. Psoriasis affects both sexes equally, but among children it occurs more frequently in girls, and among adults – in men. Disease is less common among Eskimos, Japanese, Africans, and South American Indians. In the general structure of the skin pathology psoriasis specific gravity achieves 8 to 15%, i.e. nowadays it remains an urgent problem of dermatology and common disease of population.

Etiopathogenesis. For 200-year study history of psoriasis the aspects of pathogenesis (from the dermatosis with violation of keratinocytes proliferation to T-cell autoimmune disease), clinic (from skin disease to polysystemic disease) and treatment (from ectylotics to highly selective drugs) have been repeatedly revised. A psoriatic disease as autoimmune genetically determined disease has been thoroughly investigated only during the last decades.

Hereditary conception of psoriasis pathogenesis, based on the registration of disease cases among the members of the same family, is generally accepted. According to the different data, familial psoriasis occurs in 5-40% of cases and more. Close relatives of the probands on the father's side suffers more frequently than the ones on the mother's side. The literature describes the cases of psoriasis in twins, with that, the highest concordance is observed among monozygotic individuals. The recent researches established the multifactorial character of inheritance of psoriasis, at which the high risk of disease is observed in the carriers of histocompatibility antigens HLA A1, A9, A11, A28; HLA B13, B 17, B27, B38, B39; HLA CW2, CW3, CW4, CW6. Due to the fact, that the hereditary transmission of psoriasis of the majority of psoriasis patients cannot be established, there exists the suggestion, that the disease is not inherited but disposition to it, which in a number of cases is realized as a result of complex interaction of genetic factors and adverse environmental effects.

However, although a family history is common, there is often no clear-cut inheritance pattern. What does seem clear is that the ***cascade of changes probably***

result from an interaction between T-cells and keratinocites, with the involvement of various cytokines and chemoattractants – notably interleukins 1 and 8, tumor necrosis factor-alpha, E selectin and intercellular adhesion molecule-1. It is now considered to be due to T-lymphocytes mediated disease of abnormal keratinocyte proliferation in genetic predisposed subject.

According to the modern ideas, ***immune system disorder*** and the development of weak immune response of the psoriasis patients is caused by the antigenic mimicry, genetic factors controlling the process of normal differentiation of immunocompetent cells, or disorder of neurohumoral mechanisms. The characteristic feature of immunogram of these patients is the reduction of T-lymphocytes, change of T-helpers to T-suppressors ratio due to significant increase of T-suppressors, the increased level of immunoglobulin IgG, IgA, components of complement C_3, C_4 that indicates the activation of the autoantibody formation processes, circulating immune complexes and, accordingly, the suppression of defense mechanisms. On this basis, it was concluded, that the pathogenesis of psoriasis is largely autoimmune. The leading pathogenetic link of immune disorders in case of psoriasis is deviation of cytokine profile by Th1-type with increased level of interleukins (IL-8) and tumor necrosis factor as the key mechanism of disease development.

Clinical picture and course. Psoriasis vulgaris is characterized by monomorphic eruption, based in most cases symmetrically on the extensor surfaces of the extremities and the hairy part of the head. The nails and musculoskeletal system is often affected. Psoriasis can be accompanied by itching of different intensity (usually in progressing stage) and feeling of tissue contraction.

The primary element of rash is epidermic-dermic inflammatory papule. Psoriatic papule is round with distinct boundaries, of pink-red colour of different intensity: the recent elements are bright red and the existing longer ones are more faded. The surface of rash elements is covered with silvery white (silver color is connected with



Fig. 5.1. Guttate psoriasis.



Fig. 5.2. Large-plaque psoriasis (pseudoatrophy Voronov's rim can be seen around papules).

the presence of air bubbles) furfuraceous and fine scales, which are easily removed during scraping. On the recent papules the scales are located in the center, and narrow bright circle remains on their periphery. Subsequently, the scaling increases, covering the entire surface of rash element. At the beginning the papules have correct rounded shapes and diameter of 1-2 mm. With the progression they are enlarged, form plaques, often achieving significant size and acquiring all possible shapes. Therefore, depending on the sizes of rash elements, the following clinical forms of psoriasis are distinguished:

- *Punctate psoriasis* (papules ranging in size from millet grain to match head);
- *Guttate psoriasis* (elements ranging in size from 3-4 mm to 7-10 mm);
- *Psoriasis nummularis* (papules from 10 mm to 30 mm);
- *Plaque psoriasis* (papules in size up to 6-7 cm);
- *Large-plaque psoriasis* (isolated plaques with size up to 15 cm and more);
- *Diffuse-plaque psoriasis* (dense confluent lesions, covering separate areas of body, such as back or abdomen, extremities);
- *Erythrodermic psoriasis* or *psoriatic erythroderma* (the patient's skin is the entire affected surface).

According to the infiltration rate of the plaques there are *moderate, marked and severe* (with presence of fissures) pathological skin process.

Depending on the extension of this process there can be *localized*, when the isolated plaques can be visualized on the skin of scalp or extensor surfaces of elbows, knees and other body parts, and *disseminated* or *extensive psoriasis* with numerous elements in different parts of the body.

Psoriatic erythroderma (*erythrodermia psoriatica*, *seu psoriasis universalis*) develops in the result of the effects of adverse exogenous factors, including stress situations and irritating treatment. Psoriatic erythroderma affects 1,5-3% of people with psoriasis, these people are often noted with reduction of immunological indices



Fig. 5.3. Diffuse-plaque psoriasis.



Fig. 5.4. Psoriatic erythroderma.

and high allergic reactivity. And often, the cause of erythroderma cannot be determined. The entire skin surface acquires bright red color with brown shadow. Edema and infiltration are not equally expressed on different parts. There is sharp skin flaking (furfuraceous desquamation in the hairy part of the head, and lamellate one in other parts), increasing of lymph nodes, possible temperature rise, nails destruction, occurrence of purulent paronychia. Such process without advance psoriatic anamnesis can be difficult to differentiate from other primary and secondary erythroderma.

For the diagnostics of psoriasis a range of symptoms, which include psoriatic triad and isomorphic reaction *(Koebner's phenomenon*), is significant. A psoriatic triad includes three consecutive phenomena, in case of scraping of psoriatic papule, these are *phenomenon of stearic spot*, characterized by intense desquamation, when with light scraping in the result of dyshesion of keratinized plates, the affected skin area looks like porphyrized stearic drop; *phenomenon of terminal film* appears in the result of the further scraping of papule surface and squamosa erosion, when the wet surface of the spinous layer of epidermis is exposed; *phenomenon of pinpoint bleeding* (Auspitz' phenomenon), determined by the traumatization of capillary vessels of alpine papillae after light scraping of terminal film. Isomorphic reaction (*Koebner's phenomenon* or *psoriasis traumatica*) involves appearing of psoriatic rash in the areas of physical or chemical lesions of skin cover. It takes on the average 7-9 days after skin injury to the isomorphic reaction development.

There are three stages in the course of dermatosis, these are *progressiv*e, *stationary* and *regressive* ones. The *progressive stage* is characterized by the appearance of new papules, peripheral enlargement of old elements, the presence of inflammatory peripheral rim of papules increase, psoriatic triad, Koebner's phenomenon, the formation of new plaques due to fusion of papules or enlargement of old elements, sometimes accompanying by itching. For *the stationary stage* the



Fig. 5.5. Neglected large-plaque psoriasis.



Fig. 5.6. Exudative psoriasis.

itching is uncharacteristic or weekly expressed, the new elements do not appear, peripheral rim of growth is absent, the surface of papules is entirely covered with silvery white scales, which are easily peeled, Koebner's phenomenon does not occur, pseudo atrophy Voronov's rim appears around the papules (slightly wrinkled white shiny ring up to 5 mm). In *the regressing stage* the elements of psoriasis are resolving and fading, the desquamation reduces and stops. Whitening of rash elements in the central part gradually leads to the appearance of the secondary eruption rests of various configurations in the form of hypo-, more rarely hyper pigment spots. With the disappearance of psoriatic eruptions, the remission is defined. The spontaneous remissions are marked approximately in 20% of cases, usually in the worm season.

Psoriasis is characterized by the process recurrence, appearing under the influence of various factors (climate, neuropsychic traumas, endocrine disorders, exacerbation of chronic infection). On grounds of climate and meteorological factors the *winter* (exacerbation in cold season)*, summer* and *off-season,* or mixed, types of dermatosis are distinguished. The winter type of psoriasis occurs much more often than the other types.

The nature of popular elements determines typical course of psoriatic process on the skin. Accordingly, they distinguish between *psoriasis vulgaris (common)* and *atypical psoriasis*. Psoriasis vulgaris is characterized by typical popular rash, on the grounds of location they distinguish between linear psoriasis *(psoriasis linearis),* gyrate psoriasis *(psoriasis gyrata)*, figured or geographical psoriasis *(psoriasis geografica seu figurata),* and annular psoriasis *(psoriasis annularis)*. With atypical course of skin pathological process, the signs of other skin diseases are defined in the setting of characteristic clinical picture of psoriasis. Of atypical clinical forms of psoriasis, the most frequent are *follicular, verrucous (papillomatous*), ostraceous *(rupioides), intertriginous*, *exudative*, *eczematous, pustular, plaque, seborrheic, reverse, irritating* etc.

With follicular psoriasis *(psoriasis follicularis)* the presence of small conical papules, located in the sebaceous follicular areas, is noted. Papillomatous, or verrucous, psoriasis *(psoriasis papillomatosa seu verrucosa)* is characterized by significant infiltration and verrucous enlargement of rash elements. Rupioides psoriasis (*psoriasis rupioides*), in its turn, is presented by lamellate crusty scales on the eruption surface, giving them a conical shape, "snail shell" like. Rupioides and verrucous psoriasis are very often caused by the neglected pathological process *(psoriasis inveterata)*, in which in the



Fig. 5.7. Pustular psoriasis.

basis of pathological foci, there is significant infiltrate with massive scales, which are difficult to remove, and, as a rule, not fully. Asbestoslike psoriasis is a kind of neglected psoriasis. Intertriginous psoriasis *(psoriasis inversa, plicarum)* develops in nursing infants, suffering from severe diabetes, rheumatism, and in people, suffering from obesity, in advanced age and with high sensibilization. It is characterized by atypical localization on the flexor surfaces of the extremities, joints, on the skin of inguinofemoral and other folds, axillary hollows, on the palms and plantae. Its manifestations usually are nummular exudative plaques of purple red colour with sharp boundaries, insignificant desquamation, wet and macerated surface. It is often accompanied by itching and burning sensation. It is possible, that the given form is, in fact, exudative psoriasis, the clinical picture of which has changed somehow due to localization of the process in the skin folds. With exudative, or wet, psoriasis *(psoriasis exudativa seu humida)* the elements of rash are impregnated with exudate with the subsequent formation of yellowish-grey loose scaly crusts. With eczematous psoriasis *(psoriasis eczematoides)* the phenomena of exudation, crust, scratches layer and the pathological process looks like the eczematous one.

Two types of pustular psoriasis (*psoriasis pustulosa, seu suppurativa*) are distinguished; these are *Cymbush* type and *Baber's* type. The first type can appear primarily without typical picture of dermatosis and develops more frequently secondarily in the result of transformation of vulgar or intertriginous psoriasis. It is severe general illness, accompanied by temperature rise, general ailment, leukocytosis. First, there appear numerous disseminated erythematous and erythematous-edematous foci, which spreading over the entire skin cover, form various figures and diffuse bright red lesions. In this setting there are disseminated pustular elements, which shrivel into yellowish-brown crusts and crusty scales. Dermatosis can have malignant course with lethal outcome. With second type of



Fig. 5.8. Psoriasis of palms and plantae.



Fig. 5.9. Scalp lesion with psoriasis.

pustular psoriasis, symmetrically located pustular and psoriasiform foci, of small size at the beginning, develop in the area of palms and plantae in the erythematous setting. The content of pustules is sterile. Process generalization sometimes is possible. Along with the described lesions in the areas of palms and plantae, the typical psoriatic eruptions can be observed in the other areas of skin cover.

Often in dermatological practice the plaque psoriasis *(psoriasis exanthematica)* is observed, which is characterized by weakly expressed infiltration of elements, looking not like papules, but spots, that is similar to toxicoderma. With seborrheic psoriasis *(psoriasis seborroica)* the rash is localized on the seborrheic sites, herewith the scales adhere and acquire the yellowish colour due to secretions of the sebaceous glands, resembling clinically seborrheic eczema. With localization of the rash on the flexor surfaces of extremities, the inverse psoriasis or flexion psoriasis *(psoriasis inversa seu flexuratum)* is distinguished. The psoriasis of palms or plantae *(psoriasis palmaris et plantaris)* is ranked to atypical forms in the case, if psoriatic plaques acquire hyperkeratotic character, simulating clavuses formation *(clavi psoriatici)* or resembling callous eczema *(eczema tyloticum)*.

Diffuse or sharply limited layerings of scales can occur in the hairy part of the head, which often cover smooth skin, though the hair in never damaged. Psoriasis starts from the hairy part of the head approximately in a quarter of cases, and is combined with the eruptions in the other parts of the skin in more than 60% of cases. Scalp lesion is often of focal nature, occurring in the hindhead, temples, parietal area in the form of sharply raised plaques.

Approximately 25% of psoriasis patients have their nails affected; this pathology has got the early and late forms. Among the early forms of psoriasis of nail plates there are *punctate onychodystrophy,* or *pitting symptom* (characterized by punctate parakeratosis of proximal matrix), *symptom of oil stains* (presence of yellowish-brown subungual stains, mostly, in nail walls, most frequently it occurs in the progressive stage of psoriatic diseasea). With the late stages of the nail psoriasis more frequent are *hypertrophic onychodystrophy,* or *onychogryphosis* (in the form of «bird's claw» in the result of hyperkeratosis subungual), *atrophic onychodystrophy* or *onycholysis*, *transverse and longitudinal sulci on the nail plates, subungual petchiae* (Leventhal's symptom), ponychium defect *(Popov's symptom)*.



Fig. 5.10. Nails disorder with psoriasis.

10-12% of psoriasis patients have got additionally to the skin eruptions, progressive changes of joints from

periarticular injury (enthesitis, tendovaginitis) to arthritis with frank osteoarticular changes, that is crtified radiologically. Most of patients have got the joints lesion occurring in three-five years and more after the first psoriatic eruption. Symmetric multiple lesions of small peripheral joints and bones (osteoporosis, mainly in pineal glands, and the joint space narrowing) with the gradual involvement in the process of large joints, sometimes spine is characteristic. With the severe forms there occurs dispersion of end phalanges of hands and feet, and appearing of exostoses (osteophytes).

The development of pathological process during psoriasis can occur according to two types. The first type supposes the early manifestation of the disease (with peak at the age of 16-20). It is characterized by the large area of lesion, torpid course and frequent relapses. The second type has got later signs (peak at the age of 40-50). With the first type, the hereditary link is evident (in 44% of cases), whereas in the second type this connection is set only in 1% of cases.

Pathomorphology. Hyperkeratosis, parakeratosis, acanthosis in the inter-papillary areas of Malpighian layer and thickening of its above-papillary sites, intercellular edema, spongiosis, accumulation of neutrophils in the intercellular spaces, penetrating from dermis (Munro micro abscesses) is observed in epidermis. The horny layer over papule is thickened, loosened; it consists mainly of parakeratotic cells with elongated rod-like nuclei. There are numerous gaps between the plates, filled with air, in the result of which the scales are silver. Hyperkeratosis in the old elements is more pronounced, than parakeratosis. The nuclei in the horny layer occur regardless the age of the papule. Granular layer disappears or only interrupted series of its cells remains. In the severe cases, the shiny layer is absent. Malpighian layer over the papillae is thickened, epidermal outgrowths elongated. Acanthosis is sharply pronounced in the spinous layer between the papillae. Capillaries of the papillary layer are expanded, greatly curled and overfilled with the blood. Inflammatory infiltrate of lymphocytic histiocytic origin is observed around the vessels.

Electron microscopical study observes intense coloring of nuclei of basal layer, indicating increased proliferative activity of the cells of epidermis. The cell cycle of conversion of basal keratocytes in the horny scales reduces dramatically (up to four days, when the norm is 28).

Differential diagnostics. The skin manifestations of psoriasis should be differentiated primarily from the diseases, for which the characteristic rash



Fig. 5.11. Psoriasis arthropica.

element is a papule, covered with scales, namely, lichen planus, parapsoriasis, pink Gibert's lichen, atopic dermatitis, secondary syphilis.

In contrast to psoriasis, in case of *lichen planus*, the papules are polygonal squamous; desquamation on the surface of the rash elements is weakly pronounced; the color of efflorescence is purplish-red on the skin and pearl on the oral mucosa; waxy shine of eruption surface and the presence of umbilication in the center of papule is characteristic; texiform pattern on the surface of papule (Wickham's striae) is localized most frequently on the oral mucosa and on the skin of the flexor surfaces of forearms and lower legs; there is pronounced itch in the rash areas and negative psoriatic triad.

In case of *parapsoriasis*, the presence of characteristic phenomena is typical, such as wafer (a round scale is removed from the surface of the papule), occult desquamation (it is evident during scraping of surface of papule), collarette (the central site of papule is covered by greyish-brown scales, which are flaked off peripherally), purpura symptom (it is caused due to intense scraping of rash elements).

Pink Gibert's lichen is characterized by the presence of herald patch on the trunk, distribution of the daughter, mainly spotted, rash along the cleavage lines, symptom of "crumpled tissue paper".

Atopic dermatitis differentiates by the presence of erythema of dull color, pronounced lichenification, excoriations, localizations of eruptions on the skin of face, neck, upper chest, flexor surface of knee and elbow joints, allergological anamnesis.

Psoriasiform syphilides are characterized by pale red with copper color of rash elements, the absence of peripheral growth, the presence of Biett's collarette around papules, the absence of psoriatic triad, detection of pale treponema in the rash elements, positive serological reactions.

The differential diagnostics of atypical clinical forms of psoriasis should be carried out as well. Besides, nail psoriasis is often differentiated from onychomycosis on the basis of detection analysis for pathological fungi in the material studied; psoriatic erythoderma from toxicodermas, skin lymphomas and arthropathic psoriasis from the range of chronic arthritis. Arthropathic psoriasis is more frequently differentiated from rheumatoid arthritis.

Treatment. Pathogenetic treatments of psoriasis include systemic and topical treatment, skin care and additional methods of therapy, such as physiotherapy, balneotherapy, climate, psychological, herbal therapy etc. (Table 5.1.)

Systemic treatment. The volume of therapeutic interventions with psoriasis is determined by the main parameters of skin (stage, type, duration, course, etc.) and articular (lesions amount and symmetry, clinical anatomic and clinicoroentgenological variants of course etc.) pathologic processes and the degree of systemic manifestations.

Systemic treatment is aimed at the elimination of dominating manifestations of associated lesions, reduction of systemic symptoms of psoriasis and the use of

Table 5.1.
Agents for treating psoriasis

Topical	*Systemic*
Emollients	PUVA (psoralen +ultraviolet A)
Tar	Rethinoids
Salicylic acid	Cytotoxic, e.g. methotrexate, azathioprine, hydroxicarbamide (hydroxiurea)
Topical steroids	Systemic steroids * (see precaution below)
Dithranol (anthralin)	Cyclosporin
Vitamin D analogues (e.g. calcipotriol, tacalcitol)	'Biological' (cytokines): various monoclonal antibodies
Tazarotene	
Ultraviolet radiation	

preventive and curative interventions in order to improve functional state of skin and articular apparatus in psoriatic processes.

Systemic treatment is aimed at the reduction of psoriatic process activity by slowing of cutaneous syndrome progression and destruction of bone structure of articular apparatus. Systemic suppressive therapy of psoriasis is recommended with moderate and severe degree of cutaneous and articular sickness syndrome and includes the use of:

- glucocorticosteroids;
- disease modifying drugs (DMD) – cytostatic immunosuppressants (methotrexate, cyclosporine), sulfasalazine, gold preparations, leflunomide, aromatic retinoid;
- preparations of biological effects – monoclonal antibodies to tumor necrosis factor and its soluble receptor (infliximab, adalimumab, etanercept);
- other biological agents (anakinra, alefatsepta, efalizumab, abatacept).

Prescription of systemic *corticosteroid hormones* in the therapy of psoriasis requires comprehensive study. It should be kept in mind that systemic therapy with use of glucocorticosteroids frequently results in destabilization of psoriasis with formation of torpid, severe and atypical forms of dermatosis. Accordingly, the indications for use of such therapy in psoriasis are only generalized arthritis with pronounced exudative components, malignant form of arthropathic psoriasis, sharply pronounced organ manifestations, the combination of articular syndrome and atypical or extensive cutaneous psoriatic process (pustular psoriasis, psoriatic erythroderma, and extensive exudative psoriasis), intolerance to disease modifying drugs. Disease

modifying drugs (DMD) are the preparations of pathogenic effect with immunosuppressive property and capable of inducing remission of psoriasis or reducing the rate of development of articular destruction and cutaneous pathologic process. Curative effect of DMD appears in one to two months and more after the start of treatment, what is connected with the necessity of their accumulation in organism. In psoriasis those DMD are used, as a rule, which are widely used in rheumatology. Not only methotrexate, cyclosporine, sulfasalazine, leflunomide and the preparations of biological effects are dominating among them, but also colchicine, derivatives of fumaric acid, mycophenolate mofetil, somatostatin, aromatic retinoids.

Retinoids, which are already used about 30 years in dermatological practice, are characterized by high efficiency in moderate and severe course of psoriatic disease, psoriasis of hairy part of the head, arthropathic psoriasis and with psoriatic lesion of nail plates. The developments of the recent years have led to the appearance of new aromatic synthetic analogue of retinoid acid – acitretin, mechanism of action of which lies in inhibiting the proliferation of epithelial cells, normalization of keratinization processes and stabilization of membrane structures of cells, including liposomes.

Prolonged use of SMD and DMD gives the possibility to control the activity of psoriasis and its main syndromes, slow down the rate of disease progression, contribute to preservation of working capacity of patients and improve their quality of life. The use of DMD in therapy has a positive effect on the course not only of the pathological articular process, but cutaneous syndrome, as well, that provides for reduction of use of external therapy.

Topical therapy. Among many methods of psoriasis treatment, the preparations of external therapy and skin care products are essential. Rationally found external therapy for psoriasis is of great and often key importance. For the majority of patients with limited plaque form of psoriasis, this choice of therapy under condition of elimination of main initiating agents becomes the only. With other, more severe clinical forms and extensive pathological process, the external therapy is rather ponderable addition to the systemic one.

External treatment is carried out first of all considering the process staging. Local therapy is also divided into non-suppressive and suppressive. Non-suppressive treatment of psoriasis provides for use of skin care means (local means with softening and/or moisturizing effect, which do not contain the active substances – emollients), and means, which include salicylic acid (2% in progressive stage, 4% – in stationary stage and 10% – in regressive stage) or urea (2-10%), tar preparations, as well. The use of urea and salicylic acid is connected with their cheratolic, antimicrobial and keratoplastic properties. The best studied pharmacological agents of psoriatic suppressive treatment are topical glucocorticosteroids (TGCS), analogues of vitamin D_3, topical retinoids (TP), hydroxiantrons.

Topical glucocorticosteroids are important means of external therapy of psoriasis due to their rapid anti-inflammatory effect and pronounced wide range of actions. The strongest TGCS of the IV class of activity such as clobetasol propionate in the form of

ointment and cream can be used in the severe recurrent course of psoriasis during short course (one to two weeks), after that it is advisable to prescribe the other, less strong TGCS, in particular, of the III or the II class (Locoid, Eloson, Momederm, Moleskin, CelestodermV, Cutivate, Laticort, Flucinar etc). However, prolonged use and application of corticosteroids on the large surface, inhibition of the function of adrenal cortex and the development of undesirable side effects are possible. For such a reason, thorough selection of TGCS is essential, with optimal efficiency and low possibility of occurrence of local and systemic side effects. It especially concerns the prescription of TGCS for children with psoriasis. In this aspect such TGCS as fluticasone propionate (Cutivate), hydrocortisone butyrate (Locoid), methylprednisolone aceponate (Advantan) have the advantage. Combined therapy of TGCS combined with salicylic acid (LorindenA) or urea (Betasalic) is appointed with the pronounced skin flaking.

Emollients are the key skin care products for the patients, suffering from psoriasis, providing restoration and protection of the horny layer of epidermis, maintaining hydro lipid balance and preventing transepidermal water loss.

By origin the emollients can be hydrophilic, lipophilic and combined (amphiphilic). These means can contain various compounds of mineral and organic origin, these are the higher fatty acids, triglycerides, ceramides, phospholipids, squalene, cholesterol, liquid paraffin, white petrolatum, urea, glycerol, etc. Depending on production technology emollients can be presented by simple emulsion in the form of «water in oil» or «oil in water», laminar emulsions, liposomes/microspheres, nanoparticles and other forms.

For the local therapy of moderate and moderately severe psoriasis *synthetic retinoids* (Tazarotene) and analogues of vitamin D_3 (Calcipotriol, Tocalcitol) in the form of ointment, cream, gel are used.

Phototherapy is one of the effective treatments of psoriasis. The following forms of light therapy are recommended:

- Natural insolation (heliotherapy);
- Ultraviolet irradiation – selective phototherapy (wave length of 280-320 nm, dose of 0,05-0,1 J/cm^2 in a day, during the period up to two months);
- PUVA-therapy (systemic and local);
- Re-PUVA-therapy (retinoids + PUVA).

Photochemotherapy is used in case of moderately severe and severe forms of psoriasis. However, it must be taken into account the possibility of side effects development (itching, erythema, blisters, stimulating of malignant course of neoplasms) and the risk of skin cancer. At the Department of Dermatology and Venereology of Bogomolets National Medical University, zonal UV-irradiation by means of quartz lamps according to the schedule, developed by Professor I.I. Pototsky, is widely used, ensuring the achieving of significant clinical effect in the treatment of different forms of psoriasis.

Additional methods of treatment of psoriasis involve physiotherapy, balneal and climate treatment, phytotherapy, psychosocial therapy, surgical treatment and others.

Physiotherapy is widely used in dermatological practice as stage treatment of psoriasis patients. Complex methods of treatment are worked out, involving the effects of ultrasound, magnetic and laser therapy and phonophoresis on the affected sites.

Psychosocial therapy is important in the treatment of psoriasis, as it is often necessary to consider the possible disease impacts on social, emotional and psychic aspects of each patient. In case of serious patient sufferings, significant deterioration in his life quality, the consultation with specialist in psychosomatics and psychotherapy should be recommended. Psychosocial therapy can be used only in case of patient wish and consent.

Balneal and climate treatment has a positive effect both on cutaneous and articular syndromes of psoriatic disease. Health resort balneal treatment (hydrogen sulfide, radon, salt-water baths, seabathing) is recommended In intercurrent period, in particular, in the sanatoriums of Nemyrov, Synyak, Khmelnyk, Solotvyno, in Crimean resorts and others.

Phytotherapy, treatment by means of herbal preparations must be considered as an addition to the main therapy during stabilization of pathological psoriatic process in the form of baths, phytoapplications, wraps, ointments use etc.

Since psoriasis is of polyetiological nature and there is no absolutely explicit method of its treatment for today, the main rule of a doctor must be individual approach and selection of the most effective therapy, which reduces the disease activity, accelerates manifestation of clinical effect of treatment, prolongs remission of not only cutaneous but articular pathological process as well.

Therapeutic regimen and skin care. In order to avoid the development of isomorphic reaction, hydrotherapeutic procedures without strong direct irritant effect should be favoured. After a shower (bath) the skin must be moisturized by applying emollients. It is recommended to live a healthy lifestyle, avoid alcohol abuse and smoking. The diet of psoriasis patients should support the correct acid-base balance in organism with a predominance of alkaline reaction. The positive reinforcement is also essential, as negative emotions contribute to exacerbation of psoriatic process.

1. What is the most typical localization of eruptions in psoriasis process?

A. Flexor surfaces of extremities
B. Extensor surfaces of extremities
C. Interdigital folds
D. Skin around physiological ostia
E. Mucous membranes of genitals and oral cavity

2. What symptom is not used to confirm a psoriasis diagnosis?

A. Psoriatic triad
B. Koebner's phenomenon
C. Auspitz' symptom
D. Phenomenon of pintpoint bleeding
E. Phenomenon of apple jelly

3. Which clinical sign is not characteristic for the progressive stage of psoriasis?

A. Trend to fusion
B. Presence of psoriatic triad
C. Silvery white scales in the center of papule
D. Koebner's phenomenon
E. Silvery white scales over the entire surface of papule

4. What is characteristic for psoriatic papule?

A. Yellowish red color
B. Umbilication in the center of papule
C. Oval form
D. Surface covered with white scales
E. Shiny surface

5. Clinical types of psoriasis do not include:

A. Seborrheic
B. Foliaceous
C. Exudative
D. Follicullar
E. Rupioides

6. What is identified in case of psoriatic erythroderma?

A. Pronounced infiltration of rash elements with warty growth
B. Continuous fusion of rash elements with infiltration and edema
C. Pustular rash with increased temperature and lymph nodes enlargement
D. Ulceration of rash elements
E. Articular and edema syndrome without cutaneous symptoms

7. Psoriatic lesion of nails is characterized by the following, except:

A. Symptom of pitting
B. Symptom of oil stain
C. Symptom of apple jelly
D. Onychogryphosis
E. Onycholysis

8. What of the following is not occurred?

A. Jerky appearance of pustules on the places of eruptions or visually healthy skin, not connected with hair follicles
B. Sterile pustules
C. Sudden onset with fever, leukocytosis and increased ESR
D. Hypertrophic growth of papules on the palms and plantae
E. Possibility of disease transformation into another form of psoriasis or disability

9. Clinically peripheral arthropathic psoriasis is presented by:

A. Lesion of three joints of one finger
B. Tenosynovitis of separate fingers
C. Sausage-shaped configuration of fingers
D. Arthritis of distal interphalangeal joints
E. All of the above

10. What of the following is not qualified as pathomorphological characteristics of skin with psoriasis?

A. Hyperkeratosis
B. Acanthosis
C. Acantholysis
D. Parakeratosis
E. Munro micro abscesses

Answers to the quiz of the first level of complexity
1 – **B**; 2 – **E**; 3 – **E**; 4 – **D**; 5 – **B**; 6 – **B**; 7 – **C**; 8 – **D**; 9 – **E**; 10 – **C**
Answers to the quiz of the second and third levels of complexity
1a – **A**; 2a – **A**; 3a – **E**; 4a – **A**; 5a – **B**

Task 1. A patient at the age of 20 has disseminated papular rash of bright red color, of the size from the millet to lentil grain on the extensor surfaces of extremities, back, and hair part of the head, the surface of the elements in the center is covered with whitish scales. Applying the method of scraping the symptoms of stearin spot, terminal film and pinpoint bleeding are identified.

a) Which diagnostic test was used to confirm the diagnosis?
- **A**. Psoriatic triad
- **B**. Koebner's phenomenon
- **C**. Balser's test
- **D**. Phenomenon of falling the probe
- **E**. Phenomenon of apple jelly

b) Which histopathological processed are associated these symptoms with?

Task 2. A patient at the age of 45 has numerous inflammatory rashes consisting of pink-red papules, covered with whitish scales in the center, on the skin of the hair part of the head and trunk, appearing gradually during the period of two weeks. The eruptions of this nature were observed a few years ago in wintertime, and gradually disappeared without treatment by the end of spring.

a) What is the most probable preliminary diagnosis in this patient?
- **A**. Extensive psoriasis, progressive stage
- **B**. Extensive psoriasis, psoriatic erythroderma
- **C**. Extensive psoriasis, stationary stage
- **D**. Limited psoriasis, psoriatic arthropathy
- **E**. Limited psoriasis, stationary stage

b) Determine the complete clinical diagnosis with appointment of treatment.

Task 3. A woman is complaining about periodic appearance of eruptions during the year in the area of elbow and knee joints, which she associates with frequent nerve strains. During preliminary outpatient examination the diagnosis of psoriasis is set. At presentation: rash consists of numerous plaques, surface of central part of which is covered with easily falling-away silvery scales.

a) Determine medical tactic.
- **A**. Sedative therapy
- **B**. Antihistamine therapy
- **C**. Aevit appointment
- **D**. Application of 2% salicylic ointment
- **E**. All of the above is correct

b) Conduct a differential diagnostics of the indicated disease.

Task 4. A woman at the age of 52 is complaining about the rash, swelling, pain and stiffness of hands and feet movement. She has been sick for more than 15 years, relapses occur in the wintertime. *Physical examination*: numerous plaques with diameter of 2 cm. are observed on the skin of the hair part of the head, trunk, upper and lower extremities, which in some places are merged in large foci. The rash elements are rose-red with silvery white scales in the center, which easily fall-away. Small joints of the hand and feet are edematous, their mobility is limited. There is pitting on the nail plates of some fingers.

a) Set a preliminary diagnosis:
- **A**. Extensive, arthropathic psoriasis
- **B**. Extensive psoriasis, psoriatic erythroderma
- **C**. Extensive psoriasis, stationary stage
- **D**. Limited, arthropathic psoriasis
- **E**. Limited psoriasis, stationary stage

b) Suggest the examination plan and treatment scheme for this patient.

Task 5. A patient has got rash on the skin of chest and extremities in half and a month after suffering a shingles. *Physical examination*: rose-red papules of various sizes covered with white scales, which do not reach the healthy skin, leaving peripherally narrow pink line, are visualized on the skin of trunk, extensor surface of forearms and lower legs. Dotted papules with white scales are observed on the right lower leg along the scratch.

a) Put the preliminary diagnosis:
- **A**. Lichen planus
- **B**. Extensive psoriasis, progressive stage
- **C**. Extensive psoriasis, stationary stage
- **D**. Secondary syphilis
- **E**. Tuberculosis cutis lichenoides

b) Which diagnostic tests are necessary to make for setting a clinical diagnosis?

6 TOPIC

Lichen planus

Lichen planus (*lichen ruber planus*) is a peculiar reaction of organism of undetectable etiology, which is manifested as monomorphic papular rash on the skin and mucous membranes. This skin disease is usually regarded as multifactorial. Endogenous and exogenous factors along with genetic anomalies can be essential in the formation and character of the course of pathological process with lichen planus.

TRAINING AND EDUCATIONAL PURPOSES

- To determine the possible conditions and triggers of appearance of lichen planus
- To perform classification and define general peculiarities of various forms of lichen planus on the skin and mucous membranes
- To interpret clinical picture and course of lichen planus
- To generalize the principles of treatment of lichen planus

TO KNOW:

- etiological, pathogenetic and epidemiological features of lichen planus;
- clinical forms of lichen planus and current peculiarities of its course;
- diagnostic criteria of disease manifestations on the skin and mucous membranes;
- principles of preventive and curative interventions and preventive medical examination of the patients with lichen planus.

TO BE ABLE TO:

- correctly collect anamnesis of patients with lichen planus;
- make a differential diagnostics with dermatoses, which have similar clinical presentation;
- prescribe rational treatment for a patient with lichen planus.

Etiology of lichen planus cannot be regarded as finally established. In the development of dermatosis a significant part is assigned to infectious factors (viruses), toxic-allergic effects, as well as neurological and immune disorders. The researchers, who speak in favour of infectious nature of dermatosis, make reference to the good results of treatment with use of antibiotics, cases of familial disease, as well as identification of intracellular viral inclusions in these patients. The theory of neurogenic genesis of the disease is confirmed by frequent cases of lichen planus appearance after stressful situation, effectiveness of hypnosis or reflex-segmental therapy in some patients, and the location of rash sometimes along the nerves. Endocrinal theory of disease appearance is based on the hormonal and metabolic disorders in organism. A genetic predisposition to such pathology, transmitted in an autosomal-dominant pattern of inheritance is established.

Pathogenesis of lichen planus has got a lot of links, the interaction of which is diverse and not completely studied. According to the current judgment, the main organ, where there appears a pathological picture, is a skin, as it is the place, where the pronounced dystrophic and inflammatory reactions occur. The reasons and mechanisms of pathological skin changes in lichen planus are studied insufficiently. Currently, changes in an immune system, including those of autoimmune processes, are proved to be significant in the development of lichen planus.

Epidemiology. Lichen ruber planus (LRP) occurs quite often. According to the data of most researchers, the people at the age of 30 to 60 years prevail among the patients with lichen planus. Lichen planus in children is rare. In general structure of dermatological morbidity, lichen planus constitutes from 1 to 1.5%, it makes from 11 to 30-35% among the disease of oral mucosa. Lichen planus occurs in all countries and in different climatic geographical areas, the incidence of disease varies over a wide range.

Classification. Lichen planus of skin and mucous membranes is characterized by a great variety of atypical forms that significantly complicates diagnostics.

Clinical forms of lichen planus:

– *typical (classical or usual) form;*

– *atypical forms:*

- linear lichen planus *(lichen ruber linearis seu lichen ruber striatus)*;
- annular lichen planus *(lichen ruber anularis);*
- lichen rubber monoloformis (Wise-Reindisease, Kaposi's disease) *(lichen ruber planus monitiformis Kaposi);*
- lichen planus of the scalp *(lichen ruber planus capillitii);*
- lichen planus of the palms and soles *(lichen ruber planus palmarum et plantarum);*
- erythematous form *(lichen ruber erythematosus Kaposi);*
- hypertrophic (verrucous) form *(lichen ruber hypertrophicus seu verrucosus);*

- follicular form *(lichen ruber follicularis seu spinulosus);*
- lichen planus obtusus (Unna) *(lichen ruber obtusus Unna);*
- atrophic form *(lichen ruber planus atrophicus);*
- bullous or pemphigoid form *(lichen ruber bullosus seu pemphigoides);*
- pigmentary form *(lichen ruber pigmentosus);*
- psoriasiform lichen planus *(lichen ruber planus psoriasiformis Broca);*
- tropical lichen planus *(lichen planus tropicalis).*

It is accepted to distinguish between six forms of lichen planus on the mucous membrane of the mouth and vermillion border:

- typical;
- exudative-hyperemic;
- erosive-ulcerative;
- bullous;
- hyperkeratotic;
- atrophic.

Clinical picture. Typical form of lichen planus is characterized by monomorphic rash, formed by lenticular inflammatory shiny polygonal papules, on the surface of which there can be observed pathognomonic for the disease Wickham's striae opal-like white and grayish dots and stripes. Striae becomes more visible, if the surface of papules is moisten with water, plant or vaseline oil. Its formation can be explained by uneven granulosis. There is umbilication in the center of some papules. Merging with each other, small papules can form plaques with distinct boundaries of bluish discoloration, covered with fine plaques. In advanced stage of disease the positive Koebner's phenomenon (the appearance of rash in the sites of even insignificant skin traumatization) is observed, as well as itching. The rash is localized predominantly on the skin of inner forearms, wrist and ankle joints, sacrum and externalia area. The rash can spread throughout the entire skin cover (except face). With the regression of the process the secondary pigmentation remains on the sites of the papules. Sometimes there occurs cicatrical alopecia on the hairy part of the head.

In 25–70% cases of lichen planus, together with skin lesion there occur lesions of oral mucosae (cheeks, tongue, gingivae, palate) and externalia, which can be isolated or combined with skin lesion. Firstly, there appear small papules of greyish-white color, sharply defined on a pink background of mucosa, then the plagues form. The papules on the mucosae do not have typical shine, the infiltrate can be moderately expressed, and the elements hardly rise above the mucosal surface. They are mainly localized on the internal surface of cheeks on the line of the contact of teeth (molars), where they form whitish figure, similar to frond.

Change of nail plates in lichen planus is characterized by the formation of sulci, grooves, sites of opacification; the nails can become thinner, or they can be even destroyed in part or in whole, in this connection there are two the most common types of nail changes in this dermatosis, these are onychorrhexis and onycholysis.

Thus, the main clinical morphological primary element of rash in lichen planus is lenticular dermo-epidermal inflammatory papule, with the following characteristics for this dermatosis:

- polygonal outsides;
- umbilication in the center;
- absence of tendency to peripheral enlargement;
- presence of so-called Wickham's striae, which becomes visible in the deep of papules after their surface are moisten with water or oil;
- bluish-red (or lilac) pearly papules and polished shine of their surface with side lightning.

The course of dermatosis. Typically the localized forms of dermatosis are of long-term chronic course with periodic exacerbation. Sometimes the process can begin acutely, with fever, rapid generalization of the rash, skin edema and erythema is possible, erythroderma with fine (unlike psoriatic) desquamation may appear. Acute lichen planus can rather quickly regress, but mainly it becomes chronic. Quite often in the time of paracme the rash is not everywhere regressing, remaining on the lower legs and genitalia.

Diagnostics. Diagnostics is based on the clinical and histological data.

Pathomorphology. The main pathomorphological signs of typical lichen planus are hyperkeratosis, granulosis, acanthosis, vacuolar dystrophy of the basal layer, diffuse band infiltrate in the upper dermis, intimately adjacent to epidermis, the lower boundary of which is blurred by the infiltrate cells.

Differential diagnostics. Differential diagnostics is carried out with psoriasis, toxic-derma, neurodermatitis, verrucas plantar, papular syphilides. For clarification of diagnosis a skin biopsy is usually made.



Fig. 6.1. Lichen planus.



Fig. 6.2. Lichen planus of oral mucous membrane.



Fig. 6.3. Lichen planus.

Treatment. Currently, due to absence of a common conception of etiology and pathogenesis of lichen planus there are numerous methods of treatment of this disease. Taking into account the complexity of pathogenesis of lichen planus, success is possible only in the complex pathogenetic individualized therapy with use of modern methods. Thus, it is important to take into account the conditions, enabling disease appearance, risk factors, accompanying pathology, the presence of foci of focal infection, previous treatment. Traditional treatment involves antibiotic therapy, sedatives and antihistamines, topic corticosteroids, vitamins (A, D, E), retinoids (vitamin A derivatives), with use of exogenous interferon and interferonogenes, phonophoresis with sedative and anti-inflammatory drugs, cryomassage and cryodestruction (especially with verrucous form).

Retinoids (tigason, neotigason, etretinete) reduce the intensity of inflammatory reaction, influence the state of cell membranes and normalize the processes of proliferation. Retinoids are more effective in lesion of oral mucosa and vermillion zone. In the therapy of lichen planus the analogues of vitamin A carotenoids are used as well, especially in atypical forms, including erosive ulcerous, and in lesions of oral mucosa and genitalia as well.

Of topical corticosteroids the preparations of strong and very strong action are used in complex therapy of lichen planus. In case of severe lesion the appropriate therapy should be started according to the principle of "powerful start", using the drugs of the IV power category of action with short courses of administration (one-two weeks) with the following transition to the TGCS of the III or II classes.

Prognoses of lichen planus is favorable. However, the malignant transformation of papules is described in lichen planus. Its erosive ulcerous form on the oral and lips mucosa is considered to be precancerous condition. In this relation, the methods of treatment connected with irritation and cauterization should be avoided. In the long course of erosive ulcerous forms of lichen planus, hardly answering the treatment, it is necessary to carry out a histological study in order to detect malignification.

1. Indicate the clinical manifestations, common for psoriasis and lichen planus:

A. Polygonal popular elements with impression in the center
B. Frequent mucosae lesion
C. Isomorphic Koebner's reaction
D. Very strong itching
E. Paints in the joints

2. Which form of the following is not typical for lichen planus?

A. Exudative hyperemic
B. Hypertrophic
C. Typical
D. Palmoplantar
E. Intertriginous

3. What is a patient with lichen planus complaining of?

A. Temperature rise
B. Itching
C. Dyspepsia
D. Paints in the joints
E. Catarrhal signs

4. Clinical symptoms of lichen planus are:

A. Localization of the rash on the oral mucosa
B. Monomorphic rash
C. Long duration of disease (several years)
D. Appearance of rash in the areas of mechanical trauma
E. All of the above is correct

5. What clinical characteristics are typical of papules in lichen planus?

A. Polygonal
B. With waxy shine
C. Violetish
D. With umbilication
E. All of the above is correct

6. Specify the areas of rash localization in lichen planus:

A. Hairy part of the head
B. The front surface of the tibia
C. Elbows and knees
D. Neck
E. Palms and plantae

7. Which clinical forms are not observed in lichen planus?

A. Anular
B. Pemphigoid
C. Atrophic
D. Verrucous
E. Dyshidrotic

8. Which clinical forms of lichen planus are not observed on the vermillion border and oral mucosa?

A. Typical
B. Pigmentary
C. Exudative hyperemic
D. Hyperkeratotic
E. Erosive ulcerous

9. In lichen planus the most frequent localization of rash on oral mucosa is:

A. Contact line of teeth
B. Hard palate
C. Soft palate
D. Tongue
E. Mouth floor

10. Fort the treatment of lichen planus the following drug is not used:

A. Antimycotic agents
B. Immunomodulators
C. Retinoids
D. Vitamines
E. Antihistamines

Answers to the quiz of the first level of complexity
1 – C; **2** – E; **3** – B; **4** – E; **5** – E; **6** – B; **7** – E; **8** – B; **9** – A; **10** – A
Answers to the quiz of the second and third levels of complexity
1a – A; **2a** – E; **3a** – D; **4a** – D; **5a** – D

Task 1. A patient after past influenza has got itching rash on the trunk and extremities. *Physical examination*: there are lenticular papules of bluish red color with umbilication in the center on the sites of the trunk, flexor surfaces of the forearms and extensor surfaces of the lower legs. A linear grouping of rash elements in the areas of skin trauma attracts attention.

a) The described clinical picture corresponds to:
A. Lichen planus
B. Psoriasis
C. Herpes zoster
D. Herpes simplex
E. Eczema

b) From what dermatoses should these presentations be differentiated and how?

Task 2. A patient at the age of 27 is complaining of rash on the trunk, upper extremities and itching. She associates her disease with nervous overstrains. *Physical examination*: there are polygonal papules with shiny, like waxed surface on the trunk and on the flexor surfaces of forearms. Umbilication occurs in the center of some elements. There are whitish papules on the oral mucosa.

a) What dermatosis should be considered in this case?
A. Eczema
B. Psoriasis
C. Herpes zoster
D. Herpes simplex
E. Lichen planus

b) What therapeutic and preventive measures should be carried out?

Task 3. A patient at the age of 43 is complaining of itching rash on the sites of both lower legs. *Physical examination*: there are brownish red plaques covered with dry horny wartlike masses, tightly adhering, on the flexor surfaces of the lower legs; polygonal lenticular papules with umbilication in the center and shiny like waxed surface are sometimes observed.

a) To which disease does the described clinical picture correspond?
A. Eczema
B. Psoriasis
C. Allergic dermatitis
D. Lichen planus
E. Mycosis of the skin

b) Which methods of therapy should be prescribed for the treatment?

Task 4. A patient after past otitis has got rash on the oral mucosa appeared. *Physical examination*: there are strip plaques of the whitish opal color on the cheeks and palate, isolated papules of bluish red color with umbilication in the center on the flexor surface of the forearms.

a) Which diagnosis can be set?
A. Eczema
B. Psoriasis
C. Allergic dermatitis
D. Lichen planus
E. Mycosis of the mucosae

b) What are the features of the tactics and follow-up of this patient?

Task 5. A patient of 45 after prosthodontic treatment has got whitish papules appeared on the oral mucosa, which gradually grouped, forming the irregular figures, similar to frond. A patient has not self-medicated.

a) What is the most probable character of this disease?
A. Eczema
B. Mucosal candidiasis
C. Allergic dermatitis
D. Lichen planus
E. Leukoplakia

b) What are the peculiarities in the scheme of examination of this patient?

7 TOPIC

Fungal Infections of Skin and Mucous Membrane

Fungal infections of skin and mucous membranes (mycosis) is a nosological concept that combines a number of diseases of skin and its appendages and human mucus membranes, which are caused by pathogenic and opportunistic fungi.

TRAINING AND EDUCATIONAL PURPOSES

- To understand the relevance of mycotic skin and mucous membranes lesion; the ways and conditions of mycosis infection.
- To understand basic essentials of epidemiology and pathogenesis of mycotic lesions of skin and mucous membranes.
- To classify mycotic lesions with due account for the localization of pathological process, the peculiarities of pathological manifestations, prevalence, lesion depth, the relation to the skin appendages.
- To single out characteristic clinical features of mycotic lesions of skin and mucous membranes.
- To generalize the principles of diagnostics, therapy and prophylaxis of mycotic lesions of skin and mucous membranes.

TO KNOW:

- Modern classification of mycotic lesions of skin and mucous membranes;
  The general flow and clinical manifestations of typical forms of mycotic lesions of skin and mucous membranes and possible complications;
  The principles and methods of diagnostics of mycotic lesions of skin and mucous membranes;
  The principles of treatment and prophylaxis of mycotic lesions of skin and mucous membranes.

TO BE ABLE TO:

- Correctly collect an anamnesis of a patient with mycotic lesions of skin and mucous membranes;
- Correctly conduct clinical examination of the patient with mycotic lesions of skin and mucous membranes;
- Conduct differential diagnostics of typical manifestations of mycotic lesions of skin and mucous membranes with diseases that have similar clinical picture;
- Assign a rational complex treatment to the patient with mycotic lesions of skin and mucous membranes;
- Define and take necessary measures for the prevention of mycotic lesions of skin and mucous membranes and their complications.

Epidemiology. Mycoses (fungal infections) of skin, its appendages and mucous membranes constitute a large group of lesions caused by the action of specific micro-organisms i.e. fungi that modern science included in a separate kingdom called *Fungi* or *Mykota*.

Biodiversity of fungi in nature is rather wide. Based on the taxonomists' data, there are nearly 1.5 million species of fungi, of which only 4% have been studied, to include over than five hundred registered species of fungi that are pathogenic to humans and animals.

The risk to humans and the need for commitment to antimycotic therapy against fungal infections is caused by:

the development of pathological changes in the skin, hair, nails and internal organs and breach of their functions;

prolonged chronic course, which is accompanied by serious complications (erythroderma, abscesses, erysipelas, elephantiasis, granulomatous and other neoplastic processes, etc.);

the formation of mycotoxicosis;

intolerance of antibiotics due to the presence of common antigenic determinants of fungi and antibiotics that are based on molds;

the development of secondary immunodeficiency;

prolonged duration of fungal infections, when fungi contribute to the development of allergies and can induce such diseases as eczema, atopic dermatitis, asthma, vasculitis, vasomotor rhinitis, etc.

Based on WHO data for different years, fungal infections occupy the first place in the structure of registered infectious diseases.

Opportunistic fungi cause so-called opportunistic fungal infection. Their development requires serious disorders in common resistance and especially in the immune status of the organism. In recent decades, the importance of opportunistic fungi and opportunistic fungal infections that they cause has increased dramatically in the context of HIV infection.

The sources of fungal diseases infection may steam from a sick person or an animal, as well as from plants and soil. Sometimes the cause of the spread of infection is a healthy-looking person, who is classified as an asymptomatic carrier of pathogenic fungi.

Conditions and channels of infection. Basic conditions for the development of mycoses are the presence of pathogenic fungus as well as various factors that reduce the body's defense in general and the skin in particular and, thus contribute to human disease. Only a relatively small number of pathogenic fungi – the agents of dangerous fungal infections, can cause disease in humans without any additional conditions.

The reasons leading to the development of fungal diseases are conventionally divided into two groups – the exogenous and endogenous. The first basically determines physiological decrease relative to the protective function of the skin against fungal infections, while the second adversely affects the human body as a whole and reduces its resistance.

Exogenous factors are rather diverse, where the leading role is played by superficial and deep trauma. Increase of skin moisture, maceration of horny layer of epidermis associated therewith and occurrence of surface erosion reduces the resistance of epidermis and creates confortable conditions for the penetration of fungi. Abundant sweating results in disruption of physicochemical properties of the skin, in particular in reduction of its acidity.

A contributing factor in the development of fungi is a combination of excessive humidity and temperatures.

Hypothermia and hyperthermia, certain anatomical defects (plastypodia, narrowness of feet interdigital folds), peripheral blood circulation disorder (acrocyanosis, eritrocyanosis, Friedlander's disease), trophic disorders (thinning of the skin, xerosis, callosity, keratoses) play a significant role in the development of fungal infections of skin.

The dynamics of some fungal diseases is influenced by seasonal factors.

Contamination of fungal infection may be contributed by certain habits and national traditions (smearing of hair with vegetable oil, common hats).

Endogenous factors that reduce the body's defenses against infection include intercurrent diseases, especially cancers of different origin, autoimmune diseases; metabolic diseases and hormonal disorders (hypo-and disproteinemiya; impaired glucose metabolism, impaired functioning of sexual and adrenal glands, thyroid gland; hypo-and avitaminosis; dysbiosis; malnutrition; gastrointestinal tract diseases; long-term use of antibiotics, corticosteroids, immunosuppressive and cytotoxic drugs). In recent years, greater importance has been gained by primary and secondary immunodeficiencies (especially the latter, in particular HIV-infection).

A certain role in the development of fungal diseases is played by the age, gender, ethnicity, socio-economic conditions, as well as genetic predisposition of some people to infection by fungi. Children and elderly people are more susceptible to it. Scalp mycoses are mainly observed in children, while adults often suffer from fungal infections on the feet and onychomycosis.

There are two main ways of infection and spread of fungal diseases i.e. direct and indirect. *Direct infection* occurs through direct contact of a healthy person with the sick one. Indirect infection occurs more often and is performed through various items contaminated with infectious material (skin flakes, nails particles, hair etc.) containing pathogenic fungi.

The spread of fungal diseases is largely dependent on the type of agent, source of infection, clinical presentation and localization of lesions.

Direct infection occurs via the contact with lesions on the skin, in common bed, during sexual intercourse, by kissing, as well as in public baths or bath if the latter is used by both sick and healthy people.

Direct infection often occurs in people who have domestic or professional contact with sick animals, whereat the animals are not only the source of infection, but also the carriers of pathological material from sick to healthy people.

The possibility of indirect fungal infection is caused by extremely high survival of pathogenic fungi in infectious material, whereat the fungi are not only able to exist for a long time in the environment outside the body of the patient, but also, under certain conditions, are able to reproduce on different subjects.

Infection can occur in hairdressing when you have you haircut, shave, manicure etc. Schools and kindergartens are the most common sites of fungal infections of children. Infection is contributed by the accumulation of children, their close contact with each other and sharing of infected objects. In the kindergartens fungal infections, especially microsporosis, often lead to epidemic outbreaks. From school or kindergarten the infection can get into the family. Most often, patients infect linen, slippers, socks, stockings, handkerchiefs and gloves.

A laundry can also be the source of spread of fungal infections. Poor laundered, not boiled and dried linen, which preserved fungi, can cause infection of healthy people.

Significant role in the spread of fungal infections, especially fungal infection caused by *Trichophyton rubrum*, is played by the foci of infection in the family.

Pathogenesis. Fungi are members of microbiota, and therefore have the properties of both animals and plants. The relativeness of fungi with animals is conditioned by the presence of chitin in the coat and that fungi are involved in nitrogen metabolism (splits the urea) and carbohydrate metabolism (splits the glycogen). Besides, fungal cells contain cytochromes that are involved in the process of breathing. The relativeness of fungi with plants is conditioned by the mode of eating (not through the absorption of dietary components, but through their absorption via the entire wall of the fungus) and their unlimited growth in the medium.

The development of fungal diseases of skin is determined by several factors i.e. pathogenicity and virulence of the pathogen and the state of human and environmental conditions that may contribute to infection and impact the course of the disease.

Clinical manifestations of mycoses, on the one hand, are caused by the destruction of horny layer of epidermis, hair and nails due to the growth and reproduction of fungi therein, and on the other hand – by diverse degrees of inflammatory reaction in dermis.

There are three main types of direct pathogenic effects of fungi on the human body i.e. *intoxication*, *sensitization* (mycetogenic allergy) and *infection* (the development of fungal infections of skin and other organs).

Many fungi are the causes of specific sensitization of human body, which has a peculiar form of allergic disease and induces different allergic reactions. Mycetogenic sensitization can manifest by general symptoms (e.g. by the symptoms of hay fever). Almost all pathogenic fungi cause specific sensitization of the patient's organism, which is accompanied by a kind of allergic complications, including secondary allergic rash.

Classification of mycotic lesions of skin and mucous membranes

It should be noted that today there is no any classification of these lesions that could be ideal and standard for everyone. At the same time, all over the world they use different classification of mycotic lesions of skin and mucous membranes, which determine only individual aspects of clinics, microbiology and pathology of fungal infections, but none of them, can solve a complex problem of diagnostics of these diseases.

In accordance with the latest recommendations of WHO Commission on terminology of nosologic forms of diseases and their causative agents, the names of infectious diseases are primarily determined on the basis of gender of their causative agent (e.g. rubromycosis, candidiasis, malassezia etc.).

In many foreign textbooks and manuals they use the classification of mycoses, which is based on the characteristics of localization of pathological process:

- scalp mycosis – *tinea capitis*;
- smooth skin mycosis – *tinea corporis*;
- face skin mycosis – *tinea faciei*;
- beard and mustache growth site mycosis – *tinea barbae*;
- mycosis of large folds of the body – *tinea cruris*;
- feet and hand mycosis – *tinea pedis et manuum*;
- onychomycosis – *onychomycosis, tinea unguium*.

This classification is useful from a practical point of view, but it does not take into account etiological peculiarities of the agents and pathogenetic features of the process.

There is a well-known classification of Professor Arievich A.M., modified by Professor Sheklakov N.D., under which they distinguish between the following classes of mycoses:

1. *Keratomycoses*: tinea versicolor, nodular piedra, tinea-imbricata.
2. *Dermatomycoses*: jock itch, mycosis caused by rubrophytosis, trichiphytia, microsporia, favus.
3. *Candidiasis*: superficial candidiasis of skin and mucous membranes, visceral candidiasis, chronic generalized (granulomatous) candidiasis;
4. *Deep (visceral, systemic) fungal infections*: histoplasmosis, coccidioidomycosis, blastomycosis, cryptococcosis, geotrichosis, chromomycosis, rhinosporidios, aspergillosis, penicilliosis, mucormycosis.

At the same time, recent microbiological studies have demanded to highlight some of the diseases that have traditionally been considered in a group of fungal infections as a separate group of pseudomycoses (surface forms – erythrasma, inguinal trichomycosis and deep forms – actinomycosis, micromonosporosis, nocardiosis, mycetoma) for the reason that their pathogens have been allocated to the special microorganisms occupying an intermediate position between fungi and bacteria.

Some authors' inclusion of pseudomycoses (as well as the name itself) into the aforementioned classification is hardly feasible and is only a tribute to the tradition.

Also, certain changes have taken place in regard to nosological term «tines versicolor», which is recognized today as one of the many clinical forms of skin *Malassezia*.

For clinical practice, classification of disease should contain data on the pathogen, form of infection (acute or chronic), the peculiarities of pathological manifestations (clinical, morphological and pathophysiological) – systemacity, type, prevalence, depth of lesion, relation to skin appendages (hair, nails), localization and epidemiology.

Clinical classification of mycotic lesions of skin and mucous membranes

1. Keratomycoses (nodular piedra, tinea-imbricata)

2. Dermatomycoses (epidermomycoses)

2.1. Tinea pedis

2.1.1. Intertrigo form

2.1.2. Squamous form

2.1.3. Dishydrotic form

2.1.4. Acute form

2.1.5. Mixed forms

2.2. Smooth skin dermatomycoses (Tinea corporis)

2.2.1. Smooth skin microsporosis

2.2.2. Smooth skin trichomycosis

2.2.3. Rubromycosis

2.2.4. Clinical types of smooth skin mycosis

2.3. Dermatomycosis of hands (Tinea manuum)

2.3.1. Squamous (hyperkeratonic) form

2.3.2. Dishydrotic (eczematoid) form

3. *Trichomycoses*

3.1. Surface forms (scalp microsporosis, trichomycosis)

3.2. Deep forms (pustular form, infiltrative-purulent form)

3.3. Favus: surface (pustular) and deep (infiltrative) forms

4. *Onychomycoses*

4.1. Subungual onychomycosis distal-lateralis

4.2. White surface onychomycosis

4.3. Proximal subungual onychomycosis

4.4. Total dystrophic onychomycosis

5. *Candidiasis*

5.1. Skin candidiasis

5.2. Mucosal candidiasis

5.3. Chronic (granulomatous) candidiasis of skin and mucous membranes

6. *Skin Malassezia*

6.1. Surface (furfuraceous) non-inflammatory forms of Skin Malassezia

6.2. Follicular forms
6.3. Inflammatory forms
6.4. Neoplastic forms
7. Deep mycoses
7.1. Subcutaneous mycoses
7.2. Opportunistic deep mycoses
7.3 Endemic deep mycoses
7.4. Visceral and systemic mycoses
9. *Allergic and paraallergic reactions in fungal diseases*

Laboratory diagnostic methods. Clinical picture of fungal diseases of skin is very polymorphic, so in all cases, the diagnosis should be confirmed by laboratory tests.

Laboratory diagnostics of fungal infections consists of several stages. In clinical practice they usually limit themselves with microscopic and culture studies of contaminated material. If necessary, these methods are supplemented by immunological, molecular, histological studies and infection of experimental animals. In some skin mycoses an important supporting role in the diagnostics is played by luminescence method.

Immediately prior to sampling pathological material the lesion should be treated with 96% alcohol or xylene solution. It is better to take material from fresh but already fully developed lesions. Skin scales should be scraped off from the periphery of lesions. In patients with fungal infections of scalp, the hair is usually pulled with epilation forceps.

Scrapings from surface lesions of affected nail plates shall be done with scalpel, while thickened nail plates should be cut with scalpel or nail clippers; subungual hyperkeratosis material can be obtained using a dissecting needle.

Liquid pathological material is collected aseptically in a sterile container, while skin scales, nails and hair particles – to the sheets of ordinary or soft parchment paper.

Mucous discharge to inoculate is taken with absorbent cotton swab which is then placed in a dry sterile tube or a tube with 2 ml of medium. For microscopy purposes, white-grayish plaque from mucous is taken with Volkmann's spoon or a glass slide.

If necessary, pathological material is transported to the laboratory in a special container or metal boxes. Received material is tested within one hour after sampling and at room temperature storage or within not more than three hours when stored in a refrigerator at 4°C.

Keratomycoses

Keratomycoses (*keratomycosis*) is a collective term, in which modern mycology combines mycoses affecting superficial part of horny layer of skin or hair cuticle. These mycoses include nodular piedra and tinea-imbricata.

Nodular piedra (synonym: piedra – from Spanish piedra, which means «stone») is a hair cuticle disease that is accompanied by the formation of white (*piedra alba*) or black (*piedra nigra*) nodules on the hair.

Etiology and pathogenesis. The causative agent of white nodular piedra is *Trichosporon Beigellii*, while of black nodular piedra – *Trichosporon Hortai*, which belong to yeast-like fungi. The development of the disease is favored by warm climate, wash of hair with standing water, sour milk and processing with mineral oil.

Epidemiology. White nodular piedra is sporadically met in Central Asia, the Caucasus, but mostly occurs in the UK, Hungary, Spain, France, USA and Japan.

Black nodular piedra is distributed mainly in Central and South America, Africa, India, China, Burma and Thailand. The disease is hardly infectious, but in endemic areas, its outbreaks are possible. It can be transmitted via brushes and combs.

Clinical picture. Subjective feelings are absent. White nodular piedra affects scalp, hair in the beard and mustache and in the genital area. Black nodular piedra affects only hair on the head. Multiple small, but very hard nodules are formed on the hair shaft (up to 20-30 nodules on each hair). They have irregular oval spindle-shaped form and almost completely cover the hair. Sometimes they merge, forming a short, in black piedra (1-2 mm) and long, in white piedra (up to 10 mm or more) sheath consisting of tightly bonded mycelium and spores of the fungus. Hair, in nodular piedra, does not break off.

Diagnostics. The diagnostics is based on clinical picture with due account for the anamnesis and the dynamics of symptoms. In complicated cases, the diagnosis can be confirmed by microscopic and cultural studies.

Treatment. Often, there is only local treatment of white and black nodular piedra. The patients are advised to shave the affected area, apply an antiseptic (such as hot solution of mercuric chloride 1:1000-1:2000, 0.01% sublimate vinegar or 2% solution of salicylic acid). You can also assign imidazole shampoos, lotions, creams.

Tinea-imbricata (synonyms: tokel, tropical circular mycosis) is a tropical fungal infection, characterized by the appearance of small brown spots on the trunk and limbs, which are eccentrically increasing in diameter and are covered with imbricate scales accompanied by mild itching.

Etiology. The causative agent of tinea-imbicata is *Trichophyton concentricum* – an anthropophilic cutaneous fungus, which does not hit the hair.

Epidemiology. Tinea-imbricata is a typical epidermomycosis of tropical countries, especially common in areas with high humidity. Epidemic foci are concentrated in Africa, Southern India, China, Indonesia, Vietnam, Laos and the Pacific Islands.

Factors contributing to the emergence of this disease include lack of hygiene of the body, excessive moisture and related maceration and stratification of epidermis. It is especially contagious in adults. Children get sick less often. Routes of infection may be both, the direct contact with patients and household items, especially bed clothes and underwear.

Clinical picture. Tinea-imbricata is characterized by skin itching, which is particularly enhanced in hot days with excessive sweating, as well as with consumption of alcohol, salty foods and swimming in the sea water.

The process is mainly localized on the trunk, extensor surfaces of extremities, buttocks, and rarely in other parts of the body. The disease begins with the appearance on the trunk of non-inflammatory small spots of light brown color, sometimes surrounded by barely perceptible narrow inflammatory aureole. Progressively as the eccentric growth and increase in size, in the center of each spot there appears, at first, small and then more noticeable desquamation.

In fully-formed elements of rash the central zone is slightly discolored and edged with an aureole of hanging scales, which in its turn is surrounded by dusky brown ring of hyperpigmentation. In a few months after infection the patient's skin is covered with numerous round plaques having eccentrically located rings of desquamation. They are often compared to the tiles or fish scales. The process can cover large areas of the body, where only face and scalp remain intact. The spread of the disease to the feet may cause hyperkeratosis and painful cracks when walking. As a rule, there are no abnormalities in general condition of the body.

Treatment. Usually they indicate daily warm bath with further processing of lesions with a pumice stone and use of various keratolytic ointments, creams or emulsions with salicylic acid. In acute cases, azole antifungals and terbinafine, topically, within two weeks are indicated.

Prophylaxis. To prevent recurrence of the disease and reinfection it is necessary to take a complex of sanitary and anti-epidemic measures, which include personal hygiene, detection and treatment of infected people, disinfection of clothing, underwear and household items.

Dermatomycoses (epidermomycoses)

Dermatomycoses are infections of skin and its appendages caused by cutaneous fungi. *Cutaneous fungi* are a group of filamentous fungi which attack dead skin keratinocytes. Dermatomycoses are divided into: *epidermomycoses* (infection of horny layer of epidermis), *onychomycoses* (nail infections) and *trichomycoses* (hair infections).

Etiology. There are more than forty species of cutaneous fungi, ten of which cause dermatomycoses. There are three genera of cutaneous fungi i.e. *Microsporum, Trichophyton, Epidermophyton*.

Epidemiology. Depending on the relation of cutaneous fungi with environment, they are divided into *anthropophilic* (transmitted from person to person via everyday objects and in contact), *zoophilic* (transmitted from animals in contact with a person or objects in use) and *geophilic* (found in soil).

Pathogenesis. Cutaneous fungi synthesize keratinase, which allows them to break down keratin, grow and develop in dead skin keratinocytes. The resistance to cutaneous fungi is determined by the state of cellular immunity and fungicidal activity of neutrophils.

Diagnostics. Dermatomycoses should be diagnosed with due account for:

- the clinical picture;
- fluorescent diagnostic data using a Wood's lamp (in microsporosis of hair affected by *Microsporum*, which gives greenish glow);
- the results of microscopic analysis of pathological material conducted to detect fungus elements (mycelium, spores etc.);
- the isolation of causative agent in the culture with its subsequent identification on Sabouraud 's medium (glucose-peptone agar-agar).

Treatment. External(local) therapy is effective only with smooth skin lsions. In case of affecting the hair or nails, it is ineffective.

Topical products: terbinafin, ketoconazol (gel, spray, cream) miconazole (cream), clotrimazole (cream), etc.

More effective are *systemic medications* that are indicated for the treatment of dermatomycoses, trichomycoses, onychomycoses in case of large lesions, inefficiency of topical products and significant inflammatory response. Systemic medications are those that are administered in different ways in the blood system and affect lesions via blood. *Systemic products*: griseofulvinum, ketoconazol, itraconazole, terbinafine, fluconazole.

Griseofulvinum has a fungistatic activity. It is mainly used in trichomycosis, especially microsporosis. Side effects: headache, epigastric syndrome, photosensitivity, hepatotoxicity. It requires regular blood, urine tests and hepatic function control.



Fig. 7.1. Tinea pedis (intertrigo form).



Fig. 7.2. Tinea pedis (squamous-hyperkeratotic form).

Ketoconazol has a fungistatic and partially fungicidal activity. It is used in treatment of dermatomycosis, candidiasis and malassezia. Side effects: epigastric syndrome, hepatotoxicity. It requires regular hepatic function control.

Itraconazole has a fungistatic and fungicidal action. It is used to treat dermatomycosis, candidiasis, malassezia, any cause of onychomycosis and deep mycoses. Side effects: epigastric syndrome, increased levels of hepatic enzymes.

Terbinafine has a fungistatic and fungicidal action. Amongst all systemic antifungals, it is the most effective against cutaneous fungi. Side effects: epigastric syndrome, aplastic anemia.

Fluconazole has a fungistatic and fungicidal action. It is used to treat superficial and deep candidiasis, cryptococcosis and tinea versicolor.

Tinea pedis is a chronic fungal infection of feet caused by cutaneous fungi.

Etiology. The agents of tinea pedis are: *Trichophyton rubrum, Trichophyton mentagraphytes, and Epidermophyton floccosum*. There is possible superinfection by yeast-like and mold fungi, to include staphylococcus microbiota.

Classification. Tinea pedis can be of intertrigo, squamous, dishydrotic, acute and mixed forms.

Clinical picture. *Intertrigo form* is manifested by maceration, desquamation, peeling of epidermis, cracks, erythema in the fourth, rarely in the third interdigital fold. In case of acute course of the disease it is often accompanied by bacterial (Gram-negative) flora with unpleasant odors.

Squamous form is characterized by well-demarcated erythema, mucous desquamation, keratinization first on the soles, in the interdigital folds, then on the lateral surfaces of feet and toes. With the affection of rear side of foot the lesions are outlined by typical inflammatory demarcated scalloped shape border. By moccasin type, the affection of feet can be integral.

Hyperkeratotic form is manifested by dense hyperkeratotic layers resembling corns.

Dishydrotic form is characterized by rash of vesicles and blisters on the instep that contain clear fluid and accompanied by itching. There is possible bacterial infection with formation of pustules. The course of the disease is not stable and is characterized by exacerbations in spring and autumn.

Acute form is manifested by erythema, edema, maceration, the formation of vesicles and blisters with considerable desquamation, erosion and



Fig. 7.3. Tinea pedis (dishydrotic form).

ulceration. Accession of a secondary infection may cause deterioration of health and fever, impetigo, lymphangitis, lymphadenitis, odor, itching and pain.

Differential diagnostics. Interdigital candidiasis is different from intertrigo tinea pedis by the appearance of bright red erosion with macerated whitish horny layer on the edges, often joined by candida onychia and paronychia. Squamous form of tinea pedis should be differentiated from psoriasis, tyioticum eczema, neurodermatitis, while dishydrotic and acute forms from impetigo, allergic contact dermatitis and dishydrotic eczema.

Treatment. Systemic therapy is prescribed for common forms, lack of effectiveness of external medications in dishydrotic and acute forms along with hyposensitizing drugs and antihistamines. Usually they prescribe itraconazole and terbinafine.

In acute inflammatory forms, external therapy involves, first, foot bath or lotion with aniline dyes, creams with antifungals in conjunction with antibiotics or corticosteroids, after remission of acute events – combined anti-inflammatory, anti-fungal, anti-bacterial creams (Lorinden, Oxycortum, Pimafucin, Pimafucort etc.).

In squamous forms it is recommended to apply creams and ointments with anti-fungal agents for two to four weeks.

In hyperkeratotic form first they usually prescribed dressings with creams or ointments containing antimycotics and keratolytics, and then – antifungal ointments and creams.

Prophylaxis. *Primary prophylaxis* is the use of individual rubber footwear during visits to public baths and pools, after which you should wash your feet with Myramistinum or Benzoyl peroxide solution. *Secondary prophylaxis* involves washing and treatment of feet with Myramistinum or Benzoyl peroxide solution, the use of antifungal creams, powders, boiling of cotton socks and disinfection of footwear with 20% formalin solution.

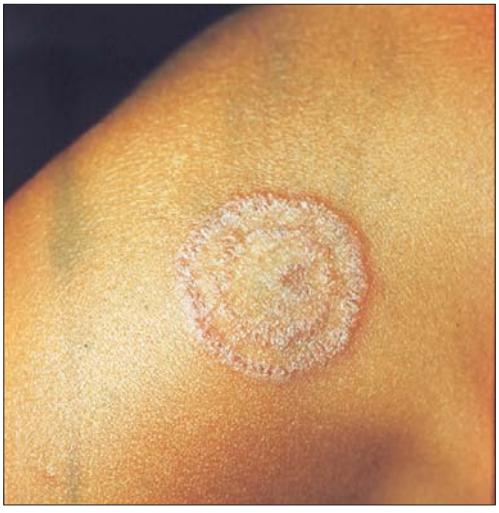


Fig. 7.4. Smooth skin microsporosis.



Fig. 7.5. Smooth skin trichomycosis.

Smooth skin dermatomycoses is a nosological concept that combines the affection of any part of the body, including rear sides of hands and feet, except for the soles, palms, scalp and axilla.

Etiology. The causative agents of smooth skin dermatomycoses are: *Trichophyton rubrum, Microsporum canis, Epidermophyton floccosum, Trichophyton mentagrophytes, Microsporum audouinii*.

Clinical picture. Clinical picture of smooth skin dermatomycoses depends on the type of pathogen.

Smooth skin microsporosis. On private parts of the body there are small lesions in the form of medallions with minor inflammatory phenomena, papules and vesicles, possible peripheral «ring in the ring» growth.

Smooth skin trichomycosis. In open areas of skin that are prone to friction and trauma, there appear annular lesions with clear margins and inflammatory border at the periphery, typical desquamation and hyperpigmentation in the center. If chronic, the clarity of foci is often lost. Trichomycosis and microsporosis are often combined with scalp affection.

Smooth skin rubromycosis is the most common form, naturally combined with feet rubromycosis and onychomycosis, and least with rubromycosis of folds and palms. There can be any localization of lesions; it is asymmetrical; often the disease begins on large folds, palms and soles. It is characterized by peripheral growth and fusion centers with the emergence of coherent site of moderate erythema and desquamation with general scalloped border.

Clinical types of smooth skin mycosis are: classic ringed with flaking and medallions; psoriasiform; verrucous; deep infiltrative dermatomycosis caused by zoophilic and geophilic fungi.



Fig. 7.6. Palm rubromycosis.



Fig. 7.7. Inguinofemoral rubromycosis.

Differential diagnostics. Differential diagnostics of smooth skin dermatomycosis is conducted with:

- seborrheic dermatitis, which in contrast to smooth skin dermatomycosis, is localized on the scalp, face, seborrheic areas in the form of low inflammatory yellowish-pink spots with fuzzy boundaries, and is accompanied by itching;
- contact dermatitis, differing by the appearance of erythema after the exposure to irritants obligate, edema, vesicles, cracks, erosion, and then followed by lichenification, excoriation, burning;
- psoriasis, which is characterized by skin lesions in different locations and the appearance of bright red papules, with silvery white scaly lesions on the surface, clear boundaries, a characteristic symmetrical peripheral location, merging of elements, and observation of three psoriatic phenomenon when scraping;
- limited neurodermatitis, which is characterized by the appearance of lichenification on the skin, flat papules on the periphery, hyperpigmentation, lack of vesicles and oozing and significant itching;
- white lichen manifested by confluent pale pink spots of irregular shape, with small scales on the surface and a slight itching;
- microbial eczema, which, unlike smooth skin dermatomycosis, is characterized by the appearance of round-shaped foci with sharp edges of different localization and size, slight oozing, exudation on the background of erythema and purulent crusts on the surface.

Treatment. Systemic antifungal therapy with Terbinafine or Itraconazole is assigned in common forms, in case of relapses and lack of effective local therapy. External treatment is carried out by means of creams and ointments with an antifungal action

Prophylaxis. Prophylaxis includes examination of organized children's groups and control of household contacts during six weeks, treatment of fungal infections and prevention from contact with people and animals sick for mycosis.

Hands dermatomycoses is fungal affection of palms caused by cutaneous fungi.

Etiology. The causative agents of hands dermatomycoses are: *Trichophyton rubrum, Microsporum mentagraphytes, Epidermophyton floccosum*.

Clinical picture. There are *squamous* (hyperkeratotic) and *dishydrotic* (eczematous) forms of hands dermatomycoses. In *squamous form* the skin on palms becomes yellowish-red with desquamation more pronounced in areas of folds; appears hyperkeratosis, sometimes – cracks, pain, itching. In *dishydrotic form*, you may observe erythema, microvesicles, itching, burning.

Differential diagnostics. In comparison with hands dermatomycosis:

- contact dermatitis is characterized by the appearance of erythema, edema, vesicles and cracks after the exposure to irritants obligate;
- palms psoriasis is characterized by hyperkeratosis, slight inflammation of skin around the periphery, bright red papules or pustules and nail infections;

- limited neurodermatitis is characterized by the appearance of lichenification, hyperpigmentation, flat papules and itching;
- dishydrotic eczema is characterized by a symmetrical process of vesicle deep in the skin filled with clear liquid and itching.

Treatment. Is similar to the treatment of tinea pedis.

Prophylaxis. Is similar to the prophylaxis of tinea pedis.

Trichomycoses

Trichomycoses are diseases that occur when hair is affected by cutaneous fungi. Depending on the location there are scalp and beard and mustache mycoses.

Etiology. The causative agents of trichomycoses are: *Microsporum canis, Microsporum ferrogineum, Microsporum aundouinii, Trichophyton violaceum, Trichophyton verrucosum, Trichophyton Shoenleinii*.

Clinical picture. Clinical features of trichomycosis depend on the type of pathogen and the depth of penetration of pathological process.

1. Surface forms of trichomycoses:

a) *scalp microsporosis* is characterized by the appearance of one or more lesions with clearly defined boundaries between 2 and 5 cm in diameter; smaller "drops" between 1 and 2 cm in diameter on the periphery; the hair on the site of lesions is broken off at the one and the same level i.e. above the surface of the skin for 4-6 mm; the skin is reddened, covered with grayish small scales. There is possible exudation with crusts, pustules and itching,

b) *scalp trichomycosis* manifests in the appearance of multiple isolated foci of up to 2 cm in diameter, with clear boundaries of irregular shape; the affected hair breaks off at a height of 2-3 mm above the surface of the skin; hair fragments are bent like a hook. Sometimes, hair is broken at the skin level, where it remains «stubs» or «black spots». Vesicles, crusts, pustules can be observed in the lesions. In chronic



Fig. 7.8. Scalp microsporosis.

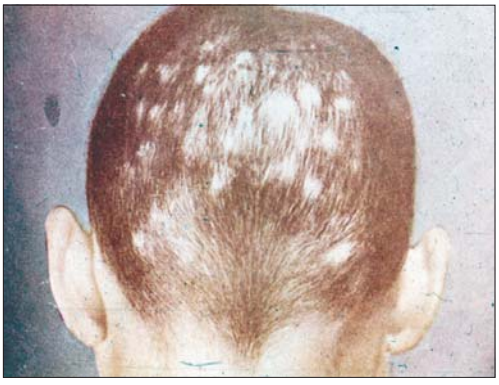


Fig. 7.9. Scalp trichomycosis.

trichomycosis adults may have focal or diffuse unobtrusive scaling, small atrophic lesions and «black spots»;

c) *favus (scald head)* causes the formation of a red spot on scalp skin , followed by the appearance of papules. In the center of papules there appears yellow pustule, which forms a skutula (fungal colony) in the form of a dry saucer-shaped dirty gray or yellow crust of 1-3 cm in diameter. Hair in the lesion become ash-gray, it is easily pulled out and does not break off. Later, the lesion is covered with solid crust, which has an unpleasant «mouse» odor. After skutula rejection, there is a scarring alopecia on its place. There are also atypical forms of favus without skutuls i.e. squamous and impetiginous.

2. Deep forms of trichomycoses:

a) *surface (pustular) form* is manifested by the presence of folliculitis, pus, crusts, which coalesce to form plaques (barber's itch);

b) *deeper (infiltrative-purulent) form* occurs on the scalp or on the face in beard, mustache, eyebrows areas; it is characterized by the appearance of pustules and formation of kerion – a painful purple-bluish infiltrative node of 6-8 cm in diameter. The kerion has a rounded shape, clear boundaries and bumpy surface. Then the node softens, yellow pus (a symptom of honeycomb) releases when pushing the hole, the hair is easily removed, it drops out and alopecia begins. The disease may be accompanied by such common conditions as fatigue, fever, malaise, headache and regional lymphadenitis. Dermatomykida appear in the form of patches, papules, eczematids, erythema nodosum.

Differential diagnostics. Unlike trichomycoses:

- staphylococcal impetigo is manifested by follicular pustules up to 5 mm, with hyperemia aureole or crusted papulo-pustules;
- abscess is characterized by the emergence of red unclearly-defined foci of irregular shape with tight edema, skin infiltration, hemorrhagic purulent exudate, pain, common symptoms of intoxication;



Fig. 7.10. Favus.



Fig. 7.11. Infiltrative and purulent (deep) form of trichomycosis.

- a boil arises where there is the hair shaft, around which there is a bright red infiltrate with tight-elastic consistency without clear boundaries, swelling, pain; then there is a softening that releases purulent-necrotic core that is removed together with a pus after breaking through; after regression boils remain scars;
- carbuncle, in contrast to deep forms of trichomycosis, is manifested by tight and painful infiltration with pustules and boils, followed by ulcers with uneven bottom and undermined edges, which then remain a scar;
- seborrheic dermatitis and malassezia eczematids differ from surface trichomycoses by inflammatory yellowish-pink spots on the face, scalp, in the folds and seborrheic areas, blurred focus, greasy scales, itching;
- psoriasis is characterized by skin lesions in different locations, especially scalp and nails, the appearance of bright red papules, with silvery white scaly lesions on the surface, clear boundaries and observation of three psoriatic phenomenon when scraping;
- limited neurodermatitis differs from surface trichomycosis by the appearance of lichenification on the skin, flat papules, hyperpigmentation and itching;
- alopecia areata is a hair loss that occurs for no apparent reason, without inflammatory changes in the skin, lesions are round, total baldness is possible and the hair is easily pulled out;
- vulgar (staphylococcal) sycosis occurs in men and is characterized by the formation of multiple drain folliculitis on the face in the beard and mustache areas on the background of erythema and edema, and chronic course.

Treatment. Systemic antifungals such as terbinafine, ketoconazole, griseofulvinum are applied. Locally, ointments and creams with antifungals are prescribed. In case of layering of a staph infection they use local combined antibacterial agents, while in severe course – systemic antibiotics or GCS. In case of kerion formation, it is recommended to make applications with antiseptics and remove hair manually.

Prophylaxis. Prophylactic methods include investigation of collective and household contacts during six weeks and washing head with ketoconazol shampoo.

Onichomycoses

Onichomycoses are infectious multifactorial diseases of nails, the causative agents of which are cutaneous, mold and yeast-like fungi.

Etiology. In the majority of cases onichomycoses are caused by antropophilic fungi: *Trichophyton rubrum, Trichophyton mentagraphytes, Trichophyton violaceum, Epidermophyton floccosum, Candida and zoofilnymi fungi Trichophyton verrucosum*.

Clinical picture. Depending on the localization of pathological process there are:

a) *subungual onychomycosis distal-lateralis* – on the free or side edge of nails of the first and fifth toes there appears a white spot, which soon becomes black, nail

plate loses its transparency and becomes thinner, can be separated from the nail bed, crack and crumble;

b) *white surface onichomycosis* – in the proximal part of the nail plate of the toes there appears a milky-white spot, which is growing and can take the entire area of the nail, leading to its destruction; the affected part is easily removed with a curette, the disease may be associated with subungual onichomycosis distal-lateralis;

c) *proximal subungual onichomycosis* – under rear nail fold of the toes there appears a white spot that extends distally;

g) *total dystrophic onichomycosis* is observed in case of loss of connection between a nail and its bed.

Differential diagnostics. Unlike onichomycosis:

- nail psoriasis is characterized by dotted deepening (a "thimble" symptom), loosening and thickening of nails, onichogriphosis, subungual hyperkeratosis and other psoriatic symptoms on the skin;
- trauma is manifested by nail changes resulting from subungual haematoma, nail destruction and affection of soft tissues;
- candidial onychia and paronychia are manifested by inflammation of nail folds, pus, change of a nail on the fixed edge, pigmentation, destruction, cracks, hyperkeratosis and are to be confirmed by laboratory microbiological tests.

Treatment. *Systemic therapy* includes application of Griseofulvinum during 4–12 months in hands onichomycosis and during 12–18 months in feet onichomycosis; of Itraconazole – during 2 months and 3 months respectively (by way of pulse-therapy courses); of Terbinafine – during 1,5 months and 3 months respectively and of Fluconazole – during 4–6 months and 6–12 months. *External therapy* is performed by smearing nails with 5% of iodine solution and topical antifungal preparations.

Prophylaxis. It is necessary to keep hygiene of nails and hands and feet skin, especially when staying in the area abundant for fungi (in the swimming pools, sauna,



Fig. 7.12. Onichomycosis.



Fig. 7.13. Onichomycosis.

public shower rooms, on the beaches etc.). Also it is necessary to disinfect footwear with 25% of formaldehyde solution. It is recommended to wear antifungal socks.

Candidiasis

Candidiasis is a group of infections of skin, its appendages and mucous membranes caused by fungi of Candida genus.

Etiology. The main causative agent of candidiasis is *Candida albicans*, seldom – *C. tropicalis, C. parapsilosis, C. glabrata* etc. These belong to normal flora of oropharynx, gastrointestinal tract and vaginal area. They are yeast-like fungi that reproduce by budding and form pseudomycelium. *Candida* quickly grows on nutrient media, and after 48 hours, forms characteristic colonies.

Epidemiology. Exogenous candidiasis is rare. Candidiasis is primarily an endogenous infection. Due to unfortunate circumstances, own Candida goes into a pathological condition and cause candidiasis. Such risk factors include age, endocrine pathology (especially diabetes), impaired immunity, HIV infection, tuberculosis, prolonged use of corticosteroids, cytotoxic agents, anti-metabolites, immunosuppressants, oral intake of broad-spectrum antibiotics, especially without medical supervision**.**

Classification. Candidiasis is classified as follows.

1. *Skin candidiasis*: interdigital candidiasis; large folds candidiasis, small folds candidiasis, Candida folliculitis, diaper dermatitis, bandage dermatitis, candidiasis of nails and nail borders, paronychia and onychia, chronic candidiasis.

2. *Mucosal candidiasis*: a superficial mucosal candidiasis (stomatitis, glossitis, sore throat, thrush, atrophic candidiasis, candida leukoplakia, angular fissure), genital candidiasis (balanitis, balanoposthitis, vulvitis, vulvovaginitis), deep mucosal candidiasis (esophagitis, tracheitis, bronchitis, cystitis).

3. *Chronic (granulomatous) candidiasis of skin and mucous membranes*.



Fig. 7.14. Skin folds candidiasis.

Skin candidiasis is clinically divided into:

1. *Candidiasis of folds*. First appear erythema and phlyctena. Then on the place of phlyctena appears pink-red erosion, oozing, fusion followed by formation of a locus with scalloped edges, the periphery of which is covered with small «subsidiary» phlyctena. Patients complain of itching and burning.

2. *Intertrigo candidiasis* occurs in the interdigital skin folds of feet and hands in those who are in frequent contact with

the water. First appear phlyctena, on the places of which there is erosion and cracks, oozing. Then, there appear lesions covered with white bloom with a border of exfoliating epidermis. It is often associated with Candida paronychia and onychia.

3. *Diaper dermatitis* occurs in children in the buttocks, perineum and inguinal folds and on the inner thigh. It is manifested in the form of erythema, swelling, phlyctena, papules, erosions, oozing and lesions with peeling epidermis.

4. *Bandage candidiasis* occurs under occlusive plaster cast or in bedridden patients on the skin of a back or buttocks. It is manifested by erythema, edema, phlyctena, papules, erosion, ulceration, oozing.

5. *Candidiasis folliculitis* occurs in the same places as bandage candidiasis, and is characterized by the appearance of small papules delineated near the hair follicles.

6. *Candida paronychia and onychia* is typical of women – housewives, laundresses, dishwashers, waitresses etc. Initially, near the nails, there appears erythema, swelling of the skin around nail borders. When pressed, creamlike pus is released, palpation is painful. One may observe degeneration of the nail plate, discoloration and onycholysis.

Diagnostics. It is necessary to carry out a microscopy of pathological material after it being treated with alkali or the investigation of native or Gram stained preparation on the subject of finding both *Candida* cells and kidney cells and the presence of pseudomycelium, also they count CFU (colony forming units). To identify *Candida* species and enzyme activity it is necessary to carry out an inoculation on Sanuro medium or wort agar.

Differential diagnostics. Differential diagnostics should be performed with:

- seborrheic dermatitis and malassezious eczematid in which there are areas of inflammatory patches of yellowish color with fuzzy boundaries, in the folds and seborrheic areas, fat scales and itching;
- psoriasis, which in contrast to candidiasis, is characterized by skin lesions of various locations, the emergence of bright red papules with a silvery-white scales



Fig. 7.15. Candida paronychia.



Fig. 7.16. Intertrigo candidiasis.

on the surface, characterized by clear lines, with the observation of three psoriatic phenomenon when scraping;

- dermatomycosis that differs by spots with clear boundaries, desquamation on the surface with peripheral growth, a fold with papules and vesicles on the edge, positive for cutaneous fungi;
- simple contact dermatitis occurs after exposure to obligate irritants and is characterized by the appearance in the impact place of erythema, swelling, vesicles, erosions, oozing, subjectively felt burning sensation;
- staphylococcal folliculitis is characterized by inflammation of the follicles with the appearance of purulent crusts and hair in the center;
- staphylococcal felon has a more pronounced inflammatory reaction, erythema, pain, pus;
- onichomycosis, unlike Candida onychia and paronychia, is characterized by nail infections on the free edge without inflammation of the nail fold, subungual hyperkeratosis, nail destruction and positive tests for cutaneous fungi.

Treatment. First, you need to pay attention to trigger factors (diabetes, immunodeficiency, chronic infection, vitamin deficiency, metabolic disorders, receiving of corticosteroids, cytotoxic drugs, antibiotics etc.).

General therapy involves administration of itraconazole 200 mg per day for 3-7 days, fluconazole – 150 mg per day for 1-3 days, in case of torpid process – 150 mg per day once a week for 2-3 weeks. Also they assign restorative drugs, immunomodulators and vitamins.

Topically they use 1-2% solution of methylene blue or 1% brilliant green, fucorcinum; creams with nystatinum and its derivatives. Smear the lesions until they completely disappear and then apply the cream for another week.

Prophylaxis. Preventive measures are aimed at keeping skin clean and dry. The folds should be daily treated with talc containing miconazole. In case of prolonged use of antibiotics and corticosteroids it is recommended to go through the preventive course of 150 mg of fluconazole per day once a week.

Mucosal candidiasis. The given pathology is clinically divided into:

1. *Superficial mucosal candidiasis* (stomatitis, glossitis, sore throat, thrush, atrophic candidiasis, candida leukoplakia, angular fissure):

- stomatitis, glossitis, pharyngitis and thrush are located on the tongue, buccal mucous and are manifested by the appearance of multiple white plaques 1-2 mm in size on an erythematous background, which are easily removed with dry gauze;
- in atrophic candidiasis there are smooth red lesions of atrophy;
- candida leukoplakia is characterized by dense white plaques, which are difficult to remove;
- with angular fissures, the corners of the mouth are covered with erythema, cracks, white coating, and pain.

2. *Genital candidiasis* (balanitis, balanoposthitis, vulvitis, vulvovaginitis)

- vaginitis and vulvovaginitis are characterized by hyperemia, swelling of mucous membrane of the vagina and cervix, white cheesy discharge, itching and burning, pain, exacerbation of these effects before menstruation;
- with balanitis and balanopostitis, first the glans penis and foreskin are covered with erythema, papules, phlyctena, then they are followed by erosion, pain, burning, swelling, cracks.

3. *Deep mucosal candidiasis* (esophagitis, tracheitis, bronchitis, cystitis).

Diagnostics. The diagnostics is similar to the one for skin candidiasis.

Differential diagnostics. Differential diagnostics should be conducted with:

- leukoplakia, which is characterized by the appearance of one or more sites of a whitish-gray color of different shapes and sizes without significant inflammation, sometimes joined by papillomatosis, hyperkeratosis, erosions and ulcers;
- lichen planus, which in the mucous manifests itself by the fusion of white (pearl) papules, Wickham's net and umbilical impression in the center of papules (if located on the skin), the formation of arcs, rings, waves in the form of a fern leaf (if located on the buccal mucosa);
- secondary syphilis, which unlike candidiasis, is characterized by patches of red circular shape with a smooth surface and sharp edges, and the pea size papules of red color with bluish tint, painless, dense, smooth surface, eventually becoming opal-white; sometimes there are erosions and ulcers; serological reactions are positive; manifestation of secondary syphilis are observed on the skin;
- other, primarily sexually transmitted infections, are sometimes similar to candidiasis, but do not have the typical clinical presentation, thus laboratory tests are required.

Treatment. *General therapy* involves the use of Fluconazole, Ketoconazole, Itraconazole, Pimafucin.



Fig. 7.17. Chronic candidiasis.

Externally it is recommended to apply as follows:

a) in glossitis, stomatitis, pharyngitis – nystatinum or clotrimazole in lozenges;

b) with angular fissure – 1.2% alcoholic solution of methylene blue or on a pre-dried surface;

c) with vaginitis, vulvovagintis – vaginal tablets Tergynan (to enter 1 tablet deep into the vagina at bedtime for 10 days) or vaginal capsules Lomexin (1 capsule at night inside the vagina for 3-6 days); clotrimazole are applied by softly rubbing or smearing the skin and genital mucous 1-2 times a day for 6-12 days.

Chronic (granulomatous) candidiasis of skin and mucous membranes. Clinically this disease is characterized by lesions of erythema with marked infiltration and hyperkeratosis, vegetations (called granulomas) tended to increase and then group. Often this disease affects children. In the mouth, there are widespread erythema with infiltration, erosion and angular fissures. One may observe paronychia, affection of palms. In some patients, such candidiasis is associated with HIV infection, immunodeficiency.

Treatment. *General treatment* includes the use of fluconazole, itraconazole.

Skin Malassezia

Skin Malsssezia (*malasseziosis cutis*) is a disease of skin and its appendages, which is caused by yeast-like lipophilic fungi of *Malassezia* genus.

Etiopathogenesis. According to the decision of the International Committee on Taxonomy of Fungi *Malassezia* genus is one of the fifteen genera of yeasts-like fungi that make up *Cryptococcaceae* family, which is part of a group of imperfect yeasts and refers to an anamorphic basidiomycetes.

The main factors of skin malassezia pathogenesis are disorders in proliferation and differentiation of epithelial cells; changes in the chemistry and physical properties of sebum; metabolic disorders (such as melanin disorder) caused by the impact of metabolic products of the fungus on to the host cells; immune disorders; inflammation and development of sensitization.

The source and the transmitter of the infection can be people, animals and plants. The spread of some forms of skin malassezia depends on the age, sex, profession etc.

Clinical picture. There is a diversity of clinical manifestations of skin malassezia, which is caused not so much by the kind of fungus, as by the patient's organism reactions (degrees and types of reactivity) that vary in a wide range – from asymptomatic carriage to systemic manifestations of infection.

Skin malassezia in patients is manifested not only as one nosology entity, but as a combination of two, three or even four entities.

Clinical forms of skin malassezia:

a) surface (scaly) non-inflammatory:

- Daria's Kerosis is a common hypertrophy of horny layer with a trend towards slight desquamation, coloring of skin into dirty yellow, dark brown or grayish color, openings of sebaceous glands pores (skin glands mouths' keratosis) and changes in the chemistry of sebum;



Fig. 7.18. Tinea versicolor (Balzer's test).

- simple common and limited pityriasis of trunk and limbs skin – unclearly delineated areas of defurfuration of non-inflammatory trunk and limbs skin with several layers of white or yellowish, dry or greasy scales or without them;
- simple pityriasis capitis of newborns (gneiss) and adults (dandruff) – unclearly delineated defurfuration of non-inflammatory areas of scalp, with several layers of white or yellowish, dry or greasy scales or without them;

b) follicular:

- comedones («black spots») are the formation of sebaceous plugs in the hair follicle consisting of fat and horny scales and have the form of black point;
- non-purulent malassezious folliculitis of trunk and limbs skin – a chronic dermatosis, which is manifested by small follicular inflammatory papules with pike-shaped scales on the surface etc.;

c) inflammatory (inflammatory and allergic)

- tinea versicolor – a dermatitis, which is characterized by the appearance on the skin of neck, torso and shoulders of slightly scaly spots of pink or yellowish-brown color;
- pitiriasiformis malassezia of smooth skin and scalp (pitiriasiformis Daria's eczematid of smooth skin) – clearly defined, red or reddish-yellow spots with scaly surface different in size, dry or fatty, circular or often ring-shaped;
- seborrheic dermatitis of scalp, trunk and extremities – chronic dermatitis, which is localized in seborrheic areas and is characterized by clearly defined common inflammation lesions, the surface of which is covered with fatty yellowish scales, also exudation phenomenon is observed;

d) neoplastic:

- confluent and reticulated papillomatosis – a dermatosis that is characterized by the appearance in the chest, epigastric and interscapular areas, as well as on the back of the hands, of small red quickly darkening and coarsen papules that coalesce into diamond-shaped lesions;
- granulomatous skin malassezia – an erythematous, with plaque and nodular granulomatous infiltrate of the walnut size with rough weeping pus, often vegetating surface or ulcers covered with thick scales, crusts.

Skin malassezia triggers the appearance of acne, eczema or complicates the course of other skin diseases (psoriasis, rosacea, atopic dermatitis etc.).

Diagnostics. The diagnostics is based on clinical picture, anamnesis and determination of pseudomycelium and yeast-like form of fungus in *uncoated, potassium alkali cleared or methylene blue-stained preparations*.

If you carry out fluorescent diagnostics of colored lichen, when viewing the smooth skin and scalp lesions via the light of Wood's lamp, you'll observe golden-yellow, yellow-brown or brown glow, which is considered to be typical (if the patient has thoroughly washed before the test, the results of this study may be falsely negative).

Baltzer's iodine test is used to determine latent desquamation when diagnosing pityriasis (tinea) versicolor – the spots are smeared with 2-5% alcohol solution of iodine; due to loosening of horny layer, the solution within rash areas is absorbed intensively and the spot becomes more contrast than the surrounding healthy skin. It should be noted that with leukoderma, which remains after tines versicolor, Baltzer'a test is negative, especially in persons, who were exposed to UV radiation. This test is also positive in Fox's impetigo.

Differential diagnostics. Unlike skin mallasezia:

- ichthyosis simplex is a chronic long proceeding dermatosis; at first there appears dryness, desquamation on the skin; soon it increases forming thin white scales across the surface;
- dry streptococcal impetigo is characterized by the appearance of pale pink irregular shaped spots with fine scales on the face, upper extremities, trunk, mainly in children and women;
- Devergie's lichen is a hereditary dermatosis, which is characterized by the appearance of pointed conical red papules around the follicle with a whitish-gray scales, which coalesce and form a generalized rash (erythroderma); one may observe "grater" syndrome and hyperkeratosis on the palms and soles; nails and har change;
- contact dermatitis caused by tar and oils occur in the event of prolonged exposure of the skin to these stimuli; the latter becomes dry with slight desquamation; first appears follicular hyperkeratosis and then it is followed by purulent folliculitis;
- at toxicoderma, after taking some medication, on the 7-10 day there appears itching and polymorphic rash prone to mergers; in 10-14 days all symptoms disappear even without treatment;
- lichenoid tuberculosis is characterized by the appearance of small papules on the trunk up to millet grain round and yellowish-brown in color; they are disseminated, sometimes grouped, with scales; other manifestations of tuberculosis are also important, thus additional tests are recommended;
- small-papular syphilid causes the appearance of small brown-red round or conical shape papules on the skin near the mouths of hair follicles; the surface is covered with scales or horny spikes, "grater" syndrome is observed; serological tests are positive, other manifestations of syphilis are present;
- bacterial folliculitis begins with genital inflammatory follicular pustules, in the center of which there is a hair, around – pink-red aureole and infiltrate in the recess, the affected area is painful; then a pustule dries up, purulent-hemorrhagic crust appears and pigmentation takes place;
- acne vulgaris – first they appear in the form of comedones on the face, back, then there is inflammation and the formation of papules; pus accumulates, results in formation of acne that breaks up and forms a crust, which is followed by the appearance of atrophic scar; acne vulgaris is typical of puberty;

- candidosis begins with the appearance of erythema, then phlyctena, erosion with scalloped edges, subsidiary pustules mainly in the folds; tests for *Candida* fungi are positive;
- Unna disease means the appearance on the scalp, the face, seborrheic areas of pale pink spots with yellow tint without clear boundaries of any size that fuse and greasy scales appear on their surface; the patient feels itching;
- Gibert's disease is characterized by the appearance of pink «mother» spot followed by pink spots of various sizes on the body that are not merged and have clear boundaries; first spots resemble crumpled paper then desquamation and itching start;
- psoriasis is characterized by skin lesions at various sites, especially the scalp, nails, the appearance of bright red papules with clear boundaries and silvery-white scales on the surface;
- vitiligo is characterized by the appearance of depigmented patches of various sizes and configurations in any area, often confluent, with bloodshot aureole; subjective feelings do not arise;
- dermatomycosis appears in the form of inflammatory patches of different sizes of round shape with sharp edges and desquamation on the surface, as well as with peripheral growth; a fold with papules on the edge; fungi tests are positive;
- atopic dermatitis is characterized by the appearance on the trunk, limbs and in the folds of lichenified and infiltrated areas of the skin that are merged; there are also small flat shiny papules, hyperpigmentation and hemorrhagic crusts;

The course and prognosis. Skin malassezia runs chronically, with relapses and stage-based transformations. The prognosis if favorable provided that the treatment is done properly and timely. But it is difficult to prevent re-infection via carriers or infected household items. Some forms of skin mallasezia are contraindications for certain types of professional activities.

Treatment. It is important to consider together all manifestations of skin malassezia and the nature of concurrent diseases in each patient, as well as their characteristics, since different forms of malassezia require different methods of treatment and may worsen or become complicated in case of irrational therapy.

Combination therapy:

- systemic antifungal therapy – oral intake of azole antifungals (fluconazole or topical causal treatment (application of selenium disulphide preparations to damp skin and hair daily for 10-14 days and then a cream, lotion or shampoo with other antifungal ketokonazole azoles once a week).

Prophylaxis. To prevent the relapse and re-infection, it is necessary to take a complex of sanitary-antiepidemic measures, which include: identification and treatment of infected people, disinfection of clothing, linens and household items.

Deep mycoses

Deep mycoses include subcutaneous mycoses, opportunistic and endemic deep mycoses. *Subcutaneous mycoses* affect dermis, deep muscle tissue and sometimes bones. Infection is caused by skin injury and penetration of a causative agent contained in soils and plants therein. This is the way how chromomycosis, sporotrichosis, eumycetoma and other disease appear. *Opportunistic deep mycoses* are infectious diseases caused by opportunistic fungi on the background of severe immunodeficiency. They affect visceral organs and deep tissues. Their causative agents are quite common soil fungi that infect humans by spores that enter the body via medical instruments during blood transfusion or via contamination of wounds and dressings. A part of opportunistic fungal infections are AIDS-associated infections (cryptococcosis, candidiasis, aspergillosis etc.). *Deep endemic mycoses* (respiratory) are caused by dimorphic fungi, which parasitize in the soil of certain geographic regions. These mycoses are represented by histoplasmosis, blastomycosis, coccidioidomycosis, endemic penecilliosos and manifest as an acute pneumonia with abortive course. Causative agents of these diseases do not transmit from person to person, but infection is poaaible via work with a particular culture.

The most spread deep fungal diseases are: chromomycosis, sporotrichosis, eumycetoma and pseudomycosis (actinomycosis).

1. The causative agent of tinea versicolor is:

A. *Microsporum* genus fungi
B. *Trychophyton* genus fungi
C. *Malassezia (Pityrosporum*) genus fungi
D. *Candida* genus fungi
E. *Rhodotorula* genus fungi

2. When viewing skin lesions of tines versicolor via Wood's lamp their color is:

A. Bright green
B. Golden yellow
C. Dark blue
D. Violet
E. White

3. Which of the below stated disease is real mycosis?

A. Mycosis fungoidea
B. Trichomycosis axillaris
C. Actinomycosis
D. Erythrasma
E. Candidiasis

4. Which of the below stated preparations is not an antimycotic agent meant for local therapy of mycoses?

A. Ketoconazole
B. Metronidazolum
C. Clotrimazole
D. Sulfur ointment
E. Nystatinum

5. Which of the below stated disinfection matters is reasonable to use against mycoses?

A. Ethyl alcohol
B. Formalin
C. Medicinal soap
D. Benzyl benzoate
E. Paracetamol

6. To conduct mycological test for cutaneous fungi they use inoculation for:

A. Sabouraud's medium
B. Peptone water
C. Muller broth
D. Price's medium
E. Bordet-Gengou potato blood agar-agar

7. The causative agent of actinomycosis is:

A. *Microsporum audouinii*
B. *Trichophyton mentagrophytes*
C. *Epidermophyton floccosum*
D. *Actinimyces bovis*
E. *Malassezia pachydermatis*

8. Which of the below stated do not belong to clinical forms of onichomycosis?

A. Subungual distal-laterallis
B. Interdigital
C. White surface
D. Proximal subungual
E. Total dystrophic

9. Which of the below stated is not a highly contagious infection?

A. Rhinosporidiosis
B. North American blastomycosis
C. Histoplasmosis
D. Coccidioidomycosis
E. Rubromycosis

10. Which of the below stated is typical of scalp trichomycosis?

A. In place of the lesions all hair is broken off at a height of 4-6 mm from the skin surface
B. The hair is broken off at a height of 2-3 mm from the skin surface; also there are "stubs" or "black spots"
C. Presence of skutula
D. Nikolsky's symptom
E. Hardy's symptom

Task 1. A farm worker complains of the appearance of painful rash on the scalp. *Objectively*: there are three well-defined infiltrated circular focus of 3-4 cm in diameter are found on the scalp; the surface is covered with crust, after removal of which there is pus in the hair follicles. Submandibular and cervical lymph nodes are enlarged to the size of a plum and are painful.

a) What preliminary diagnosis can be set?
- **A**. Scabies
- **B**. Scalp microsporosis
- **C**. Surface scalp trichomycosis
- **D**. Scalp psoriasis
- **E**. Infiltrative-purulent scalp trichomycosis

b) Which is the most possible course of the given disease?

Task 2. The dermatologist has been addressed by 62 years old patient complaining of change of color and thickening of nail plates on the feet. The patient has been ill for more than 10 years. *Objectively:* nail plates on all feet fingers are thickened and of dirty yellow color. In the course of microscopic examination of nail plates material treated with alkali solution, there were defined mycelium threads.

a) What diagnosis can be set?
- **A**. Panaricium
- **B**. Onichya candida
- **C**. Nail psoriasis
- **D**. Dystrophy of nails
- **E**. Feet rubroonichomycosis

b) Which dosage forms and pharmaceutical combinations would be reasonable to use for local therapy in this case?

Task 3. Four months old child's mother is complaining of reddening of the baby's skin between buttocks and inguinal region, which appeared on the 16th day after birth. *Objectively:* the skin between buttocks and inguinal folds of a baby is bright red, the lesions are big and clearly bordered and the surface is wet, covered with easily removable white film. Pseudomycelium was found during microscopic tests.

a) What diagnosis can be set?
- **A**. Diathesis
- **B**. Eczema
- **C**. Cutaneons diphtheria
- **D**. Toxicodermia
- **E**. Candidiasis

b) What pathogenetic feature the physician should pay attention to?

Task 4. Thirty one year old patient addressed the doctor with complains of rashes on the feet. She associates the disease with increased sweating. *Objectively:* the soles, side surfaces of fingers are covered with erythematous, vesicular elements, some of which have merged and formed lesions.

a) What diagnosis can be set?
- **A**. Restricted neurodermatitis
- **B**. Contact dermatitis
- **C**. Psoriasis
- **D**. Dishydrotic form of tinea pedis
- **E**. Erythrasma

b) What is the examination plan for this patient?

Task 5. Nineteen year old patient addressed the doctor with complaints of rash in inguinal area and itching. *Objectively:* inguinal-hip folds are covered with circled sharply delineated pin spots; their peripheral part is elevated and is surrounded with an area of vesicular elements.

a) What diagnosis can be set?
- **A**. Lichen ruber planus
- **B**. Big folds epidermomycosis
- **C**. Pemphigus vulgaris
- **D**. Scabies
- **E**. Eczema

b) Make up a treatment plan. What peculiar features it has?

Answers to the quiz of the first level of complexity
1 – C; **2** – B; **3** – E; **4** – B; **5** – B; **6** – A; **7** – D; **8** – B; **9** – E; **10** – B

Answers to the quiz of the second and third levels of complexity
1a – E; **2a** – E; **3a** – E; **4a** – D; **5a** – B

8 TOPIC

Dermatitis and Eczema

Dermatitis and Eczema are considered diseases caused by the immune response of the body to various allergens, which is accompanied by damage to its own tissues.

TRAINING AND EDUCATIONAL GOALS

- To form the modern concept of the allergodermatoses' etiopathogenesis
- To identify ways and likely conditions of the organism sensibilization
- To distinguish the factors affecting the course of allergodermatoses
- To generalize the characteristics of the allergodermatoses' clinical course
- To establishes the general principles of differential diagnosis of allergodermatoses
- To determine a rational treatment strategy of patients with allergic skin diseases

8.1 DERMATITIS

Dermatitis is considered an inflammatory lesion of skin caused by a direct effect of various exogenous factors.

TO KNOW:

- etiopathogenic characteristics of dermatitis;
- features of classification and clinical manifestations of dermatitis;
- meaning of 'monosensibilization' and 'polysensibilization';
- comparative characteristics of simple and allergic dermatitis;
- principles of treatment and prevention of dermatitis.

TO BE ABLE TO:

- properly collect patient history on dermatitis;
- make a diagnosis on clinical grounds;
- run diagnostic (skin) tests to confirm the diagnosis;
- make a differential diagnosis;
- assign individual pathogenetic treatment.

Etiology. The cause of dermatitis may be mechanical, physical, chemical and biological exogenous factors. Depending on the nature of skin exposure, the stimuli may be subdivided into unconditional (obligate) and conditional (optional).

Unconditional or *obligate* factors are the stimuli which may cause inflammation of patient's skin subject to considerable strength and duration of exposure: *mechanical* (friction, prolonged pressure), *physical* (UV radiation, high or low temperature, electric current, ionizing radiation), *chemical* (concentrated acids, bases, salts), and *biological* ones (some plants such as nettle, parsnip, etc.; insect bites). Due to exposure to skin of the unconditional factors, the patients may have easy contact dermatitis.

Conditional, or *optional* factors (allergens) – are the stimuli of physical, chemical or biological nature, to which patients become hypersensitive (sensibilization). Due to their exposure to skin, allergic contact dermatitis advances.

Classification. They distinguish between *simple contact dermatitis and allergic contact one*. A variety of simple contact dermatitis is an *artificial* dermatitis, which can occur due to excessive use of external dosage forms (with vigorous rubbing them or imposing the occlusive dressings, etc.), the use of too high concentration of solutions, wrong physical therapy appointment (too high doses of UV radiation, etc.).

For the duration of the flow, dermatitis may be of *acute* (up to two months) and *chronic* (more than two months) nature.

Development of chronic dermatitis is promoted by both exogenous (meteorological factors – long-term sun exposure, high humidity, strong winds; drafts; use of tight shoes or clothes) and endogenous factors (presence of vegetative-vascular disorders, endocrine diseases, metabolic disorders, decreased immune responsiveness, disorder of microcirculation and the like).

Simple contact dermatitis

Etiology. Simple contact dermatitis can occur in any person as a result of exposure to skin of unconditional stimuli. Mechanical factors (friction) may cause diaper rash, limited hyperkeratosis, when exposed to high temperatures – burns (*combuscio*), low – frostbite (*congelacio*) or freezing (*perniones*); when exposed to sunlight – solar dermatitis (acute or chronic), ionizing radiation – radiation dermatitis; if skin contacts with chemical agents – acute contact dermatitis, with biological factors – phytodermatitis. In this case, the clinical picture of simple contact dermatitis first of all depends on the irritating factor – its concentration, temperature, duration of exposure, etc., as well as on the individual characteristics of the patient's skin.

Clinical picture. The features of clinical manifestations of simple contact dermatitis are an acute onset after exposure to the irritant, absence of the latent period, rapid flow, lack of sensibilization. The lesion focus occurs in the region of contact of the pathogenic factor with the skin, has clear boundaries, precisely

reproducing the place of its contact with the skin, with no tendency to dissemination and diffusion of the process on the focus periphery. Patients are concerned about feeling pain and burning in the affected area. Typical signs are also considered continuous nature of the foci, monomorphic eruption, rapid regression of inflammatory processes in the skin after exposure to stimuli is over.

Depending on the nature, strength (concentration) and duration of the stimulus and individual characteristics of the patients' skin, there are following clinical forms of simple contact dermatitis:

a) erythematous – there are hyperemia and swelling of the skin in the foci;

b) vesiculobullous – appearance on the erythematous background of vesicles and bullous elements drying out along with formation of crusts or destroying with the formation of erosions, which are further epithelized;

c) necrotic ulcerous – development of tissue necrosis and ulceration with subsequent scarring.

With the development of chronic simple contact dermatitis (due to prolonged pressure, friction, sun exposure, exposure to ionizing radiation, etc.), there moderate hyperemia, dryness, peeling, hyper- or depigmentation, telangiectasia may be observed in the lesion foci; thickening and lichenification or, conversely, thinning with loss of skin elasticity, cracks may advance.

Differential diagnosis. The diagnosis of simple contact dermatitis is not complicated, it is made on the basis of complaints (pain, burning), the history data (rapid development of inflammation of the skin at the first contact with the irritant), characteristic clinical signs (development of dermatitis in contact with the irritant, clear boundaries of the foci, continuous nature of the lesion, monomorphic eruption). Simple contact dermatitis should be differentiated from epidermolysis bullosa (occurs in early childhood, has long relapsing course, some secondary changes in the skin areas of previous lesions); streptoderma (primary rash elements in the form of phlyctens, there are festering scabs); acantholytic pemphigus (often begins with the mucous membrane of the mouth, has a torpid course, positive Nikolsky's symptom and Asboe-Hansen sign, in smears from the bottom of erosions there are acantholytic Tzanck cells).



Fig. 8.1. Simple contact dermatitis (vesiculobullous form).

Treatment. The first step is to stop the exposure of etiological factor to the patient's skin. For small in size and mild forms of simple contact dermatitis, they use only external anti-inflammatory

therapy: if there an edema and sharp hyperemia in the focus – cool (2-3% aqueous solution of boric acid), corticosteroid creams. With the development of bullous elements, they should be pierced, smeared with aqueous solutions of aniline dyes; for moisting surfaces soaking therapy shall be prescribed; on erosive areas an epithelizing ointment shall be applied.

In the chronic form of a simple contact dermatitis during the exacerbation, they use corticosteroid ointment, and in the period of recourse – softening salicylic containing and absorbable ointments (with tar, sulfur, naphthalan, ichthyol).

For common skin lesions, the presence of multiple bullous elements and disorders of general condition of the patient, it is indicated a systemic corticosteroid therapy; to prevent secondary pyoderma, antibiotics or sulfa drugs shall be prescribes, to accelerate epithelialization – bio timulants, B vitamins, vitamins A and E, nicotinic acid.

Allergic contact dermatitis

Etiology and pathogenesis. Allergic contact dermatitis is caused by exposure of the skin to optional factors (allergens) that cause inflammation of the skin only in individuals with hypersensitivity to these factors (sensibilization, predominantly of monovalent one). According to WHO, in recent decades, the world has been recording an increase in the incidence of allergic diseases of the skin as a result of sensibilization of the population of chemical environmental factors. The number of patients with allergic contact dermatitis in the overall number skin pathology comprises more than 20%.

The most common causes of allergic contact dermatitis are considered chemicals (nickel, chromium salts, etc.); some industrial chemicals; household chemicals, insecticides; cosmetics; metal jewelry containing nickel and molybdenum; synthetic

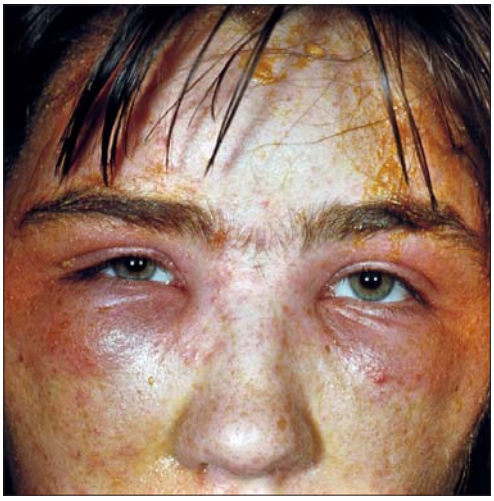


Fig. 8.2. Allergic contact dermatitis (after application of mascara to eyes).



Fig. 8.3. Allergic contact dermatitis (after the application of cosmetics).

clothing; external medicine, and so forth as well as physical (sunlight) and biological (ragweed and other plants) factors.

The basis of histopathological processes in the skin upon contact allergic dermatitis is comprised in immunological delayed reaction. Period of sensibilization to exogenous factors can last from days and months up to years, which is largely dependent on the patient's genetic susceptibility to allergic reactions, and the level of immune reactivity of the nervous, endocrine and other systems of the patients.



Fig. 8.4. Allergic contact dermatitis (after application of eye drops).

Clinical picture. Features of clinical manifestations of allergic contact dermatitis are considered its development after re-exposure of skin to exogenous factors (allergen), subacute onset (presence of the latent period – sensibilization period) and subacute or acute course.

The lesion occurs in the area of contact with the allergen, however, in contrast to the simple contact dermatitis, it has fuzzy boundaries with a tendency to spread the process beyond allergen contact with the skin. Lesions are of discontinuous nature, rash areas are alternates with those of healthy skin. The rash is characterized by polymorphism (patches, papules, vesicles less). Patients suffer from itching in places of rashes.

Contact allergic dermatitis is characterized by long duration after cessation of exposure stimulus and tendency to relapse after re-exposure to the allergen.

The diagnosis of allergic contact dermatitis is based on the patient's history (relapse after exposure to the allergen), clinical manifestations, and positive results of allergy skin tests**.**

Pathomorphology. There are intercellular edema in the epidermis, hyperplasia and hypertrophy of endothelial and perithelial vessels, narrowing of their lumen, perivascular infiltration**.**

Differential diagnosis. The diagnosis of allergic contact dermatitis is not complicated, it is made on the basis of complaints (itching of the rash), the data history (development of dermatitis after repeated exposure to the allergen), characteristic clinical signs (development of dermatitis in place of contact with the stimulus, fuzzy boundaries and discontinuous nature of the lesions, polymorphism of the rash). Contact allergic dermatitis should be distinguished from eczema, which is characterized by the formation of polyvalent sensibilization, presence of microvesicles and microerosions (symptom of serous wells) with phenomenon of oozing lesion, often has a multifocal nature of the skin lesions.

Contact allergic dermatitis should also be differentiated from the scabies, which is characterized by itching mainly in the evening and at night, symmetric localization of rash in typical for scabies areas, paired localization of rash elements, and presence of burrows and pathognomonic symptoms (Cesar, Hardy-Gorchakov, Michaelis) identification of same rashes in the family.

Treatment. First, it is required to determine the etiologic factor and to eliminate its effect on the skin. Patients are encouraged to hypoallergenic diet (to exclude the obligate food allergens, extractives substances, acute-irritating dishes, alcohol). Drug treatment should be comprehensive. With a limited process and moderate clinical signs of the disease, antihistamines (Cetirizine, Cetrine etc.) and corticosteroid creams or ointments of moderate impact shall be prescribed. In severe clinical manifestations of dermatosis, intense itching, sleep disturbances, complaints of neurotic nature, it is recommended an injectable form of antihistamines, sedatives (3% solution of sodium bromide, valerian extract, tincture of peony), vitamins A, E and C. In the event of multiple skin lesions or presence of the torpid form, systemic glucocorticoid medications (prednisone, dexamethasone, betamethasone, triamcinolone) on short-term courses should be administered.

Preventive measures. The patient should avoid repeated exposure to allergens, in case of confirmation of a professional nature of allergic factors, the suitable employment is required. Rational skin care, eliminating dryness by applying a number of emollients is recommended.

8.2 ECZEMA

Eczema is a chronic relapsing allergic skin disease that occurs on the background of a polyvalent sensibilization of the body and manifests through the inflammatory processes in the superficial layers of skin with the appearance of polymorphic rash and intense itching.

TO KNOW:

- etiopathogenic characteristics of eczema and its varieties;
- features of classification and clinical manifestations of eczema;
- stages of development of eczematous process;
- differential diagnosis of this disease;
- principles and features of dermatological tests helping to identify the allergens;
- principles of treatment, prognosis and prevention of relapse of eczema.

TO BE ABLE TO:

- properly collect patient history on dermatitis;
- make a diagnosis on clinical grounds;
- run diagnostic tests to confirm the diagnosis (Brocq scraping, skin tests);
- make a differential diagnosis;
- assign individual pathogenetic treatment.

Epidemiology. Eczema is one of the most common dermatitis; share of eczema in the structure of dermatological disease is 20 to 34%. Both men and women suffer from eczema most often at the age of 30-60 years.

Etiopathogenesis. Eczema is considered as *polyetiological* allergic disease, which is caused by the impact of a complex set of exogenous and endogenous etiologic and pathogenetic factors. Among the exogenous causes of eczema they distinguish *exogenous allergens* of chemical and biological, and environmental factors – risk factors of environmental, climatic, physical, occupational, psychological, hygienic, social plan. Endogenous pathogenic factors are important in the development and course of eczema – family history, changes in immune responsiveness, disorder of the nervous and endocrine regulation, presence of chronic foci of infection, impaired microcirculation, concomitant diseases of the digestive system, metabolic disorders, etc. They contribute to the formation of *endo-* and *autoallergens*.

Most often, patients associate debut and relapse of eczema with exposure to chemical agents (detergents and disinfectants, petroleum lubricants, construction materials, cosmetics, external dosage forms), trauma, microtrauma and burns of skin, use of trophallergens (milk, eggs, mushrooms, honey, chocolate, canned and smoked products, citrus fruits, etc.), exacerbation of varicose symptoms, nerve trauma or nerve strain, carried over colds, etc.

Clinical picture. Eczema occurs acutely, but subsequently acquires the features of chronic dermatosis with a tendency to relapse and resistance to treatment. The disease develops due to combined effect of exogenous and endogenous factors in patients with congenital or acquired predisposition to it.

There is no standard classification of eczema, on clinical manifestations and course there are following clinical forms of eczema: *true* (idiopathic), *microbial* (paratraumatic, varicose, mycotic, nummular), *seborrheic*, *professional* and *infantile*. According to the course of disease, one may subdivide *acute*, *subacute* and *chronic* eczema stages.

True (idiopathic) eczema occurs mainly after exposure to chemical agents encountered in industrial activity and in the home, or after use of certain cosmetics and drug products, as well as after eating trophallergens, endured neuropsychiatric stress or no apparent reason. Lesions are characterized by symmetry with the localization on the face, arms and legs with alternating areas of healthy and diseased skin. The foci have fuzzy boundaries with a tendency to spread, characterized by the current and evolutionary polymorphism of rash, severe itching. In the setting of severe erythema, there are multiple exudative papules, microvesicles, point erosion ('serous wells') with moist varying intensity. After drying appear the serous crusts, occurs desquamation. Around the main foci and in remote areas, allergids as eritemato-squamous and papules vesicular rash appear. In patients with long chronic dermatosis phenomenon of infiltration, thickening, congestive hyperemia, lichenification, dryness, peeling, cracks may be observed in the lesions.

Dyshidrotic eczema (clinical variety of true) occurs predominantly on the sides of the fingers, palms and feet, has a subacute course. In the lesions in the setting of low hyperemia, may appear small (pinhead) dense vesicles resembling the grains of cooked rice, and characterized by intense itching, sometimes burning.

Eczema keratosis (coarsen, tilotice) is a true manifestation of chronic form of eczema with localization in the palms of hands with the transition to the side and rear areas. Foci are characterized with clear boundaries, moderate erythema and severe infiltration with phenomena of lichenification, on the surface there are deep painful cracks with bloody crusts and big lamellar peeling. Resistance to treatment is marked. To exclude rubromycosis the patients are subject to mycological study of scaly crusts on mycology.

Among the clinical varieties of microbial eczema, the often recorded paratraumatic eczema, which occurs around nonhealing wounds after injury (micro traumas, cuts, burns of skin) due to sensibilization to pyococcus. In most patients, dermatosis is characterized by asymmetry, localization in the open areas of the skin (hands, arms, legs, face, neck). Lesions have clear limits with trimming like lamination of epidermis along the edge of the focus. At the core of the lesion in the setting of erythema and edema, it is observed a moderate oozing of point erosions, multiple seropurulent crusts, and on the periphery – pustular elements. On the lower extremities, the lesions are characterized by hyperemia of bluish tinge. In the case of exacerbation of chronic microbial eczema, the allergid eritemato-squamous and papular or vesicular papules elements appear around the principle focus and in remote areas.

Varicose eczema is a kind of microbial eczema, which occurs predominantly in elderly patients with chronic venous insufficiency during exacerbation of thrombophlebitis. Lesions are localized on the lower legs and feet, often around venous ulcers, characterized by clear boundaries, swelling of the skin, bluish tint, severe oozing, itching and feeling of painfulness, burning sensation.

Mycotic eczema is a kind of microbial eczema, which develops in the setting of course of a longlasting foot mycoses, confirmed by clinical and laboratory data. Lesions first appear on the skin of the feet, then spread to the lower legs, which is accompanied by a sharp itching, erythema, edema, vesiculation, weeping, painful cracks and erosions in the interdigital folds.

Intertriginous form of eczema is diagnosed mainly at persons of hypersthenic built, often in the setting of concomitant diabetes mellitus. Lesions in these patients are located in the major



Fig. 8.5. True eczema.

folds (armpit, groin, under the breasts in women), have fuzzy boundaries, characterized by all the signs of eczematous process – presence of hyperemia, edema, polymorphous rash, oozing, might be accompanied by widespread allergids. Mycological study should be conducted in order to eliminate candidiasis of the folds.

Nummular eczema occurs mainly during the cold season, often for no apparent reason, sometimes – after suffering a cold. Its development is associated with sensibilization to the patient's chronic foci of infection. The patients have multiple symmetric clearly demarcated round or oval lesions of coin size preferentially localized on the extensor surfaces of the extremities, at least – on the back and sides of the torso. The skin in the foci has signs of hyperemia and infiltration, on the surface appear miliary papules, vesicles, occasionally – a small soak, and serous and serous purulent crusts, scaly crusts.

Foci of **seborrheic eczema** are localized mainly on seborrheic areas of the skin (scalp, postaural folds, face, sternum, interscapular region of the back), accompanied by intense itching. In the setting of erythema, in areas there are layers of scaly crusts, under which some moist erosive surface with moderate soak may be found, and on the edge of the lesions one may see an inflammatory rim with clear boundaries, covered with scales and crusts (seborrheic 'crown'). In the area of ears and postaural folds, the skin is flushed, swollen, wet, with diffuse oozing, in the folds of auricles – painful cracks. In the sternum area, the patients may have seborrheic dermatitis – round yellow and pink erythematous patches covered with greasy yellowish scales.

Infantile eczema develops at an early age against atopy as a manifestation of the exudative phase of atopic dermatitis. Often infantile (atopic) eczema is localized on the face and scalp, although it may be common. In areas, there are signs of true, microbial and seborrheic eczema in various combinations.



Fig. 8.6. Microbial eczema.



Fig. 8.7. Microbial eczema.

Occupational eczema is caused by exposure to sensitizing substances in conditions of production with primary localization on exposed skin (back of the hands, arms, face, neck, sometimes legs, feet), has clinical manifestations of true eczema. In areas against hyperemia and edema, multiple vesicles, oozing lesions may be observed. The course is continuous, regression of clinical symptoms occurs after removal of contact with the allergen. Diagnosis shall be made by occupational pathologist on the basis of history, clinical picture, disease course, and skin allergy tests.

Pathomorphology. In the acute phase of eczema, an intercellular edema of Malpighian layer, spongiosis with vesiculation may be detected on the skin. In the dermis, especially in the papilla, there is a notable expansion of blood vessels with perivascular, predominantly lymphocytic infiltration. In the chronic stage, acanthosis, parakeratosis and hyperkeratosis, and a powerful perivascular infiltration of cell (lymphocytes, histiocytes and tissue basophilic cells) may be revealed.

Diagnosis of eczema with typical clinical manifestations is not complicated. Polymorphic elements with microvesicles and microerosions with formation of 'serous well', oozing, typical localization of the foci, significant pruritus, duration of flow, tendency to relapse – are characteristics of it.

Differential diagnosis. Eczema is differentiated with allergic dermatitis (the process is limited, microvesicles occur occasionally, no oozing), atopic dermatitis (the dominant is infiltrative component of inflammation with marked lichenification, no polymorphism of primary morphological elements, oozing lesions with typical 'serous wells' are not observed), scabies (itching mainly in evening and night, symmetrically localized rash in typical for scabies areas, pair location of the rash, presence of burrows and pathognomonic symptoms of Sezary, Hardy-Gorchakov, Michaelis, revealing a similar rash in the family), Duhring dermatosis herpetiformis (characteristic



Fig. 8.8. Seborrheic eczema.



Рис. 8.9. Infantile eczema.

grouping of rash, eosinophilia in the blood and in the content of bubbles, positive Jadassohn test – new elements appear after the applicative test with 50% potassium iodide ointment). Squamous hyperkeratosis form of rubromycosis of hands and feet differs from chronic hyperkeratosis eczema with mucosa-like desquamation of the epidermis in the folds of skin, in cultural studies of scaly crusts fungus may be detected.

Treatment. The treatment program includes a hypoallergenic diet, systemic and topical treatment of dermatosis, and correction of neural and neuroendocrine disorders, sanitation of foci of chronic infection, limiting contact with water.

Hypoallergenic diet involves eliminating the obligate food allergens, extractive substances sharp-irritating dishes, alcohol, limiting of salt and carbohydrates.

Systemic therapy of patients with eczema includes antihistamines (chloropyramine, clemastine, loratadine, desloratadine, etc.). In the case of common and torpid forms of eczema the patients shall take glucocorticoids for systemic use (prednisolone, dexamethasone, betamethasone, triamcinolone). In case of sleep disorders, neurotic disorders, psychotropic drugs shall be prescribed: tranquilizers (diazepam, nitrazepam), sedatives drugs. The external treatment for eczema patients shall be administered differentially. In the acute stage of eczema with symptoms of oozing, the cold lotion with 2% solution of boric acid and 0.25% solution of silver nitrate is indicated. In severe forms (acute and subacute stages), the topical corticosteroids on a hydrophilic base containing mometasone furoate, fluticasone propionate, clobetasol propionate, etc. shall be prescribe. The oozing is over in severe dry skin, the moisturizing drugs contain fluocinolone acetonide shall be administered. If complicated with infection (fungal, bacterial, fungal and bacterial), combined corticosteroid drugs containing substances with antibacterial and antimycotic activity should be applied. Chronic forms of the disease (severe infiltration and lichenification) require drugs on the hydrophobic base, with prednisone, urea, betamethasone valerate, salicylic acid.

Prevention. Affected areas require constant care, which involves the use of neutral creams, emulsions and ointments, which, if necessary include corticosteroids and keratolytics, and emollients. In varicose eczema, the surgical removal of varicose veins, use of elastic bandages, rational treatment of venous ulcers may become obligatory. Patients are encouraged to hypoallergenic diet. They have contraindications to work with production allergens irritating the skin, and polluting substances, as well as to work in high humidity and high psycho-emotional stress.

8.3 TOXIDERMIA

Toxidermia or **toxic and allergic dermatitis** are diseases of skin, frequently of mucous membranes, mostly in the form of acute inflammation, caused by an allergic or toxic-allergic effects of substances penetrated into the patient.

TO KNOW:

- etiopathogenic characteristics of toxidermia;
- features of classification and clinical manifestations of toxidermia;
- meaning of 'monosensibilization' and 'polysensibilization';
- comparative characteristics of toxidermia;
- principles of treatment and prevention of these diseases.

TO BE ABLE TO:

- properly collect patient history on toxidermia;
- make a diagnosis on clinical grounds;
- make a differential diagnosis;
- assign individual pathogenetic treatment.

Epidemiology. The term 'toxidermia' is considered conditional one, since in most cases the basis for their development are allergic mechanisms. The most common are *drug toxicoderma*, second in frequency is *food toxicoderma*, *occupational toxicoderma* is rarely seen. In foreign medical literature, the concept is limited only with medication exanthemas.

Etiopathogenesis. Development conditions of toxidermia are:

1) penetration of allergen, substances into the bloodstream,

2) presence of immunity to these substances, which may be congenital in the form of idiosyncrasy or acquired as a monovalent or polyvalent sensibilization

The causes of toxicoderma are *drugs* (antibiotics, sulfonamides, nonsteroidal anti-inflammatory drugs, analgesics, vitamins, etc.), *food* (food allergens or substances formed during their long-term storage or damage, as well as food additives – preservatives, dyes) *industrial and household chemicals*. Drug toxicodermatoses are the most frequently observed in clinical practice. Severe forms of toxicodermatoses often may cause a death.

The main mechanism of toxidermia development is considered *allergic* one, rarely – *toxic* one. Drug allergy is the result of penetration into the body of minimum amount of the drug; its manifestations do not conform the pharmacological action of drugs. Allergic skin damage is realized through immunological mechanisms (B- and T-immunity) in the form of various types of ***allergic reactions*** (on humoral or cell type): *type I, anaphylactoid* (allergic reactions of immediate type) – caused by IgE, most often occurs with the introduction of drugs and manifested, as a rule, as a urticarial rash (urticaria, angioedema, anaphylactic shock); *type II, cytotoxic* – caused by IgG and IgM or complement and is often manifested as a purple rash*; type III, immune deposit* – caused by circulating immune complexes, and often manifests itself in the form of vasculitis and urticaria; *type IV, cellular* (delayed allergic reaction) – caused by T-cells and occurs mainly in the form of papular rash.

They also distinguish ***non-immune mechanisms*** of acute drug toxidermia development – *idiosyncrasy* (congenital intolerance to certain drugs), and *polypragmasy* (concurrent use of large amounts of drugs from different groups, metabolism products of which may increase the allergenic effects of each other).

Clinical picture. Clinical manifestations of toxidermia with few exceptions are considered non-specific. One and the same substance can cause different patients have different symptoms. One and the same clinical picture may develop under the influence of different chemical substances. However, for most toxidermia are characterized by the following *common features*: acute onset and rapid course, patient complaints of itching skin rash; spread and symmetry of the rash; rash is localized not only on the skin, but also on the mucous membranes; disseminated nature of the rash location; the rash frequent polymorphism; the presence of urticaria elements; presence of intoxication syndrome, etc.

Depending on the nature of the rash, *macular, papular, urticaria, vesicles bullous, pustular,* toxicodermatoses may be distinguished.

According to severity, toxidermia may manifest themselves in:

I. Mild forms characterized by itching, limited urticaria, fixed erythema, multiforme exudative erythema, the reaction on lichen planus type.

II. Moderate forms in which there are generalized urticaria, angioedema, bullous toxicoderma, hemorrhagic vasculitis, bromide and iodide acne, common toxic and allergic dermatitis.

III. Severe forms means the appearance of Lyell's syndrome, Stevens-Johnson syndrome, bromoderm, ioderma, systemic lupus erythematosus, syndrome of dermatitis herpetiformis.

Mild forms of toxidermia

The patient complains of ***itching*** after using drugs, there are no primary morphological elements rashes on the skin, secondary elements in the form of bloody crusts and excoriations may occur.

Limited urticaria. Characterized by the appearance in some areas of urticarial elements (blisters) pink-red in color, protruding above the skin, patients suffer from severe itching.

Fixed erythema *(sulfanilamide).* Erythematous patches (single or multiple series) red in color appear on the skin of the trunk, extremities, genitals, mucous membranes, when getting a long time the secondary brown pigmentation is preserved; no subjective feelings; in case of repeated exposure to a provoking factor, the rash occurs on the same areas (hence the name 'fixed erythema'), as well as on new ones.

Erythema multiforme. Polymorphic rash of swollen spots or papules of right round shape coin-sized with a bluish sunken center; on the surface may appear vesicles or bullous elements.

The reaction on lichen ruber planu types. There is a common symmetrical rash of typical papules (flat polygonal with pearlescent shine and navel-like sunken centre) patients suffer from severe itching.



Fig. 8.10. Drug toxicodermatosis.



Fig. 8.11. Bullous fixed toxicodermatosis (on barbiturates).

Toxidermia of moderate severity

Generalized urticaria. Urticaria is characterized by multiple elements on large areas of skin, sharp itching, ephemeral elements.

Angioedema. There is a limited asymmetrical swelling of hypodermis; sense of increasing the organ size, asphixy, no itching.

Bullous toxicodermatosis. Disseminated bubbles with erythematous borders appear on the skin, often on the mucous membranes; erosion may form after their explosion, and upon drying – crusts, after healing the secondary spots may be preserved for a long time.

Hemorrhagic vasculitis. One may observe disseminated purpura, petechiae, ecchymosis on the skin, after their recourse – secondary hyperpigmental pots.

Bromine and iodine acne. May appear on the seborrheic areas due to accumulation of bromine or iodine drugs in the body; rash looks like pustules, acne elements.

Common toxic and allergic dermatitis. They are characterized by the appearance on the skin of the trunk and limbs of common symmetric polymorphic rash (spots, blisters, papules); sudden itching, burning skin, body temperature may increase to low grade, fever, indigestion, weakness, myocarditis.

Severe toxicodermatoses

Lyell's syndrome or ***acute toxic epidermal necrolysis*** is considered a severe form of toxidermia, manifested through acute generalized inflammation of the skin and mucous membranes with exfoliation of the epidermis, visceral injuries, intoxication. Lyell's syndrome arises in the setting of the polyvalent sensitization as a result of adequately re-prescribed and appropriately administered medicines. Manifestations of the disease are caused not so far by the pharmacological properties of drugs, but by many features of patient's immune system and his constitutional and genetic predisposition.

Etiology. Lyell's syndrome most often occurs after the administering the sulfonamides, antibiotics, barbiturates, thiamine, serums, etc., and might also be caused by chemicals, poor quality food, infectious factors (staphylococcus of various serotypes), and therefore the following forms of the syndrome may be distinguished:

1) drug,
2) staphylococcal,
3) combined,
4) idiopathic (where the cause is unknown).

The pathogenesis of the syndrome is complex and poorly studied. It is believed that at the heart of toxic epidermal necrolysis is an immediate cytotoxic response with the binding of antigen and antibodies on the surface of the basal epidermal cells, and formed antigen-antibody complex causes the lability of cells' lysosomal membranes, release of hydrolases and other enzymes and destruction of epithelial cells.

Clinical picture. The body temperature rises suddenly, the patients complain of malaise, drowsiness, headache, possible vomiting and diarrhea. On the skin, there is a

painful erythema which is spreading rapidly, there are bullous elements appear, one may observe a rapid exfoliation of the epidermis (the 'symptom of wet laundry' – wrinkled epidermis, gathered in folds and peeled); sharply positive Nikolsky's sign. A characteristic feature of toxic epidermal necrolysis is soreness of affected and unaffected skin. On the skin and mucous membranes there are widespread erosions; it is possibly an exfoliation of the mucous membranes of respiratory tract and internal organs.

Research data: a general analysis of blood shows iron-deficiency anemia, eosinophilia, agranulocytosis, pancytopenia, probable leukocytosis, increased ESR.

Positive allergological tests: intradermal, intraoral, drip, scarification, sublingual.

Positive immunological tests: PHT (passive hemagglutination test); direct and indirect degranulation of basophils or mast cells; neutrophils damage indicator; IFA for the detection of antibodies of class IgG, IgM, IgE; RIML (reaction of inhibition of leukocyte migration).

Pathomorphology of skin: epidermal necrosis with its subsequent exfoliation between the epidermis and dermis without defeat of the dermis itself. Staining the preparation in case of medical syndrome, they might detect cuboidal cells with large nucleus, in the case of staphylococcal – large epithelial cells with a small core.

Stevens-Johnson syndrome (form of bullous multiforme exudative erythema) – heavy, form of toxidermia, which manifests itself in the form of bullous multiforme exudative erythema with lesions of the skin and mucous membranes of at least two organs.

Etiology. Multiforme exudative erythema – a disease which is based on vascular lesions of the dermis with characteristic repeated changes in the skin and mucous membranes. They distinguish its infectious-allergic (idiopathic) form, which occurs in 93% of cases, and infectious-toxic one. A 'small' form (Gebre type) caused by a viral or mycoplasma infection, and 'large' (actually Stevens-Johnson syndrome) as a manifestation of drug toxidermia (because of penicillin, streptomycin, tetracycline, sulfonamides, griseofulvin, barbiturates, acetylsalicylic acid, chlorpromazine, codeine, vaccines, etc.) are also distinguished. Multiforme exudative erythema can also be observed in diseases of the connective tissue, malignant tumors, etc. The **pathogenesis** is not fully understood, hypothermia and focal infections are of big value. Dermatosis is understood as hyperergic reaction to drugs, infections and toxic factors, aimed at the keratinocytes.

Clinical picture. Diseases begins suddenly and acutely with fever and disorders of general condition of the patient. The process of the skin is spread, it damages not only the skin, but also the mouth, eyes, genitals, anus. Bronchitis, pneumonia, myocarditis, nephritis, diarrhea, arthritis, otitis media, paronychia might also develop. On the skin one may observe a patchy papular bullous rash with elements of considerable size, which is characteristic of the exudative multiforme erythema. On mucous membranes numerous bullous elements might appear, which are followed by the formation of large-sized erosions, massive hemorrhagic crusts may form on the lips on the erosion surface. The development of catarrhal or purulent conjunctivitis, ulcerative keratitis and uveitis is quite probable; that is can lead to vision loss. On the

genitals and in the perianal area, one can observe bullous elements, painful erosion that can affect urination and bowel movement difficulty. Simultaneously, the process involves the internal organs with development of pneumonia, bronchial pneumonia, pleurisy, myocarditis, glomerulonephritis, diarrhea, damage to the cardiovascular system and liver with symptoms of general intoxication.

Data of laboratory studies: a general analysis of blood indicates leukocytosis, stab shift, lymphopenia, eosinopenia.

Pathomorphology. Histologically it is possible subdivide dermal, mixed epidermal-dermal and epidermal types of skin lesions. Dermal changes are characterized by swelling of the endothelium of blood vessels and perivascular lymphohistiocytic infiltration with neutrophils and eosinophils, edema of the papillary layer, extravasations of red blood cells. Epidermal changes are accompanied by epithelial cell necrosis, spongiosis, vacuolar degeneration of the basal cells, the formation of bullous elements, basal membrane is intact. Histological changes in hemorrhagic rash look like anaphylactoid purpura as a result of degenerative disorders of the endothelium of the capillaries and perivascular accumulation of neutrophils and eosinophils.

Treatment. The treatment program regarding toxidermia patients includes stopping the impact of drugs as etiological factors and the removal of these substances residues from the body.

Systemic therapy involves the use of enterosorbents (polyvidone, dioctosmectite), detoxification therapy (polyvidone, sodium chloride, potassium chloride, calcium chloride, magnesium chloride, sodium bicarbonate, furosemide, 0.9% sodium chloride solution); antihistamines. With widespread and severe toxidermia, the patients are prescribed glucocorticoids for systemic use (prednisone, triamcinolone, dexamethasone, betamethasone), with marked edema – diuretics (furosemide, hydrochlorothiazide), and complications of secondary infection – antibiotics to choose from (cephalexin, erythromycin, azithromycin, doxycycline, ciprofloxacin, moxifloxacin, levofloxacin, etc.).

External therapy is prescribed depending on the nature of the rash. On erythema, urticaria, bullous and papular rash, steroid creams or ointments shall be applied.

Prevention. The causative agent of the disease is identified with the help of specific biophysical and immunological tests; the risk factors contributing to the development of sensitization shall be eliminated if possible; sanitation of lesions of focal infection shall be made;

Rehabilitation measures are generally aimed to prevent sensibilization to allergens, to eliminate them and treat the diseases, caused the development of toxidermia, to sanitate the focal lesions of chronic infection.

8.4 ATOPIC DERMATITIS

Atopic dermatitis is considered a chronic allergic skin disease that occurs in people with a genetic tendency to atopy, has a relapsing course and age features of clinical manifestations. Typical clinical signs of atopic dermatitis are eritemato-squamous, eczematous and lichenoid eruptions, arising as a result of hypersensitivity to the specific (allergens) and non-specific stimuli. The relevance of atopic dermatitis is defined by intense itching, presence of common skin rashes, often relapsing disease course that is the cause of a neurotic state of the patient, violation of his working capacity, reducing the quality of life and social maladjustment.

TO KNOW:

- the definition and epidemiology of atopic dermatitis;
- its etiopathogenetical features;
- age-related clinical features and classification of atopic dermatitis;
- principle and additional criteria of clinical manifestations of the disease;
- principles of treatment and prevention of atopic dermatitis.

TO BE ABLE TO:

- properly collect patient history on atopic dermatitis ;
- make a diagnosis on clinical grounds;
- make a diagnostic tests to confirm the diagnosis (identification and evaluation of dermographism);
- make a differential diagnosis;
- assign individual pathogenetic treatment.

Etiopathogenesis of atopic dermatitis is multifactorial and not fully understood. In addition to genetic determinism – (two genes were identified in the chromosomes, which are responsible for the abnormal hyperproduction of IgE), central and autonomic nervous system damages, dysfunction of the gastrointestinal tract, of hepatobiliary system in particular, presence of helminths and other foci of chronic infection (ENT-organs, teeth), and changes in immune responsiveness (decrease in subpopulation of T-suppressor cells, reduced phagocytosis), microcirculatory disorders, etc. are of great value in the pathogenesis of atopic dermatitis.

Clinical picture. The first clinical manifestation of atopic dermatitis occur on the skin of three months old children (early weaning, or coming to artificial feeding), and in older children. First rash usually occurs on the face (in 65% of children), scalp (34%), elbows and / or knees and on the extensor surfaces of the extremities. In the course of atopic dermatitis, there are three age periods with different clinical manifestations on the skin: the first period (up to two years) – during infancy (exudative stage); the second period (from two years to adolescence) – infiltrative stage; and the third period (juvenile and mature age) – lichenification manifestations.

Classification. In different age periods, one can observe different clinical manifestations of atopic dermatitis. Depending on the type of rash character, it is possible to distinguish the following clinical forms of atopic dermatitis:

- eritemato-squamous;
- vesicle crusted (eczema);
- eritemato-squamous with low lichenification;
- pruriginous;
- lichenoid.

Eritemato-squamous form is more likely to occur in infants at the age of four months and children under two years old and characterized by the appearance of erythematous patches with edema and desquamation on the face, neck and scalp. In their centers one might see microvesicles with weeping, crust and crust-scales by type of seborrheic, true or microbial eczema – it is a ***vesicle crusted form***. Then, symmetrical rash may spread to the trunk and extremities. In the period of acute dermatosis, the child is restless, not sleeping, itching the skin. Atopic dermatitis is characterized by alternating exacerbations and remissions, but even in remission behind the ears and near the lobes one can observe deep cracks,



Fig. 8.13. Atopic dermatitis.

which get wet and become infected. Dermographism in most patients (80%) remains red.

Eritemato-squamous form with low lichenification (from two years to puberty) is characterized by appearance of eritemato-squamous foci in areas of typical lesions, and lichenoid papules on the skin of the flexor surfaces, large folds, neck, where the skin is infiltrated, becomes dry, compacted and covered with scaly scales, excoriations and hemorrhagic crusts.

At ***pruriginous form*** (from adolescence to adulthood) amid the signs of atopic dermatitis, which manifest as mild or clinically erased eritemato-squamous form with signs of xeroderma, one might observe dense pruriginous multiple papules or papule-vesicles, localized on the extensor surfaces of the extremities, usually legs, shoulders and upper arms, and resemble s prurigo rash (strophulus like). Patients suffer from severe itching, so on the skin frequently the signs of scratching and hemorrhagic crusts might be observed.

At ***lichenoid form***, which occurs in adults, in the setting of xeroderma one might observe flat polygonal lichenoid follicular papules, the color of which varies from normal skin to pink-gray. They are located on the flexor surfaces of the extremities with subsequent formation of foci of lichenification, over time, these areas become pigmented. In some patients, the lesions become of widespread or even generalized nature with the formation of atopic *diffuse dermatitis (diffuse neurodermatitis)* involving the skin of perineum, genitalia, and gluteal and infrabuttock folds. In these cases, the disease course is severe, general condition of patients gets worse, the biopsy skin itch leaving a linear scar may occur, the secondary infection often joins. Dermographism is resistant, white. The course of diffuse atopic dermatitis is torpid; it responds poorly to treatment, the remission is of temporary nature. Patients suffer from insomnia and chronic fatigue, psychic and emotional exhaustion.

Diagnostic criteria and assessment of severity of atopic dermatitis. The diagnosis of atopic dermatitis shall be made when the patient has three major and at least three additional clinical criteria.

I. Major criteria:

1) itchy skin;

2) typical morphology and localization of skin rashes: in infants – eczematous rash on the face and extensor surfaces of the extremities, in older children and adults – lichenification on flexor surface of the limbs;

3) chronic relapsing course;

4) atopy in a personal and family history.

II. Additional criteria:

1) xerosis (dryness) of the skin;

2) ichthyosis, mostly of palms;

3) immediate hypersensitivity reaction in skin tests with allergens;

4) localization of cutaneous process on the hands and feet ;

5) cheilitis;

6) nipple eczema;
7) susceptibility to infectious skin lesions due to impaired cellular immunity;
8) dermatosis beginning in early childhood;
9) erythroderma;
10) relapsing conjunctivitis;
11) Dennie-Morgan fold;
12) keratoconus (conical protrusion of the cornea);
13) anterior subcapsular cataracts;
14) cracks behind the ears;
15) high level of IgE in the blood serum;
16) darkening of the areas around the eyes;
17) pallor or erythema of the face;
18) tinea alba (white lichen);
19) food sensitization;
20) intolerance to wool and lipid solvents;
21) perifollicular localization of the rash;
22) influence of emotional factors on the disease course;
23) white dermographism or delayed blanching.

To assess the severity of atopic dermatitis it is required to determine in SCORAD index in points by the formula: SCORAD Index = A / 5 + 7xB / 2 + C, where A – the rate of process spreading on the skin (as a percentage), B – rash manifestation intensity indicator (erythema, edema/papule, crust/weeping, excoriation, lichenification, dry skin from 0 to 3 points), C – indicator of the subjective state of the patient (pruritus and sleep disturbance from 0 to 10 points). The severity of atopic dermatitis index SCORAD: 20 points – an easy, 20-40 points – moderate, more than 40 points – severe.

Methods of laboratory diagnostics. General blood analysis indicates eosinophilia, elevated levels of immunoglobulin E; immunologic blood study – reducing the total number of E-rosetting lymphocytes and the relative number of T-suppressor subpopulation of lymphocytes, impaired immunoregulatory index; disimmunoglobulinemia, colonization of the affected and surrounding skin with Staphylococcus aureus, etc.

Pathomorphology. In the epidermis – hyperkeratosis, acanthosis, parakeratosis; in the dermis – edema and perivascular infiltration of lymphoid cells and neutrophils. In long-term course of the dermatosis, the dermal papillae are swollen, twisted, sclerosal, with marked changes of elastic and collagen fibers, increased number of capillaries.

Differential diagnosis. The diagnosis of atopic dermatitis is not complicated, and shall be made on the basis of complaints (itching, sleep disturbance), history data, characteristic clinical signs (major and additional criteria). Atopic dermatitis should be differentiated from scabies (itching occurs mainly in the evening and at night, paired

arrangement of elements of the rash; it is localized in typical scabies areas, there are burrows and pathognomonic signs of Hardy-Gorchakov and Sezary, such a rash might be revealed in the family), from streptoderma (primary rash elements in the form of phlyctens, there are purulent crusts), from eczema (often begins at an older age, and there are multiple microvesicles and microerosions with the symptom of 'serous wells' and the phenomena of weeping; often the skin lesions are of common multifocal nature without characteristic for atopic dermatitis additional clinical criteria), from limited neurodermatitis (dermatosis starts, according to history, in adolescence or adulthood without a rash of early childhood, no characteristic of atopic dermatitis additional clinical criteria).

Treatment of atopic dermatitis should be individualized, taking into account the patient's age, clinical symptoms, degree of activity and severity of disease. Therapeutic measures are aimed at eliminating the inflammatory process, as well as the extension of the state of clinical remission and relapse prevention.

First of all, patients are encouraged to conduct elimination activities in the home – avoid contact with pets, daily wet cleaning of premises, etc. Patients must follow a hypoallergenic diet for exceptions obligate food allergens, extractives, sharp-irritating foods, carbohydrates, alcohol and restriction of salt.

In period of exacerbation patients shall receive comprehensive medical treatment: detoxification drugs (Neohaemodes, Rheopolyglucinum, Reosorbilact, etc.), antihistamines (Chloropyramine, Clemastine, Loratadine,), with severe clinical manifestations of dermatosis – their injectables forms, stabilizers of mast cell membranes (ketotifen), psychotropic drugs (in sleep disorders, presence of neurotic disorders) for one to four weeks before the normalization of emotional states, sedative drugs. In severe atopic dermatitis and resistance to other therapies the patients shall be administered immunosuppressive agents (cyclosporine, systemic glucocorticosteroid drugs).

External treatment of atopic dermatitis involves the use of aniline dyes, topical calcineurin inhibitor, including the drug tacrolimus ("Protopic"). In severe sharp-inflammatory manifestations (acute and sub-acute stages), topical corticosteroids on a hydrophilic base containing mometasone furoate, betamethasone valerate) shall be prescribed, and after cessation of exudation in severe dry skin – moisturizing drugs containing fluocinolone acetonide. Correct daily skin care (cleansing and moisturizing it) is of great value. The products containing emollients shall be applied. The patients with atopic dermatitis are also indicated physiotherapy techniques – selective phototherapy, PUVA therapy

Preventive measures. To prevent relapses of atopic dermatitis, topical calcineurin inhibitors might be applied, in particular – tacrolimus in the form of ointment. Such patients are advised to respect the hypoallergenic diet with the exception of extractive foods and refined carbohydrates, and continuous care of the skin (its cleansing and moisturizing), which requires the use of indifferent emollient containing drugs. Questions for self-control of the first level of complexity

1. Characteristic feature of simple contact dermatitis is:

A. Fuzzy boundaries of the lesion
B. Clear boundaries of the lesion
C. Occurrence only in sensitized patients
D. Occurrence in 12-74 hour after exposure to a certain factor
E. Possible generalization of the process.

2. It is not observed in allergic contact dermatitis:

A. Rash on the place of influence of a certain factor
B. Clear boundaries of the lesion
C. Occurrence in sensitized patients
D. Subacute onset and course
E. Possible recurrence after re-exposure to the allergen.

3. Which of the following is not used for the treatment of allergic contact dermatitis:

A. Glucocorticoids containing creams and ointments
B. Antihistamines
C. Hyposensitizing drugs
D. Vitamins
E. Photosensitizers

4. Toxicodermatosis is not characterized by:

A. Acute onset
B. Symmetry of rash
C. Polymorphic rash
D. Development of lichenification
E. Possible lesion of mucous membranes.

5. Fixed erythema is not characterized by:

A. Occurrence as a result of taking sulfonamides, antibiotics etc.
B. Occurrence due to exposure to obligate irritants
C. Rash of several red spots 2-5 cm in diameter
D. Localization on the skin, genital and oral mucosa
E. After recourse pigmentation remains for a long time.

6. Which of the following is not applied for the treatment of toxicodermatosis:

A. Enterosorbents
B. Photosensitizers
C. Antihistamine drug
D. Detoxification drugs
E. Glucocorticoid creams

7. Lyell's syndrome is characterized by:

A. Isomorphic Koebner response
B. Auspitz triad
C. Nikolsky's symptom
D. Meshcherskiy-Besnier's symptom
E. Jadassohn's symptom

8. Which of the following form is not characteristic for eczema :

A. Idiopathic
B. Microbial
C. Herpetiform
D. Occupational
E. Seborrheal

9. Which of the following does not belong to the main diagnostic criteria for assessment of the severity of atopic dermatitis:

A. Skin itch
B. Ichthyosis, mostly of palms
C. Typical morphology and localization of skin rashes: in infants – eczematous rash on the face and extensor surfaces of the extremities, in older children and adults – lichenification on flexor surfaces of the extremities
D. Chronic relapsing course
E. Atopy in personal and family history.

10. Primary morphological element with urticaria is considered:

A. Vesicle
B. Bulla
C. Macule
D. Boss
E. Knot

Task 1. The plumber came to the doctor complaining of redness, burning sensation, pain in the right forearm. Some rash appeared in 10-15 minutes after contact with hot pipes. *Objectively*: on the skin of the right forearm extensor surface there is a severe focus with clear boundaries of 3x6 cm; there is skin hyperemia in the focus, some individual bullous elements with clear content.

a) Make a diagnosis:
- **A**. Dermatitis herpetiformis Duhring
- **B**. Allergic contact dermatitis
- **C**. Eczema
- **D**. Simple contact dermatitis
- **E**. Pemphigus vulgaris.

b) What should be the behavioral tactics of the patient?

Task 2. 32-years old female patient consulted the dermatologist complaining of some rash on the skin of neck and chest, accompanied by itching. Rash appeared after taking aspirin and kept on the skin for about two hours and then without any action gradually disappeared appearing at new areas. *Objectively*: there are multiple palm-sized urticaria elements. The patient has red dermographism; eosinophilia is revealed in the blood.

a) What kind of skin disease can be thought of in this case:
- **A**. Urticaria
- **B**. Allergic dermatitis
- **C**. Eczema
- **D**. Simple contact dermatitis
- **E**. Atopic dermatitis

b) Make a differential diagnosis of the disease.

Task 3. A boy of 7 years complains of feeling unwell, pain on swallowing, painful rashes on the lips and in the mouth, itchy rash on the face and body, which appeared three days after receiving analgin because of acute otitis. *Objectively*: the general state of the child is severe; body temperature is 38.6 °C. On the skin of the lips and oral mucosa, there are common erosions with massive hemorrhagic crusts. On the face and body – multiple erythematous spots and edematous papules with deep bluish center, on the surface of which there are vesicles and blisters; the elements tend to be drained. Nickolsky's sign is negative.

a) What kind of emergency prehospital care should be provided to the child:
- **A**. To prescribe corticosteroids orally, canceling all other drugs
- **B**. To prescribe corticosteroids parenterally, canceling all other drugs
- **C**. To prescribe corticosteroid ointments, canceling all other drugs
- **D**. To prescribe antihistamine drugs, canceling all other drugs
- **E**. To prescribe purgatives, canceling all other drugs

b) What preventive measures are required in this case?

Task 4. Female patient, 37 years old, employed as a manipulative nurse, complains of feeling unwell, weakness, headache, muscle and joint pain and skin rash, accompanied by severe pain and burning sensation. Some rash appeared two days after receiving ampicillin because of sore throat. *Objectively*: general condition of the patient is severe; body temperature is 39.2 °C. The entire skin is bloodshot. On the trunk and extremities, there are multiple bullous elements, erosion, fragments of epidermis observed. The skin is painful on palpation. Nikolsky's sign is positive.

a) What kind of emergency pre-hospital care should not be provided to the child:
- **A**. Stop taking ampicillin
- **B**. To prescribe corticosteroids parenterally
- **C**. To prescribe enterosorbents
- **D**. To refer the patient to the intensive care unit for further treatment
- **E**. To refer the patient for consultation and supervision of the allergist

b) Make a differential diagnosis of the specified disease.

Task 5. 34 years old woman consulted the dermatologist about the skin lesions of hands and lower third of the forearm as a significant

swelling, redness, vesiculation, weeping. Got ill six months ago. The disease appeared after four months use of 'Lotus' washing powder. In the past, the patient has no skin diseases.

a) What is the most likely diagnosis in this patient:

A. Contact allergic dermatitis
B. Simple contact dermatitis
C. True eczema
D. Toxicodermatosis
E. Microbial eczema

b) What diagnostic tests should be carried out to establish the clinical diagnosis?

Answers to the questions of the first level of complexity
1 – B; **2** – B; **3** – E; **4** – D; **5** – B; **6** – B; **7** – C; **8** – C; **9** – B; **10** – B
Answers to the questions of the second and third levels of complexity
1a – D; **2a** – A; **3a** – B; **4a** – E; **5a** – C

9 TOPIC

Professional dermatosis

Professional dermatosis is the skin disease caused by impact of production factors.

EDUCATIONAL AND TRAINING PURPOSES

- To determine the general progress and clinical findings of different professional dermatoses
- To determine the diagnostic criteria and terms of occurrence of professional dermatoses
- To analyze the principles of therapy and preventive treatment of professional dermatoses

TO KNOW:

- Etiopathogenesis of professional dermatoses;
- Classification of professional dermatoses;
- Clinical peculiarities of their modern progress;
- Diagnostic criteria of professional dermatoses, skin test meaning;
- Methods and principles of medical and preventive measure for the persons who have professional dermatosis.

TO BE ABLE TO:

- Collect anamnesis of the person who has professional dermatosis;
- Analyze clinical findings and results of laboratory research;
- Hold differential diagnostics on diseases with similar clinical findings;
- Put on reasonable treatment for the people who have professional dermatoses;
- Recommend the necessary preventive measures against professional skin diseases.

Most of the professional dermatoses are caused by chemical agents.

Professional dermatoses are divided into:

I. Professional dermatoses of chemical etiology

1. Professional dermatoses caused by obligate irritants: simple contact dermatitis, epidermitis, chemical burns, skin and mucous ulceration, onychia and paronychia.
2. Allergic professional dermatoses: allergic dermatitis, eczema, toxicodermia, uticaria.
3. Professional dermatoses caused by hydrocarbon compounds: toxic melanodermia, folliculitis, acne, limited hyperkeratosis.
4. Dermatoconiosis.

II. Professional dermatoses caused by impact of physical factors

1. Professional dermatoses caused by thermal, actinic, mechanical factors: freeze injuries, burn injuries, perfrigeration, photocontact dermatitis, cheilitis.
2. Professional signs (stigmae): temporary – colour staining, callosity, pigmentation, cracks, excoriation; and stable – penetration (contamination), scars, telangiectasia, nail changing.

III. Professional dermatoses of infectious and parasitical etiology

1. Erysipeloid, paravaccinia, mycoses.

Professional dermatoses of chemical etiology

Simple contact dermatitis is mainly an acute skin inflammation arisen directly at the place of irritators' activity and is clearly spread within the boundaries of its activity. The degree of response manifestation depends on the etiological factor, exposition period, localization and individual sensitivity.

Etiopathogenesis. The cause of occurrence is the impact of the irritators of chemical etiology (concentrated acids, alkalies, paints, lacquers), physical factors (mechanical impact, freeze injuries, burn injuries etc.) and biological factors. Simple contact dermatitis develops without incubation period.

Clinical findings. Clinical findings of the simple contact dermatitis are skin redness, edema, vesicular and bullous eruption which causes after cutting off the numerous erosions and madescence. The lesion focus is clearly distinguished from the unaffected skin area. It is localized in the place of contact with irritator.

Diagnostic. Diagnosis of the simple contact dermatitis is based on anamnesis data and clinical findings, inspection of the working conditions and detection of the contact with irritators of chemical etiology. It is differentiated with the allergic dermatitis, eczema, toxicodermatosis.

Treatment. It is necessary to eliminate the skin contact with the working chemical factor which caused the contact dermatitis. The affected area shall be rinsed with water. In case of small affected areas and mild form of the simple contact dermatitis

only the local anti-inflammatory therapy shall be applied, in particular cold lotion with 2% boric acid solution, Rivanol/Furacilin solutions as well as the madescence ceases.

Epidermitis is the skin inflammation with chronic progress which occurs as the result of frequent impact of organic solvents, coolants, solutions of oxides, alkalies and other degreasing agents.

Clinical findings. Clinical findings of the epidermitis are skin dryness, peeling, there may be deep cracks without clear inflammation and infiltration. The subjective symptoms are itchiness and soreness. Affection is mainly localized in hands.

Diagnostic. Diagnosis is based on anamnesis data and clinical examination, fact of contact with production factors.

Treatment. Detoxication, antihistamines (Cetrine, Aerius, Claritin etc.) and local agents (indifferent and corticosteroid pastes) are used.

Chemical burns occur at the working place as the result of skin contact with obligate irritants (acids, alkalies, salts of heavy and alkaline metals etc.).

Clinical findings. According to the clynical progress there are four stages of disease: I – erythematic, II – vesiculobullous, III – sphacelous, IV – necrosis of all skin layers.

Diagnostic. Diagnosis is based on anamnesis data, peculiarities of clinical findings, results of laboratory research complex, fact of contact with chemical irritants.

Treatment. Impact of the production factor shall be detected and eliminated; the place of impact of chemical irritants shall be washed with water under pressure. The acid residues shall be neutralized by 2% soda solution and in case of alkaline burns by 2% acetic/citric acid solution. Detoxication, keratoplastic and steroid cr#mes and antihistamines are used in treatment.

Prevention. Sanitary standards for manufacturing areas and work hygiene rules shall be observed. Personal prevention means are also used.

Allergic professional dermatoses

Allergic professional dermatitis results in the repeated contact of skin areas with irritants in unfavourable working conditions. In such case univalent sensibilization to one of the impact factors is shown.

Etiopathogenesis. The allergens can be different chemical agents used in work (paints, lacquers, solvents, oils and lubricants, medical drugs, nickel and chrome salts, insecticides etc.).

On the repeated contact with the allergen the sensibilizing lymphocytes flow towards the allergen excitation focus followed by lymphoquin release and leukocyte involvement which causes skin inflammatory reaction as the result of release of inflammatory mediators by the abovementioned cells.



Fig. 9.1. Professional eczema.

Clinical findings. The process is widely spread, with the trend to peripheral growth. Eruptions are polymorphous. Clinical findings are erythema, edema, papula, microvesicles, cometimes vesical eruptions which cause anabrosis in case of opening them up. The affections are localized in hands, forearms, face. The subjective symptom is middle itchiness.

Diagnostics. Diagnosis is based on anamnesis data, clinical findings, results of laboratory research and skin samples which is compulsory fir determining the allergen and making a diagnosis of the allergic professional dermatitis.

Treatment. The repeated contact with irritants shall be eliminated. The antihistamines and sedation medications are used. In severe cases the glucocorticosteroid hormones are used. External therapy depends on the clinical findings: anabroses are cured by aniline ink water solution and then by indifferent pastes or corticosteroid pastes and creams.

Prevention. Sanitary standards for manufacturing areas and work hygiene rules shall be observed.

Professional eczema is a chronic skin disease (often recurrent) caused by contact with sensibilizing occupational irritant. The details of professional eczema are described in the chapter *Dermatites and Eczema*.

Professional dermatoses caused by hydrocarbon factors

Toxic melanodermia results in long-term work contact with oil and coal products.

Clinical findings. The general intoxication is shown on face, neck, arms, rarely on body and legs, with erythema, pigmentation, follicular hyperkeratosis, telangiectasia and peeling. The typical colour of skin is brownish grey, the skin becomes rough and wears thin.

Treatment. The production factor shall be detected and the contact thereto shall be eliminated. In order to stabilize the general condition the detoxification therapy, antihistamines, B and C vitamins, external corticosteroid pastes or creams are used.

Folliculitis and acne. Engineers, tractor drivers suffer oil, resinous, tar, chloric folliculites due to contact with machinery lubricant, oil, petrol, petroleum oil and in case of direct permanent contact with oil-soaked clothes.

Typical localization of affection: hands, forearms, thighs, stomach.

Clinical findings. Black spots occur in hair follicle mouths; further the development of inflammatory nodules with transformation to furuncles is possible.

Treatment. Contact with production factor shall be eliminated. The general treatment provides antibiotics, sulfanilamides and anti-inflammatory drugs; in case of folliculate transformation to furuncles the antihistamines (Cetrine, Aerius, Claritin etc.) are used, 1-2% salicyl or boric spirit, pure ichthyol are applied externally, physiotherapeutic procedures (ultraviolet irradiation) are also used.

Limited hyperkeratosis develops on skin after long-term contact with coal tar and oil products. Its main feature is increased keratosis of epidermis at the highly contaminated skin areas: face, back of hand, thighs, forearm extensor surface.

Clinical findings. Solid pea-size flat round grayish verrucas occur. No subjective symptoms.

Treatment. The production factor shall be detected and eliminated. A and E vitamins, keratolytic pastes and creams are used.

Dermatoconiosis is resulted in impact of chemical, mineral, plant and animal powdery substances which occur in work conditions and cause mechanic or chemical irritation on penetration to skin and blocking excretory ducts of oil and sweat glands. Affection is localized in opened skin areas.

Clinical findings. The colour skin changes, the non-inflammatory and erythematic spots, follicular papules, excoriations occur. The subjective symptom is itchiness. The disease is differentiated with atopic dermatitis.

Treatment. Depends on the clinical findings, like for common dermatoses.

Professional dermatoses caused by physical factors

Freeze injuries occur under long-term impact of low temperatures, under the contact with coolants etc. It may cause both local and general hypothermia. According to the clynical progress there are four stages of freeze injuries: first stage is characterized by stagnant cyanochrous colour and edema of the affected skin areas accompanied with feelings of tingling and itchness; the second – by appearance of vesicles filled with serous or haemorrhagic fluid in the setting of stagnant cyanochrous skin; the third – by necrosis of the affected skin areas and deep soft tissues; the fourth – by necrosis of soft tissues and bones.

Treatment. At the responsive stage in case of first degree freeze the diseased person shall get warm in the room with the temperature of 18-20 °C followed by rubbing the affected skin areas by 5% tannin or boric spirit and applying the warm aseptic dressing. In case of second degree freeze the affected areas shall be cured with spirit, the vesicle tectorium shall be cut off and the lotion with disinfecting solution shall be applied. In case of third and fourth degree freezes the surgical stationary treatment is indicated.



Fig. 9.2. Photocontact dermatitis.

Perfrigeration is caused by impact of cold jointly with humidity (at the water transport, in fishing and forestry industry, agriculture). Its clinical findings are the limited edema, solid or soft consistence and cyanochrous reddish colour of the affected skin areas.

Photocontact dermatitis occurs under the impact of sun rays at the persons who work in the open space (house builders, agricultural workers) or who work with welding machine under the impact of artificial radiation and at the persons who contact with photodynamic substances (tar, creosote, sulfanilamides, mercury agents, aromatic hydrocarbons, manganese and iron salts, oil and coal tars). Sun dermatitis usually occurs in spring and summer.

Etiopathogenesis. As the result of direct impact of ultraviolet rays on skin the DNA structure destroys and the inflammation mediators are histamine, prostaglandins, interleukins which cause pain and edema.

Clinical findings. On the open skin areas (face, neck, arms) the hyperaemia and edema occur in the setting of itchiness, soreness (first degree), large amount of vesicles appears (second degree). General condition disorder (high temperature, weakness, anxiety, sleep disorder, loss of appetite). In three or four days inflammation is replaced by peeling and the stable brown pigmentation develops which prevents recurrence.

Diagnostic. Diagnosis of photocontact dermatitis is based on anamnesis and clinical examination. Differential diagnostics is held with protoporphyria and drug-induced phototoxicity.

Treatment. Insolation and contact with photosensitizer shall be avoided. B vitamins are indicated in standard doses, coolants, glucocorticosteroid pastes and creams are applied. Series of cosmetological means are used for skin care.

Prevention. Solar radiation shall be avoided, the reasonable clothes made of solid protective fabric shall be worn, photoprotective pastes and creams (Anthelios XL SPF 50+, Anthelios AC SPF 30 etc.) shall be used.

Cheilites occur as the result of impact of meteorological, mechanic, chemical and biological factors in working conditions.

Clinical findings. Inflammation of vermilion zone is shown in the form of dryness, peeling, scabs, cracks of mucous and skin around the mouth.

Treatment. The basic treatment is elimination of impact of etiologic factors. The B vitamins are used, the lotions with anti-inflammatory and disinfecting solutions are

used in case of acute events. After decrease of inflammatory events the corticosteroid creams are spread on the affected areas.

Prevention. Impact of factors which cause the disease shall be eliminated.

Burn injuries are caused by impact of high temperature on skin.

Clinical findings. There are four stages of burns: I – erythema and edema accompanied with itchiness and soreness, II – erythema and large vesicles filled with serous or haemorrhagic fluid, III – derma necrosis, IV – necrosis of all skin layers.

Treatment. In case of limited first degree burns the anti-inflammatory, anti-allergic and antipruritic means are applied on the affected surface. In case of limited second and third degree burns the skin around the burnt area is cured with spirit, the physiological solution or hydrogen dioxide is applied on its surface, the vesicle tectorium is cut off and the sterile dressing with disinfecting solution is applied on the diseased area; later pastes and creams with glucocorticoids are used. In case of deep fourth degree burns the surgical treatment is indicated.

Professional signs (stigmas)

There are temporary and stable professional stigmas. *Temporary* stigmas are:

1. **Colour staining** is caused by penetration of colouring agents inside skin, hair and nails. Its stability depends on the depth of penetration and colouring agent features (typical of lacquerers, painters etc.).
2. **Callosity** is thickening of skin corneous layer (hyperkeratosis) which is caused by long-term friction or pressure (typical of refining miners, diggers etc.).
3. **Pigmentation** is skin colour changing up to brown caused by crusting and solar radiation (typical of seamen, fishermen etc.).
4. **Cracks** is the skin integrity disorder with loss of skin viscoelasticity caused by impact of mechanic factors, crusting, freeze injury (typical of solderers, tinsmiths etc.).

Stable professional stigmas are:

1. **Penetration (contamination)** is occurrence of stable dim-grey skin colour as the result of contact with metal dust jointly with mineral oils (typical of miners, steelworkers, combat engineers etc.).
2. **Scars** are caused by small injuries in working conditions due to penetration of hot or molten metals, hot liquids, steam onto skin typical of mill roller, moulders).
3. **Telangiectasia** is a stable expansion of surface blood vessels which appears on the opened skin areas (typical of hot shop workers, steelmakers, glassblowers, coal heavers, cooks, smiths etc.).
4. **Nail changing** is the result of mechanic and chemical impact (typical of watchmakers, laundresses, enamellers etc.). Clinical findings are cracks in nails, nail malacia, thinning, tarnish. In order to prevent their affection by mycotic infection (onychomycosis) the water-repellent gel *Nailexpert by Wartner* is recommended to be applied locally. The unique formula of such product creates a special pallet on the

nail surface, creates conditions unfavourable for fungus existence and prevents infection of healthy nails.

Professional dermatoses of infectious and parasitical etiology

Erysipeloid *(erysipeloid Rosenbach)* is the most widely spread professional skin disease of infectious etiology.

Etiology. Caused by swine erysipelas *(Rhusiopathiae suis).*

Epidemiology. It is the most widely spread among the meat factory, leather/fur industry, canning\fish factory workers. Developent of the disease is caused by injuries and penetration of the irritant through the affected skin. Rodents are the main infection carriers. The disease usually does not transmit from the ill person to the healthy one.

Clinical findings. The incubation period lasts from several hours till two or five days.

The affections are mainly localized on the skin of hands and fingers. At the place where the irritant penetrates inside the limited acute painful swell occurs with dark red erythema (further replaced by cyanochorus blue-grey colour), papules and vesicles may appear. The process trends to spread over the finger joints. High temperature, weakness, shiver, enlargement of regional lymph nodes are possible. The disease lasts from two till six weeks and may become chronic with repeated recurrences.

Diagnosis. Diagnosis is based on the anamnesis, clinical findings and the result of laboratory research complex.

Treatment. Antibiotics (erythromycin, penicillin), pastes and creams with antibiotics and corticosteroids are used.

Prevention. Sanitary standards for manufacturing areas and work hygiene rules shall be observed, deratization shall be held. The veterinary inspection of animals, meat and fish products, prevention of small injuries and proper cure of the affected skin are required.

Paravaccinia is the dairy-women's professional disease; zootechnicians, veterinary physicians and other workers who have contact with the infected cattle may also suffer it.

Etiology. Etiological agent is the cowpox virus**.**

Epidemiology. Disease for cows (rarely for ship and goats). As for the diseased animals the eruptions occur in utter and nipple skin. People get infected during the direct contact with such animals. The disease does not transmit from the ill person to the healthy one.

Clinical findings. The incubation period makes up three or four days. The affections are mainly localized on hands, forearms, face. The painful solid pea-size nodules with

hollows in the center appear in the setting of hyperthermia and edema. Further the blackish brown scab appears on the hollow and when it deops off the dark spot and the scar remains. The eruption lasts up to two months.

The progress is favourable in general.

Diagnostic. Diagnosis of paravaccinia is based on anamnesis, clinical findings and the result of laboratory research complex.

Treatment. In order to accelerate the nodule dispersion and to prevent the development of secondary infection the antivirus pastes and aniline dyes are used.

Prevention. Work hygiene rules shall be observed, the veterinary inspection of animals shall be held, small injuries shall be cured properly.

Professional mycoses (trichophytia, microsporia, favus, epidermophytosis, rubromycosis, candidosis, deep fungal diseases) occur mainly at the veterinary physicians, zootechnicians, vivarium employees who contact with animals ill on mycosis as well as hairdressers, bath men and medical employees contacting with those who are ill on fungal diseases.

Etiology. The disease is caused by different species of anthropophilic, zooanthropophilic and candidal fungi. The infection occurs due to non-compliance with the work hygiene rules, due to contact with the ill people and animals.

Clinical findings. It corresponds to the clinical symptoms of non-professional diseases of the similar features.

Diagnostic. Diagnosis is based on the anamnesis, clinical findings, the results of bacterioscopic and cultural research.

Treatment. It is necessary to eliminate the contact of the ill person with the production factor. The systematic and local antimycotic drugs are prescribed taking into account the etiology of mycosis, localization and severity of the affection.

Prevention. Sanitary standards for manufacturing areas and work hygiene rules shall be observed, the current disinfection shall be held, the staff shall be provided with working clothes and shall store it correctly; the deratization is necessary if there are any rodents. They should hold periodic medical inspections and take care of the proper treatment and of taking the individual preventive measures; personal, social and health education is required.

1. The professional dermatosis develops:

A. Under the contact with different irritants in work conditions
B. As the result of genetic predisposition
C. Under viscerapathology
D. As the result of inefficient treatment
E. Due to injuries

2. What skin tests are used in professional dermatoses:

A. Application tests
B. Spot tests
C. Scarification tests
D. Intradermic tests
E. Everything is right

3. What are the features of the simple contact dermatitis:

A. Absence of incubation period
B. Long-term incubation period
C. Prevalence of the affection
D. General condition disorder
E. Strong itchiness

4. What are the causes of the professional signs (stigmas):

A. Work with dyes
Б. Work in hot shop
C. Work with plants
D. Work in open space
E. Everything is right

5. What external irritator may cause the simple contact dermatitis:

A. Use of antibiotic pastes
B. Use of laundry powders
C. Contact with synthetic fabric
D. Use of cosmetics
E. Everything is right

6. The simple contact dermatitis is:

A. Acid burn
B. Dermatitis caused by the contact with jellyfish
C. Dermatitis caused by the contact with household detergent
D. Dermatitis caused by the contact with plant
E. Everything is right

7. What is the influence of the professional signs (stigmas) on working capacity:

A. Disorder of working capacity
B. Temporary disorder of working capacity
C. No disorder of working capacity
D. Physical disability
E. Temporary disorder of working capacity

8. What are the typical features of the professional eczema:

A. Hive localization on hands
B. Asymmetric eruption
C. Hive localization in knife pleats
D. Hive localization on mucous
E. Everything is right

9. What are the symptoms of the simple contact dermatitis:

A. The affection area corresponds to the boundaries of the irritator's activity
B. The affection area is beyond the boundaries of the irritator's activity
C. Presence of incubation period
D. Degree of dermatitis manifestation does not correspond to the impact of the irritator
E. Hive of the haemorrhagic origin

10. What are the main preventive measures of the professional toxicoderma:

A. Collection of allergological anamnesis
B. Treatment of concomitant diseases
C. Use of personal protection if necessary
D. Work hygiene observance
E. Everything is right

Task 1. The worker of the cement plant visited a dermatologist with complaint on itchiness, redness, edema, madescence of hand skin. The affection boundaries are unclear; there is no eruption in other skin areas. He has been ill for almost one year with periodic recovery during vacation.

a) Choose the most probable diagnosis:
- **A**. Allergic professional dermatitis
- **B**. Chronic ulcerative pyoderma
- **C**. Seborrheic eczema
- **D**. Microbial eczema
- **E**. Professional eczema

b) Make a differential diagnostics.

Task 2. The 56-year old patient who had a permanent contact with ultraviolet radiation visited a dermatologist. He has complaint on roughening of the opened skin areas, crack and scars thereon.

a) What diagnosis may be suspected:
- **A**. Professional stigmas
- **Б**. Lupus erythematosus
- **C**. Chronic dermatitis
- **D**. Allergic dermatitis
- **E**. Toxicoderma

b) Make a diagnosis, choose the methods of treatment and preventive measures.

Task 3. The 46-year old driver visited a dermatologist with complaint on hand skin affection after engine repair work on freeze. The subjective symptoms are itchiness, feeling of tingling, burning, pain. The objective symptoms are: stagnant cyanochrous colour of skin, edema.

a) What is the provisional diagnosis:
- **A**. Perfrigeration
- **B**. First degree freeze injury
- **C**. Second degree freeze injury
- **D**. Psoriasis
- **E**. Professional eczema

b) Make a differential diagnostics.

Task 4. The 52-year old woman who worked as a yard-keeper visited a dentist. She has complaint on lip affection, itchiness in this area on eating spicy food. Has been ill for three months. Objective symptoms: dryness, peeling, cracks, scabs on the vermilion surface.

a) What is the provisional diagnosis:
- **A**. Freeze injury
- **B**. Lichen acuminatus
- **C**. Cheilitis
- **D**. Syphilis of the secondary stage
- **E**. Psoriasis

b) Determine the criteria of differential diagnostics of the present pathology, put on medication

Task 5. The 25-year old woman visited a dermatologist. She has been working in a greenhouse as flower cultivator. She has been ill for two weeks. Clinical findings are: erythematic spots, follicular papules, excoriation on the opened skin area. The subjective symptom is itchiness.

a) Choose the most probable diagnosis:
- **A**. Allergic professional contact dermatitis
- **B**. Melanoderma
- **C**. Limited hyperkeratosis
- **D**. dermatoconiosis
- **E**. Eczema

b) Name the causes of the abovementioned disease, make a differential diagnostics, put on medication.

Answers for first level self-control questions
1 – A, **2** – E, **3** – A, **4** – E, **5** – E, **6** – A, **7** – C, **8** – A, **9** – A, **10** – E
Answers for second and third level self-control questions
1a – E, **2a** – A, **3a** – B, **4a** – C, **5a** – A

10 TOPIC

Bullous dermatosis

There are non-communicable dermopathies which most components of hives is a bulla belongs to bullous dermatosis. There are following dermatosis belongs to them:

1. Pemphigus Vera (acantholytic):
   a) pemphigus vulgaris;
   b) pemphigus vegetans;
   c) pemphigus foliaceus;
   d) seborrheal pemphigus.
2. Nonacantholytic pemphigus of oral mucosa.
3. Pemphigoids
   a) bullous pemphigoid;
   b) cicatricial pemphigoid;
   c) pemphigoid gestationis.
4. Dermatitis herpetiformis:
   a) Duhring disease;
   b) Sneddon-Wilkinson disease.
5. Genetic bullous dermatosis
   a) Gougerot-Hialey-Hailey disease;
   b) Group of bullous epidermolysis.

EDUCATIONAL AND TRAINING PURPOSES

- Determine possible conditions and triggers for emergence of pemphigus vera and Duhring disease
- Examine classification and common characteristics of different forms of pemphigus vera and Duhring disease
- Examine common clinical course and clinical findings of pemphigus vera and Duhring disease
- Determine clinical findings of typical appearances of pemphigus vera and Duhring disease
- Determine principles of therapy for pemphigus vera and Duhring disease

10.1 Pemphigus Vera

Pemphigus Vera is a malignant autoimmune disease which declares itself as elaboration on uninflamed skin and mucous coats of bulla being developmental as a result of acantholysis and generalized for whole skin integument without appropriate treatment.

TO KNOW:

- classification of bullous dermatosis;
- modern conception of aetiopathogenesis of pemphigus vera;
- pathomorphological changes of skin at pemphigus vera;
- its' clinical forms;
- clinical laboratory diagnostic criterion of this disease;
- methods and principles of remedial measures and periodic health examination of patients with pemphigus vera.

TO BE ABLE TO:

- correctly determine the Nikolsky's sign;
- perform the differential diagnostics with dermatosis having similar clinical presentation;
- assign corresponding laboratory assessment required for diagnosis confirmation;
- prescribe balanced treatment for patient with pemphigus vera.

Aetiopathogenesis. Aetiology is not investigated fully but autoimmune mechanisms are very important in pathogenesis. The circulating autoimmune antibodies of lgG type related to intercellular substance of prickle-cell layer and membrane antigens of prickle epithelial cells were discovered in organism of patient with pemphigus. For the now, there is no clear vision of autoimmune antibodies' action mechanisms during pemphigus vera. The patients have been discovered autoimmune antibodies for albumins of skin keratinocyte cell-cell becoming a part by desmos and forming relations between cells – desmoglein-3 (DSG3) and desmoglein-1 (DSG1).

Interaction of autoimmune antibodies with DSG1 and DSG3 leads to acantholysis (breaking of cytoadherence between keratinocytes) resulting in formation of clefts filled up with subcutaneous water inside the epidermis and mucous coats and appearance of bulls. As far as epidermis growths the bulls are opens resulting in formation of anabrosis on skin and mucous coats.

The difference in damages being observed during pemphigus vulgaris and during pemphigus foliaceus is aligned with distinction in localization and density of DSG1 and DSG3 expression. Desmoglein-3 is expressed in deep layers of epidermis and in epithelium of mucous coats while desmoglein-1 is expressed in facial layer of skin keratinocytes. The expression of these desmogleins is observed mostly in cells of laminated epithelium. It depends on human's age and changes in accordance with allocation of cells in epidermis. It is understandable that bundling of autoimmune antibodies with DSG3 molecules on the surface of keratinocytes plays decisive role in process of acantholysis. Great significance in acantholysis induction the apoptosis has induced by failure of cells normal functioning because of lost contact with adjacent cells.

It is proved that dominant class of autoimmune antibodies at pemphigus the lgG antibodies are of lgG_4 subclasses mostly, more rarely these are antibodies of lgG_1 and lgG_2 classes. The patients with active form of disease have the immunoglobulins of lgG_1 and lgG_4 classes as main autoimmune antibodies. The patients in disease-free survival the dominant antibodies are antibodies of lgG_1 class but they also have antibodies of lgG_4 class since its dilution is much less than at recrudescence of disease. The result of antibodies action is an attenuation of intercellular substance and destroying by desmos i.e. loss of connection between epidermal cells (acantholysis). As a result of acantholysis the acantholytic bullas typical of Pemphigus Vera are appear in epidermis (in distinction to pemphigoid).



Fig. 10.1. Pemphigus vulgaris.

Clinic findings. There are four clinical forms of pemphigus vera which are vulgaris (common), seborrheal (pemphigus erythematosus), vegetans and foliaceus.

Pemphigus vulgaris occurs more often in comparison with other types of pemphigus vera. As a rule, the disease begins from damage of oral mucosa and throat which could exist separately during few months. Bulla breaks fast and transforms into painful bright-red or covered by whitish deposit of anabrosis bordered by pieces of epithelium (residues of bulla cover). Then bulla appears on skin. Bulla are located on externally unchanged skin and they full of transparent serosal content.

After existence during few days the bullas are open having been left anabrosis of bright red color. Sometimes their content becomes opacity or suppurative. Common condition of patients is satisfactory at first but it becomes worse gradually. The weakness appears and a low-grade fever. Anabrosis are epithelized slowly.

Pemphigus seborrheal (erythematosus) occurs on seborrheal areas of skin (face, hairy part of the head, cervix, dorsum). It is characterized by occurrence of spots and soft surface bulla with thin tegmentum which are fast-transformed into scaly crusts. After crusts being removed the wet eroded surface is open. The formation of bulla could be hidden resulting in impression of primary appearance of crusts which reminds seborrheic dermatitis.

As distinct from pemphigus vulgaris the course of disease is long-standing and relatively nonmalignant. The common condition of patients is agglutinin aggravates at condition of prominent prevalence rate of process only.

Pemphigus vegetans is characterized by such differential characteristic as appearance on the bottom of bulla of enlargements in form of vegetations which overhang over the faying surface. Typical places of hives localization are outer genital organs, big sentinel piles, inner surface of hips, oral mucosa.

Pemphigus foliaceus declares itself by bulla which has soft rugate tegmentum, layered scaly furfur and crusts. The differential characteristic of this form is absence of regeneration under crusts and formation of new bulla on place of cicatrization.



Fig. 10.2. Pemphigus seborrheal.

Diacrisis. The criteria of diagnostics for pemphigus vera include clinical and laboratory evidences of presence of acantholysis in epidermis and epithelium of mucosa coats.

There are seven most criteria distinguished:

1. Typical clinical picture of damage: the bulla on unchanged skin,

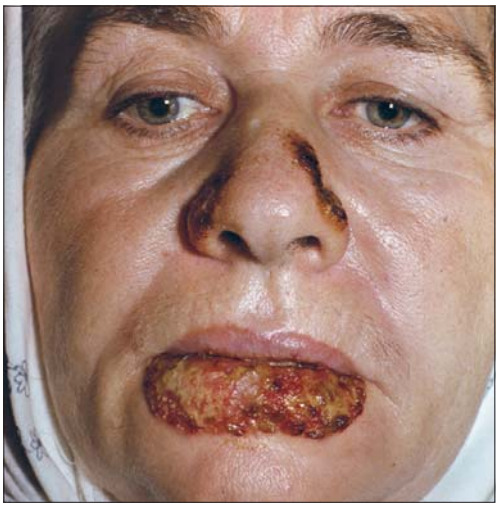


Fig. 10.3. Pemphigus vegetans.



Fig. 10.4. Pemphigus foliaceus.

long-standing anabrosis on skin and on unchanged oral mucosa, conjunctiva, nasal mucosa, genital organs. There are residues of bulla tegmentum could be observed on the periphery of anabrosis.

2. Nikolsky's sign on externally unchanged skin. At weak tension by finger of outwardly healthy skin near the bulla and sometimes far from them the lamination of epithelium surface layers occurs with formation of anabrosis. This phenomenon is considered to be most informative at diagnosis of all types of pemphigus. However, it is not pathognomonic.

3. Nikolsky's edge sign. While pulling by forceps of pieces of bulla tegmentum the lamination of epithelium out of borders of visible anabrosis occurs.

4. Asboe-Hansen sign. Pushing the bulla leads to increasing of its square.

Determination of Nikolsky's and Asboe-Hansen's signs are important diagnostic clues for establishing of provisional diagnosis. However, they are non-specific. The cytological, histologic and immunomorphologic approaches are used for diagnosis confirmation.

5. Cytological approach of diagnostics (cytodetection by Tsank) provides obtaining of impression smears from the bottom of fresh anabrosis. For this the object carrier is used which is solidly applied to the surface of fresh anabrosis. For getting of smears from anabrosis on mucosa coat of bony and soft palate and throat the mediated approach of its obtaining is used. The soft scraping of anabrosis surface is performed by blunt depressor or by nutrient spoon avoiding visible damage of surface and escape of blood after which the material being taken from the bottom of anabrosis is applied carefully to the object surface in form of smear. Obtained smears are dried and painted by the method of Romanovsky-Gimza. During further microscopic evaluation of specimens the Tsank's acantholytic cells are determined. This is a changed cells of spinous layer which were subject to acantholysis,

degenerated and thus obtained morphological and tinctorial properties which differs them from normal cells of this layer:

- they are round (oval), disengaged, and less than normal epidermal cells by size;
- the nucleus of acantholytic cells are painted intensively;
- there are two or three small nucleus could be discovered inside the enlarged nucleus;
- cytoplasm of cells is extremely basophilic and is painted unregularly; the light-blue area is formed around the nucleus and the condensation of painting in view of intense blue border occurred on periphery;
- under pemphigus the acantholytic cells could form a symplast cells which have several nucleus.

6. Histologic approach of examination is one of the most and obligatory while confirmation of pemphigus vera diagnosis. It is necessary to biopsies the fresh bulla or marginal layer of anabrosis with pinch of undamaged skin. The most earlier histologic changes in epidermis under pemphigus vera are vacuolar degeneration and disappearance of cell bridges in bottom part of spinous layer. Because of acantholysis the clefts appears inside the epidermis and then a bulla located suprabasally (i.e. over basal layer of cells, intraepithelial). The typical histologic characteristic under pemphigus vera is also discovering of separate changed prickle cells which after loss of connection with each other are left attached to the layer of unchanged basal cells.

Immunomorphologic approaches play decisive role in diagnostics of pemphigus vera. Even at early developmental stages the approach of direct ELISA on frozen skin sections allows to discover the deposits of class G immunoglobulines and complement localized in intercellular space of epidermis (greenish fluorescence). The approach of indirect immunofluorescence in blood and bulla liquid allows to discover high dilutions of autoimmune antibodies (lgG) in relation to proteins of elements by desmos. The height of their dilutions is straight correlate with heavy of section for pemphigus vera.

Treatment. Till now, the causation of pemphigus vera is not known, so the treatment of this group of diseases is left pathogenetic and directed to the depression of fusion of autoimmune antibodies to the proteins of epidermis spinous cells' desmosomal linkages. The main remedy of the systemic medication of patients with pemphigus vera are the glucocorticosteroid hormones. They are assigned independently (monotherapy) or together with cytostatic (combination therapy) – with azathioprine or methotrexate, cyclophosphamide, cyclosporine A. Combination therapy is implemented during the treatment of pemphigus which is resistant to the high doses of glucocorticosteroids and in case of necessity of its daily dose decreasing (loading or maintenance).

The treatment of patients with pemphigus vera should be started from loading doses of glucocorticosteroids, preferably from prednisolone or prednisone. The dose of prednisolone of 100–120 mg per day is an adequate loading dose allowing to stop the forming of bulla and to enforce the epithelialization of anabrosis with the physiological rhythm of provisional cortex secretion

Table 10.1.
Differential diagnostics of clinical forms of pemphigus vera

Evidences	Pemphigus vulgaris	Pemphigus vegetans	Seborrheal pemphigus	Pemphigus foliaceus
Location	Visible mucosa coats, more often in oral cavity; skin of head and body; could appear in skin folds	Mucosa coats, more often oral one, big skin folds, places of transition of skin into mucosa coats	Face, hairy part of the head, mammary gland, dorsum, rarely the oral mucosa coat could be damaged	Skin of head, mammary gland, dorsum. The damage on a face could have a shape of butterfly
Clinical implications	Soft unstable bulla on unchanged skin and mucosa coats, long-standing anabrosis under crusts (out of folds), pigment spots	Soft bulla opened fast, on unchanged mucosa coat and skin; stable anabrosis with whitish (pultaceous) vegetative surface, enlarged and interlocked	Rash is represented by weak infiltrated erythematic patches covered by furfur and lamellar crusts removing of which leads to cropping out the surface anabrosis. There are thin-shelled soft bulla could be observed on erythematic background.	The mucosa coats are not damaged. Erythematic sites of damage tend for peripheral growth, covered by lamellar furfur removing of which leads to discovering of anabrosis. Separate flat bulla on erythematic background. The peripheral growth, interlocking of sites of damage, and forming of exfoliative erythrosis are typical.
Nikolsky`s sign	+	+	++	+++

Table 10.1. (cotinued)

Evidences	Pemphigus vulgaris	Pemphigus vegetans	Seborrheal pemphigus	Pemphigus foliaceus
Cytodetection (impression smear)	Acantholytic cells	Acantholytic cells, eosinocytes	Acantholytic cells are discovered rarely	Same
Histodiagnosis	Intraepidermal, suprabasal acantholysis determines the origin of fissured cavity paved by spinous (acantholytic) cells	Intraepidermal, suprabasal acantholysis, fissured suprabasal cavities, pseudoepitheliomatous hyperplasia, acantholytic cells, numerous eosinocytes	Intraepidermal, suprabasal acantholysis, leukocytic infiltration of papillary dermis	Intraepidermal, suprabasal acantholysis determines the origin of fissured cavities under horny layer and at level of granular layer. Small inflammatory leukocytic infiltrate in dermis
Direct IF	Deposits of lgG and C_3-complement on intercellular linkages level of epidermis` spinous layer cells	Same	Deposits of lgG and C_3-complement in intercellular spaces and directly under epidermis	Same
Non-Direct IF	Antibodies against intercellular substance of epidermis (lgG)	Same	Same	Same

hormones. The maximum dose of glucocorticosteroids (usually it is two thirds of the daily dose) is being used after meals in the morning, and one third more during the day. The therapy should be started after a complete clinical examination of the patient and verification of diagnosis (biopsy of damaged skin, immune histochemical tests). Unfortunately, there are no such drugs which will decrease selectively the formation of autoimmune antibodies of pemphigus only, without simultaneous depression of biosynthesis of many other protective antibodies. A variety of other undesirable effects (Exogenetic (medicamental) Cushing syndrome, immunosuppression, water-salt balance failures, hypoproteinosis, intestine issues, and others) is opposed to the same anti-inflammatory and antiproliferative action of glucocorticosteroids.

There are water and alcohol solutions of aniline colorants used for local therapy as well as aerosols, unctures, and creams containing glucocorticosteroids.

Course and prognosis. The course is chronic with intermittent remissions and recrudescence. The use of glucocorticosteroids and immunosuppressants rapidly improves the prognosis. The cause of death for now is generally results from continuous treatment with glucocorticosteroids and immunosuppressants.

This approach is aimed at the suppression of the synthesis of autoantibodies to the desmosomal protein linkages of epidermis spinous cells. The main remedy for systemic treatment of pemphigus vera is glucocorticosteroid hormones. Despite numerous and various complications arising from glucocorticosteroid treatment, there are no absolute contraindications to their use in pemphigus, as only the use of glucocorticosteroids prevents the death of patients. Glucocorticosteroid hormones are prescribed independently (monotherapy) or in combination with a cytostatic (combined therapy with azathioprine or methotrexate, cyclophosphamide, cyclosporine A). Cytostatics cannot fully replace glucocorticosteroids. However, they help reduce the dose of glucocorticosteroids. Combination therapy is applied when treating pemphigus resistant to high doses of glucocorticosteroids and when it is necessary to reduce their daily dose (loading or maintenance).

At the present stage, biological therapy is increasingly used in the treatment of pemphigus vera, particularly with monoclonal antibody inhibitors of CD20. The most commonly prescribed drug in this group is «Rituximab.» Biological therapy can be administered as monotherapy or in combination with glucocorticosteroids, depending on the severity of the dermatological condition. The structure of the drug «Rituximab» belongs to class G immunoglobulins that can bind to the CD20 antigen of B-lymphocytes. The drug initiates immunological reactions that lead to the lysis of B-lymphocytes and selectively stimulates apoptosis. «Rituximab» is administered intravenously, drip-wise, once every two weeks.

Glucocorticosteroids, cytostatics, and CD20 monoclonal antibody inhibitors in adequate doses lead to disease remission. The success of treatment

depends on the daily dose of medications and the timing of the start of therapy. Treatment of patients with pemphigus vera should begin with loading doses of glucocorticosteroids, preferably with prednisolone or prednisone. The special literature debates the magnitude of loading doses of glucocorticosteroids, which may vary depending on the severity and extent of the condition. According to research from several leading foreign and domestic dermatological clinics, a daily dose of prednisolone of 100–120 mg is typically an adequate loading dose, which allows for the cessation of blister formation and accelerates the epithelialization of erosions. If blister formation does not cease within a week, the daily dose of prednisolone is increased by a third. Therapy should be initiated as early as possible after the onset of the disease.

Currently, there is a wide arsenal of oral synthetic glucocorticosteroids (prednisolone, prednisone, methylprednisolone, fluorine-containing preparations such as triamcinolone and its analogs like Kenacort, Polkortalon, and betamethasone derivatives such as Celeston). These have proven more effective in treating patients than equivalent doses of water-soluble glucocorticosteroids, as they are not rapidly eliminated from the body.

When prescribing glucocorticoid therapy, it should be remembered that the effectiveness of treatment increases if the daily dose of the hormone is distributed in accordance with the physiological rhythm of adrenal cortex hormone secretion. The maximum dose of glucocorticosteroids (usually two-thirds of the daily dose) should be taken after meals in the morning, with the remaining third taken during the day. Therapy should begin in a dermatological hospital after a full clinical examination of the patient and diagnosis verification (biopsy of affected skin, immunological tests). Special attention should be paid to the condition of the gastrointestinal tract, as well as the presence of chronic infection foci and other concomitant diseases.

Course and prognosis. The course is chronicity with intermitting remissions and recrudescence. The using of glucocorticosteroids and immunosuppressants rapidly improves the prognosis. Cause of death for the now is generally results of continuous treatment by glucocorticosteroids and immunosuppressants.

10.2 Duhring disease

Duhring disease is a long-lasting dermatosis of unknown causation which is characterized by continuous anticipate course with attack-like appearance of pruritic polymorphous eruption on skin of body and extremities.

TO KNOW:

- classification of bullous dermatosis;
- modern conception of aetiopathogenesis of Duhring disease;
- pathomorphological changes of skin at this disease;
- clinical forms of Duhring disease;
- its' clinical laboratory diagnostic criterion;
- methods and principles of remedial measures and periodic health examination of patients with Duhring disease.

TO BE ABLE TO:

- correctly determine the Nikolsky's sign;
- perform the differential diagnostics with dermatosis having similar clinical presentation;
- assign corresponding laboratory assessment required for diagnosis confirmation;
- prescribe balanced treatment for patient with Duhring disease.

Aetiopathogenesis. The hypersensibility of organism to the vegetable protein (protein containing in grain varieties) which is appear in intestinal canal during digestion process and to the halogens (iodine, fluorine) plays role in pathogenesis. The provoking factors are inflammatory processes in gastrointestinal tract, lumbricosis, malignant tumors, using of halogens, and contagious diseases.

Duhring disease is more often progresses with individuals who have pathematology of small bowel with intestinal malabsorbtion – malabsorbtion syndrome (gluten entheropathy) which is conditioned by absence of tolerance to gluten. It is considered that gluten plays a role of antigen of protein nature and initiates the production of lgA-antibodies inside the gastrointestinal tract. The result is that reboiling of graminoids containing gluten leads to forming of immune complexes which causes to damage of mucosa coats of small bowel with progression of villous atrophy and intestinal tract parafunction. Through the damaged papillae of mucosa the immune complexes goes to general circulation penetrating to the papillary dermis and fixing there. Most of patients with Duhring disease have deposits of lgA-antibodies in structure components of dermal papillae at area of dermoepidermal junction of skin damaged sites and around. The deposits of lgA-antibodies is often allocated in view of granules on the top of the papillary dermis and inside them and it is more rarely allocated in-line, along the basement membrane. The antibodies circulating to the gluten and its fraction which gliadine is or circulating immune complexes are discovered in blood.

Clinic findings. As regular, the disease begins from occurrence of pruritus, heat or tingling which could be accompanied by general uneasiness, rise of temperature and usually outrun the occurrence of hives for several hours, days or even months. The hives is usually symmetric, could be at any site of skin integument, but favorite places are extensor surfaces of extremities, skin of body and buttock.

Hives at Duhring disease is characterized by true pleomorphism. Following initial components could be separated:

- *erythematic* spots and papule which being interlocked and grouped forms figures with different contours (herpetiform groups);
- strained *vesicles* on edematous warp having tend to grouping and herpetiform allocation; after being opened they form anabrosis on edematous background on the periphery of which the pieces of vesicles tegmentum are observed; The crusts are formed on the anabrosis surfaces, the epithelialization occurs fast under them, often the areas of hyperpigmentation are left;
- *strained bulla* with diameter of 0.5-2 cm and more with solid tegmentum and at first with serosal and then with opacity content; bulla appear as a rule on slightly edematous erythematic but could appear on externally unchanged skin; in number of cases the soft bulla discovered with thin tegmentum; after bulla being opened the anabrosis forms on its places without tendency for peripheral growth, have relatively fast epithelialization and then left stable hyperpigmentation; bulla on oral mucosa coat appears extremely rare.

Morbid anatomy. During Duhring disease the following is discovered histologically:

- subepidermic bulla in content of which the eosinocytes are prevail;
- microabscesses located on the tops of dermal papillae and containing neutrophils, eosinocytes, polymorphonucleocytes and deposits of fibrins;
- oedema and infiltration of derma which is stipulated by angiectasis and accumulation of perivascular eosinocytes, neutrophils and destroyed nucleolus («nuclear dust»).

Diacrisis. Diacrisis of Duhring disease is based on following clinical information:

1) continuous pruritus of different gradation, sometimes esthesia of heat, tingling and painfulness appears;

2) true polymorphism of hives which could be accompanied with false polymorphism;

3) herpetiform grouping of hives components;

4) chronicity which is interrupted by complete or incomplete remissions of three months to one year duration and more.

The content of eosinocytes in blood and bulla liquid where it is far exceeds is determined for diagnosis confirmation. The patients with Duhring disease are differed by hypersensibility for iodic medical product so the three-glass test with 50% potassium iodide is used which is performed in two options – epicutaneous and per os. Analysis is considered to be positive in case of in-patient recrudescence. The negative Nikolsky's sign and absence of acantholytic cells in bulla content are typical.



Fig. 10.5. Duhring disease.

Treatment. The lifelong gluten-free dietary intervention is indicated. The abuse of wheat, corn, barley, oats and millet i.e. bread, alimentary products, manna, oat and wheat grits is excluded. There are mushes from buckwheat, rice or corn grits allowed. Moreover, the products which the presence of iodine is considered to be in are excluded (seafood).

The most effective modes of therapy for Duhring disease now are medical products of sulfonic range – diamino diphenyl sulfone (DDS), dapsone, aulosulfone, diucifone, and sulfapyridine. Usually, the DDS or diucifone is assigned by 0.05-0.1 g twice per day in cycle of 5-6 days with interval of 1-3 days (3-5 cycles and more). Course dose depends on effectiveness and tolerance of a drug.

Table 10.2
Differential diagnostic characters of pemphigus vera and Duhring disease

Indicants	Pemphigus vera	Duhring disease
Age	Children ill very rare	Any age
Start of disease	At first the oral mucosa is damaged and then a skin	The skin is damaged but the oral mucosa is not
Bulla`s nature	Soft unstrained pear-shaped bulla	The bulla ar e strained and have round shape
Location of hives	Non-grouped	Grouped
Anabrosis	Major	Small
Allocation of bulla in relation to epidermis	Intraepidermal	Subepidermal
Nikolsky`s signs	Positive	Negative
Hansen`s symptom	Positive	Negative
Three-glass test	Negative	Positive
Tsank cells	Discovered	Not discovered
Presence of eosinocytes in bulla and peripheral blood	Absent	Present
Pruritus of skin	Non-typical	Very strong
Process of epithelialization of anabrosis	Slow	Fast
Presence of antibodies	Antibodies of lgG class	Antibodies of lgA class

There are hyposensitizaton and antihistamine drugs, vitamin therapy (vitamins of B, A, E and C group), disintoxication therapy and antioxidants (folic acid, methionine, Retabolil and others), anxiolytics and anxiety medications also indicated.

While intake the sulfones the erythropoiesis stimulating agents are assigned (vitamin B_{12}, hemostimulin).

The spirits of aniline colorants are used *for local therapy* as well as aerosols, creams and unctures containing glucocorticosteroids.

Course and prognosis. The course is chronicity, anticipate with decreasing of Duhring disease's evidences intensity. The prognosis is relatively advantageous.

1. There are following types of pemphigus vera separated:

A. Vulgaris
B. Vegetans
C. Foliaceus
D. Seborrheal
E. All of mentioned above

2. For treatment of pemphigus the most effective are:

A. Antibiotics
B. Sulfanilamides
C. Glucocorticosteroids
D. Choloroquine
E. Ftivazide

3. The test provided for confirmation of Duhring disease is about tolerance to:

A. Sulfanilamides
B. Antibiotics
C. Glucocorticoids
D. Iodine
E. Procaine

4. The most important thing for confirmation of pemphigus vera diagnosis is:

A. Discovering of acantholytic cells in the impression smears
B. Eosinophilia in anabrosis of bulla surface
C. Leukocytosis in peripheral blood
D. Discovering of LE-cells
E. Frank trombocytopenia

5. Typical location of rashes at pemphigus vulgaris is:

A. Body, oral mucosa coat
B. Hairy part of the head, body
C. Palms and feet
D. Genitals and face
E. Genitals and oral mucosa coat

6. The following are typical for Duhring disease:

A. Polymorphism of rashes
B. Leukocytosis
C. Damage of oral mucosa coat
D. Discovering of acantholytic cells in impression smears
E. Positive Nikolsky's sign

7. The Tsank cells are:

A. Acantholytic cells
B. LE cells
C. Stem cells
D. Specialized ganglion cells
E. Thymic cells

8. What symptom has special diagnostic consideration at pemphigus vera:

A. Symptom of «apple jelly»
B. Symptom of «stearic spot»
C. Nikolsky's sign
D. Besnier's symptom
E. Kebner's symptom

9. Nikolsky's sign means that:

A. The peeling is increase during erasion of components
B. Lamination of top layer of epidermis when mechanical influence
C. When pressing the bosselation the slowly disappeared pitting is left on its surface
D. Presence of Wickham's mesh
E. Discharge of blood from enlarged vases at strong press

10. Leading pathological process of pemphigus is:

A. Dyshidrosis
B. Acantholysis
C. Apoptosis
D. Hyperkeratinization
E. Spongiosis

Answers for first level self-control questions
1 – E; **2** – C; **3** – D; **4** – A; **5** – A; **6** – A; **7** – A; **8** – C; **9** – B; **10** – B
Answers for second and third level self-control questions
1a – C; **2a** – B; **3a** – B; **4a** – A; **5a** – B

Task 1. Patient of 52 years old consulted a doctor concerning the eruptions on face and extremities and strong pruritus in dedicated areas. On examination: numerous of bulla on skin of jowls, metope, antibrachium, inguinal and axillary folds on extremely reddened background sized from usual grain to pea. There are grouped papulovesicles observed.

a) Which disease corresponds to the clinical presentation being described above
- **A.** Lichen acuminatus
- **B.** Psoriasis
- **C.** Duhring disease
- **D.** Herpetic fever
- **E.** Weeping dermatitis

b) What special dermatological tests should be performed for confirmation of diagnosis?

Task 2. Patient of 55 years old was hospitalized by air medical service. General state of the patient on examination is critical, active movements are embarrassed because of pain, the temperature is 38.3 °C, mouth opens hard, and there are residues of hemorrhagic crusts on vermilion surface. The numerous of major anabrosis covered by dirty pellicle are observed at skin of alvus, axillary, femoroinguinal folds and folds under inframammary crease; there are papillomatous proliferations noticed on its surface. The perilesional vesicles and bulla are on the background of healthy skin. The Nikolsky's sign is positive.

a) What dermatosis should be thought about in this case:
- **A.** Weeping dermatitis
- **B.** Pemphigus vera
- **C.** Herpes zoster
- **D.** Herpetic fever
- **E.** Lichen acuminatus

b) What diseases the differential diagnostics should be performed with?

Task 3. Patient of 47 years old was hospitalized to dermatological department after infection disease specialist's advice. From antecedent history: complains for skin pruritus, sleep paralysis, performance decrement, sourness. Patient notices the occurrence of symptoms mentioned above after disposal of courses from sea-water fish. The state is significantly getting worse and whole body and extremities eruptions after lubrication of skin by 5% iodine tincture. Dermatologic status: on skin of body and extremities the strained small vesicles, bulla, papule having tend to grouping are determined. The Nikolsky's sign is negative.

a) What diagnosis and on which grounds could be made:
- **A.** Pemphigus vera
- **B.** Duhring disease
- **C.** Allergodermia
- **D.** Lichen acuminatus
- **E.** Mycosis of mucous membranes

b) What the patient surveillance will be?

Task 4. Patient of 40 years old has got anabrosis month ago on oral mucosa and bulla on the sternum skin, which were transformed into anabrosis fast. He used antibiotics during two weeks but there was no mend. Unbiased: the bright round-shaped anabrosis of 2-3 cm in diameter and several soft bullae on oral mucosa and on the sternum. At drawing by patient of edge of tegmentum the lamination of epidermis is observed.

a) Which disease corresponds to the clinical presentation being described above:
- **A.** Pemphigus vera
- **B.** Duhring disease
- **C.** Herpes zoster
- **D.** Herpetic fever
- **E.** Weeping dermatitis

b) What else symptoms are typical for this disease?

Task 5. Patient of 57 years old complains for appearance of numerous of bullae on skin of body, dorsum and sternum. The bullae are soft, big and with serosal content. Then the anabrosis appears which epithelized gradually. The anabrosis are also observed on oral mucosa because of which the chewing is painful. The acantholytic cells are discovered in impression smears taken from the bottom of the anabrosis.

a) What the most possible nature of this disease is:
- **A.** Weeping dermatitis
- **B.** Pemphigus vera
- **C.** Allergodermia
- **D.** Lichen acuminatus
- **E.** Leukokeratosis

11 TOPIC

Viral infections of skin and mucous membranes

Viral infections of skin and mucous membranes are the diseases caused by infection of cells with the subsequent proliferation of viruses, which are small non-cellular particles consisting of a nucleic acid (DNA or RNA) and protein shell. Depending on a leading clinical sign, there are two groups of viral diseases of skin and mucous membranes:

1) Viral infections whose main symptom is blistering (herpes simplex and herpes zoster);

2) viral infections whose main symptom is verruca (verruca vulgaris, flat wart, condyloma acuminatum, molluscum contagiosum.

Both types are caused by a viral infection of epidermis. In addition, there is a fairly large group of *systemic viral infections*, in which skin rash is caused by viremia and various systemic allergic reactions (measles, rubella, etc.).

TRAINING AND EDUCATIONAL PURPOSES

- Know the current views on etiology, prevalence, pathogenesis, and the course of viral infections of skin and mucous membranes
- Explain epidemiological features and ways of transmission of viral skin diseases
- Determine clinical symptoms and the course of skin viral infections, to understand their place in the overall morbidity patterns
- Understand the role of sexually transmitted viral infections as uncontrolled and socially dangerous
- Learn to distinguish the features of the course (clinical signs) of a simple and herpes zoster, which testify of immune deficiency and may serve as markers of life-threatening or significantly reducing life quality conditions
- Recognize the role of a general practitioner and pediatrician in early diagnosis, treatment, primary and secondary prevention of skin viral diseases
- Understand the principles of rational, safe and pathogenetically substantiated therapy of viral diseases of skin and mucous membranes

11.1 Viral infections whose main symptom is blistering

The group of skin viral infections characterized by formation of blisters (vesicles), which appearance is caused by the degeneration of epidermal cells, includes herpes simplex and herpes zoster.

Herpes simplex

Herpes simplex (*herpes simplex*) is a viral disease of skin and mucous membranes caused by herpes simplex virus (HSV).

TO KNOW:

- etiology, pathogenesis and transmission of herpes simplex;
- classification and features of clinical manifestations of herpes simplex;
- histopathological features and differential diagnosis of the disease;
- principles of general and local treatment of herpes simplex;
- factors that cause exacerbation or progression of the disease;
- methods of primary and secondary prevention.

TO BE ABLE TO:

- properly collect medical history of a patient with herpes simplex;
- put a diagnosis based on symptoms and signs;
- apply additional studies to confirm the diagnosis;
- make a differential diagnosis with the diseases that have similar clinical picture;
- justify and prescribe adequate treatment.

Etiology and pathogenesis. Herpes simplex virus belongs to the family of *Herpesviridae,* subfamily *Alphaherpesvirinae* type *Simplexvirus*. There are two antigenic serotypes of HSV: first (HSV-1) and second (HSV-2).

Transmission of HSV-1 usually occurs in childhood, through a direct contact with a HIV-sick or infected person. This causes frequent localization of orofacial herpes lesions caused by HSV-1, in particular on skin areas around mouth (herpes labialis), nose (herpes nasalis), seldom on cheeks, eyelids and ears. In addition to skin, mucous membranes of the mouth (herpes stomatitis) may also be affected. Transmission of HSV-2 occurs mainly through sexual contact. HSV-2 is dominant in causing genital herpes infection (*herpes genitalis*) with the localization of lesions on skin and mucous membranes of the external genital organs of men and women. However, there is no stable relationship between antigen serotypes of HSV and localization of herpetic lesions on skin and visible mucous membranes (genital, extragenital). This is confirmed by the fact that about 20% of cases of genital herpes are caused by HSV-1.

In the pathogenesis of herpes simplex virus, the development of chronic persistent infection in sensory ganglia is crucial. Penetrating through the mucous membranes of the oropharynx, conjunctiva, urethra, cervix, rectum, or skin micro-cracks in the process of initial infection, HSV reaches nerve endings and moves to sensory ganglia through the retrograde axon, where there occurs an acute infection, when the virus replicates in the cells of sensitive ganglion. Further, virus enters into the state of persistence, which provokes the latent course of herpes. Under certain conditions (primarily, due to the lack of immune control), there occurs activation of the virus; from ganglion, the activated virus migrates along the axon of the peripheral nerve and replicates in the epithelial cells. Except general weakening of the immune control,

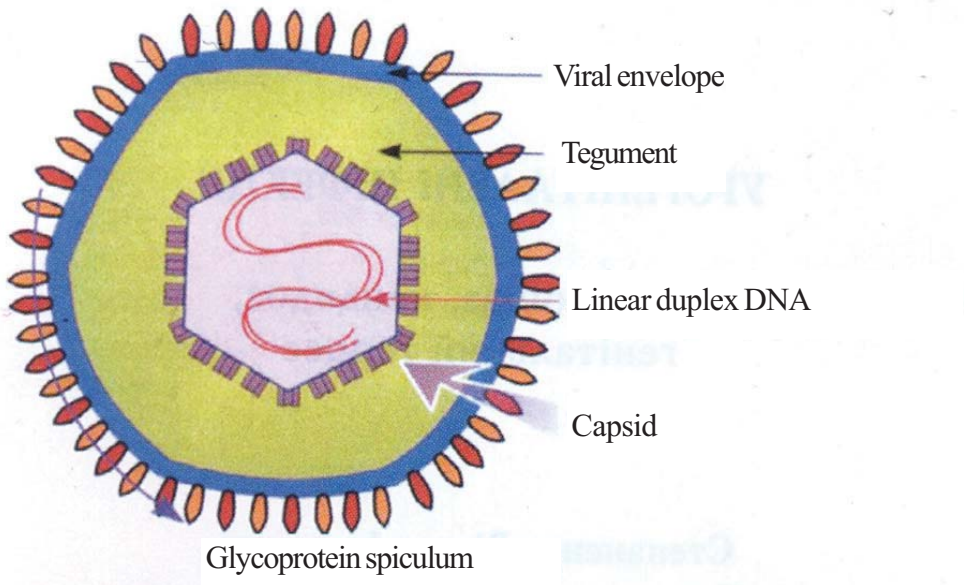


Fig. 11.1. Schematic representation of herpes simplex virus structure (HSV).

reproduction of virus is caused by a violation of local immunity in the area of the epidermis.

Epidemiology. At the present stage, herpes simplex is one of the most common uncontrolled human infections (uncontrolled human infections involve the inefficiency of vaccination or treatment methods, which allow achieving the complete elimination of the pathogen from the host's body). More than 50% of the population of developed countries and 100% of the population of developing countries are seropositive to HSV presense.

The disease features pandemic nature. Genital herpes ranks first in the list of common human infections transmitted primarily through sexual contact. The problem of herpetic infection is aggravated by the growth of cases of abortive and atypical clinical course of the disease. There is an essential difference between the number of persons seropositive to HSV and the number of people with clinical manifestations of herpes simplex.

Clinic. Herpes can be primary and simplex recurrent.

The disease begins with itching or burning, accompanied by the formation of groups of small strained vesicles amid a slightly edematous limited congested spot. The content of vesicles is transparent, becomes thick in 2-3 days. Vesicles feature a tendency to merge. After 3-5 days, vesicles dry up and form yellowish-gray crusts. After 6-8 days, crusts fall off, while secondary pigmentation is left in their place, which then disappears with no trace.

Primary herpes simplex. Primary infection with HSV-1 occurs mainly in young children. In most cases, the primary manifestations of herpes simplex are minor (redness, itching) and remain undetected. However, children infected with HSV-1 may develop primary herpetic gingivostomatitis. The disease is developed suddenly, with an increase in body temperature to 39-40 ° C and intoxication. Mucous membranes of cheeks, gums, lips, tongue, and throat are tonsils are covered with painful grouped vesicles. After their destruction, there occur painful erosions prone to a merge. Clinical manifestations of the inflammation subside in two to three weeks.

Primary genital herpes. The primary episode of genital herpes occurs after an incubation period of 1-7 days. In men, herpes rash is usually localized on the head and shaft of the penis and foreskin, while in women it is localized on small and large labia, vagina, clitoris, cervix, perineum, thighs and buttocks. On the background of significant erythema and edema, there develop grouped vesicles, first with clear, and then thick contents. On the ruins of vesicles, erosions, sometimes ulcers and cracks are formed. Subjectively, the rash is accompanied by a sensation of pain and itching. There develops painful bubonadenitis. Unlike further relapses, primary clinical episode of genital herpes features more severe and prolonged course (4-5 weeks).

Recurrent herpes simplex and recurrent genital herpes. In most cases, the initial clinical episode of herpes simplex is followed by clinical recovery. However,

virus (HSV-1, HSV-2) is stored in the body in a latent form throughout a person's life, not causing any clinical symptoms. Approximately 90% of people infected with HSV are virus carriers. Under the influence of a series of factors that reduce protective capacity of the body, which include hypothermia, overheating, infectious diseases, especially colds, etc., there occur recurrences of herpes simplex. Unlike primary clinical episode of the disease, clinical episode of recurrent herpes simplex virus features milder course. In recurrent herpes simplex, typical location of the lesion includes lips, face, cornea and conjunctiva of the eye, buttocks. At these sites, there develop grouped vesicles with clear content, accompanied by itching and burning. In further, painful erosions are formed, which may merge. On the surface of the erosion, exudate dries in the form of a crust. After the removal of crust, secondary spots are left. Clinical recurrences of herpes simplex may occur over many years and decades, with varying frequency – from one or two a year to two to four per month.

Compared with the initial episode, recurrences of genital herpes are also characterized by a mild course. Rash on skin and mucous membranes is rather sparse. Typical for herpes, lesions are located on skin and mucous membranes of the vulva.

Genital herpes can cause diverse complications, including reproductive disorders, miscarriage, intrauterine infection of fetus, and be transmitted to a baby during childbirth. In case of transplacental infection, a newborn may develop growth retardation, encephalitis, chorioretinitis. In addition, due to chronic recurrent genital herpes patients may experience significant psychosomatic disorders.

Diagnosis of herpes simplex is simple and based on presence of typical clinical symptoms: itching, grouped vesicular eruption, formation of erosions and crusts. The recurrent nature of the lesion is testified by:

1) similar clinical manifestations in the past;



Fig. 11.2. Labial herpes simplex.

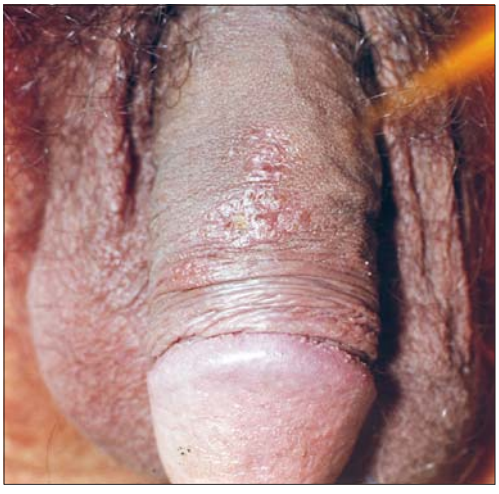


Fig. 11.3. Genital herpes simplex.

2) identification of high titers of antibodies to HSV during relapse;

3) identification of antigen in the focus of clinical manifestation.

The coincidence of the type identified from the source of HSV and type of HSV, to which the antibodies in a patient's serum are found, is the condition for diagnosis of recurrent herpes. However, it should be noted that serology and identification of viral antigen are not routine methods in the diagnosis of herpes simplex. They are applyied only in specific cases, when there is considerable doubt as to the clinical diagnosis of herpes simplex. In addition, high titers of antibodies to HSV with no clinical manifestations (recurrent episodes) are not the reason for the diagnosis of herpes simplex.

Differential diagnosis. In case of localization in the mouth mucosa, herpes simplex is to be distinguished from acantholytic pemphigus and polymorphous exudative erythema. In pemphigus, erosions are localized on a visually normal mucous membrane, they are not subject to epithelialization, Nikolsky's symptom is positive, acantholytic cells are found in the impression smears from the surface of erosions. Unlike herpes, polymorphous exudative erythema is characterized by seasonality index (spring and autumn), significant size of bubbles and erosions on a dramatically inflamed background, layering of bloody crusts on the red border.

Clinical manifestations of genital herpes localized on the genitals should be differentiated from syphilitic chancre. Unlike herpes, syphilitic erosion is characterized by smooth edges, saucer-like shape, hard bottom, indolence and peculiar regional lymphadenitis. In doubtful cases, the issue is finally resolved by microscopy examination of the material from erosions to detect the agent of syphilis – Treponema Pallidum.

Treatment. All currently existing methods and tools for treatment of herpes do not allow achieving complete elimination of pathogens (HSV-1, HSV-2) from the human body. Approaches to treatment of herpes simplex are determined by a clinical picture of the disease, severity of clinical course, frequency of relapses, as well as availability of comorbidity. In the antiviral therapy of herpes infections, preparations of acyclic nucleotides that have an ability to disrupt interaction of virus and cells, in particular inhibit reproduction of the virus through its virostatic action, play the major role.

For treatment of infections caused by herpes simplex viruses, the drugs from a group of acyclic purine nucleosides are used: acyclovir, valacyclovir (valine aether of acyclovir) and famciclovir (pro-forma of penciclovir). In the form of topical preparations (cream), acyclovir is prescribed to reduce the intensity and duration of the recurrent episode of herpes simplex. Systemic prescription of purine nucleoside analogs (internal or parenteral) is used for treatment of primary manifestations of herpes simplex virus, as well as treatment of relapse (for active clinical manifestations). With frequent recurrences of skin herpes and genital herpes, acyclovir and valacyclovir may be prescribed in long continual courses (so-called long-term suppressive therapy). For a healthy sexual partner of a patient with

recurrent herpes, prophylactic or preventive treatment has no medical meaning, since existing antiviral drugs are unable to eliminate the virus from a human body. In some countries, particularly Ukraine, Russia and Belarus, recombinant interferons and interferon inducers are used as a part of comprehensive treatment of the disease.

Prevention. Preventive measures against primary HSV infection in children are reduced to avoidance of contacts with adults that have active clinical signs of infection. Compliance with the principles of safe sexual behavior (monogamous sexual relationships, the use of barrier protection equipment) is the only way to prevent infection with HSV. Secondary prophylaxis involves the avoidance of hypothermia or excessive sun exposure, as well as the appointment of prolonged systemic antiviral therapy.

Forecast. The recurrence rate depends on a patient's sex, duration of the initial episode and the disease itself. In women, the recurrence rate is slightly higher than that of men. The longer the primary clinical episode of herpes is, the shorter the period prior to the first recurrence is, and the higher the frequency of further recurrences is. It was also found that the younger a person is at the first sign of herpes, the higher the recurrence rate of future infection is. With age, the recurrence rate is gradually reduced. It should also be noted that the majority of people infected with HSV experience no recurrences. This is explained by the proper state of their immune system, which is able to block the replication of virus in the nerve ganglia and epithelial cells.

HERPES ZOSTER

Herpes zoster (shingles) is an acute infectious disease of skin and mucous membranes caused by a neurotropic virus (*varicella zoster*), which is also a pathogen of chickenpox. The disease is characterized by the occurrence of unilateral grouped vesicular lesions within one to two dermatomes and accompanied by neurological pain.

TO KNOW:

- etiology and pathogenesis of herpes zoster;
- ways of contamination with varicella infection (herpes zoster);
- characteristics of clinical manifestations and potential complications of the disease;
- histopathologic features and differential diagnosis of herpes zoster;
- characteristics of postherpetic neuralgia;
- principles of local and general therapy for the disease;
- factors that cause exacerbation or progression of the disease;
- methods for prevention of herpes zoster.

TO BE ABLE TO:

- properly collect the history of a patient with herpes zoster;
- put a diagnosis based on clinical picture;
- identify additional studies to confirm the diagnosis;
- make a differential diagnosis with the diseases that have similar clinical picture;
- prescribe pathogenetic therapy.

Etiology and pathogenesis. Shingles and chickenpox are both caused by is the varicella-zoster virus, which belongs to the family of *Herpesviridae*.

There is a hypothesis saying that after the primary attack of varicella (manifested in the symptoms of chickenpox), the virus penetrates into the cells of dorsal root ganglion, where it is stored in an asymptomatic condition (persistent) until the moment of reactivation caused by certain factors (hypothermia, stress, cancer, immune incompetence and others). Under the influence of these factors that weaken the body immune reactivity, the virus is activated, multiplies, causing inflammation of the ganglia. In further, the virus enters the sensory nerves, causing neuritis and neuralgia, spreads around sensory nerve endings in skin and causes formation of a characteristic rash, which is located along one of the nerves. Recurrences of herpes zoster are rare; occur mainly in the background of a significant immune suppression, particularly in HIV infection and malignancy. People of any age may suffer from shingles, while elderly people are at a higher risk.

Clinical picture. The disease may begin suddenly or be precededed by a general malaise, headache, fever, neuralgia or paresthesia in the areas that are to be subject to rash. The most frequent localization of lesions includes the area of intercostal nerves, hence the name «shingles», while the rash is always localized on one side of the body (unilateral localization), rarely covers a little area on the opposite side (due to anastomotic innervation). The second most common place of the lesion is the area of trigeminal nerve. The lesion of the first and third branches of the trigeminal nerve causes the emergence of rash in the mouth mucosa. The eruption emerges in a paroxysmal way: on congested skin, there appear clusters of vesicles with clear serous contents, which quickly becomes cloudy and shrinks in serous crusts. The rash of vesicles on each individual spot occurs simultaneously, but stains emerge sequentially, with an interval of several days. Foci of the lesions may be located fairly closely, forming almost a continuous line along the nerves. After rejection of crusts, there remain brownish-red spots, which gradually disappear. In typical cases, the disease continues for two to three weeks. Burning and pain along the affected nerve are observed subjectively, especially when the rash is localized on face and mucous membrane of the mouth cavity. In herpes zoster, mucous membranes are rarely affected; typically, simultaneously with a skin lesion of a certain area. Against the background of edematous (from one side) oral mucosa, there emerge vesicles, which are rapidly destroyed, forming painful erosions, often covered with gray-white pellicle. Subjectively, burning is marked in the affected areas. Very rarely, shingles can affect vaginal mucosa and bladder.

The most common complication of herpes zoster is the development of a persistent pain syndrome, prone to a prolonged and persistent course after dermatological recovery (postherpetic neuralgia). Postherpetic neuralgia occurs in older patients, which significantly affects the quality of life. Timely administration of systemic antiviral therapy during the first 72 hours from the moment of rash emergence (erythema and vesicles) reduces the risk of this complication in a few

times. Other complications of shingles include facial paralysis, meningitis, meningoencephalitis, arachnoiditis, vestibular disorders, pneumonia, paralysis of the diaphragm, bladder paralysis, paresis of the lower extremities, myelitis with the disorder of pelvic organs, etc.

Diagnostics. Diagnosis of herpes zoster is usually based on clinical manifestations. Presence of a neurological pain syndrome preceding and accompanying rash, unilateral localization of lesions located along the corresponding nerve and herpetiform grouped localization of vesicles are considered.

Differential diagnosis. In some cases, shingles should be differentiated from bullous form of erysipelas, atopic dermatitis, and sometimes impetigo. Pain syndrome that precedes formation of rash can resemble chest pain and pain in myocardial infarction, pain with bowel obstruction, etc.

Treatment. In the antiviral therapy of both herpes zoster and herpes simplex, an important place is given to the drugs of the group of acyclic nucleosides that feature a virostatic action. Acyclovir, 800 mg orally, 4-5 times a day for 7-10 days is used. Given poor bioavailability of acyclovir, the valacyclovir, 1000 mg orally 3 times a day for 7-10 days, and famciclovir, 250 mg 3 times a day orally for 7 days are widely used in treatment of herpes.

In severe cases of herpes zoster, systemic corticosteroids in high doses (40-60 mg of prednisone per day, with a gradual reduction of the dose) are prescribed. Topical preparations of acyclovir and penciclovir (creams) are applied locally. The need for analgesics depends on pain intensity. Usually, paracetamol or indomethacin is enough. In some cases, the need to use opioids or epidural anesthesia may arise.

Expressed pain that occurs prior to or simultaneously with herpetic eruption indicates a possibility of prolonged neuralgia in the future. In prolonged neuralgia that



Fig. 11.4. Herpes zoster.



Fig. 11.5. Herpes zoster.

persists after the rash recourse, analgesics and non-steroidal anti-inflammatory drugs (infometatsin etc.) are prescribed. Patients with herpes zoster should avoid exposure to cold, exercise and stress situations.

Prevention. Primary prevention of chicken pox (and later, herpes zoster) involves a specific vaccine immunization in childhood. Patients with active manifestations of herpes zoster should avoid contact with people (especially children) that have not had chickenpox. If shingles is diagnosed in a hospitalized patient, he is to be immediately isolated to prevent nosocomial infection.

Prognosis. Shingles belongs to a group of diseases that are treated independently and feature no tendency to relapse (except in patients with immune deficiency). Elderly patients that received improper treatment may experience persistent pain syndrome, which leads to a deterioration in the life quality. Recurrences of herpes zoster testify significant violations of immune status. Such patients must be carefully examined for the presence of malignant neoplasms and HIV infections.



Fig. 11.6. Herpes zoster.



Fig. 11.7. Herpes zoster (eye form).

11.2 VIRAL INFECTIONS OF SKIN AND MUCOUS MEMBRANES THAT CAUSE THE GROWTH OF THE EPIDERMIS

The group of viral infections of skin that manifest themselves in the growth of the epidermis involves molluscum contagiosum, warts, condyloma acuminatum.

TO KNOW:

- etiological factors and epidemiology of viral infections of skin that manifest themselves in the growth of the epidermis (molluscum contagiosum, warts, condyloma acuminatum);
- features of the pathogenesis and clinical course of these viral infections of skin;
- pathogenesis, clinical manifestations and complications of molluscum contagiosum, warts, condyloma acuminatum;
- role of viral infections of skin as a marker of immunodeficiency (HIV infection, cancer pathology, etc.);
- clinical and laboratory diagnosis of these viral infections of skin;
- approaches to treatment of viral infections.

TO BE ABLE TO:

- properly collect medical history of patients with viral infections of skin that manifest themselves in the growth of the epidermis;
- differentiate clinical forms of viral infections of skin;
- identify the markers of acquired or congenital immune deficiencies;
- make a plan of the investigation of patients with viral infections of skin that manifest themselves in the growth of the epidermis;
- choose the right tactic of treatment of viral infections of skin, particularly in elderly patients;
- carry out differential diagnosis of these viral infections.

Molluscum Contagiosum

Etiology and pathogenesis. *Molluscum contagiosum* is a viral disease of skin caused by a specific virus of the *Poxviridae* family. The infection is spread by a direct contact with a patient or everyday objects used by people sick with molluscum contagiosum. Sexual route of transmission is also possible. The disease can occur in people of all ages, but is more common in children. The incubation period can last from two weeks to several months.

Clinical picture. The disease is characterized by formation of tight, hemispherical flesh-colored papules (nodules) with a waxy tint, the size of a millet grain to pea. In the center of nodules, a navel-shaped cavity is formed; at squeezing from the two sides, white curd mass is excreted from the cavity. Nodules can be solitary or multiple, may merge, forming conglomerates up to 2-3 cm in diameter. There is a selective localization of the lesion: on face, anterior abdominal wall, pubis, vulva, perineum, thighs. The rash can remain for months. Subjective feelings are absent.

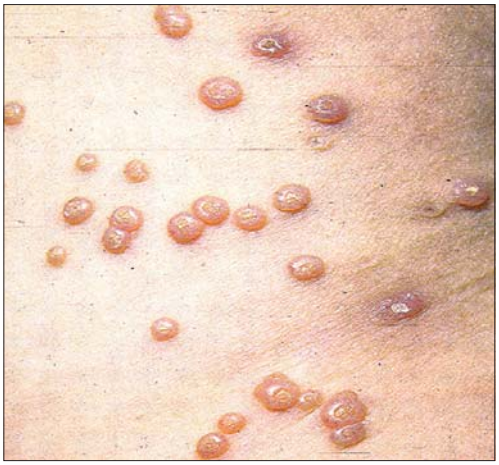


Fig. 11.8. Molluscum contagiosum.

Atypical clinical manifestations of molluscum contagiosum are also known. The disease can be warty; keratotic; cystic; furunculus; giant; solitary (with no central navel-shaped cavity); inflammatory (resembles pyogenic granuloma, prone to bleeding).

Diagnostics. The diagnosis creates no problems and is based on clinical signs.



Fig. 11.9. Molluscum contagiosum.

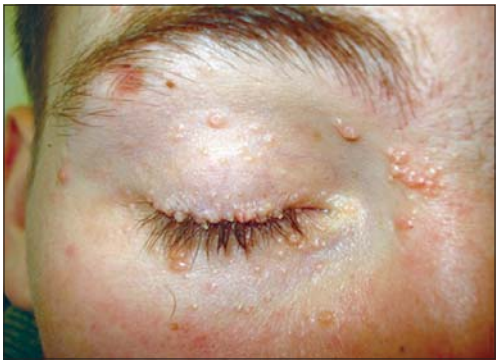


Fig. 11.10. Molluscum contagiosum.

Differential diagnosis. Differential diagnosis of molluscum contagiosum is carried out with warts, basalioma, keratoacanthoma.

Treatment. With few elements of the rash, nodules are first rubbed with alcohol, squeezed from both sides by means of forceps, and then lubricated with the alcoholic solution of iodine. Cryotherapy, curettage and retinoids in the form of a cream are also applied.

Warts

Etiology. Warts (*verrucae*) are benign epidermal growths caused by the human papillomavirus (HPV). There are more than 70 types of HPV. Most of them are caused by different clinical forms of warts of skin and mucous membranes. Some serotypes of the virus are considered carcinogenic (HPV-16, HPV-18) and can cause cervical cancer and skin cancer (Table 11.1).

Table 11.1
Types of human papillomavirus and associated clinical manifestations

HPV type	Clinical manifestations
2, 4, 7, 26–29	Verruca vulgaris (common warts)
3, 10	Plantar warts (flat warts)
5, 8, 9, 12, 14, 15, 17, 19–26, 36, 47, 50	Epidermodysplasia verruciformis
6, 11	Condyloma acuminatum
16, 18, 31, 33-35, 39–41, 51–60	Cervical dysplasia, endocervical cancer
13, 32	Oral focal epithelial dysplasia
30, 40	Pharyngeal carcinoma



Fig. 11.11. Plantar warts.



Fig. 11.12. Plantar warts.

Pathogenesis. Infection occurs through a direct contact with a patient or household items. Regardless of symptoms, familial cases are reported for all forms of warts. The occurrence of warts is caused by mechanical trauma, immune-suppression (including induced nuclear radiation, cytotoxic drugs, HIV infection, common serious diseases, etc.). HPV replication occurs in the basal layer of the epidermis. Warty growths are formed in the stratum corneum in loci of the maximum viral persistence. The infection process is limited to the outer layers of skin and mucous membranes. The incubation period is very variable: from one week to a year.

Clinical picture. Clinical features of warts depend on the species. There are common warts, plantar and flat (youthful), as well as condyloma acuminatum (condylomata).

Common warts represent one of the most common skin diseases that arise in children and adolescents. With age, the incidence is significantly reduced. Common warts are clinically manifested with hyper-keratotic papules that feature small papillae on the surface, reminiscent of the «cauliflower», common focalization involves hands and feet, seldom - skin of the forearms and legs. Warts can be located individually or in groups; often around nail plates.

Plantar warts can be single, multiple or grouped (so-called «mosaic» warts). Plantar warts are flat; a typical sign is skin thickening. If thickened skin is cut off, numerous black dots, which are thrombosed capillaries, are seen. Plantar warts are characterized with soreness.

Flat (plane) warts are most often localized on face and the dorsa of hands. They are flesh-colored, very small, with a flat surface. Often, arranged linearly as a result of viral inoculation, in a place of a random scratch.

Differential diagnosis. Diagnosis of ordinary, flat and plantar warts is clinically uncomplicated. In some cases, common warts require differential diagnosis with tuberculosis cutis verrucosa, while plantar warts are to be differentially diagnosed with calluses that are characterized by a distinct skin pattern and lack of pain.



Fig. 11.13. Verrucas plantar.

Treatment. For treatment of common and flat warts, applications of topical drugs and substances that contain salicylic acid, formaldehyde, or silver nitrate are applied. In treatment of warts, the drug called «Kollomak» (10 ml solution contains 2.0 g salicylic acid, 0.5 g lactic acid, 0.2 g polidocanol) is fairly effective. Cryotherapy with liquid nitrogen is appointed when applications of topical drugs provide no effect. Since the

procedure of cryotherapy is rather painful, it should not be used in children. Multiple warts require more than one procedure of cryotherapy, with an optimum interval of two-three weeks. Treatment of plantar warts is similar to that of common warts; though, before applying topical drugs or cryotherapy, the superficial horny layer is to be removed. It should be noted that the viral propensity to persistence may provoke relapses of warts. Effective methods of preventing the occurrence of warts are still unknown.

Genital warts (Condyloma acuminatum)

Etiology. condyloma acuminatum, Most cases of condyloma acuminatum are caused by human papillomavirus (HPV) types 6 and 11.

Pathogenesis. Genital warts are related to infections transmitted by sexual contact The incubation time lasts from two to three months. The virus enters the epidermis through minor and subtle mechanical damages, infects cells of the basal layer and provokes their abnormal proliferation.

Clinical picture. Single or multiple papules of papillary form (thin leg) or resembling cauliflower represent clinical manifestation of condyloma acuminatum. Color of papules varies from flesh (or the color of mucous membrane) to various shades of dark, in case of pigmentation. Condyloma acuminatum feature soft consistency. The rash is localized on genital skin and periproctic area. In case of infection of epithelial cells of the mucous membranes, papules appear on the mucous membrane of the mouth, urethra, vagina, rectum, cervical canal.

Diagnosis and differential diagnosis. Condyloma acuminatum are diagnosed by clinical signs: thin legs and soft consistency. However, histological examination (biopsy) may be required for the differential diagnosis with Bowenoid papulosis, which



Fig. 11.14. Condyloma acuminatum.



Fig. 11.15. Condyloma acuminatum.

is morphologically similar to dermoid cancellation and clinically characterized by the appearance of spots, papules and plaques. Condyloma acuminatum are also to be differentiated with syphilitic mucous papules.

Treatment. For treatment of condyloma acuminatum, cryotherapy with liquid nitrogen, as well as surgical removal by means of electric scalpel or carbon dioxide laser are applied. The latter method is used, if the warts are located in the vagina and cervix. Applications with 20-25% solution of podophyllin (for the full effect, 2-4 repeated applications at a certain period of time are required) are also quite efficient. However, podophyllin treatment should be carried out under a physician's supervision, since the drug features potent neurotoxicity in case of systemic absorption. The use of local applications with a solution of the Kollomak is highly efficient (the main active ingredients are salicylic acid, lactic acid, polidocanol).

1. Identify an erroneous statement:

A. Herpes simplex is a viral disease
B. Herpes simplex virus is transmitted by contact
C. Herpes simplex can be a triggering factor of pemphigus acantholytic
D. Herpes simplex virus replication occurs in the cells of ganglia
E. Manifestations of herpes simplex can disappear with no medical intervention

2. Herpes simplex virus causes the following disease:

A. Genital Herpes
B. Chickenpox
C. Shingles
D. CMV infection
E. Measles

3. Which of the following medications are not used for treatment of herpes simplex virus?

A. Acyclovir
B. Benzyl benzoate
C. Valacyclovir
D. Oxolinic ointment
E. Interferon ointment

4. What type of pathogen causes herpes zoster?

A. Herpes simplex virus
B. Cytomegalovirus
C. Varicella zoster virus (*varicella zoster*)
D. HIV
E. Gardnerella

5. Unusual features for herpes zoster are:

A. Asymmetric process
B. Grouped vesicular eruption on an erythematous base
C. Contagious pathogen
D. Expressed subjective sensations
E. Lack of subjective sensations

6. Which of the following statements is correct?

A. Warts are caused by human papillomavirus
B. Warts have a bacterial etiology
C. Warts are an air-communicable disease
D. Teenagers are not subject to warts
E. Warts resolve to form lichenification

7. Which of the following criteria are not important for the diagnosis of molluscum contagiosum?

A. Papular (nodular) lesions
B. Navel-shaped cavity in the center of the rash element
C. The disease is more common in children
D. Papules-vesicular elements
E. When squeezed, nodules excrete pultaceous mass

8. What method of therapy is used to treat molluscum contagiosum?

A. Squeezing pimple content by means of tweezers and smearing it with an alcoholic solution of iodine
B. Antibiotic treatment
C. Steroid therapy
D. UFO
E. Antifungal therapy

9. What type of pathogen causes genital warts?

A. Papillomavirus type 1
B. Papillomavirus type 2
C. Papillomavirus types 6 and 11
D. Papillomavirus types 16 and 18
E. Papillomavirus types 3 and 10

10. What complication can occur in women with chronic course of genital warts?

A. Vesiculitis
B. Cystitis
C. Cervical cancer
D. Epididymitis
E. Balanoposthitis

Answers to the questions of the first level of complexity
1 – C; **2** – A; **3** – B; **4** – C; **5** – E; **6** – A; **7** – D; **8** – A; **9** – C; **10** – C
Answers to the questions of the second and third levels of complexity
1a – B; **2a** – E; **3a** – E; **4a** – C; **5a** – A

Task 1. Parents of a two-year boy visited a doctor. Two days ago, a child's red lip border got covered with a rash of small grouped vesicles, accompanied by severe itching. The next day, parents observed a gradual increase in temperature at the end of the day, and rapid spread of the rash on skin of both cheeks. On examination, an abundant vesicular facial rash, erosions with severe oozing lesion amid lichenoid skin are detected. Oral mucosa is covered with erosion. The general condition of a child is violated, the body temperature is 38,0 ° C. A child has atopic dermatitis, moderately severe course.

a) Put a provisional diagnosis:
- **A.** Shingles
- **B.** Herpes simplex
- **C.** Streptococcal impetigo
- **D.** Vulgar impetigo
- **E.** Duhring disease

b) Make a schedule for evaluation and treatment of the patient.

Task 2. A 23 y. o. man applied to a physician with complaints of itchy rashes in the foreskin area. The rash elements appeared after a lengthy stay on the beach. When collecting the history, doctor found out the symptoms occurred in a patient previously. On examination, grouped rash of small vesicles is detected: some of vesicles opened with the formation of erosions, the bottom is bright pink and soft. Lymph nodes are not changed.

a) Put a preliminary diagnosis:
- **A**. Streptococcal impetigo
- **B**. Shingles
- **C**. Candidiasis
- **D**. Secondary syphilis
- **E**. Herpes simplex

b) Conduct a differential diagnosis and compose a treatment plan.

Task 3. Parents of a 5 y.o. boy visited a doctor with complaints that a child has a rash on his hands. On examination, grouped papular rash on the proximal part of the back of the right hand is detected. The surface of papules features marked hyperkeratosis, covered with small papillae and resembles a cauliflower. The rash is painless, with no inflammation.

a) Put a diagnosis:
- **A.** Condyloma acuminatum
- **B.** Syphilitic extensive warts
- **C.** Vegetating pyoderma
- **D.** Squamous epithelioma
- **E.** Common warts

b) Work out a treatment schedule.

Task 4. A 24 y.o. patient visited a doctor complaining of a rash on the foreskin. On examination, foreskin and perianal region featured a few small flesh-colored papules with a thin leg. Papules are soft and painless.

a) Put a preliminary diagnosis:
- **A.** Genital herpes
- **B**. Erosive chancre
- **C**. Condyloma acuminatum
- **D.** Chancroid
- **E.** Candidal balanoposthitis

b) Conduct a differential diagnosis.

Task 5. A 72 y.o. patient came to a doctor complaining of severe pain in the left chest, as well as redness of skin in the area. In the anamnesis, angor pectoris and myocardial infarction are detected. On examination, grouped vesicular rash (in the setting of erythema) is found in the dermatome Th5 to the left.

a) Put a preliminary diagnosis:
- **A.** Shingles
- **B.** Streptococcal impetigo
- **C.** Pemphigus acantholytic
- **D.** Pityriasis rosea
- **E.** Atopic dermatitis

b) Work out a schedule for examination and treatment.

12 TOPIC

Acne and Acneiform Erruptions

12.1 Acne

Acne is a multifactor multiform long-term illness of oil glands.

TRAINING AND EDUCATIONAL GOALS

- Determine classification and common characteristics of acneiform rash
- Explain role of different factors favored for development of blotches
- Understand general course of disease and clinical findings of acneiform rash
- Determine typical clinical findings of disease and distinguish the blotches different by origin.
- Know the principles of therapy and preventive treatment of acneiform rash

TO KNOW:

- modern views of causation and pathogenic mechanism of different clinical types of blotches;
- factors favored for development and advance of acne;
- principles of classification of blotches;
- symptomatology of major clinical types of acne;
- main approaches for general and topical treatment and particularities of preventive treatment of blotches.

TO BE ABLE TO:

- carry out an examination correctly and interview the patient with acne;
- place on additional examinations for the purpose of diagnosis confirmation;
- carry out differential diagnosis with diseases having similar clinical findings;
- give advices as for treatment and preventive treatment of acne.

Epidemiology. Acne is one of the most widespread long-term illnesses of skin. According to variety of researchers acne is diagnosed over 60–80% persons of growing and young age. The incidence of acne is quite high also among persons of adult and advanced years.

Causation and pathogenic mechanism. Leading factors of development of acne are compositional and production disorder of sebum, changes of hormonal and immune status of body, failure of keratinization of follicular canal, intensive colonization of aqueducts of *Propionibacterium acnes* oil glands, development of inflammatory response in perifollicular areas, and genetic disposition.

Change of composition of sebum plays certain role in formation of comedones. The deficit of keratinosomes is observed during acne and lowering of content of epidermal lipids, linolenoic acid, ceramids, and free sterols. Simultaneously on the background of lowering of epidermal lipids level the secretion of lipids in oil glands increases and the contents of follicular cholesterol sulphate in it. It increase the adhesion epithelial cells and is one of the factors of follicular retentional hyperkeratosis i.e. facilitates to abnormal keratinization of follicular ceruminous' opening.

Except qualitative changes of sebum the increase of its quantity occurs at acne. At this the hypersecretion of sebum is an important condition for acne's forming.

Important value in acne's development the microbial hyper colonization has. In particular, it was established that skin liable to be damaged by acne is colonized by three types of microorganisms – *Staphyllococcus epidermis*, *Malassezia furfur*, and *Propionibacterium acnes*. It is considerable at this that *P. acnes* plays most role in overall stage of disease.

The significant role in pathogenic mechanism of women's acne plays hormonal dysfunctions, particularly, concerned with imbalance of testosterone and other androgens levels, menstrual disorders and different gynaecological problems.

There is also the opinion regarding opportunity of certain value in acne's pathogenic mechanism for Demodex folliculorum, Demodex brevis.

Nosology and different clinical presentations of different forms of acne. There are many nosologies of acne. They are based either on clinical presentations of disease or on assessment of its severity.

Taking into consideration the severity of clinical presentations the following is separated:

- *mild disease* when up to 20 comedones are observed or up to 15 inflammatory components or up to 30 components of hives on the skin of damaged areas totally;
- *heavy-medium acne disease* which is characterized by presence of from 20 to 100 comedones or from 15 to 50 inflammatory components or from 30 to 125 components of hives totally;
- *heavy disease* is determined at presence of 5 nodes or 5 cystophorous components or 100 comedones or 50 inflammatory components or more than 125 components of hives on the skin of damaged areas totally.

With that there is no standard classification of acne till now.

The more complete clinical classification is the one proposed by G.Plewig, F.Kligman:

1. *Childhood acne*
   Acne neonatorum
   Acne infantum
2. *Acne juveniles, acne vulgaris*
   Acne comedonica
   Acne papulopustilosa
   Acne nodulocystica
   Acne furminans
3. *Acne adultorum*
   Acne tarda
   Acne inversa
   «Bodybuilding acne»
   Acne conglobate
4. Acne precipitated by external causes (*acne venenata, cosmetic acne, contact acne*)
5. Acne precipitated by mechanical agents (*acne mechanica*)
6. Acne-typed eruptions

Acne neonatorum. Occurrence of these eruptions is connected with eyesore of hormonal crisis or supersecretion of testosterone in the antenatal life. The hormonal crisis is associated by fast decrease of theelol in blood of newborns during first week of life. The hives is mostly represented by closed comedones on cheeks, metope and mentum. Closed comedones are also called as lardaceous cyst encapsulations. These components appear after born of 50% of newborn infants and have a form of pointed papule of nacre-white or yellowish color. The eruptions could be individual or multifocal, often grouped. They have been destroyed unprompted during one or two weeks and rarely require care delivery.

Acne infantum. This acne could occur of children at third to sixth month of life and progress causing sometimes quite serious injuries. As a rule, this acne exists till five-year old. Corresponding eruptions could be concerned with congenital adrenal hyperplasia or with androgen-producing space-occupying process. In connection with this child with acne requires meticulous examination.

Acne juveniles, acne vulgaris. Juveniles or vulgaris acne is the most widespread dermatosis which occurs at the beginning of adolescence, reaches top of development in ephebic age and slowly regresses during first adult period. It is considered that ephebic acne (vulgaris, adolescent) reflects natural age particularities of developmental physiology and regresses of most persons spontaneously.

60-80% of persons suffered by ephebic acne forms have spontaneous regress of dermatosis' clinical implications at the age of up to 20 years. Overwhelming majority of adolescents has acne localized on the face only and part of them have it on face, sternum and dorsum.

Comedones (*acne comedonica*). This form is characterized by predominance of comedones which are the sealed cells of hair follicles in clinical presentation. Inflammatory component is franked incompletely. Further the so called close comedones appear which have no free fenestration with surface of skin. They represented by compacted noninflammatory papule with diameter of up to 2 mm. Gradual enlargement of these papule in volume with respect to continuous production of sebum creates conditions for transformation of some of them into open comedones (black-pointed acne).

Papulopustular acne (*acne papulopustulosa*). At this clinical form the fire of different intensity appears around the open or closed comedones. Clinically it is evidenced as formation of papule and pustule. At mild case the acne papulopustulosa are resolved without cicatrization. At significant expression of inflammatory response which is accompanied by damage of dermis structures the cicatricial tissues appear on places of inflammatory components.

Nodular cystophorous acne (*acne nodulocystica*). This form is characterized by formation of deep infiltrations and cystophorous cavities filled with purulence, which could interlock between each other. At opposite development of these components of hives the cicatricial tissues always appear.

Acne furminans. It is a heavy form of acne which occurs rarely. The disease appears mostly of juveniles at age of from 13 to 18 years who suffers from acne papulopustulosa or acne nodulocystica and is characterized by spontaneous beginning of ulcerated necrotizing components appearance on skin of dorsum and sternum mostly.

Acne adultorum. This acne could persist since ephebic age or could appear in adult age for the first time.

Acne tarda. This form is observed of women mostly. 20% of adult women have regular appearance of acne on the mentum in 2-7 days before the beginning of periods. In some cases acne are permanent. Such patients have appearance of acne papulosa and papulopustular components, sometimes the acne nodulocystica could appear. Patients who suffer from acne tarda should be examined meticulously. They



Fig. 12.2. Acne juveniles (papulopustular form).



Fig. 12.3. Acne juveniles (papulopustular form).

often being discovered the sclerocystic disease of the ovary or polycystic ovarian syndrome. Adult women suffered from acne should be also excluded the growth of butterfly adrenals.

Acne inversa. This form concerned with secondary affection of apocrine sweat glands. At first, the obstruction and abruption of hair follicle's wall appears and then inflammatory infiltrate is being formed around the follicle's residues. Apocrine sweat glands are involved in process recurrently. This disease appears after adulthood and often combined with heavy forms of acne as well as with fatty degeneration. The disease begins from appearance of painful bosselated infiltrates which are open to the surface of the skin by fistulose openings. The content of infiltrates is suppurative or sanguinopurulent. The course of disease is chronicity with tend to backsets.

«Bodybuilding acne». This form of acne is concerned with abuse of anabolic steroids. The most reason of corresponding pathology is hyperandrogenism which enforces the production of sebum. The similar effect is caused also by glucocorticosteroids at chronic ingestion. Clinically, it is evidenced as appearance of acne nodulocystica.

Acne conglobate. According to the data of some researchers this heavy form of acne is most frequently observed of men with ctetosome (XYY). Clinically, the acne conglobate are characterized by gradual appearance of numerous nodular cystophorous components which are connected with each other as well as with large grouped comedones. Evidences of this disease, as usual, are not retracted after completion of adulthood and they could anticipate as long as life endures.

Acne precipitated by external causes (*acne venenata, cosmetic acne, contact acne*). The term origins from Latin word "venenum" which means "poison" and indicates on fact that comedones are formed in oil glands after epicutical influence. Comedonic and genic substances are mostly in beauty preparations. (wool fat, petroleum butter, some of vegetable greases)

Acne precipitated by mechanical agents (*acne mechanica*). Appearance of this acne is connected with pressure and friction (usual dermatosis) which causes



Fig. 12.4. Acne in dorsum area.

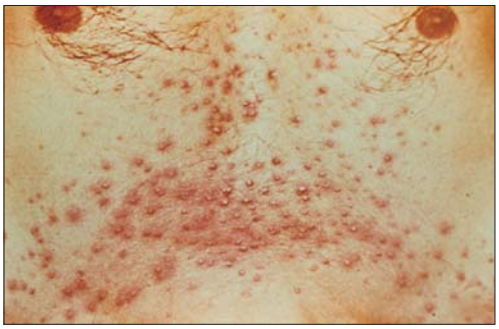


Fig. 12.5. Acne in sternum area.

mechanical blocking of follicles openings. The example could be continuous wearing of head wears, sport helmets, and plaster bandages together with excessive hidrosis.

Diacrisis. The acne's diagnostics is based on past medical history, course and clinical presentation of inflammatory process.

Differential diagnostics. The rule out is often carried out with diseases similar to acne (rosacea, demodicosis, perioral dermatitis and others) as well as with medicamental acne (iodic, bromatus, steroidal).

Curing. There are systemic and topical antiacneic solutions used in curing of acne which is assigned for breaking of main acne's pathogenetic mechanism's links, in particular, of abnormal keratinization and differentiation of keratocytes in ducts and openings of oil glands as well as hyperseborrhea, excessive activity of bacterial population in the oil glands, oil glandular obstruction and fire.

Treatment of acne should be commenced early to prevent scarring. Patients should be counseled that an improvement may not be seen for at least a couple of months. The choice of treatment depends on whether the acne is predominantly inflammatory or comedonal and its severity.

Mild to moderate acne is generally treated with topical preparations. Systemic treatment with oral antibacterials is generally used for moderate to severe acne or where topical preparations are not tolerated or are ineffective or where application to the site is difficult. Another oral preparation used for acne is the hormone treatment co-cyprindiol (cyproterone acetate with ethinylestradiol); it is for women only.

Severe acne*, acne unresponsive to prolonged courses of oral antibacterials, scarring, or acne associated with psychological problems calls for early referral to a consultant dermatologist who may prescribe isotretinoin for administration by mouth.*

Systemic treatment of acne involves using of antibiotics, 13-cis retinoic acid (isotretinoin) and cyproterone acetate.

The most effective are considered to be an antibiotics of tetracycline range (tetracycline, doxycycline) and macrolides erythromycin, josamycin and azithromycin.

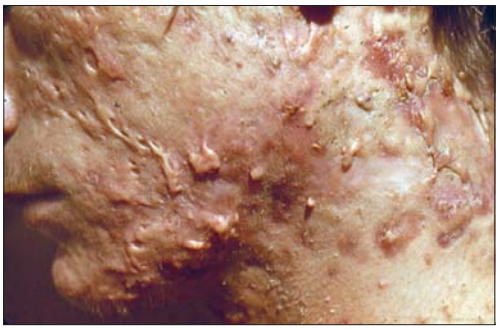


Fig. 12.6. Acne (nodular cystophorous form).

The patients with heavy and heavy-medium forms of acne are being assigned the isotretinoin per os.

Combined administration of «Diane-35» drug containing progesterone with antiandrogenic activity (cyproterone acetate) and ethinyl estradiol is particularly effective for women with acne tarda. Over 90% of patients have complete clearance of their acne and up to 80% there is no relapse. It has several

side-effects: dry lips, eyes and skin, mild alopecia, aches and pains. It also raises blood fat levels and may affect liver functions tests. The most serious problem is teratogenicity.

The group of pathogenetic remedies of acne's external therapy include topical retinoids, azelaic acid, topic antibiotics and bacterial agents as well as benzoyl peroxide. The most sebosuppressive and comedolythic effectiveness among existent remedies the local retinoids have (tretinoin, retene-A and others). According to existent algorithm of therapy of acne the topic retinoids are used for curing of different stages of severity of this disease. At acne of severity I the curing is limited by topic retinoid and benzoyl peroxide only, at acne of severity II-III the topic retinoids with benzoyl peroxide are assigned and system therapy by the means of oral antibiotics or hormonal medications, at acne of severity IV – isotretinoin, topic retinoids and hormonal androgen-deprivation therapy.

Azelaic acid is also effective anticomedogenic drug. At this, azelaic acid in contradistinction from retinoids has no sebosuppressive effect.

The existent for the now local anticomedogenic drugs containing antibiotics include «Zynerit» (erythromycin-zinc complex in form of wash).

The existent local antimicrobial drugs for curing of acne vulgaris also include benzoyl peroxide.

Individual researchers are also doubts regarding to expedience of number of cosmetic measures while acne, in particular, in sense of boosted clearing of skin by detergents, brushes, alcohol as well as carrying out the mechanical and chemical pilling, and deep cleaning of skin.

12.2 Acne-typed diseases

The term «Acne-typed diseases» is quite often occurred in modern special literature. The rosacea, perioral dermatosis, and demodicosis are considered to be placed in this group of diseases. The provisional union of these diseases into one group is conditioned by existence of a range of similar and interconnected factors which have been given a certain meaning in development of corresponding dermatosis. The common signs of rosacea, perioral dermatosis and demodicosis are location of inflammatory process on the skin of face, morphological components of exanthema as well as nature of clinical progression. At this, separate assumptions of origin and particularities of clinical presentation for this dermatosis, in particular, the type of location of inflammatory process on certain parts of face, are show for specialties of each from corresponding nosologies. Taking into account the proven leading role of acarian demodecydes in occurrence of demodicosis this dermatosis is considered in textbook in "Parasitic diseases of skin – dermatozoonosis" chapter.

Rosacea

Rosacea, symptoms: acne erythematosus – chronic dermatosis with incompletely discovered causation, which is characterized by occurrence of fixed eruption, telangiectasia, papule, and pustule on the face.

TRAINING AND EDUCATIONAL GOALS

- Publicize modern representations of rosacea's aetiopathogenesis
- Determine factors which are facilitate the disease establishment
- Know the classification particularities of dermatosis
- Determine its typical clinical presentations
- Carry out the differential diagnostics of rosacea
- Know general principles of medical and preventive measures at rosacea

TO KNOW:

- etiological and pathogenetic particularities of rosacea;
- clinical sorts of this disease;
- principles of therapy and preventive measures at rosacea.

TO BE ABLE TO:

- carry out an examination correctly and interview the patient with rosacea;
- carry out the laboratory diagnostics and determine additional examination technics with respect to discovering of acarian demodecydes, *H. pylori*;
- carry out the differential diagnostics with diseases having similar clinical performance and prove the diagnosis;
- make up a plan of advices regarding to curing and prevention of this disease.

Aetiopathogenesis. Causation and pathogenetic mechanism of rosacea are discovered incompletely. Among possible factors of occurrence of this chronic dermatosis the numerous of external and internal causes are separated.

The external causes of rosacea's progression include alimentary and meteorological factors, activity of acarian demodecydes (*Demodex folliculorum*), presence of infection which includes *H. pylori*. The range of alimentary factors (alcohol, hot drinks, spices) take stimulating effect on mucous coat of stomach which calls face hemahgiectasia reflectory. Some of authors count that excessive intake of food from meat and spices are facilitating the appearance of rosacea.

Certain role on rosacea's progression also have influence of physical agents, particularly, solar irradiation, heat and cold. It is clearly known that solar irradiation together with subsequent responses of reddening provokes the progression of erythematic form of rosacea.

The background of inflectional theory of appearance and progression of rosacea is presence of pustular components of patients' exanthema as well as effectiveness of antibacterial drugs in therapy of dermatosis.

Possible external causes of occurrence and progression of rosacea include also presence of Demodex folliculorum in pilosebaceous follicles of skin of face. At this in virtue of morphological and biological particularities of Demodex folliculorum the discussions regarding possible mechanisms of its pathogenetic effect still are. There are two types of acarian demodecydes separated (*Demodex folliculorum, Demodex brevis*) which are conditionally considered to be pathogenetic exophytes and have famous specificity regarding to human. *Demodex folliculorum* are parasitized in openings of hair follicles and *Demodex brevis* are parasitized in oil glands. The pathogenic properties of these acarian demodecydes include their ability to mechanical destroying of epithelial cells lining the follicles as well as initiate forming of granulomas and inflammatory lymphohysteocytic infiltrations in derma.

For the now one of the most pathogenetic external causes of origin of rosacea is considered to be an angioneurosis with dominating damage of vessels of face.

Clinical findings. The typical for rosacea is following location of damages – on cheeks, metope, mentum as well as sometimes in postaural areas, on hairy part of the head, front surface of neck, concha of auricles, ear lobes, and blepharons.

With due regard to clinical and morphological characteristics of rosacea there are different classifications o this dermatosis offered.

Classification on the basis of nature of morphological components and prevalence rate of inflammatory process determines six clinical forms of rosacea – smooth, localized and spreading as well as deep forms – localized with deep papular and pustular components, localized with transformation into hammer nose, spreading with deep papular and pustular rash.

On the basis of clinical course of rosacea and pathomorphological changes the classification was created according to which there are four forms of dermatosis separated – erythematic, papular, pustular and infiltrative-productive.

In addition, there is a classification of rosacea which takes into consideration the ethiopathogenetic factors of progression of dermatosis. In accordance with this classification there are four stages of progression of inflammatory process separated: prerosacea – corresponds temporary responses of skin's reddening, vascular rosacea – characterized by fixed eruption and telangiectasia, inflammatory rosacea – accompanied by occurrence of papules and pustules, delayed rosacea – corresponds to progression of hammer nose. The specialized form of rosacea is a rosacea of eyes.

Classical progression of rosacea is characterized by occurrence of tidal erythema. At first the duration of reddening varies from several minutes to several hours and is accompanied by fever sensation or warmth sense and then disappears without leaving a trace. After quite short time interval under influence of different provoking factors (insolation, atmospheric and temperature oscillations, abuse of hot or spicy food, alcohol) the tidal erythema appears again. Its location is mostly limited by central part of the face and nasal-cheek folds. The process of change of quite often erythema backsets by remissions could continue for months and even years. With this after some time the duration of backsets is increased and duration of remission between them becomes less. Erythema gradually becomes more marked, gets cyanochroic tone and goes to cheeks, metope and mentum. Subjectively the patients complain for fever sensation as well as heat and pruritus. Occurrence of pruritus is explained by range of researchers as a result of increasing of *Demodex folliculorum* population. Maybe, the pruritus is also a result of raised activity of acarian demodecydes on the background of favorable conditions for its life activity. At histological examination of this stage of rosacea there are only enlarged blood vessels and lymphangions observed in affected areas.

Later on the background of erythema and thickness of affected areas of skin the isolated or grouped inflammatory pink-red papules are occur covered by furfur. The persistence is characteristic for papules during quite long period of time (several weeks). Gradually, most of nodes are suppurate forming a papule-pustules and pustules with sterile content.



Fig. 12.7. Rosacea.

Pathomorphology. The inflammatory disorder with follicular orientation is observed in pustules at presence of lymphocytes, clasmatocytes, and neutrophils in follicle's opening. Histologically the hammer nose is a hyperplasia of oil glands and hypertrophia of connective tissue.

Diagnostics. At determination of rosacea diagnosis it is necessary to take

into account an anamnestic data, clinical presentation of damage, in particular, special clinical signs characteristic for this dermatosis in complex as well as results of microscopic investigation for presence of acarian demodecydes.

Differential diagnostics. At opposite to rosacea:

Demodicosis (*rosacea-typed form*) is characterized by fact that at progression of this disease the most etiological value have an acarian demodecydes; it begins from occurrence of follicular papules, pustules and only after some time the diffuse erythema and infiltration of skin occur.

Sebborheal dermatosis is localized on hairy part of head; its characteristic is a fatty furfur; at microscopic investigation the numerous cryptococcus of Malassezia are discovered;

Acne appears before rosacea by age criteria, in ephebic, begins from appearance of comedones, its transformation into papules and pustules and after some time only the spread erythema could progress;

Erythema centrifugum (*discoid form*) is characterized by limited discoid locuses, symptoms of follicular keratosis and progression of cicatricial;

Perioral dermatitis has typical location of process (perioral), nature of papules is non-follicular, there are no pustules and desquamation, the pruritus is observed.

Bourneville-Pringle disease (adenomatosis of oil glands) is characterized by fact that progression of adenomatosis infiltrates being started in childhood, there is no diffuse erythema;

Perniosis of nose (freezing injury) leads to uniform cyanochroic-red color in nasal area.

Menopause is accompanied by tides with hyperhidrosis.

Curing. The pustules and papules of rosacea respond to topical metronidazole or to topical azelaic acid Alternatively, oral administration of oxytetracycline or tetracycline 500 mg twice daily, or of erythromycin 500 mg twice daily, can be used; courses usually last 6-12 weeks and are repeated intermittently. Doxycycline 100 mg once daily can be used if oxytetracycline or tetracycline is inappropriate (e.g. in renal impairment). A modified-release preparation of doxycycline is licensed in low doses of 40 mg once daily for the treatment of facial rosacea (section 5.1.3). Isotretinoin is occasionally given in refractory cases [unlicensed indication]. Camouflagers (section 13.8.2) may be required for the redness.



Fig. 12.8. Hammer nose.

Perioral dermatitis

Perioral dermatitis is a chronic dermatosis located on the face's skin, mostly nearby mouth, with possible spreading of inflammatory process to the area of nosolabial triangle, mentum, and cheeks. This dermatosis is mostly registered of young and middle-age women.

Causation and pathogenetic mechanism. Perioral dermatitis is often occurs of persons with burdened allergic anamnesis, in particular, with neurodermatitis accompanied by xerodermia. Many of patients with perioral dermatitis were discovered connection of it with long-lasting abuse of outer therapeutic agents containing fluorinated corticosteroid medicinal products. Progression of this dermatosis could be provoked by cosmetic creams, washes, paints, some of teeth pasts as well as long-term staying under solar irradiation (perioral dermatitis is often recrudesces in spring and summer). According to the data of some researchers the certain role in occurrence and progression of perioral dermatitis play *Demodex folliculorum* and *Demodex brevis* acarians.

Clinical findings. The most typical clinical presentation of perioral dermatitis is occurrence of numerous small papules of red color located on the face's skin mostly around the mouth and nosolabial triangle, as well as on mentum, cheeks, bridge of the nose and periorbital areas. Later on the background of erythema these papules interlocked into largest components part of which transforms into painful pustules and nodes. The specialty of perioral dermatitis is saving of narrow strip of undamaged skin around the vermilion surface.

Clinical course of perioral dermatitis is characterized by periods of recrudescence and remission. With this even during remission period there are always separate papule-pustule components of exanthema.

Diagnosis and differential diagnostics. The differential diagnostics is carried out most often with rosacea. In contradistinction from rosacea at perioral dermatitis there are no telangiectasis, true pustulation, and nodes; the thin strip of undamaged skin is left around the vermilion surface.

Curing. The therapy of perioral dermatitis should include complex measures. In particular, the curing of concurred conditions is recommended (diseases of gastrointestinal tract at first instance), sanitation of locus of chronic



Fig. 12.9. Perioral dermatitis.

infection; if possible normalize functioning of endocrine system. The immunomodulators are used by indications, bracing and analeptic medicines as well as drugs normalizing the operation of excitatory system. There are alcohol drinks, spicy food, chocolate, and citrus should be excluded from nutrient budget as well as limit the abuse of carbohydrates and salt.

At presence of postulant exanthema it is necessary to use an antibiotics of tetracycline range, in particular, minocycline or doxycycline during 4-6 months.

The metronidazole is also used in quantity of 0.25 g twice a day during 2-3 weeks. The significant place in curing of perioral dermatosis the local therapy takes. At first instance, the patients are recommended to withdraw from cosmetic remedies. The shaken blend is used locally with 1-3% of sulphur and ichthammol (in case of fat skin) or pasts with these agents (in case of dry skin), as well as 1-2% salicylic acid, 1-2% boric acid, 2% mixture of resorcin, and 2% mixture of metronidazole. At expressed inflammatory process the cold packs are assigned with 1% solution of resorcin, 3% boric acid, 3% tetraborate sodium, as well as statutory unctures with corticosteroid medical agents.

At discovering of acarian demodecydes of patients with perioral dermatosis it is recommended to treat the skin of face by 20% suspension of benzyl benzoate or by 33% sulfur ointment during 20 days.

Prognostication. The prognosis is laudable, at condition of balanced therapy the ultimate recovery occurs.

1. Clinically the following is not included in types of acne juveniles:

A. *Acne tarda*
B. *Acne comedonica*
C. *Acne papulopustolosa*
D. *Acne nodulocystica*
E. *Acne fulminans*

2. For acne's occurrence the important thing is:

A. Pathological follicular hyperkeratosis
B. Excessive production of sebaceous matter
C. Influence of *Propionbacterium acnes*
D. Inflammation
E. All of mentioned above

3. For acne of medium severity the presence of the following is typical:

A. From 20 to 100 comedones
B. From 15 to 50 inflammatory components
C. From 30 to 125 components on skin totally
D. All of mentioned above is wrong
E. All of mentioned above is right

4. What stage of inflammatory process' progress could not be at rosacea:

A. Erythematic (Erythrosis of face)
B. Lichenificated
C. Papulopustule
D. Nodular
E. Erythematic-papular

5. The differential diagnostic of rosacea is most often carried out with:

A. Demodicosis
B. Seborrheal dermatosis
C. Erythema centrifugum
D. Bourneville-Pringle disease
E. All answers are correct

6. The following are not the types of rosacea:

A. Lupiform acne
B. Acne congolobata
C. Acne furminans
D. White acne
E. Rosacea-leukophlegmasia

7. The drugs assigned at acne have no any effect on:

A. Normalization of flake off of dead cells of skin
B. Antimicotic influence
C. Anti-inflammatory effect
D. Destroying of *Propionibacterium acnes*
E. Hormonal influence

8. What of specified drugs is not recommended for curing of rosacea:

A. "Metrogyl-gel"
B. Metronidazole
C. Glucocorticosteroid unctures
D. Antibiotics of tetracycline range
E. Azelaic acid

Task 1. The female patient of 19 years old seek advice with complains for rash on skin of face, sensation of tightness of skin after washing and stipulated by disease necessity of often washing a head. *Unbiased*: the yellow-red spots with relatively clear borders and peeling on surface are observed on the skin of hairy part of head, eyebrows, blepharons, and nasal wings. Affected skin is calloused, with rugged surface, flare. The hair is fat, flare, gummed. Rash is accompanied by pruritus, especially at excessive hyperhidrosis.

a) What the provisional diagnosis is:
- **A.** Liquid seborrhea
- **B.** Professional seborrheal weeping dermatitis
- **C.** Dry seborrhea
- **D.** Mixed seborrhea
- **E.** Seborrheal pemphigus

b) Determine the management of examination and managing of patient.

Task 2. The male patient of 16 years old seeks medical advice for dermatologist regarding to rashes on skin of face and sternum. It is known from anamnesis that patient is sick during five years, was cured periodically using only drying medical agents and medicaments of different action (antibiotics, antifungal, exfoliating) for local abuse. Clinically the variety of rash components is observed located on skin of face, upper half of sternum and dorsum in form of acne, papules, pustules, there are crusts and cyanochroic-pink cicatricial tissues in some places.

a) Determine the provisional diagnosis:
- **A.** *Acne inversa*
- **B.** *Acne papulopustulosa*
- **C.** *Acne infantum*
- **D.** *Acne nodulocystica*
- **E.** *Acne comedonica*

b) Make the complete clinical diagnosis with determination of severity of disease's course.

Task 3. The male patient of 20 years old came to the outpatient attendance to the dermatologist with complains for rashes in area of dorsum, sternum, neck (except face), which appear spontaneously, rising of body temperature up to 38 °C, pain in articulations, sickliness. It is known from anamnesis that rashes in form of acne and nodes were noticed during six years. The patient have not been examined and curried. *Unbiased*: there are numerous inflammatory painful nodes, pustules with suppurative and hemorogic content which destroyed in some places forming anabrosis and ulcerations are observed. The hematologic state is leukocytosis, and accelerated ESR.

a) Determine the provisional diagnosis:
- **A.** *Acne tarda*
- **B.** *Acne comedonica*
- **C.** *Acne papulopustulosa*
- **D.** *Acne nodulocystica*
- **E.** *Acne fulminans*

b) Determine the management of examination and curing of patient.

Task 4. The female patient of 36 years old is on institutional treatment in gastroenterology department regarding to duodenal ulcer, the advice of dermatologist is recommended in connection with presence of rashes on skin of nose, cheeks and mentum. On the basis of anamnesis and dermatological examination it was determined that disease at first observed periodically and then fixed erythema of face and telangiectasia appear. Later on the background of erythema the milliar follicular papules and pustules appear.

a) Determine the provisional diagnosis:
- **A.** Demodicosis
- **B.** Sebborheal dermatosis
- **C.** Steroid acne
- **D.** Rosacea
- **E.** Perioral dermatosis

b) Determine the management of patient.

Task 5. The woman of 34 years old complains for presence of rash without subjective sensations located around mouth. It is known from anamnesis that patient has often disorders of gastrointestinal tract. During dermatological examination the symmetric rash in form of locus

erythema of pink color is discovered around the mouth. There are grouped milliar papules, micro vesicles, micro pseudo pustules located on its background and not connected with follicles. *Demodex folliculorum* is not discovered.

a) Determine the provisional diagnosis:
A. Demodicosis
B. Sebborheal dermatosis
C. Perioral dermatosis
D. Acne adultorum
E. Rosacea

b) Cary out differential diagnostics of specified disease.

Answers for first level self-control questions
1 – A; **2** – E; **3** – E; **4** – B; **5** – E; **6** – D; **7** – B; **8** – C
Answers for second and third level self-control questions
1a – A; **2a** – B; **3a** – E; **4a** – D; **5a** – C

13 TOPIC

Cutaneous tuberculosis

Lupus (*tuberculosis cutis*) is a chronic infectious disease caused by tuberculosis bacteria. Cutaneous tuberculosis is often a manifestation of a single process of tuberculosis in the whole organism and is combined with a lesion of the upper respiratory tract, lungs, bones, joints, and other forms of tuberculosis.

TRAINING AND EDUCATIONAL PURPOSES

- Disclose the relevance of the problem of lupus, as well as ways and conditions of infection
- Have an idea of the main points of etiology and pathogenesis of lupus
- Classify typical symptoms
- Understand characteristic clinical features of lupus
- Identify principles of treatment and prevention of cutaneous tuberculosis

TO KNOW:

- current status of the theory of etiology and pathogenesis of cutaneous tuberculosis;
- classification of cutaneous tuberculosis;
- characteristic clinical and diagnostic features of the main types of skin tuberculosis (lupus, scrofuloderma, tuberculosis cutis verrucosa, tuberculosis cutis lichenoides, lichenoid, papulonecrotic tuberculid, erythema induratum, etc.);
- methods of examination of patients with cutaneous tuberculosis (dermatology, laboratory, general therapeutic);
- differential diagnosis of the diseases with similar symptoms;
- modes of treatment and principles of clinical examination in cutaneous tuberculosis;
- prevention of tuberculosis infection.

TO BE ABLE TO:

- properly interview a patient with cutaneous tuberculosis;
- formulate a complete clinical diagnosis with characteristic clinical form of the disease;
- perform differential diagnosis based on a clinical form of skin tuberculosis;
- prescribe laboratory tests to confirm the diagnosis;
- prescribe a rational therapy for a patient with skin tuberculosis, depending on a clinical form of the disease;
- prescribe a rational therapy for a patient with skin tuberculosis based on the disease case.

Etiology. The causative agent of tuberculosis is Mycobacterium tuberculosis belongs to the group of acid-fast bacilli, related to lower plants – actinomycetes, or ray fungi. Mycobacterium tuberculosis is characterized by considerable polymorphism and a strand, bacillary, granular, filter stage of development. It is a thin stick, sometimes straight, often curved, with slightly rounded ends, length of 0,8-3-5 microns and width of 0.2-0.5 mm. It is aerobic, but can also be a facultative anaerobe. Temperature limits of the growth of this bacteria are within the temperature from 29 to 42 ° C (optimum temperature is 37-38 ° C), vital activity is stored at very low temperatures, while the temperature rise to 80 ° C is stood within 5 minutes. Under intense solar radiation, vital functions of the mycobacterium are sharply reduced, while darkness and dampness allows survival for a significant number of bacteria.

In the course of phylogenetic development, the three types of human pathogens Mycobacterium tuberculosis formed: human (*typus humanus*), bovine (*typus bovinus*) and avian (*typus avium*).

Pathogenesis. Lupus represents a group of skin diseases different in clinical and histological picture, caused by a single cause: penetration of Mycobacterium tuberculosis of one of these types into skin.

For the pathogenesis of lupus, a single causative agent of the disease is not enough. It is believed that the development of the disease requires the impact of at least three factors, which include: getting of a sufficient number of virulent mycobacterium tuberculosis into skin, reduced skin reactivity to them, which is characterized by an increased content of sodium salts and water in skin, adverse effects of the environment.

Penetrating into skin, Mycobacterium tuberculosis gives rise to abnormal focal inflammation. Initially, epithelioid, and then mixed (predominantly lymphocytic) tubercle are formed. Phospholipid fractions of Mycobacterium tuberculosis are responsible for appearance of epithelioid cells, while protein fractions of Mycobacterium tuberculosis form lymphoid cells.

Classification. Numerous forms of the disease are divided into two groups: localized (focal) and scattered (disseminated) lupus.

Localized forms of skin tuberculosis include:

- primary skin tuberculosis (tuberculous chancre);
- TB erythematosus;
- tuberculosis cutis colliquativa (skrofuloderma) and tuberculosis of mucous membranes;
- verrucous tuberculosis of skin and mucous membranes;
- military-ulcerative tuberculosis of skin and mucous membranes.

Diffuse (metastatic) forms of skin tuberculosis include:

- miliary tuberculosis of skin;
- tuberculosis papulonecrotica;
- indurative (callous) erythema Bazen;

- moniliformis scrophulosorum.

In typical cases, all clinical forms of skin tuberculosis are characterized with gradual development, lack of acute inflammation and severe pain, chronic undulating course, remission and relapse in spring and fall.

Clinical picture. A variety of clinical forms of skin tuberculosis depends on many factors, which principally include immunobiological reactivity, age and sex of patients. Generally, tuberculous lupus, skrofuloderma, lichen scrofulous appear in childhood or adolescence, while verrucous and ulcerative tuberculosis, as well as erythema induratum Bazen, develop mainly in adults. Warty tuberculosis is more common in men, whereas indurative form is typical only for women.

Tuberculous skin lesions are predominantly secondary, as they develop in the body, which is infected with mycobacterium tuberculosis in one way or another. In most cases, penetration of Mycobacterium tuberculosis into the body occurs through the respiratory tract.

Localized (focal) forms of lupus

TB erythematosus *(lupus vulgaris, tuberculosis cutis luposa)****, synonyms: tuberculosis cutis luposa, or lupus,*** are most common cases. It is characterized by a slow chronic progressive course with a tendency to dissolution of tissues. The disease usually begins in childhood or adolescence; often in adults.

The primary element of tuberculous lupus rash is a tubercle (lyupoma), the size of a pinhead to a pea, somewhat above the skin level. Tubercle is of brownish-reddish color and soft (doughy) consistency. When pressed with the object carrier (diascopy), by squeezing blood from dilated blood vessels the bump turns yellowish-brown and translucent (*apple jelly symptom*); when pressed with a blunt probe, a fossa is formed (*probe symptom*) due to a significant reduction of the amount of collagen and elastic fibers in the tuberculum. The fossa remains for five to ten seconds. In some cases, its surface is easily pierced, while being accompanied by bleeding.

In further, the tuberculum decays to ulcer. Ulcers feature shall depth, grainy bottom, red surface with a predisposition to bleeding, and soft edges. After healing of the ulcer, a scar with smooth white surface is formed; new tuberculums may develop.

Most often, the process is localized on face, nose, cheeks, upper lip, ears, seldom on the neck, trunk and extremities. Mucous membranes and skin areas bordering them mainly feature ulcerous forms.

Clinical picture of tuberculous lupus features a number of varieties. Initially, the bumps are grouped closely, in the future, they slowly increase as a result of peripheral growth, merging into a diffuse infiltration, which barely rises above the skin surface, and then we talk about a flat variety of tuberculous erythematosus (*lupus vulgaris planus*). Sometimes, bums feature a significant lamellar peeling that leaves barely visible scar atrophy. This type is defined as *lupus vulgaris exfoliativus*. In long-term existence of the focal point of plane lupus, ulcers may prevail.

In this case, we talk about *lupus vulgaris exulcerosus*. If on the surface of the lesion featueres a large number of crusts, the type is called *lupus vulgaris crustosus*. If papulose elements reach the size of a pea and significantly overhang above skin surface, this form of is called *lupus vulgaris tuberosus*. If there are large soft infiltrates in the form of tumor mass formed by a merging of bumps, the type is called *lupus vulgaris tumidus*. Frequently, with the localization of the pathological process in face, upper and lower extremities and buttocks a peripheral increase of the infiltration with simultaneous decay, ulceration and scarring in the center is observed. Such state is defined as *lupus vulgaris serpiginosus*. The process has a creepy character, covers more skin area.

Destructive ulcerative changes involve the deep tissues in the process (cartilages, bone, joints) with spontaneous amputation, formation of fibrotic scars and keloids, deformation of nose, ears, fingers, eyelids and limbs (*lupus vulgaris mutilans*). With the destruction of cartilage nasal septum, nose becomes shortened and flat, there occur lid eversion and narrowing of the mouth, which greatly disfigures a patient (*lupus vulgaris vorax*).

Lesions of mucous membranes of nose and mouth are sometimes isolated. In the mouth, the process is more often localized in the mucosa of the gum and palate. Initially, there appear small bumps of bluish-red color and the size of a millet seed. Formed ulcers bleed easily; they are covered with a yellowish fur.

Diagnosis is based on clinical signs of the disease, characteristics of lupoma (apple jelly and probe symptoms), ulcers, scars, pathologic behavior and localization.

Differential diagnosis is to consider the following aspects.

Papulose syphilide. The characteristics involve the dense texture of bumps, focal localization, formation of a not solid, but mosaic scar, which consists of individual small scars with no conjugation (see «Tertiary syphilis»).



Fig. 13.1. Tuberculous lupus.

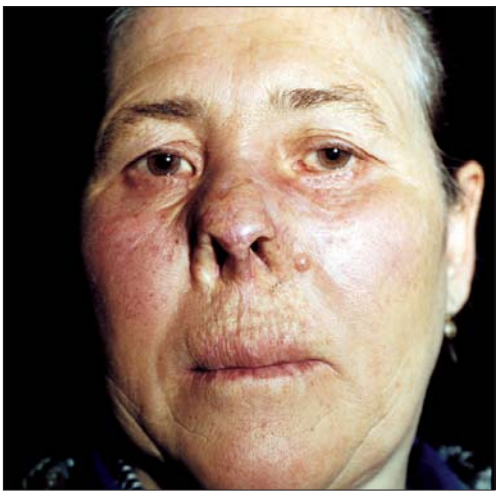


Fig. 13.2. Tuberculous lupus.

Tuberculoid form of leprosy. Unlike tubercular lupus, it features the absence of temperature and pain sensitivity in the affected skin area (see «Leprosy»).

Tuberculoid form of leishmaniasis. For differential diagnosis, history is important (a patient's staying in an endemic area), placing of bumps around the scar, their localization in the open skin areas, rapid formation of ulcers with thick copious purulent discharge, identification of Leishmania (see «Leishmaniasis»).

Some forms of tuberculous lupus (with scaling and hyperkeratosis in the cheeks and nose) may resemble erythematosus. In severe cases, biopsy and histology are applied.

Strumoderma (*tuberculosis cutis colliguativa*) or **skrofuloderma** (*scrofuloderma*). Skrofuloderma is one of the most common forms of skin tuberculosis. It is usually observed in children and adolescents, but can also develop in older people.

The lesion is the result of hematogenous infection of skin with Mycobacterium tuberculosis (*primary skrofuloderma*); more often, it occurs as the result of transition of the infection per contituitatem from the infected lymph nodes (*secondary skrofuloderma*).

The disease begins with the appearance of one or more sharply limited dense nodes the size of a hazelnut in the subcutaneous tissue. Nodes gradually increase in size. Over time, they are soldered with the covering skin. The skin over the nodes is of a bluish-red color. In further, nodes soften and turn into a cold abscess. Skin becomes thinner and then breaks. From small openings, rare liquid pus with lumps and bits of dead tissue is discharged. Then, the holes widen and form ulcers with soft deep overhanging cyanotic edges. The bottom of the ulcer is covered with yellowish flabby granulations, which bleed easily with a slight touch. After some time, typical inverted



Fig. 13.3. Tuberculous lupus complicated by erysipelas.



Fig. 13.4. Tuberculous lupus complicated by carcinoma.

jagged disfiguring scars resembling bridges with the intersections of unaffected skin and fibers are formed on the site of ulcers.

In secondary skrofuloderma caused by the lesion of lymph nodes, sores are deeper and penetrate into the tissue of the lymph node. After healing, a bumpy tight retracted scar is left.

Diagnosis. Diagnosis is based on clinical symptoms, results of Pirquet's reaction (in older children, it is strong positive with a benign course of the process, while giving versatile results in younger children). Clinical history, the results of clinical, radiological and histological studies are considered.

Differential diagnosis. It is carried out with gummatous syphilides, gummy-knotted actinomycosis, chronic ulcerative pyoderma, erythema indurativum Bazin.

Gummatous syphilides are only subject to central decay, form sores similar to a crater, surrounded by the dense infiltrated shaft, which heal in a test specific treatment.

Chronic ulcerative pyoderma develops in adults and is characterized by polymorphism of superficial and deep ulcers, not related to the location of lymph nodes and presence of the inflammatory reaction around ulcers.

Localized in the neck and under the jaw areas, gummy-knotted actinomycosis is characterized by formation of large knots of dense consistency. After they merge, there develops a solid dense infiltrate, similar to a tree, with a zone of softening in the center. Discharged pus is liquid with crumbly yellowish inclusions (nodules).

When skrofuloderma is localized on shanks, the differential diagnosis with erythema indurativum Bazin is required. It is located on symmetric parts of skin, less prone to ulcers, occurs more often in girls at puberty.

In mild cases, temporary treatment leads to the formation of a single node and a patient's recovery. In cases of persistent ulcers, the prognosis is less favorable.



Fig. 13.5. Skrofuloderma.

Warty tuberculosis (*tuberculosis cutis verrucosa*). The disease mostly occurs in people who deal with the corpses of people sick with tuberculosis, as well as in workers of slaughterhouse and leather industries, which are in contact with meat and skin of animals sick with tuberculosis. Infection may be not only exogenous, but also autoinoculation and hematogenous.

The disease is often localized on the dorsum of the fingers, seldom in feet and ankles; the lesion is observed in other parts of skin.

The disease begins with the formation of a bluish-red lentil-sized

tubercle, dense to the touch. Tubercle increases in size, the stratum corneum thickens, and the surface becomes rough, gradually turning into warty papillary ecphymas, separated by cracks. In the formed foci behind the central zone of warty mass, there is an infiltration zone, covered with scales and crusts, and finally peripheral zone of the inflammatory rim.

This is one of the most benign skin tuberculosis, slowly evolving and relatively easy to treat. With no treatment, the process can occur for months or even years, with a gradual peripheral increase in the focus (usually single), scarring or atrophy in the center.

Differential diagnosis. Differential diagnosis is to consider a simple wart. The difference is that the wart is a non-inflammatory tumor and has no peripheral inflammatory corolla. Unlike *lupus verrucosus*, tuberculosis cutis verrucosa features the enhancing mass and lack of tubercles in atrophic areas.

Acute hyperkeratosis with acanthosis is the histopathological feature of warty tuberculosis. Epidermal scallops are thickened, lengthened and go deep into the dermis. The dermis contains a significant infiltrate consisting of epiteioid cells, a small number of giant cells and lymphoid cells.

Ulcerative tuberculosis of skin and mucous membranes, or miliary tuberculosis, ulcerative skin (*tuberculosis ulcerosa cutis et mucose*). This is a rare form of tuberculosis, found in patients with active tuberculosis of the internal organs (lungs, larynx, colon, urinary tract) caused by the autoinoculation with Mycobacterium tuberculosis. The lesion is often localized near the natural openings, at the junctions of skin transition into the mucous membranes: mouth, nose, genitals, and anus. In these patients, mycobacteria are excreted with sputum, urine, and penetrate into skin or mucous membranes.

Dense spherical lumps of red light color the size of a pinhead are the first clinical manifestation of the disease. They are rapidly destroyed, forming small painful ulcers with scalloped soft slightly undermined edges and uneven grainy bottom with limp grayish bleeding granulations.

Diagnosis. The diagnosis is based on presence of active tuberculosis of the internal organs, Thrall's grainules, typical clinical picture and identification of mycobacteria in bacterioscopic study.

Differential diagnosis. When recognizing tuberculous ulcers, a differential diagnosis with ulcerative syphilides of the secondary period of syphilis is primarily required. For this purpose, the firm texture of their edges



Fig. 13.6. Verrucous lupus.

and bottom, detection of pale treponemes, positive serological tests and the availability of other clinical signs of secondary syphilis are considered. In papulose tertiary syphilis, ulcers are deep, right round, with thick cushion edges, nontender. In gastric form of tuberculous lupus, the characteristic lupomas with positive probe and apple jelly symptoms are observed on the periphery of ulcers. Positive tuberculin skin tests, as well as general good condition are considered. Epitheliomas are characterized by thick edges of ulcers, presence of pearl-gray «pearls» on the periphery of ulcers, lymph node density.

The prognosis depends on the course of tuberculosis.

Disseminated forms of skin tuberculosis

Lichenoid tuberculosis (*tuberculosis cutis lichenoides*) **or shingles scrofulous** (*lichen scrofulosorum*). Scrofulous lichen is a disease that occurs most often in children. It develops in people who have other symptoms of active tuberculosis: lesions of lymph nodes, bones, internal organs and skin. The rash is localized on the lateral body surfaces, abdomen, and consists of miliary nodules with color from pale pink to reddish-yellow, covered with scales. The elements are disseminated, but mostly in groups.

Differential diagnosis. The disease is to be differentiated with miliary syphilides, in which the rash has bluish-red color, while its tendency to grouping and, sometimes, formation of various shapes (rings, half rings) is more pronounced; and finally, positive serological reactions decide the issue of *lichen syphiliticus*.

Histopathological features lie in the fact that a perifollicular infiltrate composed of lymphoid, epithelioid and giant cells is formed the upper layers of the dermis. Areas of infiltration feature quite expressive contours.

Tuberculosis papulonecrotica (*tuberculosis cutis papulonecrotica, acnitis, folliclis*). Tuberculosis papulonecrotica is caused by the contact of mycobacteria with skin by the hematogenous pathway. The disease begins with the appearance of knots the size of a lentil seed, of firm texture and bluish-red color. After some time, nodules in the center get necrotized and a pustule is formed, which soon is covered with a tight brownish crust. After removing the crust, a small ulcer is formed. When healing, the crust falls away, while leaving a bluish-purple scar. Gradually, it becomes colorless.

The lesions are located on the extensor surfaces of the upper and lower extremities, knee and elbow joints, ears and face (*acnitis*) and not accompanied by subjective sensations.

Differential diagnosis. Tuberculosis papulonecrotica is to be differentiated with oil folliculitis, which develop from blackheads. **Erythema induratum** (*erythema induratum Basin*). This form of skin tuberculosis is characterized by formation of nodes in the subcutaneous tissue caused by penetration of mycobacteria into skin by a hematogenous pathway. At the beginning of the disease, nodes of bluish-purple color, different sizes and dense texture appear most frequently on legs. Nodes feature

round or oval shape, sometimes are elongated in the form of a band, not sharply separated from the surrounding tissue, project above the skin level and are usually painful. Skin over them turns dark red with a bluish tint, gradually turning into a color of the surrounding tissue. Nodes split, forming rounded ulcers with undermined edges.

Diagnosis. It is based on clinical and histological data. The greatest difficulty appears during the differential diagnosis with erythema nodosum and skrofuloderma with its localization in legs. Erythema nodosum is characterized by severe inflammation, fever and soreness, localization across the front surface of the lower leg, with no predisposition to frequent relapses, disintegration and formation of ulcers. Pirquet's reaction is negative. In clinically severe cases, the effectiveness of a specific treatment is considered. Skrofuloderma is characterized by soft texture of the nodules and presence of fistulas.

Miliary tuberculosis of skin, or miliary disseminated lupus of face (*tuberculosis luposa miliaris cutis, lupus miliaris disseminatus faciei*). The disease affects almost exclusively adults aged 20-40 years, mostly women. The disease is characterized by facial enanthesis in the form of scattered non-homogenous brownish-pink bumps, the size of a pinhead to lentil seed. Existing for several months, bumps leave a faint pigmentation or superficial atrophic scars («stamped ribs»). Pirquet's reaction is generally positive.

Pathohistological study of the lesion focus reveals the accumulation of epithelioid cells in the loops of argyrophilic fibers in the center, and on the periphery – a zone of lymphoid and some plasma cells. Multinucleated giant Langerhans cells are an indispensable companion of the specific inflammation.

Diagnostics. In addition to histological examination, lupus can be confirmed by carrying out tuberculin tests (Mantoux and Pirquet's reaction), thanks to positive results of instilling pathological material in experimental animals (mostly guinea pigs, which are very sensitive to Mycobacterium tuberculosis), detection of Mycobacterium tuberculosis when plated on nutrient media.

Treatment. For treatment, different tuberculostatic drugs in combination with pathogenic agents (vitamins, anabolic steroids, therapeutic feeding and the use of physical therapy methods) are applied.

For therapeutic effect, tuberculostatic drugs are divided into the following groups:

- the first group includes most effective drugs (isoniazid, rifampicin, etc.);



Fig. 13.7. Tuberculosis papulonecrotica.

- the second group includes the drugs of average efficiency (ethambutol, streptomycin, kanamycin, pyrazinamide, and so on);
- the third group includes preparations of moderate activity (paraaminosalicylic acid, tibon or tiotsetazin etc.).

Treatment with tuberculostatic drugs is carried out in two stages. In the first phase, at least three drugs for three months are prescribed, in the second phase two drugs daily or two to three times a week (intermittent mode) are prescribed. After three or four months, a combination of drugs is changed to prevent drug resistance.

In dermatological practice, treatment begins with the application of a combination of tuberculostatic drugs of the first group (e.g. rifampicin and isoniazid), sometimes pyrazinamide or tiotsetazin are added. Further, these drugs are replaced with streptomycin, ethambutol, paraaminosalicylic acid. The main course of treatment is carried out in a specialized (but not lung) hospital (luposorium) for 5-7 months, then a question of the appointment of anti-relapse treatment is decided individually (3-4 courses with an interval of 3-6 months). In resistant cases of tuberculosis papulonecrotica and miliary tuberculosis of skin, as well as some of its other forms an additional treatment with corticosteroids is required.

Prevention. Preventive measures are the same as in the general tuberculosis infection. They are based on improved living and health conditions of the population, early detection and treatment of early forms of tuberculosis.

1. Of the listed factors, following contribute to the emergence of skin tuberculosis:

A. Long-term exposure to the sun
B. Gastrointestinal diseases
C. Tuberculosis of other organs
D. Vascular disorders
E. Frequent colds

2. What are the skin manifestations characteristic of tuberculous lupus?

A. Spots
B. Telangiectasia
C. Pustules and papules
D. Tubercles
E. All of the above, except for tubercles

3. Which of the following symptoms is detected in tuberculous lupus herpes?

A. Symptom of a woman's heel
B. Biett's collarette
S. Koebner's Phenomenon
D. Apple jelly symptom
E. Nikolskiy's symptom

4. The most common penetration route of tubercle bacilli into skin is:

A. Insect bites
B. Hematogenous or lymphogenous
C. Sexual
D. All of the above is not true
E. All of the above is true

5. Lupus is caused by mycobacteria:

A. Human type
B. Bird type
C. Bull type
D. All of the above types
E. All of the above is not true

6. Optimal temperature for the growth of Mycobacterium tuberculosis is:

A. 37-38 degrees
B. 40 degrees
C. 42 degrees
D. 29 degrees
E. 0-15 degrees

7. Ulcerative tuberculosis of skin and mucous membranes is most often observed on:

A. Extremities
B. Trunk
C. Hairy part of the head
D. Mucosa of the mouth and around the natural orifices
E. Toes

8. Tuberculous lupus is often complicated with:

A. Erysipelas
B. Elephantiasis
C. Eczematization
D. Epithelioma
E. All true, except eczematization

9. Skrofuloderma is characterized by:

A. Ulceration of the nodes often in the submandibular region
B. Availability of chronic inflammatory sites
C. Presence of fistulas between ulcers
D. Hypertrophic scars with papillary growths and bridges of healthy tissue
E. All versions are possible

10. Treatment of skin tuberculosis:

A. Should not last more than three months
B. Is not significantly different from treatment of tuberculosis of the internal organs
C. Should not exceed five months
D. All of the above is true, except that treatment should not last more than three months
E. Should not exceed one month

Task 1. A female patient aged 35 years visited a doctor complaining of spot eruption on the extensor surfaces of the upper arms and thighs, within a period of about one year. At these sites, there are nodules the size of a small pea, of brownish-bluish color. Near the nodules, hollow, as if stamped, ribs surrounded by a pigmented border are observed.

a) The described eruption is characteristic of:
- **A.** Tuberculosis lupus
- **B.** Psoriasis
- **C.** Planus
- **D.** Skrofuloderma
- **E.** Tuberculosis papulonecrotica

b) What diseases require differential diagnosis?

Task 2. A female patient aged 43 years has single tight tubercules on legs, not soldered to the underlying tissues. Skin over the tubercules is red with a bluish tinge. Subjectively, slight soreness is detected. In history, pulmonary tuberculosis is diagnosed.

a) Put the initial diagnosis:
- A. Miliary tuberculosis of skin
- B. Acnitis
- C. Erythema indurativum Bazin
- D. Verrucous lupus
- E. Miliary-ulcerative tuberculosis of skin.

b) Determine the therapeutic approach.

Task 3. A patient works as a veterinarian; on the dorsum of the right hand, an infiltration with warty layers is observed. Peripheral part of the infiltrate is free of warty layers and features a reddish rim.

a) Put the diagnosis:
- **A.** Primary tuberculosis of skin
- **B.** Tuberculosis lupus
- **C.** Strumoderma
- **D.** Verrucous lupus
- **E.** Miliary-ulcerative tuberculosis of skin

b) Determine the methods of treatment and prevention.

Task 4. A 30-year-old patient has the papules the size of a sesame seed of reddish color with a bluish tinge and dense texture on the extensor surfaces of the upper and lower extremities. In the central part of some papules, tight brown crusts are observed, after their removal an ulcer with steep edges is opened. At the site of ulcers, «stamped» scars are formed.

a) What kind of disease is this?
- **A**. Miliary tuberculosis of skin
- **B**. Acnitis
- **C.** Indurativnyy erythema Bazin
- **D.** Verrucous lupus
- **E.** Miliary-ulcerative tuberculosis of skin

b) What additional tests are required to put the diagnosis?

Task 5. A 12-year-old patient has a brown-red tubercule of dense texture, the size of a walnut, in the right submandibular region, within a period of four weeks. A few days ago, an irregularly shaped ulcer with undermined edges formed on the site. *Subjectively*: pain.

a) Put the initial diagnosis:
- **A**. Acnitis
- **B**. Strumoderma
- **C.** Tuberculosis lupus
- **D**. Verrucous lupus
- **E.** Miliary-ulcerative tuberculosis of skin

b) Identify ways to clarify the diagnosis.

Answers to the questions of the first level of complexity
1 – C; **2** – E; **3** – D; **4** – B; **5** – D; **6** – A; **7** – D; **8** – E; **9** – E; **10** – B
Answers to the questions of the second and third levels of complexity
1a – E; **2a** – C; **3a** – D; **4a** – A; **5a** – B

14 TOPIC

Lepra

Lepra *(lepra),* ***synonyms: leprosy, Hansen's disease, St. Giles' disease, Saint Lazarus disease,*** – a chronic generalized infection with an indefinite duration of the incubation period, a variety of clinical manifestations, involvement of numerous organs and systems in the pathological process. In leprosy, ectoderm derivatives – skin and the peripheral nervous system, the organ of vision, as well as internal organs, bones and joints are involved in the pathological process.

TRAINING AND EDUCATIONAL OBJECTIVES

- To describe the urgency of the problem of leprosy, ways and conditions of infection
- To identify key issues of the etiology, pathogenesis and epidemiology of leprosy
- To identify typical clinical manifestations of leprosy
- To understand characteristic clinical features of different types of leprosy
- To determine general principles of diagnosis, differential diagnosis, therapy and prevention of leprosy

TO KNOW:

- current state of knowledge about the etiology and pathogenesis of leprosy;
- epidemiology and incidence of leprosy in the world and in Ukraine;
- classification and typical clinical and diagnostic characteristics of the main types of leprosy (lepromatous, tuberculoid and undifferentiated);
- principles of diagnosis and treatment of leprosy.

TO BE ABLE TO:

- correctly collect medical history of a patient with suspected leprosy;
- formulate a complete clinical diagnosis with characterization of the clinical form of the disease;
- perform diagnostic tests to assess the level of sweating (Minor's test), peripheral nervous sensitivity disturbance;
- perform differential diagnosis depending on the clinical form;
- prescribe laboratory studies confirming the diagnosis;
- prescribe rational therapy of leprosy patients depending on the type of the disease;
- undertake preventive actions in the infection focal point.

Epidemiology. Lepra is one of the most ancient diseases known to the humanity long before our era. Lepra was most widely distributed in the European countries in the 11th-12th centuries. Since then, a number of European countries started to create special detention centers for lepers (leprosariums). These special buildings were built outside the cities, and their inhabitants (leprosy patients) were isolated from the outside world. Due to the isolation of these patients in the 17th century, the incidence of leprosy has decreased significantly, and at the end of 19th century the infection almost disappeared in the European continent, except for some countries. Now there are about 15 million leprosy patients, mainly among the poor population in the countries of Africa, Asia, Indochina and South America. In economically developed countries, there are only isolated cases of lepra.

Etiology. The causative agent of lepra (*Mycobacterium leprae hominis*) was discovered in 1874 by Norwegian doctor G. Hansen. He found it in a scraping from the surface of the node cut of a leprosy patient, and in 1879 German microbiologist A. Neisser proposed a method of staining lepra bacteria. Therefore, in the literature, the causative agent of lepra is sometimes described as Hansen-Neisser mycobacterium. The causative agent of lepra to some extent resembles that of tuberculosis; this is a gram-positive and alcohol-and acid-resistant mycobacterium, 1.5-6 мм long and 0.2-0.5 мм wide. Usually mycobacteria are found in fresh leproma in large numbers. Like other mycobacteria, lepra mycobacterium are stained red by Ziehl-Neelsen; they are found in tissue cells as clusters of spherical form in which separate mycobacteria are arranged parallel to each other, resembling cigarettes in a pack («cigarette packs»).

Pathogenesis. Once in the body, the causative agent of lepra overcomes the mucocutaneous barrier, enters the nerve endings, the lymphatic and circulatory system, and gradually spreads throughout the body, without causing any significant changes (hidden generalization). In cases of sufficient immune resistance of the body, lepra mycobacteria pass into the latent stage of indefinite duration or die (cases of self-healing have been reliably established in paucibacillary lepra).

The pathogenetic mechanism in leprosy is the formation of immunocompetent granulomas. These granulomas occur when pathogens entering the body are not completely destroyed by macrophages. This leads to the induction of cellular and humoral immune response. «Leproma» (leprous tubercle, granuloma lepromatous) is the general name of specific granules observed in leprosy.

The incidence of leprosy among the population in different countries depends primarily on socio-economic factors, the standard of living, and the general health culture. Lepra is a low-contagious disease; it is believed that the main, and perhaps the only source of infection is a patient excreting mycobacteria with sputum, saliva, urine, breast milk, semen.

The problem of bacilli carriage in leprosy needs to be clarified. Thus, detection of Hansen mycobacteria on mucosae in healthy individuals, particularly medical personnel of leprosariums and family members of leprosy patients is not a sign of the

disease by itself. A precondition for confirm the diagnosis of latent lepra in such mycobacteria hosts is their multiple detection in nasal scrapings.

Incubation period and precursors. The incubation period in lepra can range from 2-3 to 10-20 years or more. At the end of the incubation period, which is sometimes referred to as the latent phase of the disease, there are various, poorly characteristic symptoms of this disease.

In a number of cases, the disease begins with rapidly progressing anemia, general weakness, drowsiness, joint pain. Paroxysmal neuralgia in the extremities, paresthesia, acroasphyxia, impaired sweating, and later sensitivity precede the development of explicit polyneuritis. There are frequent cases of rhinitis, nasal bleeding. After some time (from several weeks to several years), the disease enters a phase of marked clinical manifestations of a certain type.

Classification. In practice, there are three types of lepra – the lepromatous (lepra L.), tuberculoid (lepra T.) and undifferentiated (lepra J.) type.

Clinic. The most characteristic symptoms in lepra are lesions of the skin and nervous system; they are often combined, but primarily, as a rule, there are cutaneous manifestations, which are later supplemented with neurological disorders.

Lepromatous type of lepra. This is the most severe form of lepra, affecting the skin, mucous membranes, eyes, lymph nodes and many visceral organs. Patients emit large amounts of mycobacteria. At this stage they are the most dangerous to others. The lepromatous type of lepra develops independently or is formed on the basis of other types and is characterized by polymorphism of clinical manifestations.

Typically, the process begins with appearance of red spots of different sizes on the skin, with a purple or cherry shade; they are round or irregular in shape and have



Fig. 14.1. Lepromatous type of lepra – *«facies leonine»*.



Fig. 14.2. Lepromatous type of lepra (elbow lepromas).

distinctive shiny surface. At initial stages, the sensitivity within the spots may be preserved, but sometimes their hyperesthesia is observed. Over time, the sensitivity decreases and then disappears. Gradually, the spots become more dense, form massive infiltrates becoming rusty in color; along with the skin the process involves the subcutaneous fatty tissue. Lepromas are formed. Spotted infiltrates may be observed anywhere on the skin. On the face this leads to mimic disorders and distortion: development of an angry expression (lion's muzzle symptom – facies leonine), which caused the emergence of one of the synonyms of lepra – «leontiazis».

With further progress, bundles are formed. The fusion results in a large infiltrate with an uneven bumpy surface. Palpation can detect infiltrations, even conglomerates of tumors consisting of separate lepromas. Infiltration of the superciliary archs leads to permanent hair loss in the lateral part of the brows.

On the mucous membranes, as well as the skin, the process may begin with appearance of separate lepromas or diffuse lepromatous infiltration. Typical signs of lesions of the mucous membranes of the nose are dryness and the presence of stubborn crusts. In the course of evolution and spread of infiltration on the cartilage and nasopharyngal bone tissue, nasal septum perforation may appear. When the epiglottis is involved, voice becomes hoarse (aphonia) and even respiration may be compromised.

Another typical sign of the lepromatous of lepra is injury of the vision organ. Conjunctivitis, keratitis, episcleritis, iritis, iridocyclitis, damaged lens may develop. Leprosy lesions often result in blindness.

Among the internal organs, the lepromatous infection mostly affects the spleen in the form of splenomegaly. Impairments of the renal, hepatic and pulmonary function are observed.

Noticeable changes occur in the genital area. In men, the testis, prostate, and especially the scrotum organs may be affected. In women, due to sclerotic changes in the ovaries there occurs strong disturbance of the menstrual cycle, leading to premature menopause.

The lymph nodes are affected very early. Mycobacteria of lepra are found almost always in their punctates. Lepra in general and its lepromatous type in particular is characterized by recurrent exacerbations, or leprosy reactions (usually in spring and autumn).

The peripheral nervous system is affected relatively late and is rare, usually in the form of symmetrical polyneuritis.

Tubercuoid type of lepra. This is the most benign clinical form of lepra, which develops in subjects with frank resistance and confirms high resistance of the body (positive lepromin test). In the tuberculoid type of lepra the pathological process involves mainly the skin and nerves, seldom – other organs, and there are no express clinical symptoms. Due to scarcity of the rash, it is difficult to determine the pathogen.

Diversity of skin rash depends on the depth of the eruption, its nature (acute, subacute, chronic), and the phase of the disease. The basic elements of skin rash in

the tuberculoid type of lepra are small reddish-bluish flat polygonal papules that tend to merge. A characteristic feature of this type of lepra is presence of a cushion along the periphery, whose outer edge is somewhat elevated, clearly defined and is reddish-bluish. The inner edge is indistinct and imperceptibly merges into the central pale part of the lesion. Elements of rash are localized anywhere on the skin and can be isolated or multiple, but the scalp is never affected.

Lepromas are characterized by cacesthesia, which is especially clearly expressed in the central part of the rash element. As always in lepra, at first thermal, then pain and finally tactile sensitivity disappears. In addition to full anesthesia, occurring during a more or less prolonged period, hyperesthesia, various paresthesias can be observed. Sweating in the tuberculoid type of lepra, as in lepromatous, around rash elements disrupts, then disappears. Hair become dull, often fall.

A monotonous and steady course of the tuberculoid type of lepra can sometimes be violated by acute reaction.

Tuberculoid neuritis occur manifest themselves through thickening of skin branches in the area of skin rashes, damage of major nerve stems can occur.

Undifferentiated or nondescript type of lepra. This type of lepra is intermediate between the lepromatous and tuberculoid types. It often develops in either tuberculoid (more favorable outcome), or lepromatous type with decrease of immunobiological resistance and body defenses.

Undifferentiated type of lepra is characterized by frank neurological symptoms and absence of typical lesions on the skin. A patient with this type of lepra is less dangerous to others than those with the lepromatous type.

With this type of lepra neurological symptoms are presented with leprous neuritis, which develop gradually. In addition to loss of sensitivity, reflexes impairment is



Fig. 14.3. Undifferentiated type of lepra (eyebrow and eyelash loss).



Fig. 14.4. Lepra (deformation of the hand joints and muscle atrophy).

observed. Amyotrophies of different muscle groups develop. Amyotrophies of facial muscles cause development of «St. Anthony's mask» (face becomes sad and resembles a mask), palm amyotrophies – formation of the «monkey paw».

Diagnosis. For diagnosis of lepra, in addition to typical clinical picture (taking into account appropriate anamnestic data about stays in endemic areas) special methods are of particular importance. This is primarily microscopy and a series of clinical and functional tests.

After a thorough inspection of the skin and mucous membranes, determining the state of nerve stems and lymph nodes and sensitivity testing, it is necessary to perform a bacterioscopic examination, which is very important for early diagnosis.

Laboratory diagnostics. For bacteriologic examination, scrapings from the mucous membranes of the nose and from the affected area of skin and skin of the superciliary arch, earlobes, chin, distal parts of the limbs are taken. To take skin scrapings, pinch the crease with two fingers and make a small 1-2 mm deep incision using a scalpel, then scrape the section walls material to be transferred on a microscope slide and stained by Ziehl-Neelsen to detect mycobacteria.

Functional tests. Pharmacodynamic tests help to identify very early lesions of the peripheral nervous system, manifesting (in addition to sensory) through vasomotor, secretory and trophic disorders. At first, perform tests using histamine, morphine and dionin. Apply one drop of 0.1% aqueous solution of histamine (or 1% morphine, 2% dionin) on the test area of the skin (both affected and unaffected). Pierce the skin through these drops without affecting the capillaries. In a healthy person, in 1-2 minutes a limited erythema should appear on the injection site, replaced with a reflex erythema several centimeters in diameter, with a blister or pimple in the center, in another minute or two. In leprosy lesions, there is no or mild reflex erythema.

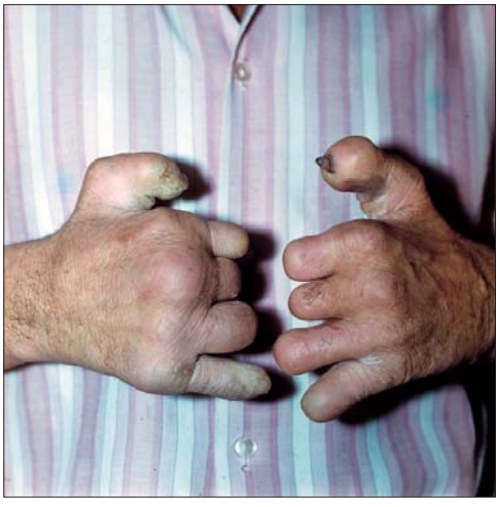


Fig. 14.5. Lepra (mutilation of finger phalanges).

In order to detect leprosy process, nicotine test is used (flash phenomenon). After one to three minutes after administration of 5.8 ml of 1% aqueous solution of nicotinic acid, an erythema appears and gradually increases, disappearing after 10-15 minutes. The affected areas remain bright red and swell; sometimesblisters appear on the surface.

Lepromin test. A specific antigen (lepromin) derived from lepromas is used as a starting material. The test is performed by intradermal injection of lepromin into the skin of the forearm

flexion. «Orange peel» should appear at the site of lepromin injection. In healthy people, swelling and redness appear at the injection site on day 2 or 3.

Interpretation of lepromin test findings

1. Negative reaction: after injection a papule is formed, less than 3 mm in diameter, and disappears in the end of day 2.

2. Mildly positive reaction: a swollen nodular infiltrate is formed, 3 to 5 mm in diameter, surrounded by a barely noticeable sore rim.

3. Positive reaction: an infiltrate is formed, 5 mm to 10 mm in diameter; the swelling is expressly elevated above the skin level and is surrounded by an inflamed aureola.

4. Acutely positive test: a sappy papule appears that turns into a node of more than 10 mm in diameter; inflammations are frank; often an ulcer is formed.

The said allergy test is very important to differentiate the type of lepra, as well as to determine the course of the disease, effectiveness of treatment and prognosis. The transition of lepromin test from negative to positive always means improvement, and the transition from positive to negative – decreased immunobiological reactivity of the body. This test may help forecasting in the undifferentiated type of lepra, especially in an exacerbation reactions (in this case, the transition of lepromin test from positive to negative evidences the transformation of lepra in the lepromatous type). In healthy people who never contacted with leprosy patients, the lepromin test is positive. This is important when examining the population in endemic areas, as well as families of patients and staff of leprosariums. The diagnostic value of this reaction is relative. It can be considered in conjunction with other data obtained in the patient examination. As is known, in all infants it is negative. The vaccine of Calmette and Guerin may be used for transition of negative lepromin test into positive.

Differential diagnosis. Differential diagnosis in lepra is performed in accordance with the symptoms as dermatological, neurological and special (with eye and upper respiratory tract diseases).

Dermatological differential diagnosis is performed with:

- erythematous dermatoses (erysipelas, erythema multiforme, secondary and tertiary syphilitic roseola);
- erythematous-squamous dermatoses (psoriasis, parapsoriasis, lupus erythematosus, pityriasis rosea);
- dyschromias (syphilitic leucoderma, leucoderma after pityriasis versicolor, vitiligo);
- papulose and nodular dermatitis (skin tuberculosis, tertiary syphilides, mycosis fungoides);
- ulcerative dermatosis (Raynaud's disease, varicose ulcers and hypertonic).

Treatment and prevention.

The main etiotropic means at the time are several groups of drugs. These are sulfone class drugs: diaminodiphenylsulfone(DDS), dapsone, avlosulfone,

diuciphonum, diazonium, etc.; thiourea derivatives (tibon, diamide, Ciba-1906 or thiambutosine), antibiotics and anti-tuberculosis drugs – rifampicin, izoprodian, klofamizin, ethionamide, isoniazid, tubazid, protionamide; fluoroquinolones – ofloxacin, pefloxacin. Several etiotropic medicines are prescribed concurrently, as each of them in monotherapy is not sufficient to inhibit sulfone mycobacteria, which are used for many decades, so that a lot of drug-resistant strains of Mycobacterium have developed.

Until now, the form of leprosy patients' isolation (and more recently – its necessaity after all) has been questionable.

Prognosis. Prognosis in lepra depends on the type of disease, stage of the process at the time of treatment and proper selection of drugs. With the tuberculoid type of lepra, the prognosis is more favorable than in undifferentiated and especially lepromatous. After treatment in leprosariums, subject to resorption of clinically visible manifestations on the skin and mucous membranes, repeatedly negative results of lepra mycobacteria (Mycobacterium lepre) tests in scrapings from the nasal mucosa and lymph node punctate, patients can be discharged for outpatient treatment with dispensary control of a leprologist or dermatologist.

1. Mark a wrong definition of lepra:

A. General infectious disease
B. Skin infectious disease
C. Skin and mucosae infectious disease
D. Toxico-allergic disease
E. Chronic infectious disease of the skin and internal organs

2. The following are skin manifestations in lepra:

A. Macula
B. Tubercle
C. Nodules
D. Bulla
E. All of the above

3. The causative agent of lepra is:

A. Protozoa
B. Mycobacteria
C. Treponema
D. Myceliums
E. Viruses

4. The following is characteristic of the tuberculoid type of lepra:

A. Polymorphic rash bothering the patient
B. Benign course
C. Early desensitization
D. Erythematous spots and hypopigmentation
E. All of the above

5. The lepromatous type of lepra develops:

A. Independently
B. Based on other types
C. As a result of new infection
D. All of the above is false
E. Independently and forms from other types

6. The following is characteristic of undifferentiated lepra:

A. Severe neurological symptoms (paresis, paralysis)
B. Absence of typical rash on the skin
C. Continued stabilization process
D. All of the above is true

7. The following type of staining is performed when examining materials for the presence of lepra causative agent:

A. Argentation
C. Ziehl-Nielsen
D. Methylene blue
E. Romanovsky-Giemsa

8. The following is used to treat lepra:

A. Dapsone
B. Rifampicin
C. Ofloxacin
D. Thiambutosine
E. All of the above

Task 1. A 47-year old patient consulted a doctor. In the past this patient worked for several years in the Middle East, and complained of rash in the form of skin nodes, replacing spots that appeared several months ago. Examination showed multiple nodes on the face, body and extremities, merging into tumor infiltrates with uneven surface. Some nodes break down to ulcers. There is no reaction to touch, pain, heat and cold.

a) Which disease is best characterized by these symptoms:
A. Spinal gliosis
B. Scrofuloderma
C. Syphiloma
D. Lepra
E. Lupus

b) Which additional studies are necessary to establish a definitive diagnosis?

Task 2. A 30-year old patient has numerous small reddish-blue flat polygonal papules on the skin of the body and limbs that merge to form elements of shaped as rings, semicircles, ovals, with elevated outer edges, clearly defined, of reddish-bluish color. There is no thermal and tactile sensitivity in the central part of the rash elements.

a) Which disease is characterized by this clinical picture:
A. Lichen acuminatus
B. Papule necrotizing tuberculosis
C. Tuberculoid type of lepra
D. Leishmaniosis
E. Tuberculous chancre

b) This is the dermatologist's tactics in this case?

Task 3. A patient consulted a doctor complaining of deformation of the face and the limb phalanges, and skin rashes. There is dyschromic erythematous skin rash with clear boundaries on the body and upper extremities, amyotrophy of different groups of facial muscles. There is no mimic («St. Anthony's mask»). As a result of mutilation the palm resembles a seal's paw.

a) This clinical picture is typical for:
A. Undifferentiated type of lepra
B. Lepromatous type of lepra
C. Tuberculoid type of lepra
D. Syphiloma
E. Lupus

b) What is the prognosis for the disease?

Task 4. A 45-year old patient consulted a doctor complaining of skin rash. There is rash in the form of hyper- and depigmented spots on the skin of the body, upper and lower extremities, as well as amyotrophy of different groups of facial muscles, and atrophy of the majority of small phalange bones. There is no or reduced pain, temperature and tactile sensitivity within the spots. From past history it is known that the patient lived in Yemen for five years.

a) Which disease can be suspected?
A. Lupus
B. Lepromatous type of lepra
C. Tuberculoid type of lepra
D. Syphiloma
E. Undifferentiated type of lepra

b) Make up a plan of rehabilitation measures.

Answers to the questions of the first level of complexity
1 – D; **2** – E; **3** – B; **4** – B; **5** – E; **6** – E; **7** – C; **8** – E
Answers to the questions of the second and third levels of complexity
1a – D; **2a** – C; **3a** – A; **4a** – C

15 TOPIC

Leishmanioses

Leishmanioses (*leishmanioses), **synonym: Borovsky's disease*** is a group of vector-borne protozoan diseases of humans and animals, whose pathogens (Leishmania) are transmitted by winged insects – mosquitoes.

TRAINING AND EDUCATIONAL OBJECTIVES

- To disclose the urgency of the problem of leishmaniosis, routes and conditions of infection
- To identify key aspects of etiology and pathogenesis, and epidemiology of leishmaniosis
- Identify typical symptoms of this disease
- To distinguish characteristic clinical features of dermal leishmaniosis
- To summarize the principles of treatment and prevention of skin leishmanioses

TO KNOW:

- modern views of etiology and pathogenesis of dermal leishmaniosis;
- factors that trigger the development of this disease;
- classification and characteristic clinical and diagnostic features of the main varieties of dermal leishmaniosis;
- principles of diagnosis and treatment of dermal leishmaniosis;
- measures to prevent dermal leishmaniosis.

TO BE ABLE TO:

- to correctly collect past history of patient with dermal leishmaniosis;
- to formulate a complete clinical diagnosis of the disease;
- to perform diagnostic tests to confirm the diagnosis;
- to perform differential diagnosis with diseases that have a similar clinical picture;
- to prescribe rational therapy to patient with dermal leishmaniosis.

Epidemiology. According to the WHO, more than 400 million people around the world have leishmaniosis every year.

Etiology. The causative agent of leishmaniosis *Leischmania tropika* is a *Protozoa*, found and first described in 1898 by P.F. Borovsky. The life cycle of Leishmania occurs in two stages with change of the host – amastigote and promastigote. The amastigote form (nonflagellate stage) parasite intracellularly in the body of vertebrate animals and humans. The promastigote form (flagellate stage) parasites in the intestinal lumen of the invertebrate pathogen mediator – Mosquito.

Pathogenesis. Leishmania as intracellular parasites multiply in the mammalian body in cells of the reticuloendothelial system, or in free macrophages. Mosquitoes become infected by sucking blood of an animal or person with leishmaniosis. After sucking the blood a female mosquito is contagious for 6-8 days. Parasites persist in the insect's body throughout its life. A patient with leishmaniosis is not hazardous for others in absence of a carrier.

The parasite is abundant in macrophages as well as skin lesions. NNN (Novi Nicole Nicole) medium is widely used to cultivate Leishmania, on which their growth is observed on day 7-21. Leishmania have common antigens with mycobacteria, which can cause diagnostic errors when performing serological tests.

Classification. There are two forms of human leishmaniosis.

Visceral leishmaniosis (synonyms: internal leishmaniosis, children leishmaniosis, kala azar) is characterized by impairment of the lymphohistiocytic system with relapsing fever, cachexia, progressive anemia, leukopenia, abrupt spleen enlargement.

Dermal leishmaniosis (synonyms: pendin ulcers, Ashgabat disease, Kokand disease and many others) which predominantly affects the skin (mucous) includes Old World and New World dermal leishmaniosis.

Both forms have different geographical and clinical and epidemiological variants.

Dermal leishmaniosis

Dermal leishmaniosis it is a transmissible protozoan disease with typical clinical symptoms and clear endemic nature of spread in many tropical and sub-tropical climates, where there are mosquitoes. There are a great number of local names of this disease, which originate, as a rule, from geographical names.

Pathogenesis. After a mosquito bite (Leishmania carrier), promastigote (flagellated) forms of the parasite get in the skin, which quickly penetrate into macrophages, acquire the amastigote (nonflagellate) form and begin to proliferate. In the area of Leishmania penetration there is accumulation of a large number of macrophages, «stuffed» with amastigotes. They are surrounded by lymphocytes and plasma cells, whose number tends to increase. As a result, granuloma begins to form. Further there is elimination of parasitic cells, epithelioid and giant Langerhans cells

appear. During the period of active decay of parasites its products directly affect the surrounding skin, thus causing swelling of the surface layer of the dermis, damage of collagen and elastin fibers (often their necrosis).

In dermal leishmaniosis there is early formation of increased delayed cellular sensitivity. Gradual increase of its activity promotes development of diffuse dermal leishmaniosis. The pathological process caused by *leischmania panamiensis et brasiliensis* is characterized by damage of not only the skin but also the mucosa of the nose and pharynx (mucocutaneous leishmaniosis) with damage of the palate and nose cartilage. Persons who had dermal leishmaniosis retain lifelong immunity to the Leishmania strain, which had caused the disease.

Classification. According to epidemiological features, dermal leishmaniosis is divided into:

Old World leishmaniosis (anthroponotic and zoonotic subtypes), which is found in countries of the Eastern Hemisphere (carrying agents – mosquitoes of *Phlebotomus* class);

New World leishmaniosis (American dermal leishmaniosis) which is found in countries of the Western Hemisphere (carrying agents – mosquitoes of *Lutzomyia* class).

Depending on the biological characteristics of the pathogen, epidemiology and clinical presentation are two types of dermal leishmaniosis:

1) **urban**, or late-ulcerous (chronic) anthroponotic type;

2) **rural**, or acute necrotising (zoonotic, desert) type.

The pathogen's reservoir in the urban type is a sick person from which mosquitoes become infected, while in the rural type these are rodents with dermal leishmaniosis (squirrels, gerbils).

Clinical picture of Old World dermal leishmaniosis. The clinical picture and course of dermal leishmaniosis largely depend on its type. Each type has certain regularities, which is reflected in the length of the incubation period, the rate of development process, peculiarities of the clinical course and duration of the disease.

Anthroponotic, first type of dermal leishmaniosis (synonyms: Ashgabat ulcers, Kokand disease, salek, yearling, dry or chronic leishmaniosis). This type of the disease is also called *anthropophilic*, because the pathogen's reservoir *(L. tropica minor)* is a human, contrary to the 2nd type – zoonotic, whose pathogen's reservoir *(L. tropica major)* is wild rodents.

The incubation period of the first type varies between 2-4 months to 1-2 years. The pathological process starts with appearance of a 2-3 mm bump. The bump is flat, slightly raised above the surrounding healthy skin, without inflammation. The bump is brownish, frequently with a small central hole filled with dry scale in the middle. As the bump increases, it gradually rises above the skin level, is often round in shape, sometimes with slight protrusions at any edge.

The bump grows slowly and 2-3 months later becomes reddish. The bump's surface in the first two months is smooth, later thin scales appear. 3-6 months later,

dense brown lamellar flaky crusts develop. Scraping reveals shiny erosive surface. Once formed, the ulcer gradually increases as the granuloma grows, but the ulcer's growth is slower than the increase in the infiltrate. Light squeezing of the ulcer's sides exposes very scarce serous secretion, sometimes with small purulent lumps on the surface. As the ulcer develops, slow formation of scars begins.

Zoonotic, or second type of dermal leishmaniosis. *Synonyms: desert-rural type of dermal leishmaniosis, Murhab ulcer, Pendin ulcer.* Due to the fact that the pathogen's reservoir in this type is wild rodents, it is also called zoonotic. This type of the disease (pathogen – *L. tropica major*) is found in Africa, mostly in Sahara deserts, the Arabian Peninsula and the Central Asian countries. Here, large infestation of rodents is recorded, and often outbreaks of disease affecting large numbers of people are observed.

The incubation period in the acute necrotizing form is shorter, it is from 1 week to 1-2.5 months (usually 10-20 days).

This disease begins with formation of a compacted bump (5-10 mm in diameter) or node (10 to 20 mm in diameter), most often around the extremities (especially the lower).The second type of dermal leishmaniosis differs from the first type by sudden onset, presence of swelling around the bump or node with rapid growth of rash elements. In a number of cases the process may begin with a formation resembling a furuncle with its typical acute inflammatory phenomena, but differing from it by softer consistency and lesser sensitivity. Then, 1-2 weeks later, necrosis occurs in the center of the node. The resulting exudate forms a dense crust, exposing a small ulcer after removal. The bottom of the ulcer is uneven, covered with necrotic plaque. At palpation, pastiness is found in the ulcer bottom.

round the primary ulcer there are sometimes new secondary smaller leishmanioms (satellite Leishmania), which undergo the same cycle of development and turn into ulcers and gradually merge with the primary ulcer.

Tuberculoid type of dermal leishmaniosis (synonyms: metaleishmaniosis, lupous leishmaniosis, papulose leishmaniosis). From a pathogenic point of view, bumps in this type of leishmaniosis are rudimentary immature leishmanioms converted to protracted form as a result of already developed, but unstable immunity. The disease is more common in childhood and adolescence. The main element of rash in the tuberculoid form is a small yellow-brown bump. Usually bumps surround a healed ulcer with a ring or semicircle.

Diagnosis. Dermal leishmaniosis is diagnosed on the basis of clinical symptoms, taking into account climatic and epidemiological factors and laboratory detection of Borovsky's corpuscles. This requires correct sampling of the examination material. In closed leishmanioms (bumps, nodes) it is necessary to make a puncture using a sharp scalpel and obtain tissue for smear from the depth of the node. If there are ulcers, material is sampled around them, along the edge of infiltration using tweezers.

Material is applied on the glass and stained by Romanovsky-Giemsa. Borovsky's corpuscles are found in macrophages and around them.

Pathomorphology. In the initial stages, when mass reproduction of the pathogen occurs, the process begins with an inflammatory reaction. Only later granulomatous infiltrate consisting mainly of histiocytes, plasma cells and a small number of neutrophils is formed. Acanthosis is observed in the epidermis before formation of ulcers.

Differential diagnosis. Dermal leishmaniosis with syphilis, skin tuberculosis, abrasions are differentiated. An ulcer formed instead of granuloma may be easily confused with syphilitic ecthyma, tuberculous ulcer, chronic ulcerative pyoderma and some deep dermatomycoses.

Such ulcer differs from common streptococcal ecthyma by the presence of a potent iliac roll infiltrate at the edge. A similar infiltrate also surrounds syphilitic ecthyma, but near the ulcer it is more express.

Prognosis. The prognosis is favorable. The disease ends in recovery without treatment, after a development cycle from bump to ulcers and scar. Long-term immunity remains after recovery.

Treatment. Treatment of dermal leishmaniosis should be comprehensive, specific, and performed using both topical and systemic agents.

Systemic treatment should be performed using preparations of pentavalent antimony mitefosine, pentamidine salts (as a first-line therapy), amphotericin B, metaciclinus, rifampicin, dapsone are also prescribed.

In the presence of a single early small bump and without inflammation; such bump can be removed surgically (diathermocoagulation).

In the presence of acute inflammation, lotions with different disinfectants, anti-inflammatory and antiseptic creams, ointments are prescribed.

Prevention. Prevention of dermal leishmaniosis should be performed in several directions and include measures both with respect to the source of infection (human – in case of anthroponotic type, rodents – in case of zoonotic) and carrier (mosquitoes). Of special significance is the earliest possible identification of patients and their treatment, measures of personal prophylaxis are also necessary.



Рис. 15.1. Dermal leishmaniosis (zoonotic type).

It is very important to destroy rodents, processing facilities (both residential and commercial) in endemic areas using various insecticides and to use repellents

Individual prophylaxis of persons staying in endemic areas for a long time, vaccinations with live culture of zoonotic Borovsky's corpuscles are performed, which provides rapid development of immunity to both types of leishmaniosis.

1. Leishmaniosis is:

A. Systemic autoimmune diseases
B. Infectious disease of the nervous system
C. Sexually transmitted disease
D. Protozoan transmissible disease
E. Parasitic disease

2. Carriers of leishmaniosis are:

A. Flies
B. Pets
C. Fish
D. Mosquitoes
E. All of the above is true

3. Main clinical types of leishmaniosis are:

A. Urban
B. Tuberculoid
C. Desert-rural
D. Metaleishmaniosis
E. All of the above is true

4. Pathogen's reservoir of acute necrotizing leishmaniosis is:

A. Cattle
B. Horses
C. Cats
D. Wild rodents
E. All of the above is true, except wild rodents

5. The primary element of rash in leishmaniosis is:

A. Blister
B. Node
C. Bump
D. Roseola
E. All of the above is false

6. The primary acute necrotizing form of leishmaniosis occurs:

A. Predominantly in winter
B. During the autumn-winter period
C. In summer
D. During the summer-autumn period
E. Independent of the period

7. Materials to search for Borovsky's corpuscles should be stained with:

A. Methylene blue
B. By Gram
C. Brilliant green
D. By Ziehl-Nielsen
E. By Romanovsky-Giemsa

8. The following drugs are prescribed in leishmaniosis:

A. Metacycline
B. Mitephosine
C. Amphotericin B
D. Solusurminum
E. All of the above

9. The following occurs in tuberculoid form of leishmaniosis:

A. Bumps
B. Nodes
C. Ulcers
D. Scars
E. All of the above is true

10. Dermal leishmaniosis should be differentiated with:

A. Folliculitis
B. Lupus
C. Syphilophyma
D. Epithelioma
E. All of the above

Task 1. A 30-year-old patient developed an infiltration in the chin area 10 days ago, and later an ulcer formed. According to past history, 20 days ago the patient returned from Turkmenistan. Examination of the chin showed a doughy 3.5-4 cm node, with an irregular ulcer in the center with sharp edges, rough grainy, sometimes ocher deposits. Along the edge of the ulcers there was an inflammatory infiltrated aureola.

a) Set a provisional diagnosis:
- **A**. Borovsky's disease
- **B**. Lupus
- **C**. Hofmann's disease
- **D**. Scrofuloderma
- **E**. Beck's sarcoid

b) Which groups of drugs are used to treat this disease?

Task 2. Two months after returning from Uzbekistan a 12-year-old girl developed on the skin of the left lower leg an inflammatory node up to 1.5 cm in diameter, and a ulcer with sharp edges appeared later in the center. After some time small bumps developed around the ulcer, which underwent similar changes and merged with the main ulcer.

a) Which disease is this:
- **A**. Tuberculous chancre
- **B**. Lupus
- **C**. Leishmaniosis
- **D**. Scrofuloderma
- **E**. Tuberculoid lepra

b) What diseases should be excluded in differential diagnosis?

Task 3. Two months ago a 13-year-old boy developed a brownish non-inflammatory bump up to 2 mm in diameter on the cheek appeared, filled with a barely visible dry scales in the center. After 4 months the bump became red, and dark brown crust developed in the center. According to past history, in summer the boy stayed in southern European countries with his parents.

a) What is the most likely diagnosis:
- **A**. Tuberculous chancre
- **B**. Lupus
- **C**. Tuberculoid lepra
- **D**. Scrofuloderma
- **E**. Borovsky's disease

b) Identify ways to clarify the diagnosis.

Task 4. After examining the patient the dermatologist assumed that he had leishmaniosis. A scraping to detect Borovsky's corpuscles was made from the affected site.

a) What method should be selected to stain the drug:
- **A**. Staining with methylene blue
- **B**. By Gram
- **C**. By Romanovsky-Giemsa
- **D**. By Ziehl-Nielsen
- **E**. Argentation

b) What is the essence of prevention of dermal leishmaniosis?

Answers to the questions of the first level of complexity
1 – D; **2** – D; **3** – E; **4** – D; **5** – C; **6** – D; **7** – E; **8** – E; **9** – E; **10** – E
Answers to the questions of the second and third levels of complexity
1a – A; **2a** – C; **3a** – E; **4a** – C

16 TOPIC

Cheilites

Cheilites (*cheilitis*) is a group of diseases in which inflammation is localized only on the lips (on the red border, mucous membrane), as well as some diseases, whose course is characterized by predominant lesion of the red border of the lips.

TRAINING AND EDUCATIONAL OBJECTIVES

- To summarize the modern concept of the etiopathogenesis of cheilites
- To distinguish routes and possible conditions of the body's sensitization
- To identify factors influencing the course of cheilites
- To summarize characteristics of the clinical course of cheilites
- To determine general principles of differential diagnosis, treatment and prevention of cheilites To identify therapeutic tactics for patients with cheilitis

TO KNOW:

- etiopathogenic characteristics of cheilites;
- peculiarities of classification and clinical manifestations of independent (weather, exfoliative, glandular, contact and actinic) and symptomatic (atopic, of eczematous cheilitis, plasma cell, macrochilia etc.) cheilites;
- comparative description of independent and symptomatic cheilites;
- principles of treatment and prevention of independent and symptomatic cheilites.

TO BE ABLE TO:

- correctly collect past history of patients with cheilitis;
- set a diagnosis based on clinical presentation,
- determine diagnostic tests to confirm the diagnosis,
- perform differential diagnosis of patients with diseases having similar clinical picture;
- prescribe individual pathogenetic treatment.

The term «*cheilitis*» denotes not the cause of the disease, characteristics of its course and morphological changes, but only on the localization of the pathological process. The red border, the mucous membrane of the lips may be involved in this process in many dermatoses, characterized in most cases by diffuse inflammation. Lesion of the lips may be a manifestation of allergic, infectious diseases, cancer, and various other states. There is still no generally accepted classification of cheilites, and this makes it difficult to diagnose and leads to prescription of non-rational therapy.

Classification. Cheilites is divided into two groups: independent and symptomatic.

The group *of independent cheilites* includes meteorological, exfoliative, glandular, contact and actinic cheilites.

The group *of symptomatic cheilites* include atopic, of eczematous cheilitis (lip eczema), plasma cell, macrocheilitis (Rossolimo-Melkersson-Rosenthal's syndrome), cheilitis on the background of ichthyosis and caused by vitamin deficiency.

Meteorological cheilitis

Meteorological or simple cheilitis (*cheilitis meteorological)* is an inflammatory disease of the mouth caused by physical effects of various meteorological factors on the red border.

Etiopathogenesis. The factors that cause development of meteorological cheilitis may be moisture, dryness, wind, heat, cold, dust. Often the disease develops in people who work outdoors, especially in adverse weather conditions.

Clinical picture. In meteorological cheilitis, the red border of the lips is affected, usually the lower one, along its entire length. The lip becomes slightly erythematous, dry, often covered with small scales, patients suffer from dry or tight sensation, many lick their lips, which leads to increased dryness, peeling, and then the red border infiltration. When scales are removed, painful erosion is exposed and may bleed. The skin and mucous lips are unchanged.



Fig. 16.1. Meteorological cheilitis.

Diagnosis. The diagnosis is set based on past history and physical examination. Laboratory tests are not advisable.

Differential diagnosis. It is necessary to differentiate meteorological cheilitis with allergic, actinic, atopic with cheilitis and dry form of exfoliative cheilitis.

Treatment. To treat meteorological cheilitis, it is necessary to exclude or

diminish the impact of meteorological factors. Recommendation: topical barrier creams, vitamin therapy (B_2, B_6, B_{12}, PP, C).

Prognosis is favorable.

Exfoliative cheilitis

Exfoliative cheilitis *(cheilitis exfoliativa),* ***synonym: Mikulicz-Кьmmel's disease*** is a chronic disease that affects only the vermilion border. The skin and mucous membrane are never involved in the pathological process.

Etiopathogenesis is not fully studied. The disease can be caused by neurogenic mechanisms and thyroid dysfunction.

Clinical picture. There are two forms of the disease: dry and exudative, both are different phases of the same disease and can easily be transformed into each other.

The exudative form of exfoliative cheilitis is characterized by appearance of grayish-yellow scales, crusts on the red border of the lips, which cover the red border with a layer from corner to corner of the mouth, beginning from the transition zone of the oral mucosa, *Klein's line,* till the middle of the vermilion border. Sometimes the crust is rather large and hangs from the lips like an apron. The disease is accompanied by severe burning and soreness, especially when the lips are closed, when eating and talking. Such patients almost always keep their mouth half open.

The dry form of exfoliative cheilitis, just as exudative, characterized by localized lesions only on the red border of one or both lips. The lesion is in the form of a ribbon extending from the mouth corner to corner and from Klein's line to the middle of the red border of the lips. Commissure of the mouth remains free from lesions. Part of the red border belonging to the skin always remains unaffected. Gray or grayish-brown flakes are tightly attached to the red border in the center and a little behind on the edges. Patient suffers from burning and dryness. After 5-7 days flakes easily exfoliate, exposing bare shiny red surface with no erosion.

Diagnosis. Diagnosis of exfoliative cheilitis is divided into:

- *clinical* (based on past history and physical examination);
- *laboratory* (thyroid function tests);
- *instrumental* (histopathological study if necessary, if acanthosis, parakeratosis, hyperkeratosis is observed).

Differential diagnosis. The exudative form must be differentiated from exudative form of actinic cheilitis, pemphigus vulgaris, erosive and ulcerative form of lupus, other types of cheilites.



Fig. 16.2. Exfoliative cheilitis (exudative form).

Treatment. Treatment of patients with exfoliative cheilitis is a difficult task and implies correction of concomitant neurological and endocrine pathology. Local therapy should include sanation of the oral cavity, use of keratoplasty means (oil solution of vitamin A and E, kartolin). Local corticosteroids are used in the exudative form.

Prognosis is favorable. Subject to correction of endocrine and psychopathological disorders, quite stable remission is achieved.

Glandular cheilitis

Glandular cheilitis *(cheilitis glandularis)* is a disease that develops as a result of hyperplasia, hyperthyroidism, and often heterotypic form of the salivary glands in the vermilion border and the transition zone.

Etiopathogenesis. The cause of glandular cheilitis can be a congenital anomaly in which a large number of small salivary mucous glands are located in the transition zone (Klein's zone) and red border, or the glads may have normal location, and their ducts are moved to the surface of the red border. Under the influence of stimulation the glands become hypertrophied and produce discharge intensively.

Clinical picture. There are primary and secondary glandular cheilitis.

Primary glandular cheilitis is manifested mainly after puberty. In the area of the mucous membrane transition in the vermillion border of the lips, and sometimes on the red border there are prominent dilated entries of salivary glands in the form of red dots, excreting droplets of saliva. 5-10 seconds after the lips are dried, salivation from entries of the salivary glands become clearly visible, and saliva covers the lip like dew drops.

Development *of secondary glandular cheilitis* is obviously due to the fact that the inflammatory infiltrate, characteristic of the underlying disease, irritates the salivary glands, causing their hyperplasia and hyperactivity. In this case, against the background of the main manifestations of the disease, more frequently on lip mucosa in the transition zone area there are enlarged entries of salivary glands excreting droplets of saliva.



Fig. 16.3. Exfoliative cheilitis (dry form).



Fig. 16.4. Exfoliative cheilitis (dry form).

Frequent wetting of the red border with saliva in glandular cheilitis contributes to dryness, maceration and leads to chronic fissures. Later on, the mucosa and the red border may gradually coarsen.

Diagnosis. Diagnosis of the disease based on past history and physical examination is not difficult.

Differential diagnosis. Differential diagnosis of glandular cheilitis is easy due to clear clinical signs and presence of enlarged ducts of glands.

Treatment. Anti-inflammatory corticosteroid ointments, punctate electrocoagulation of hypertrophied glands or cryodestruction are used to treat glandular cheilitis.

If a patient with glandular cheilitis has a great number of abnormal glands, their surgical excision is performed. In secondary glandular cheilitis it is necessary to treat the underlying disease.

Prognosis is favorable. At superficial electrocoagulation or cryodestruction clogging of ducts of salivary glands and formation of cysts may be observed.

Contact allergic cheilitis

Contact allergic cheilitis *(cheilitis alergica contactis)* is a disease, developing due to sensitization of the vermilion border or, less frequently – mucosa, to chemicals and occurs when lip mucosa direct contacts the allergen.

Etiopathogenesis. Contact allergic cheilitis is a clinical manifestation of delayed-type hypersensitivity. Most often it is a reaction to chemicals used in lipstick, toothpaste and other cosmetic products, in particular fluorescent substances and eosin, rhodamine, etc. This disease mostly affects women.

Clinical picture. In clinical terms, contact allergic cheilitis is manifested through severe burning and itching. Usually the process is localized on the red border of the lips, sometimes it extends slightly to the skin of the lips. At the point of contact with the allergen there occurs a rather well-defined erythema and slight peeling. In long-term course of the disease the red border of the lips become dry and has small transverse grooves and cracks.

Diagnosis. Contact allergic cheilitis is diagnosed based on clinical examination findings and, where appropriate, allergy tests.

Differential diagnosis. This disease is differentiated with dry forms of exfoliative cheilitis, actinic and atopic cheilitis.

Treatment. In treatment of allergic contact cheilitis first of all it is necessary to eliminate a causative factor of the disease. If the clinical picture of the disease is mildly expressed, it is possible to prescribe only local treatment – corticosteroid ointments to be applied 5-6 times a day. In more severe cases, desensitizing therapy should be used.

Prognosis is favorable subject to maximum elimination of the allergen.

Actinic cheilitis

Actinic cheilitis *(cheilitis actinica)* is a chronic disease caused by hypersensitivity of the red border of the lips to sunlight.

Etiopathogenesis. the main causes of this cheilitis are delayed reaction to ultraviolet rays, i.e. actinic cheilitis develops in people with sensitization of the red border of the lips to solar radiation. The dry form of actinic cheilitis is considered to be elective precancer.

Classification. There are exudative and xeronous (dry) forms of actinic cheilitis.

Clinical picture. The *exudative form of actinic cheilitis* is often found in individuals with hypersensitivity to sun exposure, so the clinical picture is consistent with evidence of acute allergic contact dermatitis.

In spring the red border of the lower lip *in the xeronous (dry) form of actinic cheilitis* turns bright red, covered with small dry silvery-white scales. The lesion covers the entire surface of the red border. A number of patients develop keratinization areas on the red border; sometimes verrucous mass occur.

Diagnosis. Actinic cheilitis is diagnosed on the basis of medical history and physical examination. If necessary, a smear mark to exclude cellular atypia, and dermal biopsy is recommended.

Differential diagnosis. There is actinic cheilitis with dry forms of exfoliative cheilitis, atopic and meteorological cheilitis. A characteristic diagnostic feature is the process exacerbation under the influence of insolation.

Treatment. First of all, it is necessary to recommend that the patient avoids sun exposure and changes an occupation, if it is associated with prolonged stay in the open air. Hyposensitization drugs, nicotinic acid are prescribed. Topical steroids are used locally inactinic cheilitis.

Prognosis is favorable, however in long-term keratosis is necessary to exclude malignancy.

Symptomatic cheilites

Symptomatic cheilites is a group of cheilites, which are one of the main clinical manifestations of the underlying disease. There are atopic cheilitis, eczematous cheilitis, plasma cell cheilitis, Miescher's granulomatous macrocheilitis, Meiji's trophoderm, and Rossolimo-Melkersson-Rosenthal's syndrome.

Atopic cheilitis *(cheilitis atopica)* is one of the symptoms of atopic dermatitis, which is often the only manifestation of this disease at its certain stages.

Etiopathogenesis. Atopic cheilitis is a genetically caused disease accompanied by disorders of the central and autonomic nervous system. It is more common in girls and boys aged 4 to 17 years old.

Clinical picture. In clinical terms, atopic cheilitis affects the red border of the lips and always the skin, and the process is more intensive in the corner of the mouth. The part of the red border, adjacent to the oral mucosa and the oral mucosa remain unaffected.

The disease manifests itself through itching, erythema and lip lichenification.

Diagnosis and differential diagnosis. In exfoliative cheilitis, unlike atopic, a part of the vermilion border is always affected in the form of a strip from the Klein's line to the middle of the red border; a part of the vermilion border adjacent to the skin is intact; the process never affects the skin of the lips and does not cover the corners of the mouth; there is no erythema and lip lichenification; the course of the disease characterized by monotony and lack of remission. Past history of patients with actinic cheilitis shows a clear dependence of exacerbations on insolation; there is no frank lesion of the mouth corners characteristic of atopic cheilitis. In allergic contact cheilitis lichenification is only observed during prolonged course of the disease; there are no sores at the corners of the mouth; the course depends on direct contact with the allergen. In some cases, differential diagnosis of atopic cheilitis with symmetrical streptococcal or candida bridoes can be quite difficult. In bridoes, localization of the lesion is limited only to the mouth corners; as a rule, lichenification is not observed.

Treatment. Treatment includes prescription of antihistamines and sedatives, vitamins.

Eczematous cheilitis *(cheilitis eczematosa).* All types of eczematous cheilitis are grouped together according to similarity of clinical manifestations, but they occur for different reasons. There are eczematous cheilites:

1) caused by seborrheic eczema;

2) microbial eczematous cheilitis;



Fig. 16.5. Cheilitis of eczematous cheilitis.



Fig. 16.6. Macrocheilitis (Rossolimo-Melkersson-Rosenthal's syndrome).

3) contact eczematous cheilitis.

Cheilitis in seborrheic eczema. Cheilitis is one of the symptoms of seborrheic eczema, but only the lips may be affected. In clinical terms, it manifests through hyperemia of the red border of the lips, occurrence of easily separated flakes, bubbles. Skin of the lips and the red border is dry, cracks and flakes appear.

Microbial eczematous cheilitis cheilitis. Re-develops against seborrheic eczema due pyococcal infection (mainly streptococcal) at the site of formation. Clinical manifestations correspond to microbial eczema.

Contact eczematous cheilitis cheilitis. Develops due to an allergic reaction to a variety of chemicals (in the lipstick, toothpaste, etc.). The clinical picture is consistent with acute or chronic eczema and is quite varied: swelling of the lips, bright hyperemia, blisters with subsequent formation of crusts. Elimination of allergen leads to rapid resolution of cheilitis.

Treatment. In eczematous cheilitis treatment is similar to that of eczema. Topical steroids and antibiotics are used.

Macrocheilitis *(macrocheiliti).* This is the name for Rossolimo-Melkersson-Rosenthal's syndrome Meiji's trophoderm, Miescher's granulomatous macrocheilitis, characterized by persistent lip swelling. At this time it is known that granulomatous Miescher's cheilitis is not an independent nosological form of the disease and is a variant of Rossolimo-Melkersson-Rosenthal's syndrome with development of granulomatous infiltrate in the affected tissue. Meiji's trophoderm refers to angiotrophoneurosis. Rossolimo-Melkersson-Rosenthal's syndrome combines a triad of symptoms: macrocheilia (persistent increase in the lip), neuritis of the facial nerve, folded tongue, and a chronic disease with a tendency to recur. The disease occurs both in men and in women at any age, but most often between 16 and 35 years old.

Etiopathogenesis. The causes of Rossolimo-Melkersson-Rosenthal's syndrome are not fully clear. Neurological manifestations of Rossolimo-Melkersson-Rosenthal's syndrome often may include neuritis or facial nerve paresis and paralysis of the facial muscles.

Clinical picture. The onset of the disease is sudden. During few hours the lips get swollen. Swelling lasts 3-6 days, seldom less, sometimes longer, even up to a month. At the same time there is swelling of the mucous membranes of the oral cavity. Examination reveals deformation of the lips, the increase in their volume. The lip is dense at palpation. The mucous membrane of the mouth may be edematous, its surface becomes uneven, with a white cushion along the line of the teeth compression. There develops quite clear coarsening of the mucosa, various degrees of folding and lobulation of the tongue.

The course of Rossolimo-Melkersson-Rosenthal's syndrome is chronic. At the onset of the disease relapses are usually replaced by more or less prolonged remissions, during which all symptoms of the disease resolve. Later, macrocheilia and paralysis of the facial nerve become stable.

Diagnosis. Some patients with Rossolimo-Melkersson-Rosenthal's syndrome may lack both the folding of the tongue and paralysis of the facial nerve. The only symptom of the disease in this case is macrocheilitis.

The impairment of the facial nerve manifests through the face distortion to the healthy side, smoothing of the nasolabial fold. There are signs of the cranial nerve impairment (trigeminal, auditory, etc.).

Along with a thorough dental examination of the patient, identification of odontogenic, tonsillogenic and other sites of infection it is necessary to determine sensitivity to bacterial allergens with leukolysis reaction, as well as the neurological status.

Differential diagnosis. It is performed with angioedema, lymphangioma, hemangioma, collateral edema of the lips in periostitis of the upper or lower jaw.

Treatment. Treatment of Rossolimo-Melkersson-Rosenthal's syndrome is performed in two directions: surgical and conservative. In surgical treatment, which is performed for cosmetic purposes, a part of lip tissue is excised. However, surgical treatment does not prevent recurrences of the disease. Conservative treatment includes corticosteroids, broad-spectrum antibiotics and synthetic anti-malarial drugs.

1. What is the predominant localization of lesions in cheilites:

A. Corners of the mouth
B. Lip mucosa
C. Klein's zone only
D. All surface of the red border of the lips
E. All of the above

2. The group of independent cheilites comprises:

A. Meteorological
B. Exfoliative
C. Glandular
D. Actinic
E. All of the above

3. There are the following types of symptomatic cheilites:

A. Atopic cheilitis
B. Macrocheilitis
C. Meiji's trophoderm
D. Rossolimo-Melkersson-Rosenthal's syndrome
E. All of the above

4. Exfoliative cheilitis has two forms:

A. Dry and exudative
B. Seborrheal and genuine
C. Verrucous and intertrigo
D. Vegetative and pustular
E. None of the above

5. The following is observed in the serous form of glandular cheilitis:

A. Bloody dew symptom
B. Dew symptom
C. Apple jelly symptom
D. Stearic spot symptom
E. Probe symptom

6. Actinic cheilitis is a chronic disease caused by:

A. Hyperplasia, hyperactivity and often heterotypia of salivary glands around the red border of the lips
B. Effect of various meteorological factors on the red border of the lips
C. Solar hypersensitivity the red border of the lips
D. Sensitization of the red border of the lips to chemicals
E. Clinical manifestations of the underlying disease

7. There are the following types of eczematous cheilitis:

A. Caused by seborrheic eczema
B. Caused by microbial eczema
C. Contact eczematous cheilitis
D. None of the above
E. All of the above

8. Rossolimo-Melkersson-Rosenthal's syndrome unites a triad of symptom:

A. Macrocheilia, face angioneurosis, hoarse voice
B. Macrocheilia, sinusitis, vestibulitis
C. Macrocheilia, mitral insufficiency, optic neuritis
D. Macrocheilia, facial nerve neuritis, folded tongue
E. None of the above

9. Differential diagnosis of Rossolimo-Melkersson-Rosenthal's syndrome is performed with:

A. Quincke's edema
B. Lymphangioma
C. Hemangioma
D. Collateral edema of lips in periostitis of the upper or lower jaw
E. All of the above

Task 1. A 46 year-old patient complains of dryness, itching, peeling of the red border of the lips. The disease occurs in cold windy weather.

a) Set a provisional diagnosis:
- **A**. Atopic cheilitis
- **B**. Meteorological cheilitis
- **C**. Glandular cheilitis
- **D**. Actinic cheilitis
- **E**. Exfoliative cheilitis

b) Specify preventive measures and prognosis.

Task 2. A 34-year-old woman contacted a dermatologist complaining of oral mucosa lesions. According to past history, symptoms in the form oferythema of the red border, minor swelling, peeling, itching repeatedly occurred in this patient after using certain types of lipsticks.

a) Which is the most probable diagnosis:
- **A**. Contact allergic dermatitis
- **B**. Common contact dermatitis
- **C**. genuine lip eczema
- **D**. Contact allergic cheilitis
- **E**. Actinic cheilitis

b) Determine a treatment tactics.

Task 3. A 32-year-old woman contacted a dermatologist complaining of spontaneous increase of the red border, painful sensations in that area. *Objectively*: lip swelling and congestive hyperemia. Clearly visualized enlarged ducts of the salivary glands excreting transparent viscous secret in the form of droplets (dew symptom). Around the ducts entries there is inflammatory infiltration.

a) Which disease can be assumed:
- **A**. Urticaria fever
- **B**. Contact allergic cheilitis
- **C**. Serous glandular cheilitis
- **D**. Common contact dermatitis
- **E**. Purulent glandular cheilitis

b) Perform differential diagnosis of this disease.

Task 4. A 16-year-old contacted a dermatologist complaining of rash on the lip mucosa, surrounding skin and sensation of dryness and tightness in these areas. *Clinically*: the red border of the lips and the surrounding skin are hyperemic, with cracks and easily detaching scales on the surface.

a) What is the possible provisional diagnosis:
- **A**. Cheilitis caused by seborrheic eczema
- **B**. Cheilitis caused by microbial eczema
- **C**. Contact eczematous cheilitis cheilitis
- **D**. Rossolimo-Melkersson-Rosenthal's syndrome
- **E**. None of the above

b) Specify therapeutic and preventive recommendations.

Task 5. A woman contacted a dermatologist complaining of deformation of the upper lip, increase in its volume and itching. According to past history, the disease onset was sudden. The upper lip got swollen within a few hours. *Objectively*: there is amorphous swelling of the upper lip, its edge is twisted in the form of a proboscis and it detached from the teeth. The upper lip is bluish, dense at palpation. Swelling of the oral mucous membranes is observed.

a) Set a provisional diagnosis:
- **A**. Atopic cheilitis
- **B**. Macrocheilitis
- **C**. Purulent glandular cheilitis
- **D**. Rossolimo-Melkersson-Rosenthal's syndrome
- **E**. Urticaria fever

b) What is the necessary pre-hospitalization assistance?

Answers to the questions of the first level of complexity
1 – **E**; 2 – **E**; 3 – **E**; 4 – **A**; 5 – **B**; 6 – **C**; 7– **E**; 8 – **D**; 9 – **E**
Answers to the questions of the second and third levels of complexity
1a – **B**; 2a – **D**; 3a – **C**; 4a – **A**; 5a – **B**

17 TOPIC

Erythema multiforme

TRAINING AND EDUCATIONAL GOALS

- Publicize modern representations of erythema multiforme aetiopathogenesis
- Determine factors influenced on course of erythema multiforme
- Separate particularities of clinical progression of disease
- Determine general principles of differential diagnostics, curing and preventive treatment of erythema multiforme

TO KNOW:

- ethiopathogenetic particularities of rosacea and its pathomorphology;
- particularities of classification and clinical implications of these diseases;
- principles of diagnostics and differential diagnostics
- principles of curing and preventive measures.

TO BE ABLE TO:

- interview the patient with erythema multiforme correctly;
- represent the diagnosis on the basis of clinical presentation;
- carry out the diagnostic tests for confirmation the diagnosis, if necessary;
- carry out the differential diagnostics with diseases having similar clinical presentation;
- assign a curing.

Erythema multiforme

Erythema multiforme *(Erythema exsudativum multiforme)* – disease of skin based on damage of dermis vesicles, abruptly progressed and characterized by polymorphism of rash, cyclic anticipated course in form of strongly expressed target-typed exanthema with specific badge-typed papules, often damage of oral mucosa and genital organs in form of bulla and painful anabrosis. Disease has a tendency for self-resolving. Systematic damage occurs rarely.

Causation of erythema multiforme is pluricasual. The most possible is virus causation. The promoting agents could be a medicamental allergy, gastrointestinal disorders, endocrine and visceral diseases.

Pathogenic mechanism. The pathogenic mechanism of disease is not studied but in general it is deemed that erythema multiforme is a syndrome of hypersensitivity.

Discovering of antigens of catarrhal fever's virus and DNA in skin locus of some patients with erythema multiforme supports the theory of a fact that pathogenic mechanism could be a cellular immune response directed to destroying of keratinocytes which serves for expression of catarrhal fever's virus antigens.

Classification. There are two main forms of erythema multiforme - idiopathic and toxicoallergic.

Idiopathic form of erythema multiforme has infectoallergic genesis. Most cases provoked by virus of catarrhal fever. The erythema multiforme is also associated with contact irritants (dinitrochlorbenzene, poison ivy, tropic sorts of wood) as well as systematic diseases (autoimmune progesterone dermatosis, sarcoidosis, polyarteritis nodosa, Wegner's granulomatosis, lymphadenoma, cancer and leukaemia).

Toxicoallergic form of erythema multiforme has allergic genesis. Disease concerned with progression of immune-complex response for different antibiotics, sulfanilamides, barbiturates, serosities and vaccines on area of dermis upper seam vesicles. For the long time toxicoallergic form of erythema multiforme and Stevens-Johnson's syndrome were considered as one disease. Recently the tendency have appeared according to which the heavy and light form are considered to be a parts of spectrum of the same disease (as a rule, resulting of virus infections) while the Stevens-Johnson's syndrome and toxic epidermal necrolysis are considered as separate nosological entities, connected mostly with medicamental hypersensitivity.

Clinical findings. The disease mostly occurs resulting in suffered acute respiratory viral infections. Before appearance of rashes the general weakness and painful joints could be observed.

For erythema multiforme the typical is polymorphism of rashes. Most often rashes localized on extensor surfaces of forearms, anticnemions, hips, back side of hands. The palms and feet are also affected as well as oral mucosa, and skin of genital organs. Rash is characterized by appearance of bright-pink edematous maculas and exudative

papules of up to 20 mm and more in size having red with cyanochroic tone color. Papules are surrounded by cyanosed scyphus, have a tendency for peripheral growth, fallen in center. At first papules arranged in focus but resulting in peripheral growth they interlocked between each other. The vesicles and bulla could appear in center of papules. They resolved with formation of anabrosis or crust. So, for erythema multiforme the target-typed rashes are typical each of which has not less than three different areas:

- *central disk of dark erythema or purpura* which could become necrotic or transform into solid vesicle;
- *ring of pale edematous area* which is felt;
- *outer ring of erythema*.

Rashes are accompanied by heat esthesia, rarely weak pruritus. Disease continues for 3-4 weeks after which the remission occurs with often backsets (up to 4-5 times per year).

The Stevens-Johnson's syndrome is a heavy form of erythema multiforme. The disease begins spontaneously with rapid high raising of body's temperature, the rushes have bullous nature. Most often the oral mucosa coats, soft and hard palate, genital organs, conjunctive and cornea of the eyes are affected. The men gets the progression of urethritis, and women gets the progression of vulvovaginitis and the erythematous, papular and bulla rashes are appear on the skin of face, body and extremities. Resulting in bulla evolution the solid bleeding anabrosis and necrotic ulcers embarrasses the meal are left. The general weakness and intoxication appear. The disease often ends mortally.

Pathomorphological mechanism. Histologically the epidermis hydrops is observed and especially of all layers of dermis. The perivascular infiltration from neutrophils, lymphocytes, histiocytes and small amount of eosinocytes progresses in



Fig. 17.1. Erythema multiforme.



Fig. 17.2. Erythema multiforme.

papillary and reticular dermis, the swelling of vesicles walls and their endothelium occur, the picrinofilty of separate collagen fibers appears. In central part of locus the rapid necrobiosis of elastic fibers and small bleedings occur, and the spongiosis in epidermis.



Fig. 17.3. Erythema multiforme.

Diagnostics. Determination of diagnosis for erythema multiforme is based on the following data:

- *clinical examination* (clinical presentation of erythema multiforme on skin is characterized by polymorphism of rash, presence of rash in form of badges, typical location on distal areas of extremities);
- *laboratory examination* (complete blood cell count – deviations occur rarely, decreasing of ESR and intermediate leukocytosis is observed at heavy form of disease);
- *instrumental examination* (inadvisable because of low informational content).

Differential diagnostics. In contradistinction from erythema multiforme at:

- *urticarial vasculitis* there are no target-typed locus;
- *medicamental rashes* there are no target-typed locus, the rashes are generalized;
- *Duhring disease* the pruritus, heat, herpetiform polymorphism of rash (papules – bulla), positive test with potassium iodide, eosinophilia, and typical pathognomia are observed;
- *acantholytic pemphigus* there are monomorphic rash of bubbles observed of different size and any location, progressive course, positive Nikolsky's sign, presence of Tsank cells in impression smears;
- *secondary papular lues* – the papular rash of cyanochroic-red color and dense consistence with furfur in central part of papule and formation of peripheral Biett's collar, general impressions are absent, serological responses on lues are positive;
- *erythema annulare* there are more individual locus of different location, long-term course, absence of locus on mucosa coats typical;
- *Kawasaki's disease* there are such signs appear as red lips, strawberry tongue, water retention of palms and lymphadenopathy;
- *herpetic gingivostomatitis* there are no locus of skin affections.

Curing. In most cases especially at light form of erythema multiforme the disease resolved independently and requires for symptomatic measures only for relief of pruritus and weakness. For curing of erythema multiforme at first instance the salicylates (salicylic natrium, pyramidon or anodynine), sulfanilamide drugs (sulfadimine, norsulfazole up to 2-4 g per day) antibiotics (erythromycin by 0.3 g 4-5 times per day and others) are assigned. There are antihistaminic medicaments assigned (cetirizine, citrine Suprastin and others), large doses of cevitamic acid (not less than 1.5-2 g per day), folic acid (by 0.03 g three times per day).

At Stevens-Johnson's symptom the corticosteroid therapy is assigned (prednisolone by 45-60 mg daily) with gradual lowering to the maintenance doses.

The symptomatic therapy is used locally (neutral dusts, magmas, pastes) for protection of affected areas from secondary infection. After paracentesis of bulla, anabrosis on skin and mucosa coats the solutions of antiseptics are drawn. AT absence of exudation it is possible to assign corticosteroid unctures or

At curing of lesions on mucosa coats the care is extremely important thing. The care of oral cavity is carried out with implementation of antiseptic solutions (chlorhexidine, 3% of hydrogen dioxide) and local corticosteroid medical agents.

Long-term systematic use of acyclovir or valacyclovir is indicated at backsets of erythema multiforme concerned with herpes.

Preventive measures and prognostication. In case of affection of oral cavity the diet is indicated with exclusion of spicy food, the food in liquid form only is desirable. The sanitation of body, discovering of focal infection's locus, especially in maxillofacial area, and cold water treatment are indicated. The elimination of provoking factors is necessary (herpetic and mycotic infection).

The prognosis of disease is favorable as a rule.

1. Determine right name of pathogenetic theory for erythema multiforme:

A. Infection-allergic
B. Toxic
C. Metabolic
D. Genetic
E. Neurogenic

2. Call clinical forms of erythema multiforme depending on its pathogenetic mechanism:

A. Localized and generalized
B. Symptomatic and true
C. Idiopathic and toxicoallergic
D. Erythematosus and bullous
E. Erythematosus and pustular

3. What primary components are not encountered at erythema multiforme:

A. Papule
B. Macule
C. Bulla
D. Tubercle
E. All of above mentioned is correct

4. Call heavy form of erythema multiforme:

A. Layel's syndrome
B. Stevens-Johnson's syndrome
C. Kazabach-Merrit's syndrome
D. Martorella's syndrome
E. Gujero-Blume's syndrome

Task 1. The female patient refers to the dermatologist with complains for rashes on skin of lower extremities which appeared after intake of sulfanilamide medications. *Unbiased*: the rashes located on extensor surfaces of anticnemions and hips in form of bright-pink edematous spots and papules of up to 3 cm in size. Papules surrounded by cyanochroic nimbus, have a tendency for peripheral growth and felt in center. In some places papules interlocked between each other forming rings on the background of red-cyanochroic erythema.

a) Determine the provisional diagnosis:
- **A.** Annular centrifugal Daria's erythema
- **B.** erythema multiforme
- **C.** Nodular erythema
- **D.** Fixed erythema
- **E.** Erythema migrans

b) Give therapeutic and prevention recommendations.

Task 2. The male patient of 45 years old went to institutional treatment in dermatological department. He complains for suddenly rapid rise of body's temperature accompanied by pain in joints, throat, headaches, occurrence of rash. *Unbiased*: There are anabrosis covered by bleeding crusts on the oral mucosa, extremities, and conjunctiva and in area of genital organs on the background of slightly infiltrated erythema.

a) Determine the provisional diagnosis:
- **A.** Stevens-Johnson's syndrome
- **B.** Layel's syndrome
- **C.** Kazabach-Merrit's syndrome
- **D.** Martorella's syndrome
- **E.** Gujero-Blume's syndrome

b) Make a plan for examination and curing of the patient.

Answers for first level self-control questions
1 – A; 2 – C; 3 – D; 4 – B
Answers for second and third level self-control questions
1a – B; 2a – A

18 TOPIC

Systemic diseases of connective tissue – collagenoses

Collagenoses (diffuse diseases of connective tissue) are characterized by mucoid and fibrinoid degeneration of connective tissue, often damage of joints, serous coats, skin, internal organs, and nervous system. The basis of mechanism of progression of collagen diseases is mostly autoimmune process with affection of different morphofunctional systems. The most often in practice of dermatologist the scleroderma, lupus erythematosus and acute disseminated myositis are encountered regarding to collagenoses group.

TRAINING AND EDUCATIONAL GOALS

- Determine possible conditions and trigger factors of occurrence of scleroderma, lupus erythematosus and acute disseminated myositis
- Learn the classification and particularities of different forms of scleroderma, lupus erythematosus and acute disseminated myositis
- Determine general course and clinical implications of causation of mentioned diseases' different forms.
- Determine typical evidences of scleroderma, lupus erythematosus and acute disseminated myositis
- Determine principles of therapy of scleroderma, lupus erythematosus and acute disseminated myositis

18.1 Scleroderma

Scleroderma *(Sclerodermia)* – idiopathic disease characterized by sclerotic affection of skin of locus or diffuse nature with foregoing occurrence of fibrosis.

TO KNOW:

- modern conceptions of aetiopathogenesis of scleroderma;
- factors precipitating the progression of this disease;
- classification of scleroderma;
- pathomorphological changes in skin at scleroderma;
- clinical profile of different forms of this disease;
- its laboratory diagnostic criteria;
- principles and approaches of curing measures and periodic health examination at scleroderma.

TO BE ABLE TO:

- interview and make a diagnosis for the patient with scleroderma correctly;
- carry out the differential diagnostics with dermatosis having similar clinical presentation;
- assign corresponding laboratory examinations for confirmation of diagnosis;
- assign balanced curing for the patient with scleroderma.

Aetiopathogenesis. The causation and pathogenetic mechanism of scleroderma are studied not enough. It's progression could be concerned with suffered inflectional diseases as well as after introduction of serosities, vaccines, medicamental drugs, after physical and psychical trauma or burns.

Scleroderma belongs to multifactor diseases with polygenetic inheritance. The significant role in its progression the immune (including autoimmune) and metabolic disorders are play. Major pathophysiological processes are in three systems – vascular, immune and fibroblasts.

Classification. There are following types of scleroderma:

1. Isolated scleroderma (not more than two lesion focuses observed):
   - Circumscribed;
   - linear;
   - white-spot disease;
   - morphea;
   - Pazzini-Pierini's idiopathic atrophoderma (superficial isolated scleroderma).
2. Diffuse progressive or systematic scleroderma.

Clinical findings. Isolated and systemic scleroderma is the types of one pathological process. Isolated scleroderma could transform into systemic. There are three stages of general course of sclerotic pathological process – *swelling, induration and atrophy*.

Isolated scleroderma (*Sclerodermia circumscripta*). There are morphea guttata, linear, white-spot disease and morphea forms of isolated scleroderma by clinical course.

Morphea guttata is evidenced by pink-red spots of rounded shape with lilac peripheral collar. Then in area of spot the induration progresses which could be superficial or penetrates deeply in dermis. In area of locus skin has primrose painting reminding the

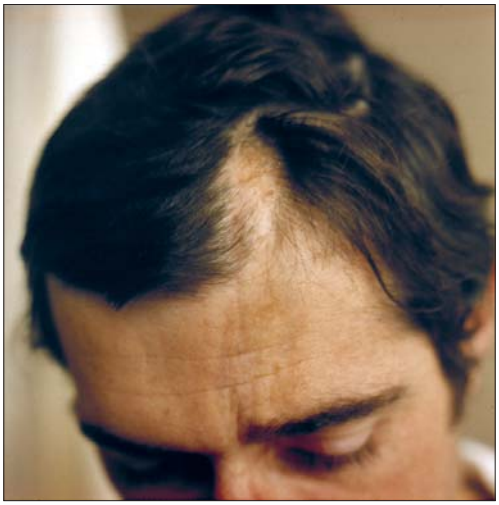


Fig. 18.1. Morphea guttata.



Fig. 18.2. Morphea guttata.

color of ivory. There is no hair on skin, no hidrosis and sebaceous excretions, the sensitivity is weak. There are light paresthesias observed. Process located on the body, extremities, and face. Further evolution of scleroderma locus is in disappearance of lilac ring, gradual resorption of induration and appearance of atrophy.

Linear scleroderma or scleroderma striata (sclerodermia linearis) is an original form of localized scleroderma which often occurs in children age. The affection is usually begins on hairy part of head then goes to sin of metope, dorslim of nose reminding the cicatricial tissue after strike by sabre (*un coup de sabre*). The lesion focuses at linear scleroderma are located on upper or more often on lower extremities. The patients with linear scleroderma are noticed the progression of atrophy and disorder of extremities bones growth, presence of *spina bifida*, and micro sclerosis. The lesion focuses at linear scleroderma could be also located along the vesicles, nerves, transfer from skin to the mucosa coat.

The course of linear scleroderma is the same as morphea guttata.

White-spot disease (sclerodermia guttata) more often located on skin of neck, sternum and alvus. This disease is usually typical for women. The glance depigment atrophic spots of pea size appear at this disease around the hair follicles with tendency for interlocking and with erythematous peripheral collar.

In rare cases the *morphea* is observed (*sclerodermia anularis*)

Pazzini-Pierini's idiopathic atrophoderma (superficial isolated scleroderma) is evidenced by slightly pigmented cyanotic rashes of round and oval shape on body, arms, hips with weak atrophy.

Localized variant is associated with CREST-syndrome called by first letters of containing symptoms (*calcinosis, Rayneud's disease, esophageal dysmotility, sclerodactyly, teleangiectasia*).

Systemic or diffuse scleroderma (*sclerodermia diffusa progressiva*). Systemic scleroderma is a systemic disease which is evidenced by affection of connective tissue and vesicles of degenerative-necrotic nature. There are prodromes observed in form of general weakness, pain in joints, and fever.



Fig. 18.3. Linear scleroderma in area of metope in association with white spot disease.

Systemic scleroderma includes *skin* (sclerodactylia, acrosclerosis, Tnibierge-Weissenbach syndrome) and *non-skin* (muscular-joint, gastrointestinal, pulmonic, cardiovascular, hepatic, and neurological) *syndromes*.

The affection of skin begins from extremities and face (*acrosclerosis*). At diffuse scleroderma the process could spread to the body. There are numerous

telangiectasis appear on skin of face and sternum, the change of ingius and defluxion are observed. In the beginning of disease the skin is diffusion and edematous, cold, not folded. For incipience of systemic scleroderma there are Reynaud's syndrome, arthralgia, polycardia, often infections of respiratory infections typical. Then skin symptomatic progresses with occurrence of induration, especially on opisthenar and dorsum of feet. Face becomes masklike, the telangiectasis appear, areas of hyper and depigmentation.

At final stage the sclerotic process is spread to subcutaneous fat and muscles bearing against bones. The movements become harder, the mimic is absent, the mucosal coats of mouth and esophagus are affected, the oral fissure is narrowed. Fingers of hands becomes thin and are in semiflexed position, its movement is limited (sclerodactylia). These sclerodermia changes can lead to the mutilation on the hands and feet. The skin over joints is hard and tensioned; the movements in joints are hindered. Most of patients are observed the fibrous changes of muscles progressed primary or after scleroderma changes of skin. Some patients with scleroderma, usually at acrosclerosis, the deposit of calcium is evidenced in subcutaneous fat (*Thibierge-Weissenbach's syndrome*), usually on hips, buttock, hands, around the joints. These deposits could burst resulting in occurrence of fistula from which the friable calcareous mass is discharged.

Pathomorphological mechanism. At histological examination in the beginning of progression of morphea process the swelling of derma is being discovered, the infiltrate consisting of lymphocytes is between fascicles of collagen fibers. The elastic tissue is dead in these locations. Infiltrate could appear also in subcutaneous fat. The thinning of spinous layer and vacuolization of cells of basal layer occurs in epidermis. During induration stage the sclerosis of collagen fibers, luminal occlusion, lymphoid infiltrate absence of hair, atrophy of oil and sudoriferous glands, sclerosis of hypoderm, thinning of epidermis and intumescence of horny layer are observed.

Diagnostics. Preventive diagnosis is hard to determine. Antinuclear antibodies are found in 97% of cases with implementation of HEp 2 cells as a substrate. Antibodies for centromeres are found in 50-70% of cases of isolated disease (CREST-syndrome), antibodies for antitopoisomerase (ScI-70) found approximately in 36% of cases at diffuse form of disease. Levels of Я-halactosidase and N-terminal procollagen III peptide is raised and it is a sign of enhancement of collagen's metabolism because of activation of fibroblasts.

Pathomorphological presentation at systemic scleroderma is mostly the same as for localized but fibrosis-degenerative changes in collagen fibers and vesicles are expressed more fully.

At diffuse scleroderma the inner organs are often affected – esophagus, lungs, heart, rarely kidney, gastrointestinal tract, bones, and often several organs at the same time. Sometimes the diseases of inner organs are progress without changes on skin. At damages of esophagus the fibrotic changes of muscle tissue, exulcerations and diverticula appear. In lungs the signs of pulmonary fibrosis are discovered radiologically.

At affection of cardiovascular system the intumescence of myocardium, endocardium and intima of aorta are observed and the fibrinoid degeneration of intima in vesicles.

At acrosclerosis the atrophy of finger bones and osteoporosis could progress. At kidney's affection the sclerodermic nephropathy is observed evidenced in form of oliguria, azotemia, uremia and being ended fatally. At histological examination the fibrinoid degeneration of arteriols, glomerulus and bleedings in cortical substance are discovered.

At diffuse scleroderma ambilateral cataract could appear which occurs in young age and sometimes before skin affections. The dry keratocnjunctivitis could progress. The telangiectasis and angioma could occur on nasal mucosa which is accompanied by nasal bleedings.

Differential diagnostics. The *localized scleroderma* should be differed from white spot disease, indeterminate leprosy, pseudoleukoderma, facial hemiatrophy, morphea-like basalioma, kraurosis vulvae, and lymphangioma.

At indeterminate leprosy the changes on skin are characterized by spotty rushes of different tone (from pink to cyanochroic). In area of spots the pain, tactile and temperature sensitivity is decreased.

Pseudoleukoderma appears of patients on place of previous locus of chromophytosis and psoriasis as well as of persons influenced to excessive solar or ultraviolet irradiation. These spots have no induration and disappear after weakening of san-tan.

It is harder to differentiate the linear scleroderma with linearly oriented keloid-typed nevus. It's typical signs could be a manifestation in first months of life and long-lasting existence of nevus without expressed changes during many years.

Diffuse scleroderma is differentiated with Raynaud's disease, acute disseminated myositis, pseudo scleroderma, Bushke's scleroderma, Arndt-Jaffe scleropoikidermia, sclerema and newborn's scleroderma, and systemic lupus erythematosus.

Curing. There is no efficient curing of scleroderma. In certain cases the prednisolone and methotrexate is advised systematically.

Preventive measures. The primary preventive measures of localized scleroderma are in sanitation of locus of chronic infection and timely curing of neuroendocrine diseases.

During secondary prevention it is necessary to remember that patients with scleroderma are counter-indicative for working in cold premises, as well as at work connected with damaging of skin and vibration.

Dermatologist examines persons with circumscribed scleroderma twice per year. Laboratory examinations (clinical and biochemical analysis of blood and urine) are carried our one or two times per year, the radiology of lungs and esophagus is carried out yearly. The duration of observance is three years if there are no backsets.

Prognosis. Course of progressive systematic sclerosis is changeable and unpredictable. The result of disease depends on damage of kidney (uremia, accelerated hypertension), heart and lungs (pulmonary fibrosis, pneumonia).

18.2 Lupus erythematosus

Lupus erythematosus is a disease characterized by fibrinoid degeneration of connective tissue with incompletely known causation and complicated pathogenetic mechanism which include participation of immune, genetic, metabolic neuroendocrine and outer causes.

TO KNOW:

- modern conceptions of aetiopathogenesis of lupus erythematosus;
- factors precipitating the progression of this disease;
- classification of lupus erythematosus;
- pathomorphological changes in skin at lupus erythematosus;
- clinical profile of different forms of this disease;
- its laboratory diagnostic criteria;
- principles and approaches of curing measures and periodic health examination at this disease.

TO BE ABLE TO:

- interview and make a full diagnosis correctly;
- carry out the differential diagnostics with diseases having similar clinical presentation;
- assign corresponding laboratory examinations for confirmation of diagnosis;
- assign balanced curing for the patient with lupus erythematosus; determine the preventive measures.

Aetiopathogenesis. The leading theory of progression of lupus erythematosus for the now is an autoimmune theory. Precipitating factors could be different B-cellular activators including infections; As a result the range of antibodies is produced against cellular antigens like DNA, RNA and RNA-protein complexes. Resulting in influence of antibodies on cells' nucleus (leukocytes) the patient gets the LE-cells. The appearance of LE-phenomena in peripheral blood and bone marrow (some nucleophagocytosis) is conditioned by unique «antinuclear factor". LE-factor is an immunoglobulin G which is antibody for nucleoprotein.

The progression of mucoid degeneration is typical and expressed depolymerization of main substance of connective tissue with following deposit of fibrinoid in affected tissues. Interaction of antibodies with antigens of connective tissue leads to liberation of mucopolysaccharides and glucoproteins (haptens). On newly formed antigens the immune competent lymphocytes produce corresponding antibodies. The patients with lupus erythematosus are discovered the malfunction of genital and other endocrine glands as well as disorder of protein, carbohydrate and adipose metabolism and others. The presence of acroasphyxia, Reynaud's disease, and perniosis leads to progression of lupus erythematosus on affected areas of skin.

Epidemiology. The incidence of lupus erythematosus is 0.25-1% among all dermatological diseases. This disease appears mostly of persons from 20 to 40 years old. The disease is widespread in countries with wet cold sea climate. Despite of good isolation the lupus erythematosus occurs rarely in tropical countries which is possible to be connected with more expressed protection of pigmented (dark) skin from influence of solar beams. Women suffers more often than men.

Classification. There are following types of lupus erythematosus:

1. Chronic lupus erythematosus
   - Discoides;
   - Disseminatus;
   - Erythema centrifugum Biett
   - Kaposi-Irgang's heavy form
2. Lupus erythematodes systemicus
   - Acute;
   - Subacute.

Clinical findings. The clinical performance of lupus erythematosus depends on form of disease.

Lupus erythematosus discoides. At lupus erythematosus discoides the process begins from occurrence (on the face as usual) of pink-red edematous spot which is sclerosed and covered by fine greyish crusts closely fitted to openings of hair follicles. On the bottom surface of crust at its removal the fine acicula are visible – these are corneal plugs tightly entered into the openings of hair follicles. At attempting of their removal the patient feels pain (Besnier's symptom). After removal of crusts the surface

of locus reminds lemon peel. Square of locus increases, the new similar locuses appear. The infiltration, keratosis, hyperemia, and swelling are intensified on the periphery of locus. There is an ulerythema gradually appears in center, the skin is thinned and easily folded. The major typical signs of lupus erythematosus discoides are erythema, infiltration, hyperkeratosis, and atrophy. In addition to this, the teleangiectasia and hyperpigmentation could be observed.

The size of locuses of lupus erythematosus (diameter from 0.5 to 5 cm and more) and quantity varies from one to a number. The typical location is nose and cheeks. The locuses of lupus erythematosus discoides are gradually spreads by periphery and have a form of butterfly which back is on the nose and wings are on the cheeks.

Subjective feelings are expressed in weak pruritus and tingling. There are weakly expressed general evidences could be observed such as anemia, increasing of ESR, decreasing of quantity of albumins and increasing of content of globulins, especially of gamma-globulins, appearance of S-reactive protein and cryoglobulins. The patients with lupus erythematosus discoides and lupus erythematosus disseminatus the dystrophic changes of connective tissues are discovered not only in lesion focuses but also on an externally healthy skin.

Lupus erythematosus disseminatus. Lupus erythematosus disseminatus is evidenced by numerous dispersed lesion focuses on the skin of face, sternum, hands, feet and other areas. This form occurs of 12.5-22% of patients with lupus erythematosus.

The locuses of lupus erythematosus disseminatus have erythematous-edematous nature or the form of disks which are typical for lupus erythematosus discoides. The infiltration and hyperkeratosis are nod observed in erythematous-edematous locuses of cyanochroic color. The lupus erythematosus disseminatus could be transformed into discoides or systematic form.



Fig. 18.4. Lupus erythematosus discoides.



Fig. 18.5. Verrucous form of lupus erythematosus discoides complicated by carcinoma.

Erythema centrifugum Biett. By its clinical findings the erythema centrifugum Biett is significantly differs from lupus erythematosus discoides by absence of infiltration, hyperkeratosis and atrophy in the locus.

Erythema centrifugum by course is different than lupus erythematosus discoides as it fast answers the medical treatment but has often backsets because of which it sometimes called migrant. Among patients with lupus erythematosus the patients with erythema centrifugum is 5-11%. ***Lupus erythematodes profundus Kaposi-Irgang.*** At lupus erythematodes profundus Kaposi-Irgang together with typical discoides locuses or independently in subcutaneous fat one or several sclerotic and movable nodular components appears. The color of skin above them at first is not changed but then it gets cyanochroic-red tone, the peeling is not evidenced.

Lupus erythematodes systemicus is a serious general disease which more often occurs of young women. Its course could be acute, subacute and chronic. The disease progresses suddenly or rarely from chronic form of lupus erythematosus discoides or lupus erythematosus disseminatus.

The most typical is an affection of skin of face in form of diffuse edematous erythema with strict borders reminding cellulitis. Erythema could be spread to the neck and upper part of sternum. Erythema and light atrophy often appear on the palms and feet. The nodes often have hemorrhagic painting.

There is also affection of many organs and systems typical for lupus erythematodes systemicus: the pain in joints and muscles, pneumonia, pleurisy, affection of liver, kidney, lien, leukopenia, anemia, trombocytopenia and others are observed.

Diagnostics. During lupus erythematosus diagnostics except data of clinical examination it is important to discover the cells of lupus erythematosus (LE-cells) which are neutrophilous leukocytes containing phagocytosed nucleoids. There are also so called rosettes could be found which are the assemblies of leukocytes around homogenized nucleus of sphacelous leukocytes containing DNA. The leukocytes containing in rosette could phagocytize the homogeneous mass and be transformed into cell of lupus erythematosus. Except LE-cells and rosettes there are Gross's hematoxylin bodies discovered in blood of patient with lupus erythematosus. These bodies are the residues of lysed but still not phagocytized nucleus which together with LE-cells and rosettes are the result of nucleolysis.



Fig. 18.6. Lupus erythematosus disseminatus.

In dry blood of patients suffered from lupus erythematodes systemicus the LE-factor is discovered concerned with function of gamma-globulins of blood plasma which comes into contact with nucleus of leukocytes and causes its destruction. The antibodies for La (SS-B) nucleus antigen coexisted with antibodies for Ro (anti-SS-A) nucleus antigen and usually absent as single antibodies.

Pathomorphological mechanism. The lesion focuses at lupus erythematodes have specific histopathology which is hydropic (vacuolar) degeneration of basal layer of epidermis with locus atrophy of epidermis; sclerotic mononuclear cellular infiltrate in upper layers of dermis, around the appendages of skin and vesicles which runs to the deep layers of dermis; subepidermal deposits of immunoglobulin in locuses (test for presence of lupus strip).

Differential diagnostics. *Lupus erythematosus discoides* and its disseminatus form could be discovered without any problems. At incipience the disease is distinguished with psoriasis, seborrheic dermatitis, Hutchinson's syndrome, pseudopelade, black-dot ringworm, favus, acne erythematosa, and lupus.

It is possible to distinguish the lupus erythematosus from psoriasis on the basis of location of rashes: at lupus erythematosus it is on face and at psoriasis it is on hairy part of head, body and extremities.

The signs on the basis of which the lupus erythematosus could be differed from seborrheic dermatitis are location of seborrheal rashes in skin folds, unclear borders of locuses covered by fat crusts, pruritus, and enhancement of course of process in summer.

At black-dot ringworm and favus the peeling and cicatrization on hairy part of the head could appear in connection with which they remind the lupus erythematosus.

Distinguish the *lupus erythematodes systemicus* from other diseases is harder than its' discoides form, especially at incipience with acute course.

At cellulitis reddening on the face the assumption could appear about presence of sacred fire. However, the hyperemia is not so bright, has bluish tone, and distinguished by torpenty of course at acute lupus erythematodes. It is necessary to distinguish the lupus erythematodes from diffuse scleroderma. At last one usually the serious general eyesores, fever, and numerous affections of inner organs are present.

The rashes at lupus erythematodes systemicus could remind the evidences of acute disseminated myositis, however, at last one they have more congestive nature.

Curing. For curing of lupus erythematodes there are system steroids (prednisolone, dexamethasone), immunosuppressive agents, aromatic retinoids (tigasone), and non-steroidal anti-inflammatory medicamental drugs used. Light-exposed areas of the skin should be protected by sun-screens with high sun protection factor. For curing of lupus erythematodes discoides the fluorinated topical steroids and injections of triamcinolone (intralesional) are used. Light-exposed areas of the skin should be protected by sun-screens with high sun protection factor.

Preventive measures and prognosis. The ultra violet irradiation (exposure to light), UHV-therapy, abuse of some medicamental drugs (antibiotics – penicillin, tetracycline; sulfanilamides; isoniazid, hydralazine, phenothiazine, vaccines) are counter-indicative.

The prognosis of lupus erythematodes discoides regarding to life and working ability is favorable, but its transformation into lupus erythematodes systemicus is possible. The prognosis regarding recuperation is doubtful as disease have tendency to the backsets.

18.3 Dermatomyositis

Dermatomyositis is a serious chronic idiopathic inflammatory myopathy characterized by bilateral affection of proximal muscles and typical locuses on skin.

TO KNOW:

- modern conceptions of aetiopathogenesis of dermatomyositis;
- factors precipitating the progression of this disease;
- classification of dermatomyositis (primary, secondary and juvenile);
- pathomorphological changes in skin at this disease;
- clinical profile of primary, secondary and juvenile dermatomyositis;
- its laboratory diagnostic criteria;
- principles and approaches of curing measures and periodic health examination of patients at dermatomyositis.

TO BE ABLE TO:

- interview and make a full diagnosis correctly for patient with dermatomyositis;
- carry out the differential diagnostics with diseases having similar clinical presentation;
- assign corresponding laboratory examinations for confirmation of diagnosis;
- assign balanced curing for the patient with dermatomyositis;
- determine the preventive measures for dermatomyositis.

Aetiopathogenesis. Dermatomyositis is an autoimmune disease of connective tissue with unknown causation. Disease appears often after infection damages of upper air passages, recrudescence of tonsillitis, pharyngitis as well as result of epidemic roseola, influenza, streptococcosis, and rheumatism. The process involves both cellular and antibody-mediated immune responses. Approximately in 15-20% of cases of clinical dermatomyositis of adults and children the specific for myositis Mi-2 antibodies are found. Some patients have the antibodies for (Jo-1) transport RNA-synthetase as immunologic marker. Nonmalignant form of dermatomyositis is associated with Mi-2 antibodies having immunogenic markers DR-7, DRw-53 and DQ-2 while the pseudotrichiniasis associated with other myositis antibodies is characterized by very increased frequency of alleles HLA-DRB1*0301 and DQA1*0501. The deposit of membrane attack complex of complement in intramuscular vesicles and fixed expression of interleukine-1 as well as molecules of cell-cell adhesion-1 and molecules of adhesion of vascular cage-1 in endothelial cell of capillary tubes are possible responsible for damage of vesicles especially expressed at juvenile form of disease. Cellular immune mechanism also plays significant role which is confirmed by presence of activated T-lymphocytes in inflammatory infiltrates.

This pathology is observed rarely, usually in age of from 20 to 50 years. The children of from 1.5 to 15 years old suffer too which is about 20% of patients with dermatomyositis. The women affected more often.

The significant association with malignant swellings is established of patients who are older than 50 years. Such patients should be examined for presence of oncologic pathology.

Classification. There are *primary* (idiopathic), *secondary* (symptomatic, paraneoplastic) and *juvenile* (more often women suffer) dermatomyositis distinguished.

Clinical findings. The disease often begins in acute form. The temperature of body is rising suddenly, the general condition is affected. Typical erythema is around the eyes, on cheeks, palpebrae, extensor surfaces of upper and lower extremities, in area of joints. The erythema is especially typical on superior eyelids and around them in form of eyeglasses. It could goes to the nose and in such cases reminds erythema in form of butterfly at lupus erythematosus. Erythema on the neck and on extremities, in area of face could be accompanied by water retention; it is often located around the joints in area of elbows, knees, ankles, on the body of hands. At spreading the erythema from neck to arms, dorsum and sternum the affection has form of pelerine. Sometimes the lichenoid rashes, bullous components, and hemorogic spots are observed in area of erythema. The bullous components could exulcerate in future. Often on the background of erythema the telangiectasis are appear which causes to more intensive coloration of skin. It is necessary to notice the affection of mostly opened areas of skin exposed to often influence of solar irradiation.

Further according to regress of rashes the peeling appears together with white-ceramic colored spots surrounded by telangiectasis. The pruritus of skin is strong

rarely. At long-lasting course of disease the changes of skin could be observed reminding the changes at poikiloderma in form of depigment or hyper pigment areas, atrophy, and telangiectasis. The changes of skin are earliest and typical sign of dermatomyositis and could be the only symptom for the long time.

Another typical symptom of dermatomyositis is an affection of muscles which is often discovered at beginning of disease. The patients complain for suddenly appeared pains or pains appeared while moving or at examination of muscles by touch. Morbidity rate is extremely expressed at extension of extremities. The affection of muscles of extremities and of rotator cuffs is progressed more often. Sometimes the difficulties occur at swallowing. The changes in muscles are evidenced in its enlargement, water retention and tenderness. At long-lasting course of disease there are contractures and atrophy of muscles progressed.

Many patients with dermatomyositis have a progress of affection of mucosal coats. Diseases of inner organs at dermatomyositis are expressed by malfunction of myocardium, endocardium, and respiratory organs. Last-mentioned is conditioned by affection of intercostal muscles and diaphragm. That's why ventilation of lungs is not sufficient which could cause to pneumonia. More often the affections of gastrointestinal tract are evidenced. Except dysphagia there are disorders of chewing process, abdominal migraine, and enterocolitis observed; almost half of patients have their kidney and lien enlarged, many of them have all lymphatic nodes enlarged.

The significant role plays relatively often evidence of malignant swelling at dermatomyositis, mostly the stomach cancer is observed.

The course of dermatomyositis is acute as usual. Thanking to curing the remissions could occur, sometimes positive, but then the recrudescences occur again with more severe course.

Pathomorphological mechanism. The most changes occur in dermis, where the delayering of collagen fibers discovered as well as their thickening and further sclerosis. In subcutaneous fat the locuses of lymphoid infiltration, fibrous tissue, and sometimes calcium tophus appear.

There are inflammatory and degenerative evidences observed in muscles.

Differential diagnostics. Dermatomyositis at incipience is distinguished with *acute lupus erythematosus*. At further course of dermatomyositis the some semblance with incipience of scleroderma systematics and myxedema could occur.

Usually the crucial significance for diagnostics the results of histological examination of muscles have as well as enzyme multiplied immunoassay.

Curing. If dermatomyositis is associated with neoplastic transformation the removal of mass lesion in most cases leads to improvement of dermatomyositis course and even to recuperation. The main curing is in assigning of oral steroids starting from loading doses (1 mg/kg of body mass for prednisolone) which then titrated to the maintenance ones (10-20 mg per day). Gradually the azathioprine is added as well as cytostatics (azathioprine 3-4 mg/kg, metatrexate, and cyclophosphamide). At remission stage the remedial gymnastics and massage are connected.

Preventive measures and prognosis. There is no primary preventive measures, and secondary provides avoiding of recrudescences. It is not recommended to abuse the antibiotics, sulfanilamides, and hormonal contraceptives. It is also should avoid the frigorism, exposure to light, and use sun-protective measures. The mortality in case of absence of curing is up to 70%, the disability is possible.

1. What of the following dermatosis are not belong to diseases of connective tissue:

A. Epidermophytosis
B. Lupus erythematosus
C. Dermatomyositis
D. Psoriasis
E. Scleroderma

2. There are following types of localized scleroderma:

A. Circumscribed
B. Linear
C. White spot disease
D. Morphea
E. All of mentioned above

3. There are three stages of course of sclerotic pathological process:

A. Induration, lichenification and sclerotherapy
B. Swelling, induration and atrophy
C. Infiltration, exulcerations and cicatrization
D. Erythematous, infiltrative stages and resorption
E. Swelling, erythematous stage and resorption

4. LE-factor is:

A. Immunoglobulin G, which is antibody for cell's cytoplasm
B. Immunoglobulin A, which is antibody for nucleoprotein
C. Immunoglobulin G, which is antibody for RNA
D. Immunoglobulin G, which is antibody for nucleoprotein
E. Immunoglobulin M, which is antibody for nucleoprotein

5. What of following forms is not belonging to chronic lupus erythematosus:

A. Bazin's disease
B. Discoides
C. Disseminatus
D. Erythema centrifugum Biett
E. Lupus erythematodes profundus Kaposi-Irgang

6. For clinical symptomatology of lupus erythematosus is not typical:

A. Infiltrated spots
B. Hyperkeratosis follicularis
C. Presence of pruritus
D. Ulerythema
E. Absence of pruritus

7. The following is not a form of lupus erythematosus discoides:

A. Lupus erythematodes gypseus
B. Lupus erythematodes papilomatosus et verrucosus
C. Lupus erythematodes tumidus
D. Lupus erythematodes dissiminatus
E. All answers are incorrect

8. The following is not a typical clinical-diagnostic criterion of dermatomyositis:

A. Affection of skin in form of swelling and erythema in form of "glasses"
B. Myositis, myodania, ceratinuria
C. Damage of digestive tract
D. Hyperkeratosis follicularis
E. Rapid reduction of weight

9. Secondary preventive of dermatomyositis provides avoiding of:

A. Abuse of antibiotics and sulfanilamides
B. Exposure to light
C. Frigorism
D. Hormonal contraceptives
E. All of above mentioned

Task 1. The female patient visit a dermatologist with complains for rash on skin and upper extremities and some numbness. According to the words of patient, pathological process began two months ago from occurrence of pink-red spot of round shape with lilac collar on periphery. Later in the area of spot the superficial induration of ivory color progressed. The patient had no curing. *Unbiased*: the infiltrated locus of primrose color is observed on the skin of arm. It could be taken into fold with hard. There is no hair on skin in area of rushes, no diaphoresis and sebaceous excretions, the sensitivity id weak.

a) What disease such symptoms are most typical for:
- **A**. Circumscribed scleroderma
- **B**. Strumoderma
- **C**. Bazin's disease
- **D**. Elephantiasis graecorum
- **E**. Dermatomyositis

b) What additional examinations should be carried out for determination of final diagnosis?

Task 2. At histological examination the swelling of dermis is discovered, the infiltrate containing of lymphocytes is between fascicle of halogen fibers. The streaming of spinous layer and vacuolization of cells of basal layer are observed in epidermis. The sclerosis of collagen fibers, lymphoid infiltrate, luminal occlusion, and absence of hair, atrophy of oil and perspiratory glands, sclerosis of hypoderm, thinning of epidermis and thickening of corneal layer are discovered.

a) What disease such symptoms are most typical for:
- **A**. Dermatomyositis
- **B**. Lupus erythematosus systemicus
- **C**. Bazin's disease
- **D**. Elephantiasis graecorum
- **E**. Scleroderma

b) Determine the patient surveillance.

Task 3. The female patient visit a dermatologist with complains for presence of rash on the right cheek appeared after excessive exposure to light. It is known from anamnesis that process began from appearance of pink-red infiltrated spot of up to 3 cm in size and covered by tightly fitted fine greyish crusts on skin of face. On the bottom surface of crusts at their removal the fine spinelets are visible. At attempting of removal the crusts the pain is filled. After removal of crusts the surface of locus reminds lemon peel.

a) Determine the provisional diagnosis:
- **A**. Bazin's disease
- **B**. Lupus erythematosus discoides
- **C**. Circumscribed scleroderma
- **D**. Erythema centrifugum Biett
- **E**. Lupus erythematodes profundus Kaposi-Irgang

b) What nosologies this disease is most often distinguished with?

Task 4. The female patient visit a dermatologist with complains for rise of body's temperature, presence of pain in muscles, joints, headache, faintness, and skin rash around the eyes. The disease began in acute form after influenza being suffered. *Unbiased*: the erythema of cyanochroic-red color in form of glasses is observed on skin around the eyes and the telangiectasis on its background which condition the more intensive coloring of the skin.

a) What diagnosis should be though for:
- **A**. Strumoderma
- **B**. Lupus erythematosus
- **C**. Dermatomyositis
- **D**. Bazin's disease
- **E**. Scleroderma

b) Carry out the differential diagnostics.

Answers for first level self-control questions
1 – A; **2** – E; **3** – B; **4** – D; **5** – A; **6** – C; **7** – D; **8** – D; **9** – E
Answers for second and third level self-control questions
1a – A; **2a** – E; **3a** – B; **4a** – C

Genodermatosis – genetic disorders of the skin

19 TOPIC

TRAINING AND EDUCATIONAL GOALS

- Discover the applicability of the problem and make a presentation of major moments of aetiopathogenesis of genodermatosis
- Determine the main groups of genetic pathological processes in skin and cutaneous appendages
- Interpret general course and clinical presentation of different genodermatosis
- Determine clinical findings of typical evidences of bullous genodermatosis
- Learn the diagnostic criteria of ichthyosis
- Determine principles of therapy and prognosis of course of genodermatosis

TO KNOW:

- classification of genodermatosis;
- etiology and pathogenetic mechanism of genodermatosis;
- clinical particularities of modern curing of bullous genodermatosis;
- diagnostic criteria for determination of different forms of ichthyosis;
- principles of curing and preventive measures being implemented regarding patients with genodermatosis.

TO BE ABLE TO:

- interview the patient with genodermatosis;
- analyze the clinical presentation and results of laboratory examinations;
- carry out differential diagnostics with diseases having similar clinical presentation;
- assign balanced curing for the patient with genodermatosis;
- carry out the psychodiagnosis and psychocorrection.

Epidemiology. According to data of WHO, about one third of all genetic diseases are the dermatosis, the genetic nature of which is proven. The crucial role of genetic factor is determined for approximately 200 of skin diseases. In other words, the genetic diseases accounts for 10% of all known dermatosis for the now. The number of genodermatosis is all the time increased year after year because of development of knowledge about reasons and pathogenesis of these diseases of skin.

Pathogenesis. The great majority of genetic diseases of skin are conditioned by drop gene-mutations which are failed to be found.

The basis of modern genetic classifications is a type of transferring of mutant gene in generations and particularities of its allocation in autosomes or in gonosomes. The penetrance (possibility of associated trait of gene depending on influence of environment) and expressivity (degree of manifestation) of gene are also taken into consideration.

The sebaceous adenoma, Hopf's disease, partial albinism, atopic dermatitis, congenital dermal aplasia, Hailey- Hailey disease, Darier's disease, keratoma of palms and feet, neurofibromatosis, porphyria cutanea tarda, ichthyosis vulgaris, psoriasis, Mibelli's disease, simple epidermolysis bullosa and others are passed by autosomal-dominant inheritance.

The dystrophic epidermolysis bullosa, acrodermatitis enteropathica, xerodermia pigmentosum, epidermodysplasia verruciformis, lamellar exfoliation of the newborn, Urbach-Wiethe disease, congenital erythropoietic porphyria, native polykeratosis of Turen, and wide range of syndrome diseases (Grenbland-Strandberg, Rothmund, Blum, Verner etc.) are passed by autosomal-recessive inheritance.

Sex-controlled (X chromosome) dominant inheritance is observed at follicular atrophic keratosis, Bloch-Sulzberger syndrome.

Sex-controlled recessive inheritance (X chromosome) is observed at anhidrotic ectodermal dysplasia, dystrophic form of epidermolysis bullosa, diffuse angiokeratoma, and ichthyosis vulgaris.

Genetic diseases of skin with dominant type of inheritance are more numerous than diseases with recessive type. This is mostly conditioned by a fact that it is difficult to trace the recessive gene of human. It is necessary to mention that genetic diseases could be evidenced either straight after born or in different periods of life (in childhood, youthful and even in adult age). The same genodermatosis could be passed by different ways either dominantly or recessively which in some degree makes impact on particularities of clinical symptomatology, course and prognosis of these dermatoses.

Classification. There was a variety of attempts for creation of clinical classification of genetic diseases of skin. For the now there are following groups of genetic pathological processes in skin and cutaneous appendages:

- *physiological anomalies* (heterochronia and hair poliosis, sunspots, lentigo etc.);
- *metabolic defects* (albinism, pigmentation of xerodermia, porphyria, xanthomatosis etc.);

- *elastic tissue developmental disabilities* (epidermolysis bullosa, Ehlers-Danlos syndrome and others);
- *dyskeratosis* (ichthyosis, keratoderma, Devergi's disease and so on);
- *ectodermal dysplasia* (alopecia adnata, anonychia, hypertrichosis) and other anomalies.

It is considered to be regular from the clinical point of view the division of genetic diseases on three main groups:

1. Skin diseases, in occurrence of which the crucial role is played by genetic factors (group of ichthyosis: ichthyosis vulgaris, lamellar exfoliation of the newborn and genetous ichtyosiform erythemas; bullous hemodermatosis, genetous dysplastic diseases, phacomatosis and others).

2. Dermatosis which genetic occurrence is also practically assured but type of inherent pass determined indistinctly and in a great measure is conditioned by environmental effect (weeping dermatitis, psoriasis, acne vulgaris, and atopic dermatitis). These diseases often called as diseases of genetic disposition.

3. Some dermatosis at which, as a rule, similar diseases are not observed among near relatives, but the hereditary transmission is registered in separate groups of patients (lichen acuminatus, seborrheic dermatitis, white spot disease).

Bullous genodermatosis

The diseases of this group are characterized by occurrence of different by size bullae on skin and in separate cases – on mucosal coats too. The bullae appear as a response for even insignificant pressure. The group of genetous bullous dermatosis includes epidermolysis bullosa, Hailey-Hailey disease, porphyry, Bloch-Sulzberger syndrome, and ichthyosiform affections.

Epidermolysis bullosa (*epidermolysis bullosa hereditaria*). As issue of certain diagnosis decided not only chronically but also with obligatory attraction of morphological examination, the meaning of simple or dystrophic forms of epidermolysis bullosa hereditaria is important for the practician physician.

Epidermolysis bullosa hereditaria was firstly described by *J. Hutchinson* (1875) and *T. Fox* (1879). *H. Kebner* (1886) name this disease the epidermolysis bullosa and *L. Broc* (1902) – the traumatic pemphigus. Epidermolysis bullosa is discovered as heterogenic group of genetically conditioned diseases of skin among which either dominantly and recessively inherited forms. They are divided by three groups in accordance with results of morphological researches. There are 24 clinical types of this disease. Accordingly to this the groups of usual, boundary and dystrophic epidermolysis bullosa are distinguished.

Aetiology and pathogenetic mechanism. Aetiology of all forms of epidermolysis bullosa is determined by numerous genetic mutations in different chromosomes. Its pathogenetic mechanism is discovered not enough. At all forms

there are genetically conditioned structural failures at level of basal membrane. At variety of clinical forms the enzymatic failures are discovered in epidermis.

Clinical findings. The common for all clinical forms of epidermolysis bullosa is an early appearance of disease, more often in childbirth or in first days after birth of child. The appearance of bullae and anabrosis on skin and mucosal coats as result of weak mechanical injury or hyperthermia is typical. Presence or absence of cicatricial tissues after regenerative process is a basis for division of clinical forms of epidermolysis bullosa by dystrophic and usual ones.

Usual generalized epidermolysis bullosa

The disease begins of child from birth or in first month of life. At first bullae appear on feet, then on hands, further – in places of friction by clothes and nappies. In 20-30 min after shear stress of skin the tin-walled bullae appear on it. After breaking the bulla's tegmentum the regenerative process occurs during several days. The cicatricial tissues are not discovered. General condition of patients is not broken, the course of disease is mild, the intellect is not suffer, the legs are not damaged, the Nikolsky's sing is negative. At adulthood the spontaneous recovery is possible.

Delayed or localized epidermolysis bullosa (synonyms: the Weber-Coccain's syndrome, summer epidermolysis bullosa of feet and hands). The disease begins in ephebic or of adults as usual in summer. The allocation of bullae is limited by palms and plantae.

Group of dystrophic bullous epidermolysis

Dystrophic bullous epidermolysis is represented by non-regular group of genetically conditioned inheritable bullous diseases, part of which is passed by autosomal-dominant and the other part is by autosomal-recessive way.

Pathogenically at autosomal-dominant forms the incompleteness of constitution of anchor fibrillas, i.e. structures connecting the basal membrane with dermis. Histopathology at all clinical forms of dystrophic bullous epidermolysis is similar. The bullae allocated under basal membrane which is away with dermis together with epidermis and is a part of bulla's tegmentum («dermolythic» bulla). The expressed swelling and homogenization of collagen fibers are observed under bulla in dermis. Elastic fibers bloat, in some places they are disorganized either in area of bulla and at well-looking areas of skin.

There are following clinical forms are distinguished in group of dystrophic bullous epidermolysis:

- hyperplastic form of habitual dystrophic bullous epidermolysis of dominant type;
- albopapuloid form;
- atrophied form;
- autosomal-recessive bullous epidermolysis in one's turn is divided for:

– polydysplatic;
– generalized;
– localized.

Hyperplastic type of dominant habitual dystrophic bullous epidermolysis. The disease begins from moment of birth or first months of life when on injured areas of skin as well as on mucosal coats the bullae appear. The spontaneous rash is rarely observed. On places of bullae regression the hypertrophic and keloid cicatrixes and verruciformis hyperkeratosis appear. The mucosal coats are affected often and seriously. The appearance of bullae on mucosal coats leads to formation of secondary ciactrical stenosis of fauces, gorge, and esophagus, and corneal opacity. Hair and teeth has no changed. The mend occurs at periods, gravidism and, as a rule, during adolescence. The duration of life of patients with bullous epidermolysis is not decreased significantly.

Albopapuloid form of dominant dystrophic bullous epidermolysis. The disease begins from two-year age and proceeds by a type of hyperplastic epidermolysis bullosa. With coming of adolescence (even earlier for some children) the occurrence of bullae in area of extremities is stopped and fine indurated white papules appear on skin, mostly on body. These components become larger and interlock gradually, their surface becomes of ivory color. General condition of the patients is satisfactory. The miliums appear on the places of bullae and the cicatricial tissues occur. The Nikolsky's



Fig. 19.1. Bullous dystrophic epidermolysis.

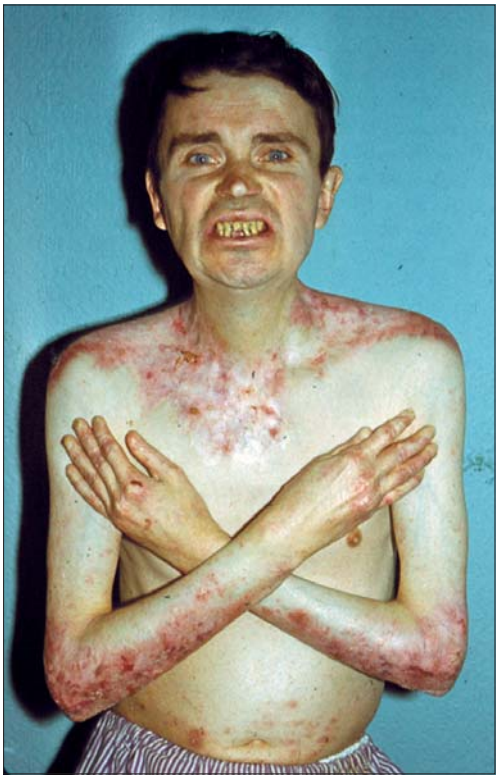


Fig. 19.2. Bullous dystrophic epidermolysis.

sign is rarely could be positive. The prognosis for life is favorable. It is considered that this form is a milder variant of hyperplastic form of epidermolysis bullosa.

Atrophic form of dominant dystrophic bullous epidermolysis. The disease begins from moment of birth. The generalized injury of skin progresses in first days of life already. The bullae appear on most injured areas of skin such as hands, feet, elbows, neck, and lumbus. The mucosal coats are not injured. Bodies of nails are burned-out of all of patients. Physical development could be postponed, and the intellectual is not suffered. With age, the bullae appear rarely, and the presence of disease of adult patients could be evidenced by dystrophy of nails and atrophic cicatricial tissues on elbows, knees and anticnemions only.

Recessive bullous epidermolysis

This group of diseases is characterized by severest course. The following is distinguished: dystrophic polydysplastic bullous epidermolysis (non-generalized and generalized) and dystrophic inverse localized.

Polydysplastic dystrophic bullous epidermolysis. The disease begins from moment of birth and could cause death at an early age. It is evidenced since first minutes of child's life and in moment of birth the bullae and anabrosis could appear on the large areas of baby's skin. In first days of life the bullae appear either as result of mild injury of skin, pressure, and friction or spontaneously. The anabrosis appear fast on the bullae's places and process gets a spread nature. The Nikolsky's symptom is evidenced. Regeneration occurs slowly with formation of atrophic cicatricial tissues. Wide cicatrization of skin in area of elbows, hands, and feet is gradually leads to progression of contractures, symphasodyctylias, and autoamputations of phalangeal bones. There are no nails from birth or gradually disappear as a result of occurrence of hyponycheal bullae. Ulerythema of hairy part of head is accompanied by diffuse rarefying of hair and its dystrophy. All of patients have their teeth injured. The caries, numerous defects of dental enamel, compromised dentitions, and paradontosis are observed. Approximately 20% of children have their mucosal coats of mouth cavity, esophagus and straight intestine injured. The bullae with hemorrhagic content are also could appear on these areas. The process of cicatrization on mouth leads to limitation of tongue displaceability, atrophy of mamelons, and mycrostomia. The most often causes of death on first year of life are dermatogen blood poisoning, asphyxia resulted by ingression into respiratory passages of bullae tegmentum and aspiration pneumonia. The ability for regeneration of injuries of skin is decreased in age of older than 30 years. The traumatisms are not healed on some areas during several months and could vegetare. The dermoid cancer could progress on long-lastly opened areas of skin.

Generalized dystrophic bullous non-mutilans epidermolysis. It is similar with clinical form described above but proceeds more mildly and differs by absence of injury of mucosal coats and by less severe course of disease in adult age (rare and more and more mild backsets). The cicatrization does not lead to autoamputations.

Localized dystrophic bullous epidermolysis. AT this form the beginning of disease is in first days of life and characterized by appearance of bullae with serosanguineous content which are located in places of maximal pressure and friction (feet, knees, elbows, and hands). The atrophy progresses in area of bullae, the milim-typed encapsulations occur, but these changes are less evidenced than at generalized form. The dystrophy of nails is evidenced on palms and feet. The injury of oral mucosa proceeds mildly. The dystrophy of nails is often encountered.

Pathomorphological mechanism. Histopathological examinations carried out by the means of submicroscopy became the basis for division of all forms of bullous epidermolysis by regular, boundary and dystrophic bullous epidermolysis.

At *regular forms* the appearance of bullae in epidermis occurs due to cytolysis of basal epidermal cells and this is reflected on electron diffraction patterns in view of full-blown swelling of their cytoplasm with abruption of cell envelopes. The bulla's tegmentum is all rafted epidermis and the bottom is an undamaged basal membrane.

The bullae at *boundary forms* appear on level of light plate of basal membrane. It is conditioned by inheritable incompleteness by desmos of basal epithelian cells and fixing tonofilaments. The bottom of bulla is made of plate of basal membrane.

At *dystrophic forms* the appearance of bullae is on the border of basal membrane and dermis which is concerned with genetically conditioned incompleteness of fixing fibrils connecting the basal membrane with dermis. The bottom of bulla is a dermis and this leads to formation of cicatricial tissues.

Differential diagnostics. The inheritable bullous epidermolysis of children should be distinguished from inheritable bullous ichthyosiform erythrodermatitis, epidemic and syphilous pemphigus, acrodermatitis enteropathica, inheritable erythropoietic porphyria, and Bloch-Sulzberger syndrome.

The inheritable bullous epidermolysis of adults should be distinguished from non-heritable bullous epidermolysis, bullous variant of multiform exudative erythema, pemphigus vulgaris, pemphigoid, Duhring disease, delayed skin porphyry, toxic epidermal necrolysis, and bullous form of mast cell disease.

Curing. From first days of life of child it is necessary to create a regime of minimal injury of skin for him (soft nappies and clothes with scarring outside). The skin should be lubricated and hydrated to make it soft, elastic and more resistant against influence of mechanical irritants.

On account of a fact that at autosomal-recessive bullous epidermolysis the excess of structurally-changed collagenase is produced the *pathogenetic therapy* is provide the abuse of drugs inhibiting of its production and activity (large doses of vitamin E, retinoids).

Symptomatic therapy is a basis of curing of patients with bullous epidermolysis. It includes the abuse of pluripotential antibiotics at secondary contamination, antihistamines at well-marked pruritus, and anabolic drugs. It is necessary to provide a due care for oral cavity (antiseptics). It is undesirable to implement systemic and

local corticosteroid therapy as it does not stop the occurrence of bullae and does not heal the anabrosis.

At appearance of contractures, symphasodyctalies and other cicatricial complications the surgical reconstructive maneuver is carried out.

Labor expertise. The labor expertise and reasonable career guidance of adult patients are carried out depending on severity and complications of disease. For the patients with heritable bullous epidermolysis the disability status could be settled.

Ichthyosis

There are changes in epidermis, leading to appearance of the crusts reminding the fish-scale on skin typical for this group of diseases.

Clinically the ichthyosis is characterized by dryness and scabrities of skin, cornual fusions of different sizes – from small tender whitish crusts to greyish-black-green fusions tightly connected with skin in center and little bit raised by the edges. In some cases the cornual fusions could reach few millimeters in width.

Aetiology and pathogenetic mechanism. Ichthyosis is the genetous diseases; its clinical types are conditioned by different genetic mutations which biochemical effect is still unknown. At ichthyosis the malfunctions of proteometabolism and amino acid exchange, changing of activity of some biocatalyzers, gaseous exchange through the skin and oxygen tension in it are discovered. The lack of vitamin A and endocrinopathy (insufficient activity of thyroid hormones, butterfly adrenal, reproductive hormones) play a role. In some cases the changes on skin of non-heritable nature are observed because of which it reminds fish-flake, – heritable ichthyosis. Such changes have symptomatic nature and could serve by evidence of hypovitaminosis, senile involution of skin, neoplastic diseases and others.

Classification. On the basis of clinical-genetic and pathomorphological data the ichthyosis is divided by heritable and non-heritable.

Heritable ichthyosis includes regular (vulgaris) ichthyosis with autosomal-dominant and autosomal-recessive X-sex-linked types, ichthyosis of fetus, congenital ichthyosiform erythroderma, single-sided, linear circumflex porcupine disease and syndromes providing the ichthyosis as a symptom.

Non-Heritable ichthyosis (ichthyosis-typed conditions) are divided by symptomatic, disk-typed and senile.

Let's bring into focus the most widespread clinical forms of heritable ichthyosis.

Ichthyosis vulgaris. Ichthyosis vulgaris is a most widespread form of disease which is up to 80% of all ichthyosis events. The frequency of spreading of this ichthyosis' form among population is 1:20000 births. Ichthyosis vulgaris is run in the blood by autosomal-dominant type.

First signs of disease in view of dryness, folding of epithelium, especially at belly-band surfaces of body, and sloughing of skin appear firstly on second or third month

of life. As a rule, ichthyosis vulgaris occurs in first three years of life but the occurrence in latest time is not excluded (up to 12-year age).

Ichthyosis vulgaris progresses gradually and reaching its maximum at adulthood. Since that time diseases become stable but the magnitude could change. Usually, process is weak in summer and is strong in late autumn and in winter.

Depending on intensity of clinical evidences there are following *clinical forms* of ichthyosis vulgaris:

- ichthyosis follicularis
- xerodermia
- ichthyosis nitida
- ichthyosis serpentine
- ichthyosis hystrix.

Ichthyosis follicularis is characterized by (together with barely perceptible dryness of skin and its scabrities in extensor surfaces of upper and lower extremities) presence of corneal plugs in openings of hair follicles having pin-head's size on which the hair is noticeably extends – *lanugo*. The significant folding of epithelium is observed at slight displacement of the skin on the belly-band surfaces of body.

At ***xerodermia*** the dryness of skin and defurfuration are more evidenced. Sin if face is dry, tensioned, covered by erubescene (face of "doll"). The folding of epithelium is noticed on the skin of body and alvus. There are underlined natural figured lines on the palms.

At ***nitida*** from of usual ichthyosis the evidenced dryness of skin comes to the fore. Skin is covered by freely sitting thin mess crusts of up to lens in size and some larger. Fusion of crusts and their size at this clinical form are more evidenced. Grooves between crusts are superficial usually but at presence of more thick crusts they become deeper. Because of air contained under peripheral part of crusts the crusts are off-



Fig. 19.3. Ichthyosis vulgaris.



Fig. 19.4. Ichthyosis vulgaris.

white, and the central part is tightly close to the underlying skin and is darkest. As result of oscillation of peripheral parts of crusts at patient's move and of typical glare they remind fish's scale (therefore the name – glare or nacreous ichthyosis). The skin of face is dry, tensioned and strenuously flaked.

At ***ichthyosis serpentine*** there are wide shells of dark-brown, dirty-grey, dark-yellow color sitting tightly observed on the extensor surfaces of extremities and body. In some places they are divided by deep and superficial grooves. The shells gives to skin cover the similarity with skin of snake or crocodile. Corneal shells could cover either small or wide areas of skin forming the affinity of carapace and left the folds of skin and bends of elbows free. At this clinical form the nails affection in view of lengthwise and diametrical streaks is registered more often than at xerodermia and nitida form.

Ichthyosis hystrix in addition to low-grade dryness of skin is characterized by presence of verruciformis appearances in view of spears or acus highly extrude over level of skin. Usually these corneal appearances are located on localized areas of skin. It has brown, brownish-black, and dirty-grey color.

At histological examination the mediate hyperkeratosis, lowering or even complete absence of stratum granulosum, large follicular plugs the pressure of which leads to atrophy of lower part of follicles and oil glands are observed. The imperceptible perivascular infiltrates, containing from lymphocytes are appear in dermis and the hyalinization of collagen fibers, oil glands and erector muscles of hairs occur in deep layers.

Diagnostics and differential diagnostics. Clinical and morphological changes at ichthyosis vulgaris are characterized by uniformity and hence the diagnostics is not so hard. Differential diagnostics of non-heritable ichthyosis is based on origination of ichthyosis vulgaris in childhood and heritable one is on the background of diseases of blood, neoplastic processes, hypovitaminosis, and allergic disorders.

Curing. Individual care includes assigning of vitamins A, E, C, ultraviolet irradiation, and hydrotherapy. The emollients containing ureal are used topically.

Ichthyosis congenita, ***synonyms: heritable keratosis, universal heritable keratoma, ichthyosis foetal, hyperkeratosis universal heritable, ichthyosis of fetus, harlequin fetus.*** Ichthyosis congenita progresses in fetal life and child is born with evidences of ichthyosis. Babies with this disease are low-birth-weight in approximately 80% of cases. The mediate oscillation of expressivity is observed, from severe fatal forms with dead birth or low-birth-weight with range of early complications to forms compatible with life, non-disabling, but always with expressed cosmetic defect as a result of crude violation of cornification. The ichthyosis congenita is inheriting in autosomal-recessive way with complete penetrance and variable expressivity of gene. This defect is considered to be rare.

The skin of newborn at birth has a view of rough corneal carapace of greyish-white color. In first hours after birth the carapace begins to dark and becomes violet-

grey and even brown and then crisped by polygonal sites divided by deep breaks. This anomaly of skin has universal nature. The rough corneal carapace on distalis of extremities creates such impression as like fingers are interlocked. The hairs on head are short and thinned out, also could be absent at all. The face is deformed and covered by large corneal sheets. Mouth is open widely because of strong infiltration of soft tissues, and the breaks in its corners. The lips are thickened and mucosal coat is inverted, hypertrophied and remind "jaw of fish". Ectropion is evidenced clearly. The corneal fusions in form of plugs are observed in nostrils and auditory pathways.

Expressed formation of scaly crusts is left for whole life. Periodically, once per 3-4 months the peeling-off is noticed. The patients with heritable ichthyosis have underlying risk for impetiginous infection, especially in childhood. Differential diagnostics is carried out with lamellar ichthyosis and range of syndromes such as Rode's syndrome, Refsum's syndrome and others.

The curing is the same as for ichthyosis vulgaris.

Brok's congenital ichthyosiform erythroderma. Congenital ichthyosiform erythroderma has bullous and non-bullous clinical form and belongs to group of ichthyosiform diseases. It is inherited by autosomal-recessive type. In recent days in medical literature a non-bullous (dry) form is called as lamellar ichthyosis and a bullous one is called as congenital porcupine skin, congenital ichthyosiform epidermolysis, and congenital universal acanthokeratolysis.

Non-bullous (dry) ichthyosiform erythroderma is evidenced with birth of child. The surface of newborn's skin reminds colloidal film or sheepskin. Corneal layer is yellowish-green, some retracted, at first movements it begins to broke and during few days or weeks is detached by large layers so some children could recuperation happen.

Bullous ichthyosiform erythroderma is characterized by expressed inflammatory evidences, especially in folds of skin. The disease begins from birth. The newborn has a skin of red color at first time, such skin is soft, manageable, wet but it becomes dry fast and in area of large folds the bullae, areas of hyperplastic peeling-off of skin appear, the superficial anabrosis are cropped out.



Fig. 19.5. Congenital ichthyosiform erythroderma.

Histologically the massive hyperkeratosis is evidenced in which the conglomerates of spinous cells with indistinct borders are involved. The spontaneous arrangement of epithelial cells and absence of border between epidermal cells is observed in injured areas in spinous layer. Spinous cells are burned-out and have no connection between each other.

At carrying out the differential diagnostics with ichthyosis vulgaris the attention is obligatory paid to the fact that at ichthyosis vulgaris the folds of skin are remain free of injuries. At distinguishing from bullous epidermolysis it is taken into consideration that there are no erythroderma and bullae appear on places of mechanical irritation. Epidermal pemphigus of newborns (staphylococcus) is accompanied by high temperature and occurrence of bullae on erythematous and edematous background.

Principles of curing of congenital ichthyosiform erythroderma are the same as principles of curing of ichthyosis vulgaris but for enhancement of further prognosis it is reasonable for the patients to assign one of the oral steroids right after determination of diagnosis (not later than ten days after birth).

At ***bullous ichthyosiform erythroderma*** of children older than ten years at spread bullae the positive effect is observed at assigning per os of sulfanilamide drugs in curative doses to bullae disappearance and the dose is further decreased up to the maintenance one.

1. Name the diseases belonging to congenital ones:

A. Atopic dermatitis
B. Lichen acuminatus
C. Strumoderma
D. Ichthyosis vulgaris
E. All of mentioned above is correct

2. The basis of genodermatosis are:

A. Somatic mutations
B. Genetic mutations
C. Induced mutations
D. Chromosomal mutations
E. All of mentioned above is correct

3. Congenital ichthyosis is evidenced by:

A. Bullae and peeling-off
B. Papules and plaques
C. Nodules and ulcerations
D. Lichenification
E. All of mentioned above is correct

4. Regular ichthyosis is characterized by:

A. Symmetric location
B. Unique contour of palms
C. Symmetric location and unique contour of palms only
D. Injury of mucosal coats
E. All of mentioned above is correct

5. The group of genetically conditioned ichthyosis includes:

A. Xerodermia
B. Symptomatic ichthyosis
C. Senile ichthyosis
D. Lichenification
E. All of mentioned above is correct

6. The following are the clinical forms of ichthyosis vulgaris:

A. Follicular
B. Nacreous
C. Xerodermia
D. Serpentine
E. All of mentioned above is correct

7. The following belongs to the group of bullous epidermolysis:

A. Hyperplastic form of dominant dystrophic congenital bullous epidermolysis
B. Albopapuloid variant of dominant dystrophic congenital bullous epidermolysis
C. Atrophic variant of dominant dystrophic congenital bullous epidermolysis
D. Autosomal-recessive bullous epidermolysis
E. All of mentioned above is correct

8. What clinical form the ichthyosis vulgaris has no:

A. Follicular
B. Xerodermia
C. Nitida
D. Lenticular
E. Serpentine

9. Individual care at ichthyosis does not provide of assigning of:

A. Vitamins A, E, C
B. Clotrimazole
C. Ultraviolet irradiation
D. Hydrotherapy
E. Prednisolone

Task 1. Since 11 days after birth the girl was discovered the anabrosis on buttock (conditioned by breech presentation) and bullae near the nails of first fingers. The bullae began to spread fast. Because of this the antibiotics were assigned which were no effect. There were no similar diseases in her family before.

a) What disease is talking about:
- **A**. Regular generalized bullous epidermolysis
- **B**. Albopapuloid variant of dominant dystrophic congenital bullous epidermolysis
- **C.** Atrophic variant of dominant dystrophic congenital bullous epidermolysis
- **D**. Delayed bullous epidermolysis
- **E**. Pemphigus

b) Give a prognosis of disease

Task 2. Two-year boy since first days after birth has strained bullae of from 4 to 6 cm in size on places of tight enclosure of clothes. The bullae are filled up with serous and serosal-hemorrhagic content. The Nikolsky's sign is positive. The familial anamnesis regarding skin diseases is not severed.

a) What diseases should be excluded:
- **A**. Congenital bullous ichthyosiform erythroderma
- **B**. Epidemic pemphigus and pemphigus syphiliticus
- **C**. Acrodermatitis enteropathica
- **D**. Congenital erythropoietic porphyria
- **E**. All of mentioned above is correct

b) Assign a curing for the patient.

Task 3. Twelve-year boy since three-month age the dryness of skin appeared especially expressed on the extensor surfaces of upper and lower extremities. The skin of mentioned areas is covered by gentle whitish crusts tightly connected with underlying skin in center and perched by periphery. Similar disease father has but it is less evidenced.

a) What disease is talking about:
- **A**. Divergee's disease
- **B**. Ichthyosis vulgaris
- **C**. Bullous ichthyosiform erythroderma
- **D**. Non-bullous (dry) ichthyosiform erythroderma
- **E**. Divergee's disease

b) What diseases the differential diagnostics should be carried out with?

Task 4. Thirteen-year girl has all her skin excluding natural folds dry, covered by fusions of silver-white crusts central part of which is tightly enclosed with underlying skin and accordingly of darkest color. The evidenced folding of epithelium is on belly-band surfaces of body. The skin of face is dry and strained («face of doll»).

a) What diagnosis will you make:
- **A**. *Ichthyosis follicularis*
- **B**. *Xerodermia*
- **C**. *Ichthyosis nitida*
- **D**. *Ichthyosis serpentine*
- **E**. *Ichthyosis hystrix*

b) What curing should be assigned?

Task 5. The patient of 25 years old who is injured since early childhood (as far back as he can remember) has all his skin dry, including palms and feet, it is covered by flat flake-crusts, which tightly enclosed with underlying skin. The ciliae are inverted, concha of auricles are deformed.

a) What is the most possible diagnosis in this case:
- **A**. Congenital ichthyosiform non-bullous erythroderma
- **B**. Divergee's disease
- **C**. Bullous ichthyosiform erythroderma
- **D**. Weber-Coccain's syndrome

b) What diseases this disease should be distinguished with?

Answers for first level self-control questions
1 – D; **2** – E; **3** – A; **4** – C; **5** – A; **6** – E; **7** – E; **8** – D; **9** – B
Answers for second and third level self-control questions
1a – A; **2a** – E; **3a** – B; **4a** – B; **5a** – D

20 TOPIC

Diseases of hairs

Group of dermatosis to which the diseases of hairs belong is very miscellaneous either by causation with pathogenetic mechanism and by clinical course with prognosis. There is no uniform universally recognized classification of diseases of hairs for the now. It is recommended to separate defluxions and pathologies of hairs by the following groups and subgroups:

1. Non-heritable defluxions – Alopecia areata, androgenic or seborrheal, symptomatic pelade (syphilous, leprous, toxic, including postpartum, after abstinence from food etc.).

2. Heritable defluxions (complete or partial) – hereditary syndromes including hypertrichosis (Gottorn's familial acrogeria), anhidrotic ectodermal dysplasia, Conradi disease, Bushe-Fischer's keratoderma, Grobe's syndrome, Unna's syndrome, trichrinophalangeal syndrome, curly hairs' syndrome, Rothmund's syndrome, and Werner's syndrome.

3. Monilethrix or moniliform hair – heritable, as a rule, familial dystrophy of hairs and hair follicles.

4. Cicatrical alopecies – pseudopelade Brocq, lupus erythematosus, Lassueu-Little syndrome, alopecia after X-ray irradiation.

5. Dystrophies and anomalies of growth of hairs – clastothrix, trichoptilosis, twisted hair, trichiasis, burrowing hairs, Nethertone's syndrome.

6. Hypertrichosis non-heritable and heritable (universal and partial), could be one of the symptoms of Morgagni's syndrome, Paraundler-Gurlier's disease, Stein-Levental's syndrome, Recklinghausen's disease, Arnold-Chiari malformation, hypertrichosis in climacterical period.

7. Mycotic lesions of hairs (microsporia, trichophytosis, favus).

TRAINING AND EDUCATIONAL GOALS

- Determine possible conditions and trigger factors of occurrence of hairs' diseases
- Determine the particularities of different diseases of hairs
- Notice and understand general course of different diseases of hairs
- Determine clinical particularities of typical evidences of hairs' diseases for different groups
- Determine the principles of ethiopathogenetic therapy and preventive measures for occurrence of hair's diseases

20 Alopecia

Alopecia or pelade is a partial or complete heritable or non-heritable absence of hairs. The non-heritable alopecia includes areata, androgenic, seborrheal, syphilous, leprous, toxic, symptomatic, including postpartum, after abstinence from food etc. The group of heritable alopecia includes congenital syndromes which are hypertrichosis, anhidrotic ectodermal dysplasia, Conradi disease, Grobe's syndrome, Unna's syndrome, trichrinophalangeal syndrome, curly hairs' syndrome, Rothmund's syndrome, and Werner's syndrome. There are also cicatrical alopecies – pseudopelade Brocq, lupus erythematosus, Lassueu-Little syndrome, alopecia after X-ray irradiation.

TO KNOW:

- modern conceptions of aetiopathogenesis of clinical forms of alopecia;
- factors precipitating the progression of this disease;
- principle of classification of alopecia;
- symptomatology of different clinical forms of alopecia;
- clinical-laboratory diagnostic criteria of determination of hair's pathology;
- pathomorphological changes in skin at different forms of alopecia;
- general and local approaches of therapy and principles of curing and preventive measures at different forms of alopecia.

TO BE ABLE TO:

- carry out the material intake and determine the structure of hairs correctly;
- carry out the differential diagnostics with diseases having similar clinical presentation;
- assign corresponding laboratory examinations required for confirmation of diagnosis;
- assign balanced curing for the patient taking into consideration his or her age and sex;
- advice required preventive measures of alopecia.

Pathological loss of hair is an obligatory deterministic regular sign of disease at one dermatosis (alopecia areata, pseudopelade Brocq) and non-obligatory and non-regular at other ones (lues venerea, lepromatous leprosy).

Alopecia areata

Alopecia areata, synonyms: alopecia, focal pelade, Cazenae's vitiligo is a widespread form of non-heritable alopecia which is evidenced by spontaneous focal or total loss of hair without occurrence of inflammation, cicatrization and atrophy of skin caused by influence of different pathological factors.

Aetiopathogenesis. The causation and pathogenetic mechanism of alopecia areata are not determined to a full degree. The possible factors include failure of immune status, neurotrophic and endocrine disorders, especially from pituitary-adrenal system, stresses, chronic and acute intoxications, injuries, results of surgical aggressions, presence of chronic focal infection etc.

Unpredictability of course of disease, vast number of clinical forms, presence of numerous comorbid conditions which significantly influence on course of dermatosis, make the explanation of cases of alopecia areata by only reason impossible which is evidence of polygenicity of this disease.

Epidemiology. Incidence of alopecia areata is 3-5% of the total number of dermatosis, the young people suffer mostly but there are cases of alopecia areata of babies and elderly persons also known. According to data of some authors, the incidence of men and women is approximately the same and according to results of others the alopecia areata is mostly encountered of women.

Classification. There are following clinical forms of alopecia areata:

focal – presence of separate or numerous allocated focuses of pelade with round-shaped contours on skin of hairy part of head;

subtotal – there is no hair on the most part of surface of hairy part of head (square of pelade is more than 2/3 of scalp's surface, only separate "bushes" of hair are left);



Fig. 20.1. Focal pelade.

total – absence of hair on whole surface of head;

universal – absence of hair on all surface of skin;

band-like or Celsius ophiasis – absence of hair in marginal layer of growth in area of hindhead and temporal fossa.

Clinical findings. Alopecia areata is characterized by focuses of loss of hair of round or oval shape without evidences of cicatrization and atrophy of skin. The

skin in lesion focuses has normal painting (could has pink tone at beginning of disease or be edematous), there are no evidences of peeling, the follicle apparatus is saved.

There are three stages of clinical course of alopecia areata depending on activity of pathological process:

progressive – random loss of hair and presence of area of «loose» hairs on periphery of pelade focuses is observed (at pulling by hairs their painless epilation occurs), there are burned-out recurrently splitting hairs discovered at microscopic examination having no radicular pore;

stable – the random loss of hair is stopped, area of "loose" hairs is not determined, at attempting of mechanical epilation the hairs stay in skin solidly, the growth of hairs in focuses of pelade is absent;

regressive – the growth of hairs in focuses of pelade is observed, the prenatal ones at first instance.

Course and prognosis. At the beginning of disease it is hard to foretell the further course of alopecia areata. Sometimes after 2-4 months of existence of focuses of pelade the growth of hair in affected areas is restored gradually. At first the discolored prenatal hairs grows, then they are pigmented and grows again reaching the length of normal hairs. But more often takes the malignant, chronic, recurrent course. Repeatable back-sets cover new areas and could lead to complete loss of hair. Thus, focal form of pelade is transformed into total one which is often occurs in children or juvenile age.

Pathomorphology. Histological changes at the beginning of disease are mostly in hair follicles: root sheathes are separate from connective tissue membranes of follicles, the structure of outer and inner root sheathes is broke, hair papilla is mummified, and the hair bulb is deformed. The lymphocytic infiltration is formed around the hair



Fig. 20.2. Subtotal pelade.



Fig. 20.1. Total pelade.

follicles. Significant changes happen also in nervously-receptor apparatus of skin: numerous nerve terminals located near the hair follicles are destroyed.

The pathomorphological presentation at stable stage is changed: the perivascular lymphohysteocytic infiltrations and enlarged capillary vesicles with thickened walls, partially non-functioning are discovered in dermis. The number of reduced hair follicles is increased; there are residues of hairs in view of striker and accumulations of corneal masses found in its openings. However, most of these follicles remain the ability for formation of hair. At regression of disease the proliferation and restoration of vesicles, hairy and nervously-receptor apparatus processes are in skin.

Diagnostics. The diagnosis of alopecia areata in most cases is not so hard to determine and could be verified by the means of microscopic examination – discovering of burned out hairs and hairs in view of striker.

Differential diagnostics. At presence of patient of pelade locuses' large number on his head it is necessary to exclude secondary syphilis. Lupus erythematosus could remind alopecia areata. In this case it is necessary to carry out the biopsy of patient's skin. At absence of hairs in view of striker and at presence of peeling of skin the dermatomycosis should be excluded. The alopecia areata should be also distinguished with congenital atrophy of scalp, leprous and toxic alopecia. Often the alopecia areata should be distinguished with androgenic alopecia for which the progressive thinning and diffuse loss of hair, signs of hirsuties and acne, significant increasing (up to 30%) of number of hairs which are in stage of telogen are typical.

Curing. Not all clinical forms of alopecia areata could be influenced by therapy. The most favorable prognosis regarding clinical recovery the patients with located clinical forms of pelade have.

Anticipate nature of course of alopecia areata, necessity of long-lasting treatment and refresher courses condition the including in complex therapy of zinc, cuprum, ferrum drugs, and drugs enhancing microcirculation. The photosensitizers – furocoumarins (meladynine, amifurin, psorelen, psoberan, beroxane and others) are used at curing of patients with alopecia areata. The modification of this approach is combined abuse of furocoumarins with ultraviolet irradiation–PUVA-therapy. It is should be noticed that abuse of furocoumarins could cause to range of complications of patients with alopecia areata such as strong headaches, sleeplessness, soreness, vomiting, biliousness, and albuminorrhea.

The assigning to the patients with alopecia areata of corticosteroids is justified at malignant course of disease only.

More often these patients are being assigned the corticosteroid medicines directly into lesion focuses by the way of pharmacopuncture.

Large group of drugs used at curing of alopecia areata are the topic stimulating drugs causing the erythema and improving the metabolism in lesion focuses.

The local abuse of minoxilide hypotensive drug as a stimulator of hairs' growth is efficient. It is reasonable to include in plan of therapy of patients with alopecia areata

the physiotherapeutic approaches – cryomassage by liquid nitrogen, phonophoresis with vitamins and corticosteroids, ultraviolet irradiation, freezing by chlorethyol (to appearance of rime frost), reflexotherapy and sanatorium-resort therapy.

Alopecia seborhoica

Alopecia seborhoica is a form of non-heritable alopecia which is evidenced by progressive loss of hair without evidences of cicatrization and atrophy of skin on the background of stable seborrhea.

Aetiopathogenesis. It is not determined definitively. The possible causative factors include genetic disposition, endocrinal disorders, malfunction of reproductive glands, butterfly adrenal, thyroid body, nervous, immune, alimentary systems, hypertrophia and hypersecretion of oil glands, and change of quality of sebaceous matter. The disease of different intensity begins mostly in adolescence; the patients are both men and women.

Clinical findings. The most reason of progress of alopecia seborhoica is a seborrhea. At this, clinical course and progression of complications are depends on form of seborrhea.

Course and prognosis. The course of disease has chronic nature with short-term incomplete remissions in summer period. More often the process progresses very slowly but implacable. At condition of efficient curing of seborrhea on the background of which the alopecia seborhoica is progresses the prognosis is favorable.

Pathomorphological mechanism. At histological examination the patients with alopecia seborhoica the extremely evidenced in openings of follicles hyperkeratosis, acanthosis, and spongiosis of cells of epidermis' spinous layer are discovered in lesion focuses. The perivascular and perifollicular lymphohysteocytic infiltrates (located more superficially than of patients with alopecia areata) are observed in superficial layers of dermis. The openings of oil-hair follicles are enlarged and filled up with corneal masses.

Diagnostics. It is based on the typical clinical representation, microscopic and histological examination (presence of atrophied hair follicles).

Differential diagnostics. The lupus erythematosus at location of lesion focuses on skin of hairy part of head could remind the alopecia seborhoica. It is necessary to carry out biopsy examination of patient's skin for clarification of diagnosis; in addition, at lupus erythematosus the skin in locuses of pelade is reddened, the follicular hyperkeratosis, peeling, and atrophy with strict borders are.

If patient has large number of fine focuses of pelade on the head the secondary syphilis should be excluded. In such cases it is necessary to find another signs of syphilis and carry out the serologic examination.

The alopecia seborhoica is distinguished from congenital atrophy of scalp by a fact that it is non-heritable disease which is not accompanied by abnormal development. Often the alopecia seborhoica should be distinguished with androgenic alopecia for which the genetic predisposition, progressive thinning and diffuse loss of hair, signs of hirsuties and acne (for women) are typical.

Curing. The complex examination is obligatory and curing of interfacing specialists (gastroenterologist, endocrinologist, gynecologist and others) in case of discovering of pathology.

The nutritional care is assigned for the patients (limitation of carbohydrates, fat and extractive products), anxiolytics. The medicine drugs of zinc, cuprum, ferrum, as well as drugs improving microcirculation and vitamins are used in order to normalize the functioning of oil glands. The significant role the reasonable care for skin and hairs plays. In cases of seborrhea adiposa the skin is lubricated by solution of salycilic acid, resorcinol, tincture of marigold. It is reasonable to use the combined corticosteroid unctures or creams containing antifungal agent. The shampoos containing the ketoconazole and urea are used locally.

Androgenetic alopecia

Androgenic alopecia (*alopecia praematura*), ***synonyms: regular alopecia, psilosis, androgenetic alopecia, alopecia presenilis, male pattern baldness*** is an immature progressive loss of hair.

Aetiopathogenesis. Androgenic alopecia is caused by genetically determined increasing of sensitivity of hair follicles' cells to influence of androgenic hormones and increasing of activity of 5-6-oxidoreductase. The men have the androgenic alopecia is conditioned by autosomal-dominant gene with different penetrance but the polygenic type of inheritance is not excluded. Women have the autosomal-recessive type of inheritance.

Epidemiology. This is most widespread type of loss of hair which diseases both men and women; however it is more often discovered of men.

Clinical findings. The disease of men began in adolescence. The process progresses slowly but implacable and ends by formation of pelade in age of 35-40 years.

There are five stages of alopecia by male pattern:

I stage – front line of hairs is going back;

II stage – thinning hair in temporal areas in view of "M" letter (if you are looking from the top) and in parietal region;

III stage – diffuse loss of hair in central-parietal region;

IV stage – the hairs are left between frontalis and central-parietal areas only;

V stage – complete symmetric pelade of frontalis and parietal area.

Women have first signs of disease at age of 20-30 years, and the full-scaled picture is formed in premenopausal age. Clinical presentation of androgenic alopecia is characterized by thinning hair in central-parietal area and its saving in frontalis and temporal areas as well as by signs of hirsuties and acne.

There are three stages of alopecia by female pattern:

I stage – insignificant thinning hair;

II stage – mediate thinning hair;

III stage – significant thinning hair.

Course and prognosis. The course of androgenic alopecia is characterized by sequence of periods of back-sets and remissions. At this, the rising of activity of oil glands, painfulness, and paresthesias in area of hairy part of head are observed. The process is more often progresses slowly but implacably. The prognosis regarding to restoration of hairs in lesion focuses is unfavorable.

Pathomorphological mechanism. At histological examination it is discovered that hair follicles are smaller in size, miniaturized, and some of them are atrophied.

Diagnostics. The diagnosis of androgenic alopecia is based on typical clinical presentation (progressive thinning and loss of hair, signs of hirsuties and acne) with taking into consideration of anamnesis (genetic predisposition), microscopic and histological examination (misbalance between hair follicles in stage of anagen and telogen to the side of the last one, presence of miniaturized hair follicles).

Differential diagnostics. In contradistinction with androgenic alopecia the alopecia areata is characterized by focuses of loss of hair with roundly or oval form without evidences of cicatrization and atrophy of skin, discovering of burned out hairs and hairs in view of striker at microscopic examination.

Symptomatic or telogen alopecia is conditioned by influence of range of endogenic and exogenic factors (stress, significant loss of blood, surgical maneuver, abuse of some medicamental drugs, inflectional diseases and others). It is characterized by diffuse loss of hair continuing from three months to one year and, as a rule, ends by complete recovery of hair growth.

The diffuse loss of hair, inflammatory evidences of different intensity, peeling, pruritus of skin of hairy part of head, excoriations and hemorrhoidal crusts, and jointing of secondary infection are typical for alopecia seborhoica.

If patient has large number of fine focuses of pelade on the head the secondary syphilis should be excluded. In such cases it is necessary to find another signs of syphilis and carry out the serologic examination.

Curing. The complex examination is obligatory and curing of interfacing specialists (gastroenterologist, endocrinologist, gynecologist and others) in case of discovering of pathology. The curing of androgenic alopecia is low-efficient but in cases of early abuse of calcium, zinc, methionine medicaments, approaches of outer stimulating therapy the decreasing of loss of hair could be observed during several

years. The positive effect is observed at using of as stimulator of hair growth or men. Recovery of hair growth is conditioned by synergizing effect of stimulation of follicle epithelium and suppression of immunological reactions mediated by T-lymphocytes.

At curing of pelade of men the antiandrogens (finasteride) suppressing the activity of 5-6-oxidoreductase are used. At hormonal disorders of women with androgenetic alopecia the assigning of hormone replacement therapy is justified, which gives valuable therapeutic effect. In recent years the approaches of surgical aggression are used widely for transplantation of hairs.

Pseudopelade Brocq or atrophic alopecia

Pseudopelade Brocq (*pseudopelada Brocq, alopecia atrophicans, synonyms: cicatricial atrophic pelade*) is a non-heritable form of alopecia which is evidenced by focal loss of hair which is accompanied by cicatrization and atrophy of skin.

Aetiopathogenesis. The causation and pathogenetic mechanism are not determined definitively.

Epidemiology. The disease occurs mostly at 35-40 years age. The both men and women are suffered.

Clinical findings. The disease begins from appearance of fine cicatricial-atrophic asymmetrically located focuses of pelade which are enlarge in sizes, get irregular crenated contours, and interlock between each other. At the incursion of disease the mediate perifollicular hyperemia, and then the atrophy of skin without evidences of inflammation (skin gets yellowish color, becomes smooth, easily folded) and peelings are observed in lesion focuses, the follicular apparatus is destroyed. Sometimes the separate visually unchanged long hairs are encountered in center of lesion focuses. The patients with pseudopelada Brocq have no subjective sensations.

Course and prognosis. The process progresses slowly but implacable. After some time the loss of hair stops, there is no complete pelade. However, the prognosis regarding the recovery of growth of hair in lesion focuses is unfavorable.

Pathomorphological mechanism. At histological examination of patients with pseudopelada Brocq the acute atrophy of epidermis, the destroyed oil-hair follicles, the perivascular and perifollicular lymphohysteocytic infiltrates located more superficially than of patients with alopecia areata in dermis, and the follicular hyperkeratosis in some places are discovered.



Fig. 20.4. Pseudopelada Brocq.

Diagnostics. It is based on typical clinical representation and could be confirmed by the means of histological examination.

Differential diagnostics. The lupus erythematosus at location of lesion focuses on skin of hairy part of head could remind the pseudopelada Brocq. It is necessary to carry out the biopsy of the patient's skin for confirmation of diagnosis. At lupus erythematosus the skin in locuses of pelade is reddened, the follicular hyperkeratosis, peeling, and atrophy with strict borders are.

In contradistinction with pseudopelada Brocq, the alopecia areata is characterized by focuses of loss of hair of round or oval shape without evidences of cicatrization and atrophy of skin.

If patient has large number of fine focuses of pelade on the head the secondary syphilis should be excluded. The pseudopelada Brocq is distinguished from congenital atrophy of scalp by a fact that it is a non-heritable disease which is not accompanied by abnormal development.

Curing. The cicatricial alopecies are nonreversible so in most cases the curing is not efficient.

For curing of patients with pseudopelada Brocq there are medicamental drugs of vitamin A1 acid (roaccutane, acnetine) used. It is also reasonable to use the physic-therapeutic approaches such as indirect diathermy or neodiathermy of neck sympathetic ganglions and dorsolumbar area, cryomassage by liquid nitrogen etc. The important part of complex curing is a reasonable care for hairs (using of medicated shampoos) and refuse from social habits (smoking, abuse of alcohol and others).

1. The non-heritable alopecies does not include:

A. Alopecia seborhoica
B. Celsius circles
C. Syphilitic alopecia
D. Conradi disease
E. Androgenic alopecia

2. Absence of atrophy and peeling in focuses of pelade is typical for:

A. Pseudopelada Brocq
B. Alopecia areata
C. Lupus erythematosus
D. Superficial Tinea capitis
E. Conradi disease

3. The following diseases proceed with evidences of atrophy of skin of hairy part of head:

A. Pseudopelada Brocq
B. Alopecia areata
C. Androgenic pelade
D. Seborrheal pelade
E. Mycotic lesions of hairs (microsporia, trichophytosis, favus)

4. Which clinical form the pelade areata does not has:

A. Focal
B. Total
C. Universal
D. Band-like or ophiasis of Celsius
E. All of mentioned above is correct

5. At second stage of androgenetic alopecia by male pattern the following is observed:

A. Displacement of front hair line back
B. Thinning of hair in temporal areas in view of "M" letter and in parietal region
C. Diffuse loss of hair in central-parietal region
D. Presence of hairs between frontalis and central-parietal region only
E. Complete symmetrical pelade of frontalis-parietal area

6. Presence of area of "loosen" hairs is typical for:

A. Cicatricial alopecia
B. Stationary stage of alopecia areata
C. Progressive stage of alopecia areata
D. Conradi disease
E. Lupus erythematosus

7. Possible causative factors of progression of alopecia seborhoica include:

A. Genetic disposition
B. Endocrinal disorders
C. Malfunction of reproductive glands
D. Hypertrophy and hypersecretion of oil glands, change of quality of sebaceous matter
E. All of mentioned above is correct

8. What disease the focal alopecia should be distinguished with:

A. Pityriasis versicolor
B. Psoriasis
C. Syphilitic alopecia
D. Lice infestation
E. Herpes zoster

9. The indications for cryomassage are:

A. Alopecia areata (stage of regress)
B. Round-typed alopecia (progressive stage)
C. Herpetic injuries of skin of hairy part of head
D. Pseudopelada Brocq
E. Mycotic lesions of hairs (microsporia, trichophytosis, favus)

10. The cryomassage:

A. Calls a pathophysiological changes in skin
B. Improves the blood circulation and trophic of skin
C. Has antifungal properties
D. Has antibacterial effect
E. Restores the innervation of tissues

Task 1. The female patient of 34 years old had consulted with dermatologist with complains for enhanced loss of hair. *From anamnesis*: had affected about three months ago when suddenly appear at first one focus on the hindhead and after month – numerous focuses of alopecia on whole surface of head. The inheritance is clear. At dermatological examination the fact was discovered that alopecia focuses have rounded contours, size of 1-4 cm in diameter and located on whole surface of head. The skin in affected places is of normal color, the hair follicles have no pathological changes. The area of "loosen" hairs is discovered by periphery of focuses of alopecia. Nail plates are burned out, nycterine and fragile.

a) Determine the provisional diagnosis:
- **A**. Alopecia areata, focal form
- **B**. Alopecia areata, total form
- **C**. Alopecia areata, universal form
- **D**. Ophiasis of Celsius
- **E**. Alopecia areata, subtotal form

b) What diseases the differential diagnostics should be carried out with?

Task 2. The male patient of 19 years old is at outpatient medicine regarding to pelade. *From anamnesis*: had affected at first year of life, lost his hairs during two months from hairy part of head, body, as well as eyebrows. Patient had cured repeatedly in hospital stay and as outpatient curing but there was no positive effect from therapy having been implemented. No trauma or operations. The inheritance is clear. At dermatological examination the absence of hair on head, body, and extremities is discovered. Eyelashes and eyebrows are saved. The skin of hairy part of head has no fire and atrophy. Follicular apparatus is completely saved. Complete lamination of nail plates is discovered.

a) Determine the provisional diagnosis:
- **A**. Alopecia areata, focal form
- **B**. Alopecia areata, total form
- **C**. Alopecia areata, universal form
- **D**. Ophiasis of Celsius
- **E**. Alopecia areata, subtotal form

b) Determine the patient surveillance.

Task 3. The male patient of 43 years old is at outpatient medicine with complains for presence of focuses of pelade. *From anamnesis*: had affected 11 years ago when after severe bronchopneumonia during three weeks all hairs of the head and body as well as eyelashes and eyebrows have been lost. Patient had cured repeatedly in hospital stay and as outpatient curing. Had passed the course of endocrinotherapy (had intake per os of prednisolone according to the schedule during two months), the plasmapheresis, hemosorption, vasodepressors, and vitamins have been assigned but there was no positive effect from therapy having been implemented. *Unbiased*: the patient has absence of all types of hairs (on head, mentum, body, extremities, in inguinal folds as well as eyelashes, eyebrows and mustache) observed. The skin of hairy part of head is of normal color, with no evidences of fire and atrophy. Follicular apparatus is completely saved. The nail plates are burned out; the complete lamination of nails is observed on fingers of upper extremities.

a) Determine the provisional diagnosis:
- **A**. Alopecia areata, focal form
- **B**. Alopecia areata, total form
- **C**. Alopecia areata, universal form
- **D**. Ophiasis of Celsius
- **E**. Alopecia areata, subtotal form

b) Make a plan of examination of patient and give a prognosis regarding to recuperation.

Task 4. The male patient of 24 years old had come for visit of dermatologist with complains for presence of focus of pelade and enhanced loss of hair. There are no subjective sensations. It is known from anamnesis that the disease had begun from occurrence of two fine symmetrically located focuses of pelade which are slowly enlarged and interlocked between each other. Unbiased: there is a round focus of pelade of up to 4 cm in size with evidences of skin's atrophy without signs of fire is discovered on temporal-occipital region of the hairy part of head. The skin in area of affection

is of yellowish color, smooth, and easily folded. The follicular apparatus is destroyed.

a) What is the provisional diagnosis could be though about:
A. Alopecia areata, focal form
B. Alopecia areata, subtotal form
C. Alopecia areata, total form
D. Ophiasis of Celsius
E. Pseudopelada Brocq

b) What examinations should be carried out for clarification of diagnosis?

Task 5. The female patient at dermatological examination had got the "alopecia areata, focal form, progressive stage" diagnosis.

a) What diseases the differential diagnostics should be carried out with:
A. Pityriasis versicolor
B. Psoriasis
C. Lupus erythematosus
D. Syphilitic alopecia
E. Herpes zoster

b) Determine the policy of curing and preventive measures.

Answers for first level self-control questions
1 – D; **2** – B; **3** – A; **4** – E; **5** – B; **6** – C; **7** – E; **8** – C; **9** – A; **10** – B
Answers for second and third level self-control questions
1a – A; **2a** – B; **3a** – C; **4a** – E; **5a** – D

21 TOPIC

Peculiarities of skin in children of tender age

TRAINING AND EDUCATIONAL OBJECTS

- Determine the physiological and morphological characteristics of the skin, its appendages and mucous membranes under normal conditions and in various pathological conditions in children of tender age
- Set display of hormonal crisis and major skin diseases of newborns
- Learn the basic general and special methods of examination in children of tender age

TO KNOW:

- peculiarities of anatomical and histological structure of the skin, its appendages and mucous membranes of the oral cavity in children of tender age;
- characteristics of the functional properties of the skin in children of tender age;
- clinical varieties of pathophysiological changes in children of tender age (telangiectasia, mongolian spots, dark line, physiological jaundice, physiological erythema, etc.);
- clinical characteristics of the manifestations of hormonal crisis and major skin diseases in children of tender age;
- methods and principles of medical and preventive measures in case of skin diseases in children of tender age.

TO BE ABLE TO:

- properly collect past medical history and examine the newborn child;
- distinguish between the types of pathological conditions in children of tender age;
- analyze the clinical picture of the main skin diseases in children of tender age;
- carry out differential diagnosis of diseases that have similar clinical picture;
- prescribe a rational treatment in case of detection of skin diseases in children of tender age.

General state of the skin, its appendages and genital organs in new-born children

The skin of a healthy new-born child is red, covered with more or less thick layer of grayish-yellow tyroid oily viscous mass called *vernix caseosa*. It is available on the entire surface of the skin, but is most pronounced on the skin of face, ears, lower back, groin, armpit areas, and the back surface of the body. The composition of *vernix caseosa* includes modified epithelial cells, soluble esters and fats, cholesterol, eleidin, glycogen.

Hair-covering. Immediately after the birth, the major part of the child's skin is covered with soft pappus (*lanugo*), which comes off to the birth or in the first week of life. The head can be covered mostly dark thick hair coming down to the forehead.

Nails. Nails of the new-born children reach the fingertips, but their weaker development does not give grounds to speak of prematurity. Nails may be missing in premature children.

Umbilicus. Umbilical cord is mummified and separated by 6 to 10 days after birth at the junction of the mucous cord with abdomen skin. Blood vessels of the umbilical cord are obliterated only at the end of the third week of life.

Dilatation of capillaries (telangiectasiea, *teleangiectasiea*). Telangiectasia is registered in 50% of new-born children in the form of dilatation of both individual vessels and groups of capillaries at the level of the skin – this is the spot, like a flat hemangioma. Dilatation of blood vessels is a physiological phenomenon. These vessels are located mainly on the back of the head, forehead, nose, eyelashes and lips.

Mongolian, or blue spots (*taches bleues mongoliques*). Mongolian spots are not signs of pathology and have a tendency to self-extinction. Most often, they are located in the sacrum area, at least in the area of the shoulder blades and buttocks. These are more or less dark bluish non-infiltrates spots on which there is no hair and which do not disappear when pressing them.

Dark line *(linea fusca).* Often between the second and eighth, and most often between the third and sixth weeks of life the children have thin pigmented strip in the midline abdomen that covers the umbilicus, and self disappears in two or three months. Pigmentation on the white line of the abdomen (*lineae albae*) often occurs in a later age.

Physiological erythema of new-born children *(erythema neonatorum).* As one of the organs which directly experiences a variety of external factors, the skin of new-born child responds to them in the form of different manifestations. After removing of *vernix caseosa* skin of the new-born child is pale cyanotic, and after the first few breaths it turns bright red. In case of true *erythema neonatorum* skin of the whole body gets the color of boiled crawfish. Usually the erythema disappears on the third day of life, then there is a common skin peeling. Cyanotic color remains only on

the hands and soles. Erythema of new-born children is called *physiological inflammation of the skin of newborns*. Erythema – is a direct result of exposure to environmental factors, it is an adaptive response to a sudden change in the conditions of existence.

Physiological jaundice *(icterus neonatorum)*. A few days after birth (on the 2-4 day of life in 60-80% of children), the skin becomes yellowish. If the general condition of the child is not violated, then this yellow color does not matter. Yellowness reaches peaks within 2-3 days, and then weakens and disappears after a few days without treatment. It is believed that the cause of such condition is an increase of the level of bilirubin due to the destruction of red blood cells associated with the transition from placental to pulmonary routes of oxygen delivery in the body

Physiological peeling *(desquamatio neonatorum)*. Due to the increased development of the epidermis of the fruit within the last months of pregnancy, the skin peels off, losing the epidermal cells, which form part of the *vernix caseosa*. On the 3-5 days of age skin peeling gradually increases in the new-born child in the form of the delicate grayish flakes. It can last from two weeks up to 1-2 months.

Sebaceous ichthyosis *(ichthyosis sebacea)*. In the first days after the birth sebaceous glands of some children are intensely functioning at the expense of estrogens derived from the mother. Sebaceous matter dries quickly, in result of which soft and velvety skin of new-born becomes dry and dense. The process continues for about a week and ends in peeling. Thus, sebaceous ichthyosis is a peculiar condition of the skin, which is based on fast drying of the sebaceous matter.

Ichthyosis-like skin dryness. The skin of some children, mostly on the elbows, wrists, ankles, is rough, dry, pale, with cracks. This condition occurs in the second week of life, and has nothing to do with ichthyosis. In case of ichthyosis-like skin dryness the skin is changing from very soft to very rough, "thick".

Mouth and mucous membranes. During the first days of life the tongue of the new-born child is largely coated with white fur. Perhaps this is due to the start of the lactation, and fur has a tendency to disappear when the new-born child begins to drink water.

Frenulum of tongue. Frenulum of tongue of most new-born children is short and taut. It should be noted that the tongue does not take much part in the act of breastfeeding. This state is not a pathology, and requires surgical interference only in exceptional cases.

Genital organs. Foreskin in newborn boys is always tight to the balanus and can not be separated for several months, so it is unacceptable to attempt to pull it back. At the same time, the foreskin may be relatively long, with a narrow opening. There are no indications for genital mutilation in case of normal urination. In 98% of the boys testicle is in the scrotum. At birth labia majora of the girls are underdeveloped and interlabial space is opened.

Skin diseases in new-born children

Reference of children to a separate group of specific neonatal skin diseases is conditional. A significant number of these diseases, even though they start in the first three – four weeks of life, can be continued after the end of this period.

Laner's toxic erythema of new-born children *(erythema neonatorum toxicum, exanthema allergicum, urticaria neonatorum).* Toxic erythema of new-born children is observed in 20-50% of infants on the 2-3rd day of life, rarely earlier and even more rarely at a later period.

Its symptoms include red spots of various sizes, multiple and very close to each other, which sometimes merge into a field of considerable size. .

Scleredema of new-born children *(scleroedema neonatorum).* This is a form of edema of the skin and subcutaneous tissue. It develops between 2-4 days of life and even later. It is more common among premature children, but can occur in normal full-term children, especially after hypothermia. Pathological process on the skin reminds a normal swelling, but the skin is smooth and swollen, heavy, cold to the touch. When pressing, a pit forms on it.

Sclerema of new-born children *(sclerema neonatorum).* It is a severe disease characterized by diffuse thickening of the skin, where it does not swell and a pit is not formed when pressing. It is observed in weak premature infants in the state of dehydration. It is detected on the 3-5 days of life.

Clinically it is an induration of various parts of skin. The sole, palm and scrotum remain free from lesions. Skin is like a tight hard cold shell and is not taken into the fold. The face is like a mask in the affected areas, ankylosis is developing..

Subdermal (focal) necrosis of fatty tissue of new-born children *(adiponecrosis subcutanea neonatorum).* It is characterized by the appearance of limited dense infiltrates or nodes with thickness of 1-2 cm and a diameter of 1 to 6 cm, and sometimes with a size of the child's hand, in the subcutaneous tissue.

Sweating fever *(miliaria seu sudamina).* Sweating fever occupies the first place by frequency among the diseases of sweat glands. It is caused by increased secretion of sweat glands. It appears in the form of vesicular and papular rash.

Seborrheic dermatitis of tender age. It occurs on the 1 – 2 weeks of life and disappears under the influence of rational therapy not later than the third month.

Steadfast and persistent symptoms of seborrheic dermatitis include redness of the skin and minor peeling, with grayish-yellow greasy scales. Pathological process is localized at the initial stages in the folds, on the face and hair-covered part of the head, then takes a common character.

In case of the mild form of seborrheic dermatitis, external treatment with disinfectants and keratoplastic means is sufficient.

1. Indicate the characteristic reaction of the newborn skin to an external environment:

A. Swelling of the mammary glands
B. Mongolian spots
C. Physiological erythema
D. Cholecystic impetigo
E. All the above mentioned is true

2. Manifestations of hormonal crisis in newborn children include:

A. *vernix caseosa*
B. Swelling of the mammary glands
C. Salmon patches
D. Mongolian spots
E. All the above mentioned is true

3. Papillary dermis is most manifested in newborn children:

A. On face
B. On hands
C. On soles
D. On hands and soles
E. All the above mentioned is true

Task 1. On the fifth day after the birth the mother found dark bluish white non-infiltrated spots that do not fade when pressing on the shoulder blades and buttocks of the boy.

a) What disease the boy is suspected to have:
- **A**. Physiological erythema of new-born children
- **B**. Toxic erythema
- **C**. Mongolian spots
- **D**. Salmon patches
- **E**. Dark line

b) What is the doctor's tactics?

Task 2. On the background of vomiting and bowel movements 3-4 times a day the two-months child was revealed redness in the folds of the trunk and extremities. The hair-covered part of skin is bright red, infiltrated with marked peeling.

a) Which disease can be suspected:
- **A**. Exfoliative dermatitis
- **B**. Toxic erythema
- **C**. Seborrheic dermatitis
- **D**. Sweating fever
- **E**. Salmon patches

Task 3. In a maternity hospital on the third day of life the premature child has thickening of the skin on the face and legs, which spread to the hips, trunk and upper extremities in a day. The skin in the affected areas is like solid spanned cold shell and is not taken into the fold.

a) Determine the preliminary diagnosis:
- **A**. Scleredema
- **B**. Sclerema
- **C**. Adiponecrosis
- **D**. Subcutaneous oedema
- **E**. Scleroderma

Answers to the questions of the first level of complexity
1 – **C**; 2 – **B**; 3 – **D**
Answers to the questions of the second and third levels of complexity
1a – **C**; 2a – **C**; 3a – **B**

22 TOPIC

Skin neoplasms

EDUCATIONAL AND INSTRUCTIONAL OBJECTIVES

- To define skin blastoma among other dermatoses
- To detect classification and pathogenesis of skin neoplasms
- To analyze the course of different skin neoplasms
- To determine the tactical technique and treatment of skin neoplasms

TO KNOW:

- Possible implications and process of skin neoplasms occurrence;
- Classification of these diseases;
- Diagnostic techniques of skin neoplasms;
- The signs of skin precancerous metamorphosis in skin neoplasms with malignant course;
- The basic anatomical and histological changes of structural elements by skin neoplasms;
- The principles of precancer and malignant skin neoplasms treatment;
- The preventative measures of skin blastomas occurrence and precancerous metamorphosis to malignant neoplasms.

TO BE ABLE TO:

- Determine the basic microscopic blastoma developments – papule, bosselation, lump, ulceration, infiltration and cyst;
- The process of palpation, dermatoscopy and evaluation of results;
- Define histogenesis of skin neoplasms on the basis of microscopic picture;
- Distinguish benign and malignant skin neoplasms according to clinical features and nature of growth, finding out the possible implication and mechanism of its development;
- Determine the metastasis clinical features, explain its mechanism of development and possible ways of initiation (lymphogenous, hematogenous, perineural);
- Prognosticate sequellae of benign and malignant skin neoplasms.

Epidemiology. Special group among dermatoses consists of blastomas, by means of its pathological processes variation, which may develop primary or as the result of metastatic disease. Malignant skin neoplasms are instrumental among human blastomas and inferior only to pulmonary mass. Women and men get sick in like manner, preferentially late in life.

Pathogenesis. The causes of skin neoplasms occurrence totally and particularly are not investigated. Skin neoplasms develop as a result of hypernormal regenerative process, hyperplasia, proliferation and metaplasia of the skin cells. This is the most pressing multifactorial theory of neoplasm occurrence, which takes into account the impact on various skin mutations.

There are defined the following risk factors of skin neoplasm development:

- physical: insolation (in nowadays is regarded as the main carcinogen) – from 90% of occasions the skin neoplasm are arising in open areas, ionizing and X-ray radiation, processing carcinogen (coal, coal tar, asphalt, arsenic), smoking;
- Nonspecific skin pathological processes with regeneration phenomenon.
- ***Immunodeficiency disorders***: HIV infection, protracted of immunodepressant admission after Major Organ transplant and etc.;
- ***Virus***: human papilloma virus (NRV), particularly the development of epidermodysplasia verruciformis associated with the 5th and 8th type NRV, skin carcinoma of external genital and perianal area – with a 16-m and 18-m type NRV;
- ***Inherited***: susceptibility to hyperkeratosis, the availability of multinomial nevi, and others;
- ***Anthropometric***: white skin, red or blond hair, blue or grey eyes;
- Aging.

Classification

1. Precancer

Facultativus pre-cancer – skin diseases, during the process of provided timely treatment of skin neoplasms with malignant course which is seldom developed. Among these are cutaneous horns, keratoses, neoplasms with benign course (papillomas, fibromas, adenomas, molluscum sebaceum), vascular and pigmented nevi, chronic skin inflammation, post-burn scars, etc.

Obligate precancerous – are neoplasms of the skin, which always assumes the malignant course. Among these are xeroderma pigmentosum, Bowen precancerous dermatosis, erythroplasia of Queyrat, Paget's disease.

2. Benign neoplasms of the skin

3. Malignant neoplasms of the skin:

- Basal cell carcinoma (basalioma);
- Squamous cell carcinoma (epithelioma spinocellulare);
- Metastatic cancer;

- Melanoma;
- Sarcoma cutis

FACULTATIVUS PRE-CANCER AND SKIN NEOPLASMS WITH (MALIGNANT) BENIGN COURSE

Actinic keratosis

Actinic keratosis – skin pre-malignant condition characterized by reduced thick hyperkeratosis on skin segments which are usually undergo insolation.

Epidemiology. The disease progresses more frequently in middle-aged white people, in response of constant long-term impact on insolation.

Clinic. There are appeared small flat plaques grayish-yellowish of round or oval shape with a rough surface on facial skin, neck and upper extremities. They bloom to the skin surface and might be individual (solitary) and multiple. In due course time, neoplasms become sealed, by the forcible separation of scales where might appear drops of blood. Actinic keratosis is supervened by pruritus. Neoplasm does not subside individually. In case of constant trauma or irrational treatment can be transformed into a malignant neoplasm.

Pathomorphology. While histologic examinations are defined irregular proliferation of malpighian layer, acanthosis and hyper parakeratosis, separate sections of papillomatosis. Malignant transformation of keratomas is supervened by signified atypical cells, mitosis activation.

Differential diagnostics. Actinic keratosis should be differentiated with seborrheic keratosis, Bowen's disease, verruca Vulgaris.

Treatment and preventative measures.

It is recommended to use sun-protection creams on open skin areas. Ectylotics might be used only in the incipient stage of senile keratomas development and beyond the cryodestruction. Formed neoplasm is removed surgically, usually administered the neodymium laser beams, cryodestruction. Good prognosis.

Seborrheic keratosis

Seborrheic keratosis – is a benign epidermal skin neoplasm which consists from cells of epidermis basal layer or keratinocytes or just a superficial part of the follicle.

Epidemiology. Seborrheic keratosis is predominantly exposed in older age (50 years). Blastoma is appeared on haired skin areas rich by sebaceous glands.

Clinic. It is clinically occurred by yellow-brown macules of small-sized. Macules may increase in size and acquire its multiple character. The macules surface with fatty crusts, which are easily removed. Seborrheic keratosis is rarely malignized. In process of dermoscopy signs of degeneration into a malignant neoplasm are absent.

Pathomorphology. While histologic examinations are defined: papillomatosis, acanthosis, proliferation of epidermis basal cells (basaloids), corneal cysts; melanin concentrations.

Diagnostics. The diagnosis assessment is based on clinical implications, histological changes, the results of dermatoscopy. Seborrheic keratosis should be differentiated with simple warts, melanocytic nevi, melanoma, carcinoma basal cell, senile (solar) keratosis nummular papule.

Treatment. In therapeutic interventions are used cryodestruction and / or curettment, laser therapy, radio-wave deletion. Good prognosis.

Cutaneous horn

Cutaneous horn – is a skin precancerous condition which is characterized by epithelial formation from the cells of spinous layer of epidermis. This pathology is determined as a variant of senile keratosis.

Epidemiology. The disease more frequently progressed in people of white race and localized preferentially in the areas of permanent trauma.

Clinic. Clinically the process is displayed by a horn-shaped in size from a few millimeters to a few centimeters. Cutaneous horn consists of indurated pressed keratin.

The course of cutaneous horn is benign, malignancy rarely occurs.

Pathomorphology. While histologic examinations are defined: signified hyperkeratosis, acanthosis and granulomatous disease.

Diagnostics and differential diagnostics. Cutaneous horn should be differentiate with squamous cell carcinoma, senile keratome, seborrheic keratosis.

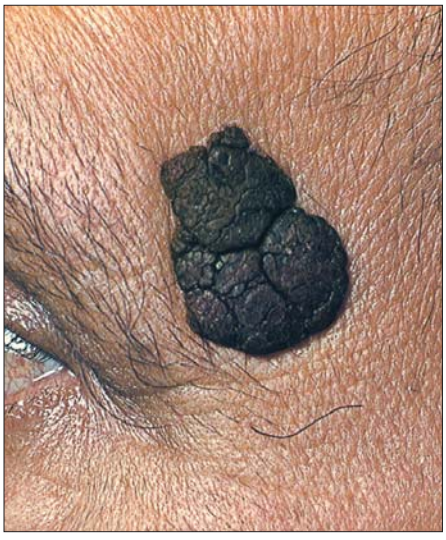


Fig. 22.1. Seborrheic keratosis.



Fig. 22.2. Cutaneous horn.

Treatment: Cutaneous horn should be differentiated from horny molluscum sebaceum types, within the bounds of healthy tissue by aggressive approach, cryodestruction, electroscission. Good prognosis.

SOFT FIBROMA

Soft fibroma – is a neoplasm of connective tissue with benign course.

Epidemiology. It is usually occurs for women.

Clinic. The formation has a soft texture, round or oval shape, different size, pink or dark brown colour. Soft fibroma is placed pedunculated. The skin is wrinkled. The blastoma is usually single, rarely multiple. It has sacculated type, often localized on neck, on the front part of the chest, back, on retromuscular and inguinal folds.

Pathomorphology. While histologic examinations were defined: assembling of posterior pyramid of collagen fibers, which are placed between the intercellular substance and cells of fibroblastic line. Elastic fibers are absent. There is defined atrophy of the epidermis and the growth of connective tissue. Fibroma is clearly distinguished from the surrounding dermis.

Diagnostics and Differential diagnostics. The disease is diagnosed on the basis of definitive histological changes. Soft fibroma should be differentiated with fibropapilloma and papillomas.

Treatment. For treatment of soft fibroma are usually used surgical removal and electroscission. Good prognosis. After removal this neoplasm does not anticipate.

Dermatofibroma

Dermatofibroma – is a benign neoplasm of skin connective tissue, which often occurs on extremities in the form of intradermal site reminded button.

Epidemiology. It is usually occurs for women.

Clinic. It is clinically occurred by the presence of nodules (solitary, rarely multiple) round, dense texture and dark brown form. It has a smooth surface. Size – 0.2-1.5 sm. In palpation is developed a hard «button», fixed within the bounds of the skin, which is moved along the subcutaneous fat layer. On impact between two fingers is formed pouch of low rate surrounding skin.

Pathomorphology. While histologic examinations were defined: accumulation of mature and young collagen fibers disposed in a different direction, fibroblasts and a large number of small capillaries, perivascular edema.

Diagnostics. Diagnosis is based on clinical and histological examinations. Dermatofibroma should be differentiated with melanoma (applying the method of dermatoscopy) dermatofibroma, xanthomatosis, seborrheic keratoses, Kaposi's sarcoma, cicatricial keloid.

Treatment. In the experiment were used surgical treatment, electroscission, cryosurgery. Prognosis: The neoplasm is indolent – from several months to a year.

Keratoakantoma

Keratoakantoma – is a benign blastoma of the epidermis, which is developed from the sebaceous glands and hair follicles and characterized by a hemispherical lump with a crater hole in the center, filled with horny masses. Keratoakantoma can be paraneoplastic development of internal organs neoplasms.

Epidemiology. It occurs predominantly for elderly people on facial skin, neck, extremities rarely on other skin areas.

More than in twice times occurs predominantly for white men older than 50 years.

Etiology. The etiology is acritical. It holds out the prospect about nature of viral disease, in particular due to human papilloma virus of type 9, 16, 19, 25 and 37. Potentially possible unfamiliar character with autosomal dominant inheritance.

Clinic. Clinically keratoakantoma is characterized by presence of dense hemispherical exophytic blastoma up to 20 mm in diameter with a crater-hole depression in the center, covered with horny masses of gray-brown color, which can be easily removed. The lips of neoplasm are wedge; the skin texture on them is smoother. The blastoma has the ability to rapidly progressive growth, but can have predilection to spontaneous regression.

Pathology. In the process of histopathlogical examination in the material are detected such processes as hyperkeratosis, parakeratosis, dyskeratosis and pseudocarcinomatous hyperplasia of epidermis. In contoured section of keratoakantoma epidermis is thickened and pressed by means of crater filled with horny masses. Two-dimensional epithelium strands from thorny layer cells penetrate deep to the dermis, destroying the basement membrane.

Diagnostics. Keratoakantoma should be differentiated with actinic keratosis, common warts, cutaneous horn, giant molluscum contagiosum, basal cell carcinoma, highly differentiated squamous cell carcinoma of the skin.

Treatment. There are represented surgical treatment (excision) electroscission, laser therapy and cryosurgery.

Prognosis. In some cases the blastoma has the predilection to malignant transformation.



Fig. 22.3. Keratoakantoma.

Hemangioma

Hemangioma – is a benign blastoma formed from blood vessels.

Epidemiology. It usually occurs for 1-2% of children. Generally, people of white race are sick.

Clinic. Hemangioma is localized on any parts of the skin area. The clinical picture depends on process development stage. There is a small red spot or papule, in the phase of proliferation, which grows in size also is potentially prospective the formation of ulcers, bleeding. In the stabilization phase of hemangioma growth rate decreases, the color becomes less intense; there are small patches of pullulation of connective tissue in blastoma. In the phase of regression can occur complete spontaneous resorption or fat connective tissue replacement of blastoma cells with saving of cosmetic defect.

Pathomorphology. While histologic examinations were defined vascular endothelial cell proliferation, expansion of the lumen of the capillaries, increasing its quantity.

Diagnostics is based on anamnesis, physical examination, palpation, ultrasound investigation, angiography, magnetic resonance imaging, dermoscopy.

Hemangioma should be differentiated from lymphangioma, on the surface of which are observed small grouped vesicles and cavernous form are followed by diffuse cutaneous dropsy and flat pigmented mole that have a dense texture and dark brown staining.

Treatment. The method selection depends on age and baby's condition, blastoma localization and phase of its development. It is suggested the erasion by method of electro and criosurgery or chemical sclerotherapy. The courses of hemangiomas are benign in the majority of cases.

Lymphangioma

Lymphangioma (lymphangioma) – is a benign neoplasm from the lymphatic vessel (congenital abnormality of lymphatic vessel), which is localized on any parts of skin areas.

Epidemiology. It is usually occurs for white women.

Clinic. Clinically are characterized isolated capillary (simple), cystic and cavernous lymphangioma. Simple lymphangioma has bumpy surface and fuzzy boundaries. In case of cavernous form the intumescence is expressed and has a soft texture. The skin over lymphangioma is not changed. In this segment the skin is thinning and cyanotic. On palpation appears the feeling of fluctuation

Pathomorphology. While histologic examinations were defined the proliferation of lymphatic vessels, the expansion of the lumen of the capillaries, increasing its quantity.

Diagnostics. Diagnostics is based on clinical performance, X-ray radiography and histological examinations. Lymphangioma should be differentiated with cysts, squamous cells, lipoma, spinal hernia, teratoma and lymphadenitis.

Treatment. In the process is represented surgical removal, sclerotherapy, radiofrequency coagulation, electrocautery. The absence of lymphangioma treatment may lead to significant recurrent deformation of soft tissues and bones of maxillofacial area, serious violations of breathing and ingestion for localization on the neck. There are not observed any metamorphosis into malignant neoplasms.

NEVI

Nevi – are benign congenital abnormality. Their origin is connected with the migration of melanocytes in fetal life from neuroectodermal tubes (neural crest) in the basal layer of epidermis of the embryo. Any melanocytes do not reach the epidermis and remain in dermis.

The huge varieties of nevoid neoplasms have almost 90% of people in number from three to one hundred, and its number increases with age. They are congenital and acquired, appear from pinafore stage of existence and save to an extreme old age.

There are clinically distinguished the following types of nevi: melanocytic nevus, congenital melanocytic nevi, dysplastic nevi, Melanosis circumscripta praeblastomatosa Dubreuilh, congenital vascular nevi, nevus of connective tissue.

Nevocytic nevus

Nevocytic nevus – is a benign skin neoplasm. It is formed as a result of proliferation of melanocytes accumulation.

Epidemiology. It is often formed for representative of white race (on average, every adult has up to 20 of these nevi).

Clinic. There are distinguishing only a few clinical types of melanocytic nevi:

1. Epidermic-dermic nevi – flat, slightly raised, brown or suntan. Usually occurs for children. There are located on palms, soles, genitals.

2. Compound nevi – are pigmented papules. Pigment cells are located on the boundary of the epidermis and dermis, and in the dermis, they are irregularly shaped, symmetrical, their surface is smooth or slightly bumpy with a pigmented center.

3. Intradermal nevi – are papules with moderate spotty pigmentation, on a surface of which are increasably marked increase of hair growth Nevi cells are diffusely located or by way of assumption in the lower parts of epidermis and on the border with the dermis reticular layer .

4. Spotted nevus – is a stain of bronze or light brown color. On its background are a huge number of small monomorphic papulous nevi of dark brown colour.

5. Blue nevus – single blue spots or dense hemispherical papules with dimensions from 0.5 to 2 sm. on head, neck, buttocks. The blue color is associated with rich

melanin (melanocytes) located in deep layers of the dermis. The consistency is dense. Blue nevus does not ail the patient, grows slowly in size, why it keep unnoticed so long.

6. Galonevus (Sutton disease) has a hypopigmentation by means of collar around the pigmented nevus.

Pathomorphology. While histologic examinations were defined increase of melanocytes in the basal layer of the epidermis, in the lower layers of the dermis, around skin appendages.

Diagnostics. Nevocytic nevus should be differentiated with malignant melanoma, hemangioma, basal cell carcinoma, seborrheic keratome.

Treatment. Nevocytic nevi do not require treatment. Surgical removal can be made in cases of traumatic location, signs of malignancy or the presence of a cosmetic defect. Prognosis most of melanocytic nevi is favorable.

Congenital Melanocytic Nevus

Congenital melanocytic nevus (naevus pigmentosus et pilosus), synonyms: Congenital nevocytic melanocytic nevus, giant pigmented nevus, giant hairy nevus – is a benign pigmented neoplasm from nevocytic melanocytes of newborn infants.

Epidemiology. The representatives of the male and female sex of any race such kind of nevus occurs with equal frequency. Large nevi are found in a ratio of 1 to 20,000 of newborn infants

Clinic. Congenital melanocytic nevus is resulted of violation of melanocyte differentiation during intrauterine growth. There were observed plaques and shapes of different sizes on any parts of the skin, light or dark brown color, with a soft texture, protruding the level of the skin, often covered with thick hair. With growth of child the plaque proportionally increases, reaching the large-sized and covering a significant part of the soma, neck and other parts of body. The surface of the nevus in the majority of cases is rough, warty, with deep cracks in the skin.

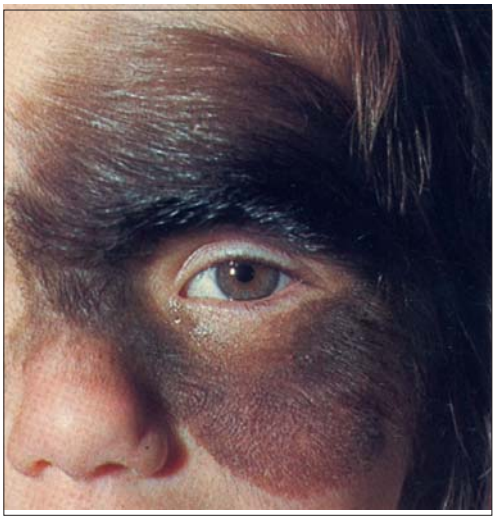


Fig. 22.4. Congenital Melanocytic Nevus.

The possibility of malignant transformation extends to all congenital melanocytic nevi, irrespective of their size. The risk of melanoma development intra vitam comprises 6-12% for giant congenital melanocytic nevi and 1.5% – for the small ones.

Pathomorphology. While histologic examinations can be defined an increase of melanocytes number in basal layer of

the epidermis, in lower layers of the dermis, around the skin appendages, accumulation of them as layers, alveoles or bands.

Diagnostics. Do not withhold the difficulties because of anamnesis and typical clinical picture.

Treatment. There is represented the surgical exsection in cases of trauma or observation.

Dysplastic nevus

Dysplastic nevus (*naevus dysplastica*), synonyms: Clark nevus, abnormal spiloma – it is acquired pigmented neoplasm.

Epidemiology. Dysplastic nevus is observed in 5% of white population. It is almost defined for all patients with familial melanoma and for 30-50% of patients with sporadic melanoma. Men and women are homochronous sicked.

Clinic. Dysplastic nevus occurs on unaffected skin, or as a component of a complex nevocytic nevus. These nevi appear intra vitam. They clinically appear by the process of skin uneven pigmentation from black-brown to red-pink with a dark area in the center of the tumor. Nevus has no clear boundaries, irregular shape, often localized on the back, legs, scalp, chest, buttocks and genitals.

Pathomorphology. While histologic examinations were defined disordered proliferation of polymorphic atypical (large-sized, polymorphism, and hyperchromasia of cores) melanocytes.

Diagnostics. Dysplastic nevus is diagnosed on the basic of clinical performance combined with epiluminescence microscopy and results of microscopic examination.

Treatment. Surgical removal.

Precancerous Dubreuil's melanosis

Precancerous Dubreuil's melanosis is nevoid skin disease predominantly of seniors and regarded to pre melanoma dermhelminthiasis.

Epidemiology. The disease occurs for people over 60, in more often than for women.



Fig. 22.5. Congenital vascular nevus.

Clinic. ***It is*** clinically characterized by the appearance of a single light-brown spot to 4-5 sm. or more in diameter with irregular polycyclic edges without packless of foundation.

The stain is gradually increased in size, gains on dark brown color, after black.

Within the limits of pathologic focus can exist areas of different colors side by side with depigmented (spontaneous regression of lesions). The most frequent localization – open body areas. For Precancerous Dubreuil's melanosis and his (75%) transformation into malignant melanoma. It is clinically presented by a significant growth, change color (to black), the appearance of lumps and papillomatous proliferation with focal hyperkeratosis, atrophy areas, the mass of erosions and hyperemias around the exposure of diseased area.

Diagnostics. Diagnostics of pigmented nevi is based on clinical presentation, anamnesis, dermoscopy, cytological and histopathlogical examinations. A biopsy is contraindicated. Removed nevus must become material for histopathlogical examination.

The differential diagnosis is primarily realized with melanoma, pigmentary basal-cell, hemangioma, seborrheic keratome.

Treatment. It is used a wide surgical excision in the range of healthy tissue, obliteration regional lymph nodes, roentgenotherapy.

Nevi, which are often injured or irradiated by sunlight, have been surgically removed or used cryo-or laser destruction. It is also performed for cosmetic purposes.

Preventive measures. All people who have such pigmented nevi should be at regular monitoring. It is important to avoid excessive sun exposure and trauma of nevis neoplasms. At the slightest sign of metamorphosis (rapid growth, color change, the appearance of inflammation, subjective symptoms, erosions, ulcers, nevoid satellites, the increase of regional lymph nodes) which is required in radical therapy.

Vascular nevi

Vascular nevus – congenital malformations of blood or lymph vessels of permanent nature (except nevus Unna). They can be combined with vascular malformations of eye and the meninges.

Epidemiology. Represented at 0.3% of newborns.

Etiology. The cause of vascular nevi onset is not determined.

Clinic. Nevi have pink-red or purple color. There are distinguished the following clinical forms:

Unna nevus (congenital telangiectasia neck); Sturge-Weber disease (a combination of blazing nevus in zone of trigeminal nerve innervation with deformities of eye vessels and meninges development);

Klippel-Trenaunay-Weber syndrome (a combination of naevus flammeus with vascular malformations of the soft tissues and bones);

Cobb syndrome (naevus flammeus in the vertebral region in combination with vascular malformations of spinal cord).

Pathomorphology. While histologic examinations can be defined primary neurodystrophy and secondary u angiopathy.

Diagnostics. Diagnostics is based on clinical symptoms and instrumental and histologic methods of examination. Vascular malformations should be differentiated with hemangioma, angiokeratoma, lupus erythematosus and limphemangioma.

Treatment. The main methods of treatment of vascular nevi are cryosurgery, electrocautery, sclerotherapy, method of selective photothermolysis. Prognosis is good.

Connective tissue nevus

Nevus connective tissue – is a skin hamartoma, which primary consists of collagen (collagenoma), elastin (elastomers) or from both simultaneously.

Epidemiology. It usually occurs for men of old age.

Clinic. There are clinically represented by the presence of clinically asymptomatic papules or plaques. They are located around the genitals, palms, nailfold, mucous membranes, has yellowish color.

Pathomorphology. While histologic examinations are revealed dense aggregates of collagen and elastic fibers.

Diagnostics. Diagnostics is based on clinical symptoms and instrumental data (dermatoscopy) and histological (biopsy) studies. Connective tissue nevi should be differentiated with scleroderma, dermatofibroma, xanthoma.

Treatment. The examination of connective tissue nevus represents the surgical removal or observation. Prognosis is good, but in some cases is possible malignant transformation.

OBLIGATE PRECANCEROUS XERODERMA PIGMENTOSUM

Xeroderma pigmentosum (it is innate chronic skin disease that is characterized by high sensitivity to ultraviolet ray, inherited by an autosomal recessive manner.

Clinic. Xeroderma pigmentosum is clinically manifested by erythema, pigmentation, swelling of the dermis, hyperkeratosis, fissures, ulcers, warty growths, lesions of atrophy, telangiectasia particularly on areas of the skin exposed to solar irradiation.

Treatment. Radical methods of therapy do not exist; it is recommended continuing the use of sunblock cream. It is also used an aromatic retinoids. On the stage of appearance of keratinization and tumor formations are recommended surgical excision, cryosurgery, diathermocoagulation.

Bowen's disease



Fig. 22.6. Bowen's disease.

Bowen's disease – is a skin neoplasm, which develops from keratinocytes and occurs on different parts of the skin.

Epidemiology. Men and women over 20 years are often affected.

Clinic. The neoplasm is clinically occurred solitary, rarely multiple plaques with brownish-red of irregular shape with size from 2 mm to a child hand.

The plaque surface may be covered with squamas and serosanguineous scabs; the atrophy may occur. After removing the scabs which cover plaques the velutinate surface remains. In other cases the plaques are covered with warty growth. The tumour is often localized on the body, arms, in perineum, rarely on genitalia mucous. .

The tumour progress is slow and usually results in squamous cell cancer.

Pathomorphology. The histological changes in the epidermis are represented by clear hyperkeratosis, parakeratosis and acanthosis. The cells of spinous layer are placed chaotically, there are many atypical cells with hyperchromic nuclei.

Diagnostics. Diagnosis of the Bowen's disease is based on clinical findings and histological examination. Differential diagnostics is made with the microbial eczema, tuberculosis cutis verrucosa, basalioma, metastatic cancer.

Treatment. For Bowen's disease there is mainly a surgical treatment; laser treatment and cryolysis are also applied.

Erythroplasia of Queyrat



Fig. 22.7. Erythroplasia of Queyrat.

Epidemiology. Elderly men are often affected.

Clinic. On the balanus, rarely on the foreskin, a bright red plaque with clear boundaries and the diameter of 2-5 cm appears. The tumour surface is velutinate or bright and humid, sensitive on palpation. In 30% of cases erythroplasia transforms into squamous cell cancer.

Pathomorphology. Histological and cytological findings correspond to the changes on Bowen's disease.

Diagnostics. Diagnostics is based on clinical findings and the results of histological and cytological research. Erythroplasia of Queyrat shall be differentiated with hard chancre, candidal balanoposthitis, squamous cell cancer.

Treatment. In case of foreskin affection genital mutilation is reasonable; if the erythroplasia is localized in the balanus area the cryolysis is recommended.



Fig. 22.8. Paget disease.

Paget disease

Paget disease is an intraductal breast cancer which develops in the mouth of output galactophorous ducts. Paget disease is connected with chronic inflammatory processes in mammary gland. Peget cells are also supposed to originate from sweat and oil glands.

Epidemiology. Women at the age of 40-70 years old are the most often affected. Its feature is the long-term progress for several years.

Clinic. Clinical peculiarities are the occurrence of dry scabs, cracks, surface erosions near the nipple, madescence. Itchiness, sometimes pain disturb the ill people. Further the nipple becomes flat, then inverted. When the pathological process is spread over the mammary gland tissue the tumour-like nodule appears and lymph nodes get larger.

Paget disease may occur on such skin areas which have apocrine sweat glands. If the Paget disease is localized near the nipple it should be differentiated with nipple eczema, nipple chronic non-specific disease, adenoma, tuberculosis, in other area it should be differentiated with eczema, sscrapie.

Pathomorphology. Paget cells are detected histologically in basal layer. They are large cells with light cytoplasm, large nucleus, absence of cytoplasmic tectum.

Diagnostics. The diagnosis is confirmed on biopsy and immunohistochemical analysis.

Treatment. Treatment of Paget disease is mainly surgical with compulsory histological control over the cut off edge of the tissue. If there is a tumour-like nodule the disease is treated as cancer of the corresponding stage.

SKIN NEOPLASM WITH MALIGNANT PROGRESS

Skin neoplasms with malignant progress are basal cell carcinoma (basalioma), squamous cell cancer, melanoma, fibrosarcoma.

Basal cell carcinoma

Basal cell carcinoma (*carcinoma basocellulare*), synonyms: basalioma, rodent ulcer, carcinoid of skin, basal cell epithelioma, basal cell cancer, *ulcus-rodens;* is a skin neoplasm with malignant progress, originated from epithelium basal cells.

Epidemiology. Basal cell carcinoma is the most widespread disease which makes up 75-90% всех of all cases of skin cancer. It is similar to cancer by typical infiltrative progressive growth, often with destruction; it is similar to benign tumour by absence of metastasis. Basilioma occurs mainly in elderly age and is localized mainly on face.

Clinic. Clinical findings distinguish five forms of basiliomas: surfacial, sclerodermal, tumoral, nodular ulcerous and pigmental (pagetoid) basilioma. The latter causes atrophy in the center of tumour and a row of small solid pearl nodes along the boundary. Such form of basilioma is prone to peripheral growth.

Surfacial basalioma is located mainly on the body skin. It is represented by a limited round/elliptic focus with a thin, quite solid spindled ring which consists of waxy small solid pearl-bright nodes. The rings turns white in the process of diascopy. There is a depression in the center of neoplasm. Basilioma can be single, rarely multiple.

An ivory black plaque with waxy shine and elevated edges is typical of *sclerodermal basilioma*.

Tumoral basilioma is globular, from lens-size to pea-size. The tumour surface is smooth, the center is sometimes covered with grayish scales.



Fig. 22.9. Basal cell carcinoma.

Nodular ulcerous basiloma may be primary or may originate from the further development of tumoral or surfacial basilioma. A small crater-like ulcer with a solid woody basis beyond its boundary is typical thereof.

Diffusive pigmentation is typical of *pigmental basilioma*.

Pathomorphology. Histological research detects tumoral cells which look like epidermis basal layer cells but differ by absence of intercellular processes and large heavy coloured nuclei.

Diagnostics. Diagnostics of basal cell carcinoma is based on clinical findings, cytological and histological research, epifluorescent dermatoscopy

Basalioma shall be differentiated with discoid lupus erythematosus, Bowen's disease, acanthoma verrucosum, melanoma, actinic keratosis, acantholytic nevus.

Treatment. Surgical, radiological and medicamental methods are applied. There is favourable prognosis for basalioma, recurrences meet rarely.

Squamous cell carcinoma

Squamous cell carcinoma (*carcinoma planocellulare*), synonyms: planocellular epithelioma, spinocellular cancer, epidermoid cancer, spinalioma, skin invasive primary cancer; is a skin neoplasm with malignant progress, originated from skin and mucous keratinocytes.

Epidemiology. Men older than 50 years old are the most often affected.

Clinic. Squamous cell cancer is a neoplasm with the most malignant progress from all epithelial tumours. It is localized on any skin areas, mainly on the opened ones, and in borders between skin and mucous (in genitalia, lower lip, nose, anal canal). There are two clinical forms of the squamous cell carcinoma: infiltrative ulcerous and papillar.

In the *infiltrative ulcerous form* first a small nodule arrears, having smooth surface or covered with hyperkeratotic layers. The nodule growth quickly, in its center an ulcer appears with rough bleeding bottom, often covered with haemorrhagic scab. In case of *keratinizing squamous cell carcinoma*, hand-glass may detect yellowish spots in the bottom – the focus of keratosis (cancroid corpuscles). The ulcer is surrounded by a solid spindle based on the solid woody infiltrate (invasive part of neoplasm) beyond its boundary.



Fig. 22.10. Squamous cell carcinoma.



Fig. 22.11. Squamous cell carcinoma.

The warty growths which look like papillas in the bottom of ulcer are typical of *papillomatous form*. They grow quickly and rise over the skin level. Squamous cell carcinoma metastasizes into the regional lymph nodes and other organs. The lymph nodes are solid, painless, immobile and fixed with each other and with the surrounding tissues.

Pathomorphology. From the histological point of view there are keratinizing and non-keratinizing squamous cell carcinomas In case of *keratinizing squamous cell carcinoma* there are epitherlial tenias, expressed polymorphism, discomplection and diskeratosis of certain cells (keratoid pearls). In case of *non-keratinizing squamous cell carcinoma* the cells with hyperchromic nuclei prevail, nest-like layers of epithelial cells flake away from the epidermis, keratosis is slight or absent at all.

Diagnostics. Diagnosis of squamous cell cancer is based on clinical diagnostics, results of histological research and instrumental research (biopsy, vitropression).

Squamous cell cancer shall be differentiated with solar keratosis, basalioma, keratoacanthoma, Paget disease.

Treatment. Surgical, radiological and medicamental methods are applied.

If there are no metastases and in case of early detection the squamous cell cancer is treated nearly in 80-90% of cases.

Melanoma

Melanoma (*melanoma malignum*), synonyms: malignant melanoma, melanocarcinoma, melanoblastoma, melanocytoma, neurocarcinoma; is a skin neoplasm with malignant progress, originated from melanocytes (pigmentary cells) which produce melanin.

Epidemiology. Melanoma is one of the most malignant human neoplasms due to quick growth and rapid metastasis by haematogenous and lymphogenous means. Skin is the most often affected (87–90% of cases). The most malignant progress is typical for melanoma among men, young men and youth.



Fig. 22.12. Melanoma.

Etiology. Cause of melanoma as well as of all malignant neoplasms is not defined.

Clinic. Melanoma may occur in different parts of the human body.

Clinical findings distinguish four clinical and anatomic forms: surfacial, nodular, acral lentiginous and mucous melanoma, sort of malignant lentigo.

Intraepidermal surfacial melanoma has two phases of development. The first phase is the horizontal radial spreading of brown plaque, absence of tumoral cell invasion in the derma reticular layer. It has favourable prognosis. The second phase, *nodular melanoma,* occurs in 15% of cases. Melanoma has a shape of flat cyanochrous nodule rising over skin level; it rarely has a form of pedunculated polyp. *Acral lentiginous and mucous melanomas* make up 10% of all melanomas and affect mainly people of elderly age. The tumour has rough black edges.

The fourth form, *malignant lentigo* (melanotic freckles) is very rare, affects mainly people over 60 years old. Multiple small nodules (diameter of 1.5–3 mm) with colour ranged from yellow to black appear on skin.

Pathomorphology. Melanoma has verified histological structure. The most typical features are the expressed polymorphism of chromogenic cell elements, their non-typicality. The tumour consists mainly of round, cubical or polygonal cells which look like epithelial ones.

Diagnostics. The basic methods are anamnesis, clinical examination, palpation of peripheral lymph nodes. Dermatoscopy, tumour thermography, cytological research, radioisotope scanning are held. Melanoma should be differentiated with pigmentary basilioma, seborrheic keratosis, haemangioma, pyogenic granuloma and angiofibroma. In case of suspecting of melanoma biopsy is not allowed.

Treatment is surgical**.** Chemical therapy, immunotherapy (with using interferon alpha, interleukine-2), hormonal therapy are applied..

Preventive measures. Preventive measures suppose elimination or limitation of impact of ultraviolet rays, ionizing radiation, electromagnetic irradiation, chemical cancerogenes, avoidance of nevi traumatization.

Kaposi's sarcoma

Kaposi's sarcoma is a malignant multifocal disease, probably of tumoral nature, which occurs in derma and originates from blood and lymph vessels. Focus is localized mainly in distal parts of arms and legs.

Epidemiology. Persons of male sex are the most often affected.

Clinic. Clinical findings distinguish several stages. *The spotty stage* is featured by separate reddish



Fig. 22.13. Kaposi's sarcoma.

cyanochrous or reddish brown spots of irregular shape, with smooth surface and with diameter of 1–5 cm. At the *popular stage* the tumour has a spherical or hemispherical shape with diameter of 2 mm – 1 cm, the colour is ranged from pink to reddish cyanochrous with brown shade, the tumour has solid elastic consistence. At the *tumoral stage* there are multiple nodules with diameter 1–5 cm. The nodules may merge and ulcerate. Lymph nodes are increased.

There is also *AIDS-associated* sarcoma.

Classical Kaposi's sarcoma may have a long-term process and a reversive character. AIDS-associated type has disseminated and malignant progress.

Pathomorphology. Patohistological research of the affected skin biopsy sample detects a chaotic incomplete angiogenesis, proliferation of spindle cells, outgrowth of granulating tissue of different maturity degree infiltrated by immune competent cell (lymphocytes, plasma cells and macrophagocytes). At the primary stage the capillary vessels with wide lumens overgrow in the upper layer of derma. Endothelial cells are increased, extended, the nuclei are hyperchromic and have irregular form.

Diagnostics is based on clinical findings and the results of histological research.

Kaposi's sarcoma shall be differentiated with Kaposi's pseudosarcoma, haemangioma, pyogenic granuloma, high differentiated agniosarcoma.

Treatment. Treatment of Kaposi's sarcoma is not always effective; the existing means (radial means, cryotherapy, chemical therapy) cause only temporary remission. X-ray radiation is used for large or painful foci. Visible therapeutic effect during the disease progress occurs only after systematic use of prospidinum and cytostatic agents.

Fibrosarcoma

Fibrosarcoma is a neoplasm from the fibrous tissue with cancerous progress distinguished by quick metastasis.

Epidemiology. Mainly old and elderly men and women are affected.

Clinic. Fibrosarcoma is localized the most often on feet, head, body. Clinical findings are non-specific. At the early stage a solid brownish blue subdermic nodule appears. The skin is intact and is involved in the process only in case of tumour aggressive progress. In 50% of cases there is a pain syndrome. Fibrosarcoma metastasizes inside lungs and bones early, by hematogenous means.

Pathomorphology. On patohistological research the typical bundles of spindle/round cells divided by collagen fibers are detected in the biopsy sample. Also the infiltrative and destructive growth occurs.

Diagnostics. Due to absence of specific peculiarities of the neoplasm diagnostics is based on the results of histological research. Fibrosarcoma shall be differentiated with dermatofibrosarcoma and malignant histiocytoma.

Treatment. The surgical treatment is applied with wide excision within the healthy tissue, X-ray therapy, chemical therapy.

1. Which skin functions are relevant to the tumour occurrence:

A. Protective
B. Immune
C. Receptor
D. Metabolic
E. Resorption

2. Which factors do not provide skin antitumoral function:

A. Killer lymphocytes
B. Urokin acid
C. Interferons
D. Cell necrosis factor
E. Growth factor

3. What belongs to facultative precancer:

A. Paget disease
B. Keratosis
C. Queirat disease
D. Bowen's disease
E. Xeroderma pigmentosum

4. What does not belong to obligatory precancer:

A. Skin atrophy
B. Xeroderma pigmentosum
C. Bowen's disease
D. Paget disease
E. Queirat disease

5. What are the skin neoplasms with non-malignant progress:

A. Basalioma
B. Spinal cell cancer
C. Melanoma
D. Dermatofibroma
E. Metastatic carcinoma

6. What does not belong to the main symptoms of nevi malignization:

A. Subjective feelings
B. Change of colour
C. Clear boundaries
D. Ulcers and erosions on the nevus
E. Hair on the nevus

7. What is typical of basal cell carcinoma:

A. High temperature
B. Slow growth
C. Occurs often in the young age
D. Metastasis into the internal organs
E. Quick metastasis

8. What is typical of squamous cell carcinoma:

A. Quick growth
B. Ulcer formation
C. Solid infiltrate
D. Absence of metastasis into the lymph nodes
E. Everything abovementioned

9. What are the main requirement to the surgical treatment of melanoma:

A. General anesthesia is compulsory for the operation
B. Wide excision of melanoma within 3–5 cm of healthy skin
C. Tumour is eliminated in one block with the subjacent subcutaneous fat and fascia
D. Regional lymph nodes are eliminated
E. Everything abovementioned

10. Which factors do not provide melanoma development:

A. Ultraviolet radiation
B. Permanent traumatization of the nevus
C. Race and sex attribute
D. Skin pigmentation level
E. Smooth skin pelosis level

Task 1. A 60-year old woman visited a dermatologist with complaint on a small bleeding ulcer appeared in the dorsum of nose. The ulcer appeared a year ago, after scratch; then it got larger and was bleeding after slight injury.

a) What is the preliminary diagnosis:
- **A**. Basal cell carcinoma
- **B**. Squamous cell carcinoma
- **C**. Precancerous melanosis of Dubreuilh
- **D**. Metastatic cancer
- **E**. Queirat disease

b) What additional methods of research should be applied?

Task 2. A 52-year old patient visited a doctor with complaint on ulcer in the left side of upper lip. He says that it occurred due to the frequent cigarette burn. *The examination revealed*: the ulcer has spindle-type edges based on a solid woody substance beyond the boundaries of occurrence, covered with haemorrhagic scab. Regional lymph nodes are not increased.

a) What is the preliminary diagnosis:
- **A**. Basal cell carcinoma
- **B**. Squamous cell carcinoma
- **C**. Queirat disease
- **D**. Metastatic cancer
- **E**. Precancerous melanosis of Dubreuilh

b) State the additional methods of examination.

Task 3. A 64-year old patient visited a dermatologist with complaint on neoplasm on the end of the nose which has tripled for two months. *The examination revealed*: the hemispheric pea-size neoplasm of a solid consistence appeared on the end of the nose. In the center there was a cystiform neoplasm covered with keratoid mass. The edges are spindle-type.

a) Make a diagnosis:
- **A**. Warty horn
- **B**. Keratoacanthoma
- **C**. Skin sarcoma
- **D**. Xeroderma pigmentosum
- **E**. Melanoma

b) Prescribe reasonable treatment.

Task 4. A 37-year old patient attended the doctor with complaint on numerous pigmental nevi which appeared after summer holidays at the seaside. The detailed examination detected an innate slate black nevus of solid consistence, with a diameter of 4 cm, under the left shoulder blade. Skin around the nevus is congested. Its surface was covered with hyperkeratotic layers. 11 similar smaller neoplasms (satellites) are at different distances therefrom. In both axillary hollows there are enlargened lymph nodes.

a) What is the preliminary diagnosis:
- **A**. Warty horn
- **B**. Keratoacanthoma
- **C**. Skin sarcoma
- **D**. Xeroderma pigmentosum
- **E**. Melanoma

b) Determine the further plan of diagnostics and treatment.

Task 5. A 53-year old woman visited a dermatologist with complaint on skin congestion in lower abdomination. She noticed changes on the skin nearly three months ago. She did not visit doctors because the neoplasm did not disturb her. Three years ago she was operated on cervical cancer (hystero-oophorectomy). *The examination revealed*: skin in the place of affection was blueish purple, with woody solid consistence, two ulceration foci were visible. Infiltrate had unclear boundaries and was fixed with the tissues adjoining to skin.

a) Make a diagnosis and prove it:
- **A**. Basal cell carcinoma
- **B**. Squamous cell carcinoma
- **C**. Precancerous melanosis of Dubreuilh
- **D**. Metastatic cancer
- **E**. Queirat disease

b) State the additional methods of research.

Answers to the questions of the first level of complexity
1 – B; **2** – B; **3** – B; **4** – A; **5** – D; **6** – C; **7** – B; **8** – E; **9** – E; **10** – E
Answers to the questions of the second and third levels of complexity
1a – A; **2a** – B; **3a** – B; **4a** – E; **5a** – D

23 TOPIC

Medical Cosmetology

Cosmetology is a branch of clinical medicine that studies the mechanisms of development and the nature of cosmetic skin defects, as well as develops methods and approaches for their correction, prevention, and concealment. Modern cosmetological procedures, enabled by advanced technologies, allow for significant changes in appearance, long-term preservation of youthfulness, and resolution of numerous aesthetic concerns.

The rapid advancement of the cosmetology field necessitates a profound level of knowledge from medical professionals. This expertise allows for the rational application of cosmetological correction methods in addressing aesthetic pathologies encountered by physicians across virtually all medical specialties.

The elimination of cosmetic imperfections not only improves a person's appearance but also positively influences their psycho-emotional state and facilitates social adaptation. This trend is closely linked to increasing demands for aesthetic appeal and the rapid progress of scientific and technological innovation.

EDUCATIONAL AND UPBRINGING OBJECTIVES

- To perform proper skin examination
- To identify skin types and subtypes
- To study the principles of instrumental skin assessment methods
- To provide recommendations for appropriate skin care
- To correctly apply the latest methods and technologies in cosmetology
- To interpret current concepts regarding the correction of cosmetic skin defects
- To determine indications and contraindications for cosmetological procedures
- To understand the techniques and methodologies of cosmetological procedures
- To possess knowledge about the outcomes, consequences, complications, and side effects of cosmetological interventions

TO KNOW:

- Definition and classification of cosmetology
- Principles of instrumental methods for skin assessment
- Characteristics of age-related skin changes
- Features of all skin types and subtypes
- Basic methods of cosmetological correction of skin defects
- Techniques for performing cosmetological procedures
- Indications and contraindications for cosmetological correction
- Adverse reactions and complications associated with cosmetological procedures
- Equipment and pharmacological agents required for cosmetological procedures
- Principles of psychocorrection in medical cosmetology

TO BE ABLE TO:

- Accurately determine the facial skin type
- Appropriately select and apply instrumental methods for skin analysis
- Select suitable techniques and methods for cosmetological correction in patients with different skin types
- Choose appropriate methods of cosmetological correction for patients of various age groups
- Collect medical history and correctly prescribe necessary examinations prior to cosmetological procedures
- Inform patients about expected outcomes and possible consequences of cosmetological interventions
- Recommend appropriate post-procedure skin care

23.1 Main Characteristics of the Skin, Its Specific Features, and Examination Methods

Skin Types and Care Guidelines

Skin types refer to the condition of the skin based on its functional activity and the performance of physiological processes. Determining skin type at first glance can be challenging. While the basic structure of the skin is the same for all individuals, sebaceous glands vary in the quantity and distribution of sebum secretion across different areas of the body. Additionally, the skin has a hereditary ability to retain or lose moisture. With age, the skin type often changes; however, with proper hygienic care, it can be maintained in good condition for a prolonged time.

There are four primary skin types: normal, dry, oily, and combination. Additionally, sensitive skin is recognized as a separate category. In approximately 90% of women, the tendency toward dry skin increases with age. It is also known that individuals with fair hair (e.g., blondes) tend to have drier skin compared to brunettes. Nevertheless, the most significant contributor to skin dehydration is improper skincare.

Normal skin is characterized by an intact hydrolipidic barrier, a slightly acidic pH, and well-balanced levels of water, lipids, and proteins. It exhibits normal sebum secretion, good elasticity, and a natural, healthy glow. This skin type is firm, smooth, free of wrinkles and enlarged pores, and feels soft and velvety to the touch. It tolerates cleansing with water and environmental stressors such as wind, cold, and heat relatively well. Normal skin consists of approximately 60% water, 30% protein, and 10% lipids, and is typically found in young, healthy individuals.

Normal skin has a matte surface, barely visible pores that are not clogged with sebum, and may exhibit slight shine in the central facial area. Sebum test results are positive in the T-zone and negative on the lateral facial zones. The rotation-compression test is typically negative but may become positive with age. To maintain this skin type, supportive skincare routines are recommended, including cleansing, moisturizing, and protection against UV radiation.

Basic Guidelines for Normal Skin Care

Caring for normal skin typically requires minimal effort. The main objective is to maintain cleanliness and a fresh appearance, along with the occasional use of cleansing masks. Overdrying the skin and exposure to harmful ultraviolet (UV) radiation should be avoided. Frequent use of lotions containing high concentrations of alcohol may also contribute to dryness.

Normal skin is well protected from environmental factors and can maintain a healthy appearance without intensive cosmetic care until the age of 30–40. To prevent early age-related involution, it is advisable to minimize the use of cosmetic products. In the morning, the face should be rinsed with cool water (for sensitive skin, a 1:1 mixture of water and milk may be used). Alternating temperature rinsing helps maintain skin firmness. After cleansing, apply a cream for normal skin along massage lines. Both semi-fat and moisturizing day creams can be used, as they nourish and strengthen the skin.

Evening cleansing should be done 1–1.5 hours before bedtime using plant oils, sour milk, kefir, lotions, or liquid emulsion creams. After removing makeup, the skin may be wiped again with cleansing milk or cream.

Face masks or wrap-masks are beneficial for normal skin but should be applied no more than once a week. Ingredients suitable for this skin type include egg yolk combined with honey or any plant oil. However, honey should be avoided in individuals with visibly dilated blood vessels. Seasonal adjustments are also recommended: for example, vegetable or berry masks are preferable in spring and summer. Regular exfoliation with scrubs, steam baths, herbal compresses, and facial massage supports skin vitality.

To protect the skin from cold, wind, or sun exposure, use protective creams (e.g., a blend of one part zinc ointment, one part plant oil, and one part spermaceti cream). After the age of forty, nourishing creams and hygienic or self-massage routines are recommended.

Normal skin is a hallmark of youth. To keep it healthy and radiant for as long as possible, consistent but relatively simple care is required–often less intensive than that needed for dry or oily skin.

Harmful Procedures for Skin and Guidelines for Dry Skin Care

One harmful procedure that can damage even normal skin is frequent washing with harsh cold water and soap. It is equally harmful to remove makeup daily with soap and water. Excessive drying of dry skin accelerates the aging process. Such skin should not be exposed to overheating from sun exposure, nor should artificial tanning products or cosmetics containing high levels of alcohol be used. Both hot and very cold water are contraindicated for dry skin.

Basic Guidelines for Dry Skin Care

This skin type is highly sensitive to external irritants and, therefore, requires constant care and protection. The first step is to ensure a balanced diet rich in vitamins A and C, found in foods such as onions, fish oil, egg yolk, and carrots. In cases of increased flaking, the skin should be treated twice a day with a rehydrating cream or oil. Cleansing should be performed twice a week using

milk or a milk-water mixture. Soap generally irritates dry skin, so alternatives like egg yolk mixed with a small amount of olive oil are recommended. As dry skin has an alkaline pH, it is also essential to use dairy products such as kefir, sour cream, or buttermilk for cleansing.

Very beneficial for dry skin are cheese-fruit masks, egg-yolk chamomile masks, as well as masks made from aloe juice and flax seeds. Dry skin should be cleansed both in the morning and evening, followed by a generous application of a rich moisturizing cream that forms a protective layer and helps retain moisture in the upper layers of the skin. Similarly, special creams for the eyes and neck are indispensable for dry and aging skin. Once a week, it is necessary to perform a procedure to exfoliate dead skin cells from the surface.

Occasional Toning Masks and Recommended Skin Care Products

In addition, it is recommended to periodically use toning masks to stimulate the production of natural skin oils. For the cleansing, moisturizing, and care of dry and very dry skin, cosmetic products from the «Physiogel» line (cream, lotion), «Oylatum» line (cream, bath emulsion, gel, dermatological soap), «Atopra» line (lipid emulsion, cream), «Excipial M Lipolotion,» «Excipial M Hydro Lotion,» «Dermalex Atopic Eczema,» «Locobase Reparative,» and others are recommended.

Oily Skin

Oily skin is characterized by overactive sebaceous glands. Such skin appears greasy, shines, and has a rough texture. Sebum, combining with dust and exfoliated cells from the stratum corneum, forms plugs that block the ducts of the sebaceous glands. The sebum test is positive, but in older individuals, it may turn negative due to the diffuse atrophy of the sebaceous glands. In younger individuals, the rotational-compression test is negative, but with skin aging, it becomes positive. This skin type is sensitive (it does not tolerate soaps or creams with an oily base) and is prone to inflammatory processes.

Oily skin most often appears on the forehead and nose. Excess sebum production typically develops during puberty. It can also occur in cases of nervous system disorders, endocrine gland diseases, chronic gastrointestinal dysfunctions, and more. Menstruation can also trigger skin breakouts. Oily skin is predominantly found in young people and persists until the age of 35–40. As people age, sebum production decreases, and in older individuals, the skin is generally not characterized by excessive sebum secretion. Wrinkles on oily skin appear much later than on dry skin.

The activity of the sebaceous glands is often enhanced by consuming spicy, high-fat, and high-carbohydrate foods, alcoholic beverages, and decreases

with the consumption of dairy and plant-based foods along with regular meals. Oily skin can become more pronounced if a person gains weight, or through excessive use of greasy creams, various cosmetic masks, and emulsions. Oily skin requires special, prolonged care, combined with appropriate treatment and a specific dietary regimen.

Basic Guidelines for Oily Skin Care

Care for oily skin begins with correcting the diet: one should limit the intake of spicy foods, alcoholic beverages, fatty, and fried foods. People with oily skin need to monitor proper bowel function, reduce the intake of animal fats and lard, drink less liquid, engage in physical exercise, and take air and sunbaths. Massage, steam baths, and drying masks are also beneficial.

This skin type requires regular cleansing using mild or neutral soap with warm (37–38°C) water once a week, and cold or room temperature water on other days. The ideal way to cleanse oily skin is with a soap cream. Light, non-greasy cleansing lotions can also be used. However, excessive washing removes too much oil, which leads to further sebaceous gland secretion. A gentle two-minute massage with fingertips during morning and evening washes, using soap or lotion, is beneficial. After cleansing, it is important to remove excess oil with an astringent product. Very oily skin does not require additional moisturizers. However, slightly oily skin should be moisturized occasionally. It is not recommended to use hard makeup brushes, as they may cause premature wrinkles. It is beneficial to wipe the face with a piece of ice made from medicinal herbs. Thermal water refreshes oily skin. When selecting a cream, one should carefully examine its composition and oil content (the cream can be either fatty or semi-fat, or a hydrant). Contrast washing is also beneficial.

Face Care After Cleansing

After cleansing, the face can be left to air dry instead of being wiped with a towel, and then wiped with an herbal infusion that contains healing ingredients to help narrow the pores. At night, it is better not to use a cream, but instead, opt for cosmetic milk or creams. A steam bath once a week will help cleanse the skin of acne. For deeper cleansing (peeling), a cosmetic scrub can be used. The use of non-greasy elements, such as «Effaclar Duo,» «Physiogel Cleanser,» and «Eucerin Dermopurifyer» mattifying cream, is also recommended.

It is not advisable to frequently wash the face with hot water, as this only intensifies the activity of the sebaceous glands. Hot water should only be used 2–3 times a week. On other days, cold water should be used, as it tones the skin, improves its nourishment, narrows the pores, and reduces oiliness. If oily skin starts to peel or feels tight and dry after water treatments, it is recommended to use a liquid cream or apply a mask before washing, and after washing, apply a

nourishing cream to damp skin. For oily, porous skin, the following masks are beneficial: protein, protein-lemon, protein-camphor, fruit-vegetable, yeast, and hydrogen peroxide masks.

Excessive sun exposure increases sebaceous gland activity, making it necessary to use photoprotective products, such as «Anthelios XL SPF 50+» (cream) and others.

Combination Skin

Combination skin (also known as mixed skin) is a skin type characterized by both oily and dry areas. The T-zone (forehead, nose, and chin), as well as the upper chest and back, are usually oily, while other areas are dry and may even experience peeling. The characteristic feature of this skin type is a shine in the middle part of the face and a matte appearance in other areas. Pores are large and filled with sebum. The sebum test is positive in the middle of the face and negative in the sides. Combination skin requires special, dual care for each area. In practice, this is normal skin with unevenly distributed oily areas. For example, the skin of the face may be normal, but around the eyes, it is dry, while the area around the nose is oily. Combination skin is the most common type.

Basic Guidelines for Combination Skin Care

To make the skin surface uniform, the areas of the nose, forehead, and chin should be treated with methods recommended for oily skin. For combination skin, differentiated care products and methods are recommended, as washing is beneficial for oily skin but not for dry skin. However, if the difference between the dry and oily areas is not significant, it is easier to use cleansing milk. Toners for dry skin should be more liquid than those used for oily skin in the central areas of the face. The dry areas should be treated more often with a moisturizing cream. Mint water can be used to wipe combination skin. Contrast washing also works well. In the morning, the face should be washed and treated with cosmetic products for combination skin. In the evening, after removing makeup with a greasy cream or cosmetic milk, a thin layer of fatty cream should be applied to the dry areas, and a cream for oily skin or emulsion should be applied to the oily areas. Masks, wraps, skin cleansing with scrubs, massage, and compresses with medicinal herbs are beneficial for combination skin. By using day and night creams according to the season, the youthfulness of the skin can be preserved for a long time.

Sensitive Skin

Sensitive skin can occur at any age. Its distinctive feature is the presence of red veins and capillaries that are visible on the surface. The appearance of such veins is the result of poor vascular elasticity, which worsens due to spicy

foods, alcoholic beverages, temperature changes–anything that causes the blood vessels to expand and contract excessively. Such skin is easily irritated and very sensitive to fragrances.

Basic Guidelines for Sensitive Skin Care

Sensitive skin care depends on the underlying skin type (dry, oily, combination), but specific cosmetic products designed for sensitive skin should be used. Dividing skin by type allows for the selection of an adequate skin care program. The main characteristics of facial skin types are presented in Table 1.

Table 23.1
Characteristics of the main facial skin types

Version	Characteristic
1. Normal healthy skin	
1.1. Skin of normal oiliness, with good tone	The skin has a matte surface with a slight shine in the central part of the face. The pores in the central area of the face are thin and barely noticeable, not clogged with sebum. The oiliness test in this area is positive, while the sides are negative. The rotational-compression test is negative. The skin tolerates external irritants well and maintains its appearance for a long time without cosmetic care. Only at the age of 30–40, depending on the care, does it transition to the next group.
1.2. Skin of normal oiliness, slightly slack	The skin surface is matte, with a slight shine in the middle part of the face. The pores are thin and not filled with sebum, only slightly visible. The oiliness test in the middle part of the face is weakly positive, while on the sides it is negative or the same. The skin around the eyes begins to weaken, and fine wrinkles appear at the corners. Skin folds form, but they are elastic. The rotational-compression test is weakly positive. If optimal cosmetic care is provided during this period, the transition to the next skin group can be delayed for many years.
1.3. Skin of normal oiliness, loose	The surface of the skin is matte with a slight shine in the middle part of the face. In the middle part, there are noticeable thin pores that are not filled with sebum. The oiliness test is weakly positive in the middle of the face, and negative on the sides. Fine lines and mimic wrinkles are clearly visible, and the skin is thin and loose. Folds form spontaneously in areas where the skin sags. The rotational-compression test is positive. Without cosmetic care, this skin type develops after the age of 50, and with at least minimal care, it appears in old age.

Table 23.1 (continuation)

Version	Characteristic
2. Dry skin	
2.1. Skin is dry, tone is good	The skin surface is matte, smooth, and wrinkle-free. The pores are fine and not noticeable. The oiliness test is negative. The skin is elastic, and the rotational-compression test is negative. The skin has an excellent appearance in youth. However, it is very sensitive to any irritants, including soap. It requires constant skincare, protection from the sun, and other external factors. Without proper care, the skin quickly transitions to the next group.
2.2. The skin is dry, slightly flabby	Its surface is matte and soft, with fine, inconspicuous pores. The oiliness test is negative. Small wrinkles appear at the corners of the eyes. Skin folds form easily while maintaining elasticity. The rotational-compression test is slightly positive. Signs of slackness in this skin type can appear as early as 30 years of age. Regular skincare is advisable to prevent the skin from transitioning to the next type.
2.3. Skin is dry, flabby	The skin's surface is matte and soft, with fine, almost imperceptible pores. The skin is thinned, particularly in the areas around the eyes and mouth. Permanent folds and wrinkles form. The rotational-compression test is positive. This skin type can be observed in patients around the age of 40 if there is no targeted skincare. Regular skincare may only partially affect the condition of the skin.
3. Oily skin	
3.1. Oily skin, good tone	The skin surface is oily, oily, with a rough structure. The pores are enlarged, funnel-shaped, but empty. The test for oiliness of the entire surface of the facial skin is clearly positive. The rotational compression test is negative. The skin is very sensitive to external influences, in particular to soaps and creams with a fat base. Most people with this skin type have a dysfunction of the sebaceous glands of the scalp. It is prone to inflammatory processes. Aging and the transition to the next skin type occur quite quickly.
3.2. The skin is oily, somewhat flabby	The skin surface is oily, with a coarse texture. The oiliness test for the entire face is positive, although the intensity of sebum secretion is slightly reduced compared to the previous type. There is increased sensitivity and a tendency

Table 23.1 (continuation)

Version	Characteristic
	to inflammatory processes. General laxity of the facial skin is noted. The rotational-compression test is positive. Folds appear spontaneously. With age, the skin transitions to the next group.
3.3. The skin is oily, flabby	There is a normalization of the process of sebum secretion. The test for fatness in some cases may even be negative. Random skin folds, wrinkles. The rotational-compression test is clearly positive.
4. Combination skin	
4.1. Combination skin, good tone	The skin surface, especially in the middle part of the face, is shiny with prominent pores filled with sebum. The oiliness test is positive in both the middle and lateral parts of the face. The skin is smooth and wrinkle-free. It is difficult to form a skin fold. The rotational-compression test is negative. This skin type is typical for individuals aged 18–30. During the transitional period, acne breakouts and inflammatory processes are common. Soap and oil-based cosmetic products should not be used. Systematic cosmetic care is necessary. After 30 years of age, the skin transitions to the next type.
4.2. Combination skin, slightly flabby	The skin surface is shiny with a coarse texture. The oiliness test is positive in the middle part of the face, while it may be negative in the lateral parts. The skin around the eyes is lax, and mimic wrinkles begin to appear. An elastic skin fold forms. The rotational-compression test is slightly positive. The skin is quite sensitive and prone to inflammatory manifestations, especially in the middle part of the face. It requires special care. The aging process is slow, and the transition to the next group occurs only in old age.
4.3. Combination skin, flabby	The characteristics of skin oiliness and its signs correspond to the type described in point 4.2. The skin is noticeably lax with mimic wrinkles. Skin folds form randomly. The rotational-compression test is clearly positive. Conventional cosmetic methods for skin rejuvenation are of little help, and plastic surgery may be necessary.

1.2 Characteristics of Skin Phototypes

A skin phototype refers to the degree of sensitivity of the skin to ultraviolet (UV) radiation. There are several conditional classifications that define the characteristic features of different human skin phototypes. However, the most widely used and popular classification is the classical skin phototype system developed in 1975 by American professor Thomas Fitzpatrick. His classification includes six skin types, each with its own distinctive features.

- Type 1 – Celtic: Typically individuals with green or blue eyes and red or light hair. Their skin is delicate, milk-white, highly sensitive to sunlight, often with many freckles; they have very light areolas. This phototype produces almost no pigment, meaning sunburn occurs instantly and tanning never happens. They always burn, never tan.
- Type 2 – Light European (Nordic or Germanic): This type includes people with blue, gray, or greenish eyes and light brown or chestnut hair. They have light skin and light areolas, and freckles are typically few or absent. These individuals are sensitive to ultraviolet radiation, tan poorly, and are prone to sunburn.
- Type 3 – Dark European (Mid-European or Mixed): This is the most common type in Ukraine. People with brown, sometimes gray eyes and dark blonde or chestnut hair fall into this group. Their skin is lightly tanned, without freckles, and the areolas are quite dark. They are less sensitive to UV rays, tan well but can get sunburned with prolonged sun exposure.
- Type 4 – Mediterranean or South European: This type is characterized by a tan, olive-colored skin, typical for people with dark eyes and hair. Those with this phototype tan easily, quickly, and almost without burning. They can enjoy immediate tanning in the sun.
- Type 5 – Indonesian or Middle Eastern: Rare in Ukraine, people with this phototype have very dark skin without freckles, dark hair, eyes, and areolas. They get a quick, even, and dark tan, rarely burn, and have few contraindications for sun exposure.
- Type 6 – Afro-American: This type includes individuals with very dark skin, black hair, and dark eyes. They never get sunburned, even with prolonged sun exposure. Their skin is dark brown and does not burn, but they do get a deep tan.

Some authors also highlight a Zero Phototype (Type 0), which includes individuals with depigmented skin (albinos). Their skin is white, often with a pinkish hue, and areas such as eyelashes, eyebrows, armpits, and the pubic area are also white and thin.

Skin Care and UV Protection According to Phototypes Depending on the skin phototype, different sunscreens with varying Sun Protection Factor (SPF) should be used for sun protection.

The Sun – the primary source of energy for the inhabitants of our planet – emits three types of ultraviolet (UV) radiation: UVC, UVB, and UVA. Let's look at each of them individually:

- UVC – Short ultraviolet waves from 10 to 280 nm, which are absorbed by the ozone layer and do not reach the Earth's surface.
- UVB – Medium ultraviolet waves from 280 to 315 nm. This is active radiation that leads directly to tanning or sunburn. These rays do not pass through glass or clothing, so protection from them can be achieved by wearing a hat, dark sunglasses, and light long-sleeve clothing.

UVA – Long ultraviolet rays ranging from 315 to 400 nm; the most dangerous type of radiation. These rays can penetrate through light clothing and window glass, reaching deeper layers of the skin than UVB rays. UVA rays primarily affect the elastic and collagen fibers, causing photoaging of the skin.

While the effects of UVB rays are visible immediately after exposure to the sun, UVA rays have a cumulative effect, with the negative results (skin dryness, pigmentation spots, or new moles) becoming apparent only at the end of summer.

All sunscreens contain UV filters that protect against ultraviolet radiation and are classified into:

- Non-stable to sunlight (non-photosensitive): Examples include ethylhexyl methoxycinnamate (EMC), benzophenones (benzophenone-2, -3, -4, -9), avobenzone, para-aminobenzoic acid (PABA).
- Photosensitive (stable to light): Examples include Tinosorb M, Tinosorb S, titanium dioxide, zinc oxide, Mexoryl SX and Mexoryl XL, octocrylene (octocrylene or Parsol 340), Parsol 5000, Parsol SLX.

When choosing a cream with maximum protection against sunburn and photoaging, it is advisable to ensure that it contains 2-3 stable filters such as Mexoryl or Tinosorb.

UV Filter Indices for UVA/UVB Protection: SPF, IPD, PPD (PA). The effectiveness and range of UV filters are expressed by widely accepted symbols. The protective power of a cream against UVB radiation is indicated by the abbreviation SPF (Sun Protection Factor). This factor was proposed by Australian scientist Franz Greiter in 1962 and has been unanimously adopted by global cosmetic and pharmaceutical companies.

The SPF protection function can be calculated using the formula: the SPF level indicated on the tube is multiplied by the number of minutes it takes for the skin to redden in the sun. For light-skinned people, this time is usually 10–15 minutes. So, if normally sunburn occurs in 10 minutes, a cream with an SPF of 15 would extend safe sun exposure to 150 minutes. After this time, the cream layer must be reapplied.

It is much harder to evaluate protection against UVA rays. Different methods for this are used, such as IPD, PPD, or PA.

- IPD (Immediate Pigment Darkening): This indicates how much the product protects against UVA rays. The maximum value is 90, meaning that with a cream with an IPD of 90, the skin will be protected by 90%.
- PPD (Persistent Pigment Darkening): This index informs how much the UVA radiation dose is reduced. The maximum level is 42. In this case, 42% less UVA radiation will penetrate the skin.
- PA: The intensity of protection is expressed with the symbols «+1», «+2», or «+3».

Therefore, for full protection from the sun's rays, you need to use a sunscreen that optimally protects against both UVB and UVA radiation. To protect against UVB, SPF is used, which is listed on all tubes. For protection against harmful UVA rays, you should look for indices such as IPD, PPD, PA, «UVA», or the phrase «Broad-Spectrum Protection», which means protection against both UVA and UVB rays.

To ensure reliable skin protection, you should apply 2 mg of cream per 1 cm^2 of skin. For specific phototypes:

- Type 0 – Maximum SPF factor 50+.
- Type 1 – Maximum SPF factor 50+.
- Type 2 – SPF factor 20, or 15 after getting used to the sun.
- Type 3 – SPF factor 20–10.
- Type 4 – SPF factor 15–8.
- Type 5 – SPF factor 6–8.
- Type 6 – SPF factor 3–4.

1.3 Methods of Skin Research

Skin research using instrumental techniques. Corneometry, assessment of transepidermal water loss (TEWL test), and skin electrical conductivity measurement allow for the determination of the skin's water balance status.

Sebummetry, visualization tests, and gas chromatography analysis assist in evaluating the skin's lipid balance. Mexametry and chromometry are used to study processes associated with skin photoaging.Skin microcirculation is studied using laser Doppler flowmetry. Topography of the skin can be examined using optical profilometry and analysis of high-resolution digital camera impressions with the aid of specialized computer programs. Exfoliation of the skin is investigated by staining scales on impressions from adhesive tapes. Optical coherence tomography (OCT), ultrasound microscopy, and magnetic resonance skin tomography (with a resolution of 0.86 mm) are employed to study the internal structures of the skin. Methods of vibration rheoelastography, transverse and longitudinal deformation, and acoustic methods are used to determine the mechanical properties of the skin.

1.4 Gender-Specific Features of Skin Structure, Physiology, and the Impact of Various Factors

Male and female skin exhibit differences in structural, anatomical, biochemical, mechanical, functional features, responses to exogenous factors, skin microcirculation, coloration, hormonal influence, and characteristics of the sebaceous-hair structures. These differences are most notable after the age of 12, although they are minimal before that time. With age, under the influence of endogenous and exogenous factors, significant distinctions develop.

Structural and Anatomical Features

Men's skin is generally coarser, with a thicker stratum corneum and dermis, while the subcutaneous fat tissue is thinner. Male skin continuously thins between the ages of 12 and 90, while in females, it does not significantly change until the age of 50, after which it begins to thin progressively (this fact is important when planning plastic surgeries for women of reproductive age).

A hormonally determined connection between skin thickness and collagen content has been demonstrated in men across all age groups. However, in women, this relationship is only observed in individuals over 60 years old. Collagen density (defined as the ratio of dermal collagen to dermal thickness) is closely associated with age in both men and women, but it is significantly higher in men across all age groups. Generally, chronological aging is associated with the overall collagen content. Initially, a lower collagen content may be one of the reasons for the earlier (compared to men) aging of female skin. In mature age, without a skincare regimen, women often appear 10–15 years older than their male peers.

One factor influencing gender differences in collagen content may be the level of androgen production. It has been established that collagen decreases linearly with age. The rate of this decrease is the same for both sexes, at approximately 1% per year throughout adult life. This must be taken into account when planning treatment and certain cosmetic procedures. The rate of aging also depends on topographic factors. For example, skin thinning in the forearm area in women begins at age 35, while in men, it starts at age 45.

Subcutaneous Fat Tissue Structure

Before the age of 12, there are no significant differences in the structure of subcutaneous fat tissue. Visible changes begin at puberty. In girls, subcutaneous fat tissue continues to increase, whereas in boys, it does not change significantly. With age, in men, subcutaneous fat accumulates in the abdominal and upper body areas, while in women, it accumulates in the thighs and buttocks.

Lipase activity in women is higher, especially in the abdominal and buttocks areas, while in men, it is higher in the abdominal region. These topographic and gender-specific differences in structural-anatomical features and lipase protein activity are the basis for the differentiation in fat distribution and are among the factors contributing to the development of cellulite in women.

Biochemical Features

In men, the composition of sphingolipids in the stratum corneum does not depend on age. However, in women, there is a significant increase in ceramide types I and II, and a decrease in ceramide types III and VI during the prepubertal and mature age stages. After puberty, the amount of ceramide type II decreases, while the amount of ceramide type III increases. These lipids are known to play a crucial role in skin hydration and the effectiveness of the epidermal barrier function. This is why women's skin requires more attention and care than men's.

Certain differences are also observed in metal content in hair. Women have significantly higher concentrations of metals compared to men, and these concentrations change with age. For example, copper concentration in women's hair increases with age, while it remains unchanged in men.

Mechanical Properties

Skin hydration in the stratum corneum and the degree of exfoliation do not differ significantly between men and women. Creams containing estriol and estradiol are effective in improving hydration of the stratum corneum and preventing wrinkle formation, particularly in premenopausal women. Functional properties of the skin and the adhesion of corneocytes also do not differ between the sexes. Skin extensibility is similar in both men and women, but after hydration, it increases only in women. Since women's skin is thinner, a reduction in the cells of the stratum corneum contributes to its quicker stretchability. The positive impact of estrogens on facial skin hydration has been proven, as the appearance of fine wrinkles significantly decreases in this case.

Functional Features

In men, eccrine secretion is twice as high as in women, and the pH of sweat is 0.5 lower. Women exhibit more pronounced pubertal sweating in the palms and soles, although these differences diminish with age. The gender differences in eccrine secretion are likely due to irreversible gene expression rather than the effect of sex hormones (androgens). Men also have a higher level of androgen-induced sebum production.

Response to Exogenous Factors

Men are significantly less prone to contact dermatitis and skin irritation compared to women. A higher level of transepidermal water loss (TEWL) has been observed in women than in men, which is linked to the level of estrogen secretion. However, some studies suggest that in the age range of 18–39 years, the level of transepidermal water loss is lower in women than in men.

Skin Microcirculation

Hormonal factors influence vascular flushes and blood circulation speed in the vascular plexuses of the dermis. Differences in skin microcirculation between men and women of reproductive age have been confirmed, resulting from the slowing down of blood circulation in superficial vascular plexuses (including

the skin of the face). However, these changes are related to symptomatic tone rather than structural or functional characteristics of the vessels. Additionally, skin microcirculation in women changes throughout the menstrual cycle. It is lower in the luteal phase and higher in the preovulatory phase. The least recovery occurs during the luteal phase. These changes must be considered when determining the timing of surgical and/or invasive cosmetic interventions. The direct impact of sex hormones on blood vessel walls has been proven. Estrogens influence the sympathetic nervous system, inducing vasoconstriction by acting on alpha-2 adrenergic receptors. Doppler vascularometry has revealed a slowdown of skin microcirculation in young women compared to men and women over 50 years old. Moreover, the corresponding reactive hyperemia in young women is lower than in men and women after 50 years. Therefore, thermal procedures for the face in women over 50 should be limited.

Sensory Function

Men's skin is less sensitive to temperature changes and pain caused by both heat and cold. Additionally, there is more pronounced asymmetry in sensitivity between the hands of men, with a stronger response on the left hand. In women, this asymmetry is less pronounced, with a dominant response on the right hand.

Skin Color

Under equal ethnic, climatic, and somatic conditions, men's skin is generally darker, which is not hormonally driven, but rather due to different levels of melanin, hemoglobin, and carotene. Women's skin color is more homogeneous compared to that of men. Colorimetric studies have shown that pigmentation and redness in men's skin are more pronounced in those aged 65-88 compared to women. However, no such differences are observed in younger individuals (18-26 years).

Hormonal Influences

All the aforementioned differences may be linked to hormonal effects. The action of sex hormones is particularly noticeable when treating postmenopausal women with estrogen (in which case, the skin thickens). Hormone replacement therapy (HRT) during menopause has a significant impact on skin elasticity and prevents skin sagging. In the postmenopausal period, skin thins, which is accompanied by a reduction in collagen content in the dermis. Collagen content in the dermis is regulated by estrogens or testosterone, or both. In men, the skin contains more collagen than in women of the same age (men's skin is 25% thicker), although the rate of reduction in collagen content is the same for both sexes, approximately 1% per year throughout adulthood. Moreover, the ratio between collagen types III and I changes. With hormone replacement therapy, dermal collagen content in women increases by 48% compared to women who did not undergo treatment. Unfortunately, similar treatments for men are not yet available.

Estrogens, the primary female sex hormones, contribute to an increase in hyaluronic acid content in the dermis by acting on estrogen receptors, thereby enhancing skin hydration. This leads to the smoothing of fine wrinkles. As a result, the use of so-called «hormonal» creams induces an increase in hyaluronic acid in the dermis and an increase in estrogen receptors in the skin. With age, the number of estrogen receptors in the skin decreases, leading to degeneration of elastic fibers.

Sebaceous-Hair Structures

Sebaceous glands and hair follicles are hormonally dependent in both men and women throughout all life stages. In men aged 20–69 years, sebum secretion levels are higher. However, there is no such difference in the 15–19 year age group. This fact is associated with a more severe course of acne in men older than 19 years. In boys over 10 years and girls after 15 years (in the absence of current or past acne), sebum excretion is primarily stimulated by androgens and increases through the third and fourth decades, respectively. At the age of 50–70 years, sebum secretion in men does not change significantly, while it decreases markedly in women. This may be related to a decrease in ovarian activity. There is no correlation between blood testosterone levels and sebum secretion levels.

The distribution of body hair in men and women is different. The most significant gender differences are that men's hair is less dense and a higher percentage of hair is in the telogen phase. The influence of androgens on hair growth in specific areas is noted in both men and women. Androgens affect the cells of the hair follicle, which in turn are influenced by melanocyte-stimulating hormone, thyroid hormones, prolactin, certain physiological states (e.g., pregnancy), and dietary habits. High testosterone levels inhibit the cells in the dermal papilla and surrounding keratinocytes, with less of an effect on fibroblasts. A low level of testosterone does not produce these effects. The actions of estrogens and cyproterone are opposite in effect.

1.5 Age-Related Features of Skin

Skin of Newborns and Children

At birth, the skin has three layers: the epidermis, dermis, and subcutaneous fat. The epidermis in children is thin, delicate, and spongy. It consists of six layers, but the stratum corneum is only noticeable on the palms and soles. In the basal (growth) layer of the epidermis, the pigment melanin is absent until about six months of age. One of the characteristics of children's skin is the absence of keratohyalin in the granular layer of the epidermis. The cells of the outer layer of the epidermis (stratum corneum) are easily shed because intercellular connections are weak.

The dermis retains an embryonic structure, containing many cellular elements and insufficiently differentiated fibrous structures. These structures contain fewer collagen fibers, which are thin and loosely arranged in

bundles. The papillary layer of the dermis is not well developed and absent in premature infants. Children's dermis has more water than adults' skin and contains significant amounts of hyaluronic and chondroitin sulfate acids, as well as a highly active enzyme, hyaluronidase, which causes increased skin permeability. Children's skin has a very developed capillary network with good blood circulation.

The basal membrane, which separates the dermis from the epidermis, is underdeveloped. This makes it easier for the epidermis to detach from the dermis even during minor pathological processes, leading to the formation of blisters or vesicles.

The thickness of the subcutaneous layer in children is relatively greater than in adults. The adipose tissue still contains embryonic tissue areas capable of accumulating fat and performing hematopoietic functions. The adipocytes are morphologically immature and contain higher levels of saturated fatty acids (palmitic, stearic) compared to unsaturated ones (oleic, etc.), explaining the frequent occurrence of adiponecrosis, sclerema, and sclerodermia in newborns. The subcutaneous tissue also contains a significant amount of brown adipose tissue. This type of tissue is rich in mitochondria, coenzymes, and cytochrome, which supports intense thermogenesis independent of muscle contraction. Brown fat is located in areas like the axilla, between the shoulder blades, pericardium, esophagus, kidneys, adrenal glands, and thyroid and thymus glands.

Upon the first exposure to environmental stimuli, infants often develop neonatal erythema or physiological skin catarrh. The skin becomes hyperemic—bright red with areas of bluish tint. After two to three days, the hyperemia gives way to peeling, especially on the palms and soles.

Newborns' skin is covered with a waxy coating known as vernix caseosa, composed of fat, glycogen, extractive substances, salts, as well as cholesterol, fragrant and volatile acids, and vitamins. This coating disappears within a few days due to wrapping and drying.

Yellowish-white spots, caused by excess secretion from sebaceous glands during intrauterine life, often appear on the nose. These spots disappear within 1–2 weeks.

As the child develops and grows, the skin thickens, and its protective functions gradually improve. However, children's skin retains several differences: the epidermis is thinner, and the cells are much smaller in size, making the skin more susceptible to irritation. The density of sweat glands is 5-7 times higher than in adults, while the thickness of the subcutaneous fat is less, making thermoregulation less efficient and making children more prone to both hypothermia and overheating. The larger number of sebaceous glands means that children's skin is more often classified as oily rather than dry. Additionally, the ability to produce melanin is lower than in adults, making children more sensitive to UV radiation.

Skin During Puberty

During puberty, the skin undergoes the final stage of its formation. Although there are no significant age-related changes, the skin often appears oily, with clogged pores, a typical issue not only for teenagers but also for young adults. The main skin problem during puberty is acne (teenage pimples), which usually fades away by the age of 25-30 as hormonal changes stabilize. However, it's important to note that acne can have a significant impact on a teenager's developing psyche, and in severe cases or without treatment, it may lead to irreversible scars. Additionally, during puberty, under the influence of female sex hormones, gradual changes in the proportion of various types of ceramides occur. Ceramides play a crucial role in the formation of the skin barrier, which regulates transepidermal water loss. Hormonal fluctuations also significantly affect the functioning of this barrier.

Skin of Individuals Over 30 Years Old

In individuals over 30, the epidermis thickens due to slower basal cell division and thinning of the basal layer. This process leads to the skin, especially dry skin, becoming parchment-like. There is also degradation of collagen and elastin fibers in the dermis, causing thickening and disorganized arrangement of these fibers, slowing their regeneration and resulting in a loss of skin elasticity. Microcirculation is impaired, leading to a dull complexion. This gradually reduces trophic support, accelerating the aging process. Additionally, blood circulation declines, further affecting complexion, and muscle dystonia (loss of muscle tone), particularly in the face and neck muscles, occurs. This causes the forehead and chin muscles to contract, forming deep horizontal and vertical wrinkles, while the cheek muscles sag, leading to the appearance of downturned mouth corners and changes to the facial contour.

Skin of Individuals Over 40 Years Old

The physiological age-related changes mentioned above become more pronounced. The process of involution, or age-related dystrophy, occurs. This involves the thinning of the epidermis, hypodermis, and the length of the hair follicles, as well as the atrophy of small sebaceous glands. Collagen fibers thicken, and the connective tissue undergoes dystrophy, with some fibers sticking together or breaking down. The skin's content of mucopolysaccharides decreases, leading to dehydration. However, these changes are still quantitative rather than qualitative, meaning with proper cosmetic care, the appearance can remain similar to that of a person in their 30s, especially if body weight is maintained.

Age-related changes become noticeable in areas where several factors combine. For example, «crow's feet» appear around the eyes because the skin in this area is:

- 3–4 times thinner than on other parts of the face,

- has a minimal hypodermis layer,
- has few sebaceous glands, whose secretions protect the skin from environmental damage,
- contains fewer elastin and collagen fibers,
- is constantly deformed due to frequent facial movements.

These factors contribute to the first visible signs of aging around the eyes. Other «problem» areas include the nasolabial fold (which deepens and becomes more pronounced), the eyelid skin (which becomes heavier, and folds appear), and the neck (where first wrinkles and folds appear, and in cases of excess weight, a «double chin» may form). In some women, hormonal changes lead to the growth of facial hair, such as on the upper lip. Microcirculation disorders cause vascular changes like couperose, spider veins, and telangiectasia.

Skin of Individuals Over 50 Years Old

At the pathophysiological level, the skin undergoes thinning of all layers, with a reduction in subcutaneous fat in the face, cheeks, and neck, and its increase in other areas of the body. The number of mucopolysaccharides in the dermis decreases, collagen undergoes degeneration, and blood supply to the skin diminishes. The skin becomes dry or «parchment-like,» with significantly slowed regeneration processes. The pH level increases to a more alkaline state, leading to reduced barrier function.

One of the key factors contributing to these external changes, especially in women, is age-related hormonal changes, such as menopause. Estrogen inhibits the secretory activity of sebaceous glands, increases hyaluronic acid content, converts collagen into its insoluble form, and regulates melanogenesis. A decrease in estrogen levels leads to reduced skin oiliness, causing dryness. This results in lower hydration and elasticity, along with the appearance of age spots.

23.2 Skin Aging: Signs and Characteristics

The first signs of aging on the skin typically become visible around the age of 25. Fine lines appear first, and over time, they become more pronounced as wrinkles develop, accompanied by a loss of volume and skin density. There are three primary manifestations of overall skin aging, each affecting the appearance of the face in its own way: wrinkles, loss of volume, and loss of skin density.

The first noticeable sign of skin aging, starting around age 25, is the appearance of mimic wrinkles, which form on different areas of the face. These small, shallow wrinkles typically appear at the outer corners of the eyes, also known as «crow's feet.» Mimic wrinkles may also appear on the cheeks. On the forehead, wrinkles become visible as horizontal lines, formed due to facial expressions. Over time, these wrinkles generally become deeper. Small

vertical lines between the eyebrows occur when we furrow our brows. Deeper wrinkles form between the nose and mouth, known as nasolabial folds, which are caused by skin sagging and often linked to a loss of volume. This loss of volume is sometimes referred to as sagging skin, loss of facial contours, «turkey neck,» or «chicken skin.» It can be difficult to identify, and unlike wrinkles or loss of volume, it changes the overall appearance of the face. A noticeable reduction in volume and the loss of clear facial contours can make a person look unhappy, sad, or exhausted, which can lead to misinterpretations of mood or emotional state.

Loss of Skin Density

Loss of density manifests as thin, weak superficial skin and is most common in women after menopause. Unlike wrinkles or volume loss, loss of density affects the entire face rather than isolated areas. This is often associated with deeper wrinkles and occurs in parallel with a decrease in skin brightness and a tendency for the skin to darken.

Understanding the Mechanisms of Skin Aging

Doctors must understand the patterns of age-related changes in the skin. There are several main hypotheses regarding the aging process, which complement each other. These include the Hayflick cell aging theory, genetic theory, free radical theory, thermodynamic theory, immunological theory, elevation theory, and alimentary theory. The role of the pineal gland and melatonin production in aging processes has also been proven. Skin aging does not occur due to a single cause, but rather as a result of multiple internal and external factors. Understanding these causes helps to develop a comprehensive approach to preventing skin aging.

Changes in Skin Structure

- Epidermis Changes: As skin ages, the process of cell renewal slows down, and lipid production on the surface decreases, leading to an increased risk of dryness. The skin becomes more sensitive to UV rays. Regeneration processes in the epidermis slow down, and reduced immune function can lead to a higher likelihood of skin infections and slower wound healing.
- Dermis Changes: Starting at age 25, the amount of collagen decreases by 1% each year. Collagen, one of the main «building blocks» of skin, along with the reduced amount of elastin, leads to disorganization of skin tissue. The skin's structure is disrupted, and wrinkles may form. The elasticity of the skin diminishes, making it more prone to damage and capillary rupture. Microcirculation disorders lead to less effective delivery of nutrients and oxygen to the skin's surface, causing a reduction in the healthy flush typically seen in youthful skin.
- Subcutaneous Changes: In deeper layers of the skin, the most noticeable changes occur in the size and number of fat cells that accumulate lipids.

This decrease leads to loss of volume, which has a domino effect, resulting in deeper wrinkles, hollow cheeks, and slower wound healing.

Internal Aging Factors

Genetics, ethnicity, and skin type play a significant role in how quickly signs of aging appear on the skin's surface. For instance, light, sensitive skin is more prone to wrinkle formation at an earlier age, while Asian skin types may experience uneven skin tone and wrinkles later in life. Age-related skin dryness can also be influenced by individual skin characteristics.

External Aging Factors

External factors that affect the speed of skin aging are primarily based on oxidative stress. This occurs when molecules known as free radicals or reactive oxygen species (ROS) are generated in the body. A free radical is a volatile atom or molecule containing an unpaired electron in its outer electron shell. Many of them are highly damaging to cellular structures, including lipids and proteins.

Under normal conditions, free radicals are captured and neutralized in the skin by antioxidants, molecules capable of absorbing and stopping them. However, over time, the skin's ability to deactivate free radicals decreases, leading to the damage of all cellular components. Oxidative stress is accelerated and stimulated by various lifestyle factors, including: UV radiation, smoking, poor diet, and insufficient skincare. Therefore, the theory of aging caused by free radicals asserts that we age primarily due to the accumulation of damage caused by these molecules.

Sun Exposure

UV radiation is the primary external factor responsible for skin aging due to oxidative stress. Damage to the skin caused by both prolonged and intermittent daily exposure to UV rays is known as photoaging, which also affects uneven pigmentation.

Pollution

Contact with various pollutants, particularly in urban areas, can lead to the formation of free radicals in the skin. Additionally, pollution enhances the effect of sun exposure, accelerating oxidative stress.

Smoking

Chemical compounds and nicotine found in cigarettes are responsible for increasing the number of free radicals in the skin. Similar to pollutants, they also amplify the effect of UV radiation, leading to oxidative stress.

Diet

Antioxidants are molecules that can neutralize free radicals, preventing damage to the skin and slowing down its aging process. If the diet lacks antioxidants, it won't effectively help slow down the skin's overall aging. On the

other hand, consuming a large amount of antioxidant-rich fruits and vegetables can be a key component in a comprehensive approach to preventing aging.

Insufficient Skincare

Without proper skincare, the skin will age more rapidly. Thorough cleansing with products suited to your skin type, along with the regular use of skincare products targeted at the skin's primary needs, can significantly impact its appearance. Using effective sun protection is a crucial part of prevention.

Skin Aging Phases

Depending on the morphological changes in the skin of the face and neck, three main phases are distinguished:

1. Age Evolution Phase (from birth to 20–25 years): The skin is still youthful and has its natural elasticity and moisture.

2. Age Change Phase (from 25–30 to 40–45 years): During this phase, changes occur primarily in the fibrous structures of the skin, and there is a gradual reduction in elasticity.

3. Age Involution Phase (after 40–45 years): During this period, atrophic changes increase in all layers of the skin. The stratum spinosum, granulosum, and lucidum layers begin to atrophy. The corneum layer becomes more fragmented and unable to retain moisture efficiently. The biochemical state of the skin and its water-lipid mantle also change, leading to dryness, thinning, and discoloration of the skin, along with circulatory issues. Atrophic changes also occur in skin appendages, with a decrease in the number of sweat and sebaceous glands. After 50-60 years, hair growth may increase in unusual areas, such as on the eyebrows, earlobes, inside the nose, and in women, on the chin, cheeks, and around the mouth. Eyelash length decreases. Progressive capillary network dilation can lead to the appearance of telangiectasia and, in some cases, the development of senile angiomas (Morgagni spots). With the accumulation of mutations in skin structures, various skin growths or neoplasms may appear.

Types of Facial Skin Aging

Based on the nature of age-related changes, the following types of skin aging are distinguished:

1. Deformational Type of Skin Aging

This type of aging is typical for fuller women with more prominent facial features. These individuals usually have thick, porous skin with a well-developed layer of subcutaneous fat. As the skin ages, facial muscle tone weakens, skin elasticity decreases, and the face loses its round shape, leading to puffiness. Common signs of this type of aging include drooping facial muscles and neck skin, bags under the eyes, and deep wrinkles in the nasolabial and nasolacrimal folds.

Anti-aging Program:

- and restore skin tone and firmness)
- Chemical peelings

- Laser rejuvenation
- Ultrasound therapy
- Microcurrent therapy
- Myostimulation
- Daily skincare with appropriate home remedies
- Face exercises

2. Muscular Type of Skin Aging (Muscular Aging)

Similar to the deformational type, the muscular type also represents an early form of skin aging. This type is more common in lean individuals (both men and women) with well-developed facial muscles and a minimal layer of subcutaneous fat. In this type of aging, facial features become overly defined and rough due to the total disappearance of subcutaneous fat, causing the skin to cling tightly to the facial muscles. Age-related changes in women with this type of aging tend to manifest later.

Recommended Procedures:

- Botulinum toxin injections to relieve muscle tension
- Mesotherapy for facial skin
- Facial contouring with hyaluronic acid-based preparations
- Mid-depth chemical peeling
- Facials and massages
- Regular home skincare
- Contrast washing for skin stimulation
- Relaxing facebuilding to relieve muscle tension

3. Pasty (Swollen) Type of Skin Aging

In this type, the face appears swollen, the corners of the mouth drop, noticeable nasolabial folds develop, and the skin becomes dull. It is important to note that a visit to a cosmetologist alone will not produce significant results. Before starting rejuvenation treatments, women with this face type should consult an endocrinologist and a gynecologist. Typically, doctors advise against using beauty injections for such conditions. The «tired face» (pasty or swollen aging type) can be rejuvenated through various hardware techniques and massages. This type is characteristic of relatively young women, typically between 30–35 years old.

Effective Methods:

- Proper rest and a balanced diet with limited salt intake
- Hardware methods and facial massage

4. Wrinkled Type of Skin Aging

This type of aging is typical for slender women with thin, dry skin. Over time, the skin loses its moisture, elasticity decreases, and the face may resemble a dried apple. Although facial volume decreases, the facial contour remains defined.

Recommended Procedures:

- Chemical peeling to cleanse the skin from dead cells
- Botulinum toxin injections
- Mesotherapy
- Laserre juvenation

Home Care:

- Hydrate both from the inside and the outside
- Maintain a healthy diet with sufficient vitamin A and essential fatty acids
- Use skincare products containing phytoestrogens
- Protect the skin from UV radiation

Women experiencing this type of skin aging can maintain a youthful appearance with proper home care, even without beauty injections or advanced cosmetic procedures. The key is consistent hydration and protection from the sun, along with the right skincare regimen.

5. Combined Type of Skin Aging

This type combines features of the fine wrinkled and deformational aging types. It is characterized by reduced skin elasticity, dryness, and wrinkles around the eyes and forehead, puffiness under the eyes, changes in the facial contour, and the appearance of wrinkles in the nasolabial region, as well as «sorrow wrinkles» around the nose.

Anti-aging Program:

- Chemical peeling
- Facial cleansing
- Professional facial massage
- Moisturizing, nourishing, and firming masks
- Invasive methods
- Facial contouring
- Mesotherapy

6. Late Stage of Skin Aging – Senile Exhaustion of the Face

This stage combines all signs of aging and, in most cases, can only be corrected with surgery. It typically occurs at an age when a woman may have become a great-grandmother.

This type of aging is associated with significant facial changes that are challenging to correct without surgical intervention.

Quantitative Characteristics of Skin Aging

Recent data allows for a more precise understanding of the aging process:

- Collagen concentration in the dermis decreases by 1% annually after the age of 30, contributing to skin firmness.
- Skin thinning occurs at a rate of 1% per year after the age of 40.
- Skin cell regeneration is capable of 10,000 to 100,000 DNA mutations daily. However, just 2 hours of exposure to bright sunlight without protection can cause up to 1 million mutations.

- Antioxidant depletion in the skin (especially vitamins C and E) occurs within 15 minutes of exposure to bright sunlight without protection, reducing antioxidant reserves by 70–90%. Recovery takes at least 2 hours.
- 40% of proteins synthesized in skin cells have structural errors and are subsequently eliminated by cellular mechanisms.
- Hyaluronic acid content in the body is about 15g, with 10g of this being in the skin. Hyaluronic acid in the skin is fully renewed every 3 days. Any disruption in its synthesis causes skin stress.

Changes in Skin Regeneration with Age

The overall quality of skin processes does not change with age, but their speed significantly slows down. For instance, a negative factor that young skin can neutralize within 12 hours may take 30 hours for older skin to neutralize. This explains why skin is equally effective as a protective barrier in youth and old age, but its ability to regenerate is markedly reduced in older years.

The Influence of Internal Pathology on Skin Changes

Many cosmetic defects are caused by internal factors. Key substances ensuring normal body function include proteins, carbohydrates, fats, salts, and water. Scientists have observed a connection between disrupted carbohydrate metabolism and the development of acne and seborrhea.

- Lipid metabolism disturbances can lead to yellow spots on the eyelids and skin (xanthomas).
- Reduced fat metabolism may contribute to fat accumulation under the chin, leading to a «double chin.»
- Disruptions in lipid metabolism can also be linked to seborrhea and the formation of comedones.

In cases of impaired water metabolism in the skin and subcutaneous tissue, water retention can lead to puffiness, especially around the eyes.

Endocrine and Organ Disorders Affecting the Skin

- Hypothyroidism (reduced thyroid function) leads to thinning, brittleness, and hair loss, especially in the eyebrows and scalp. The skin becomes dry, very thin, and wrinkled.
- Adrenal insufficiency causes Addison’s disease, which results in pigmentation disorders, giving the skin a bronze hue.

Disorders in Internal Organs can manifest on the skin as well. For example:

- Blood disorders lead to skin rashes.
- Gastrointestinal diseases often result in rashes on the face and torso.
- Liver diseases are frequently associated with pigmentation spots on the skin.

Toxic Substances in the Blood

When breakdown products from the intestines or kidneys enter the bloodstream, they can lead to various skin conditions, such as:

- Hives
- Hair loss
- Pigmentation spots
- Acne

These changes emphasize the importance of understanding the connection between internal health and skin appearance, as imbalances within the body can lead to noticeable cosmetic and dermatological issues.

Prevention of Skin Aging

Understanding the process of skin aging provides a basis for choosing the appropriate methods of skincare. The application of a comprehensive, holistic approach can help both minimize the effects of aging and prevent its further progression. This approach encompasses both lifestyle and skincare, which are considered and changed in relation to one another. Since oxidative stress is the primary external cause of skin aging, any lifestyle changes should aim to minimize its impact.

Healthy eating, rich in fruits and vegetables, provides antioxidants that can help limit the harmful effects of free radicals on the skin. The diet should be as diverse as possible. However, some foods are particularly rich in antioxidants and may even have a protective effect on the skin: carrots, apricots, other orange and yellow fruits and vegetables, blueberries, green leafy vegetables, sweet peppers, tomatoes, beans, and other legumes, fish, and nuts. At the same time, while choosing beneficial foods, some should still be avoided. It has been established that foods with excessively high levels of fats and carbohydrates contribute to the aging process.

Smoking significantly accelerates aging, reduces elasticity, and causes a dull appearance of the skin. Quitting smoking will improve the skin's appearance by eliminating nicotine and other chemicals found in cigarettes. The skin changes at each stage of the life cycle, so skincare should take into account the changing needs of the skin with age. Careful skincare is an essential part of the comprehensive approach to preventing signs of aging – loss of volume and density, wrinkle formation, and associated dryness or sensitivity of aging skin.

Skincare should consist of three stages: cleansing, care, and protection from the sun. Cleansing helps remove makeup, dirt, and chemicals from the skin's surface. This is very important, as chemicals from environmental pollution on the skin's surface can exacerbate oxidative stress. Care involves restoring and hydrating the skin; appropriate products are used to address the signs of aging, which is a primary task. With the correct selection of the necessary product and its active ingredients, such as hyaluronic acid, glycine saponin, or coenzyme Q10, significant improvements in the skin's appearance can be achieved. Protection from UV rays is the most important step in preventing future skin aging.

23.3 Therapeutic cosmetology of the face

The range of services in medical cosmetology is constantly expanding. Let's consider the most common procedures for facial skincare.

3.1 SKIN CLEANSING

Skin cleansing (most often of the face) is a procedure that can take place in several stages, depending primarily on the degree of skin contamination. There are three main methods of cleansing: mechanical, ultrasound, and combined.

Mechanical Facial Cleansing

Mechanical facial cleansing, as a procedure, has a long history, evolving from ancient rituals to modern cosmetological techniques. In ancient Egypt, natural abrasive substances (such as sand mixtures, herbs, and honey) were used to cleanse and exfoliate the skin. In Greece and Rome, where hygiene and beauty culture were of high priority, regular skin cleansing was practiced using scrubs and special tools, such as scrapers (strigils), to remove impurities and dead cells. During the Renaissance, ancient traditions of body care were revived, leading to the development of more organized methods of facial cleansing using natural components and mechanical tools. In the 20th century, with the development of science and cosmetology, methods of mechanical cleansing were systematized. Cosmetologists began to apply various techniques for exfoliating the skin and emptying comedones.

Mechanical or manual skin cleansing is a cosmetic procedure aimed at physically removing impurities, excess sebum, keratinized cells, and other particles from the skin's surface. This is the most effective and result-oriented procedure for cleansing the skin and removing comedones using hands and special instruments (Uno spoon, Vidal needle).

Indications:

- Enlarged pores
- Comedones (blackheads)
- Acne
- Oily and combination skin
- Sebaceous plugs, milia
- As preparation for subsequent procedures

Contraindications:

- Skin infections (demodicosis, pyoderma, herpes)
- Allergic dermatoses in the acute stage (dermatitis, eczema, toxicodermias)
- Menstruation during the procedure
- Acute (inflammatory) acne
- Blood disorders, anticoagulant therapy

- Hypertension, diabetes
- Fragile blood vessels
- Skin cancer
- Individual hypersensitivity to materials used in the procedure
- Presence of wounds, cuts, burns
- Irritated skin
- Recent aggressive cosmetic procedures

Protocol for Mechanical Facial Cleansing Procedure:

1. Perform makeup removal depending on the skin type.
2. Wipe and disinfect the skin with an antiseptic solution (infection prevention).
3. Apply a mask that opens the pores.
4. Perform mechanical cleansing (use the Vidal needle to puncture the sebaceous pore and express its contents with the Uno spoon).
5. After the procedure, disinfect the skin with an antiseptic solution and apply an anti-inflammatory mask that tightens the pores.
6. Finish the procedure with the application of antibiotics in powder form (e.g., Tyrothricin, Baneocin, etc.) or a post-procedure cream with SPF 50 if needed.

Expected Results:

- Deep cleansing of the skin: Removal of excess sebum, impurities, and keratinized cells, which helps clear pores and reduce the appearance of comedones.
- Improved texture and tone: Cleansing helps remove dead skin layers, stimulating the skin's regeneration process, making it smoother and fresher.
- Reduction of inflammatory processes: Regular cleansing can help reduce the risk of acne and other inflammatory processes, especially in combination or oily skin.
- Increased effectiveness of subsequent procedures: Skin that is free of excess impurities better absorbs nourishing agents, creams, or other cosmetic products, enhancing their action.
- Cell renewal: By stimulating the natural cellular exchange process, the skin acquires a healthier appearance, which is reflected in its radiance and elasticity.

Results may vary depending on the skin type, condition, and individual characteristics, as well as the method used for the procedure.

Frequency of the Procedure:

• For oily or problem skin, the procedure should be performed weekly until a stable effect is achieved. For prevention, it is done once a month.

• For dry skin, the procedure should be done once every 2 months.

Doctor's Recommendations:

- A few days before the cleansing, it is recommended to start preparing the skin at home using peels or moisturizing products. This will make the skin more elastic, and the cleansing process will be less traumatic and more effective.
- The patient should be informed that after manual facial cleansing, mild redness of the skin (up to 2 days) and some pain sensations may occur.
- Avoid washing the face for 12 hours after cleansing, and for the first day after the procedure, do not apply cosmetics.
- It is recommended to use moisturizing and sunscreen creams.
- For a few days after the procedure, wipe the face with alcohol-containing toners in the morning and evening.
- The areas cleaned during the procedure should not be exposed to UVA and UVB rays for 24 hours.
- The selection of the necessary products for mechanical cleansing should be made only after consultation with and recommendations from the treating physician.
- If the client has inflammatory processes on the skin/acne that could not be removed during the first procedure, a repeat session is recommended for deeper cleansing. This is why mechanical cleansing is often supplemented with hardware techniques.

Complications that may arise during the procedure:

- Irritation and redness: Physical impact may cause temporary redness or irritation, which can last for 2–3 days after the procedure.
- Microtrauma and skin damage: Incorrect or excessive cleansing can lead to microcracks, scratches, or other micro-damages, making the skin more susceptible to infections.
- Inflammatory processes and acne activation: If the procedure is performed on skin with active inflammatory processes or acne, inflammation may worsen or an infectious process may spread.
- Infections: Non-sterile equipment or inadequate disinfection may cause bacterial infections.
- Allergic reactions: The use of certain components (scrubs, cleansing solutions, masks, creams) can trigger allergic reactions in people with heightened sensitivity.
- Post-inflammatory pigmentation: After the procedure, dark spots or uneven skin tone may appear, especially in people with darker skin.

Ultrasonic Facial Cleansing

Ultrasonic facial cleansing is a modern cosmetic procedure that uses high-frequency ultrasonic vibrations for delicate skin cleansing from impurities, keratinized cells, and excess sebum.

The history of this technology is linked to the development of ultrasonic methods in industry and medicine, later applied in cosmetology. Initially, ultrasonic technology was used in industry for cleaning and processing parts due to its ability to dissolve contaminants on surfaces. With the development of medicine, ultrasound found applications in diagnostics (ultrasonic diagnostics) and therapy, which allowed researchers to study its effects on tissues. In the 1980s–1990s, cosmetologists began using ultrasonic devices for skin cleansing, as this method provided deep cleansing without mechanical impact, reducing the risk of irritation.

Due to high-frequency vibrations, ultrasonic cleansing gently exfoliates the surface layer of the skin, stimulates blood circulation, and enhances the absorption of active cosmetic ingredients. Modern ultrasonic cleansing devices feature adjustable intensity, allowing the procedure to be adapted to the skin type and individual needs of the client. Today, ultrasonic cleansing is commonly used in comprehensive skincare programs to maintain skin health, improve texture, and overall facial appearance.

How it Works: Ultrasonic vibrations remove dead skin cells, and the spatula gently lifts them off the surface. The procedure promotes deep penetration of cosmetic products into the skin, which results in well-hydrated skin that looks healthy. During the ultrasound cavitation vibration, the tip emits sound waves that are inaudible to the human ear. The vibration of ions (positive and negative alternating sound waves) creates a strong pressure wave on the cell membranes, which removes impurities from the upper skin layer. This also softens the keratinized layer, gently cleansing dead skin cells.

Ultrasonic Facial Cleansing Procedure Protocol:

1. Thoroughly cleanse the client's skin.
2. Apply a toning agent or water-based gel to the treated area to keep the skin hydrated for effective ultrasound penetration.
3. Use a cotton pad soaked in the toning agent to hydrate the skin before each new contact with the scrubber.
4. Move the scrubber tip along the lymphatic vessels (3-5 times in the same area) at a 45° angle.
5. Maintain skin hydration during the procedure.
6. The scrubber tip should be in constant motion to prevent the risk of burns.
7. Finish the procedure with the application of Tyrosur powder (or a post-procedure cream with SPF 50, as needed).

Indications for Ultrasonic Facial Cleansing:

- Enlarged pores, oily skin
- Small number of comedones (blackheads)
- Mild acne

- Isolated sebaceous plugs, milia
- Excessive keratinization and dryness
- Hyperpigmentation
- Delicate cleansing of sensitive skin
- Mimic wrinkles
- As a preparatory stage for other procedures

Contraindications:

- Infectious skin diseases
- Allergic dermatoses (eczema, toxicodermias)
- Herpetic skin lesions
- Menstruation during the procedure
- Acute inflammatory acne
- Acute stages of atopic dermatitis or psoriasis
- Presence of medical devices in the treatment area (implants, etc.)
- Recent aggressive procedures

Expected Results:

- Removes keratinized skin cells
- Visually reduces forehead wrinkles and fine wrinkles on the face, neck, and décolleté
- Reduces the visibility of scars from injuries and blemishes
- Slows down the skin aging process and age-related changes
- Improves skin elasticity

Recommended Course of Procedures (for preventive purposes):

- 2-5 sessions with weekly intervals, 1–3 times per year
- Combining ultrasonic cleansing with other cosmetic procedures can yield excellent results.

Doctor's Recommendations:

- The patient should be informed that slight redness may appear after ultrasonic facial cleansing.
- Do not apply cosmetics during the first 24 hours after the procedure.
- For a few days after the procedure, use alcohol-based toners in the morning and evening.
- Use moisturizing creams.
- For the first 24 hours after the procedure, avoid exposing the treated areas to UVA and UVB rays. It is advisable to apply sunscreen.

Possible Temporary Side Effects After Ultrasonic Cleansing:

1. Erythema: This is a result of intensive ultrasound and mechanical action on the skin, usually disappearing a few hours after the procedure.
2. Mild swelling: A tissue reaction to the ultrasound vibrations, typically lasting several hours, especially under the eyes or in sensitive areas.

3. Skin dryness: The ultrasound removes surface oils and impurities, which can lead to temporary dryness. It is recommended to apply nourishing creams or masks after the procedure.

4. Irritation or peeling: Intense cleansing can disrupt the upper layer of the skin, especially if the skin is dry or sensitive. It is advised to avoid aggressive skincare products for 1–2 days following the procedure.

5. Temporary increased sensitivity: After cleansing, the skin may become more sensitive to external factors (sun, wind, cosmetics). It is recommended to use sunscreen and avoid direct sun exposure.

6. Breakouts (rare): If the skin had clogged pores, ultrasonic cleansing may cause impurities to surface, leading to temporary breakouts. This is usually a normal reaction that resolves within 1–2 days.

7. Microtrauma (very rare): Incorrect use of the device or excessive intensity of the procedure can lead to minor skin damage.

Combined Facial Cleansing

Mechanism of Action:

Combined skin cleansing is performed when a single method (mechanical or ultrasound) is insufficient. It doesn't make sense to clean the skin with ultrasound if there are deep comedones (blackheads) and pustules. Similarly, there is no point in performing only manual cleansing if the patient desires a simpler method of cleaning for clean, well-groomed, and healthy skin, as combined cleansing removes deep comedones and pustules through mechanical action on the skin, while ultrasound removes more superficial impurities.

Combined facial cleansing is suitable for people of all ages and allows for gentle treatment of sensitive areas. Mechanical cleansing helps eliminate visible impurities, acne, and milia, while ultrasound treats swelling, keratinization, redness, and comedones. The procedure takes a relatively long time (about two hours) because it occurs in two stages.

Number of Procedures:

Combined facial cleansing is a one-time procedure, performed as needed based on the skin's condition, but no more often than once every 2-3 months. The effect of the procedure is not immediately visible. Essentially, combined cleansing has a prolonged action aimed at future results. After the redness subsides, the skin will appear smoother, fresher, more even, and cleared of inflammation and comedones.

Manual Cleansing Protocol:

1. Makeup Removal: The skin of the patient/client is cleansed according to their skin type.

2. Disinfection: The skin is wiped and disinfected with an antiseptic to prevent infection.

3. Pore Opening Mask: A mask is applied to open the pores.

4. Manual Cleansing: Using a Vidal needle, the fatty pore is punctured, and the contents are squeezed out using a Uno spoon.

5. Ultrasound Cleansing: Ultrasound cleansing is performed using an ultrasonic gel.

6. Aftercare: After the procedure, the skin is wiped with an antiseptic and a pore-tightening anti-inflammatory mask is applied.

7. Finish: The procedure concludes with the application of an antibacterial powder or post-procedure cream (with SPF 50 if needed).

Indications:

- Combination skin type
- Oily skin
- Keratosis, particularly age-related
- Uneven skin surface
- Comedones (blackheads)
- Presence of inflammatory processes
- Poor complexion

Contraindications:

- Dark skin
- Myomas and inflammations
- Active herpes
- Pregnancy
- Oncological diseases

Expected Results:

- Skin is cleansed from both superficial and deep comedones (blackheads)
- Pores are tightened
- Sebaceous plugs, milia, and lipomas are removed
- Complexion improves

Doctor's Recommendations:

- A week before the combined cleansing, it is advised not to consume alcohol, sunbathe, or eat spicy, salty, smoked foods, or citrus fruits (which may cause dehydration or allergies).
- Two days before the procedure, discontinue the use of anticoagulants (e.g., aspirin) to prevent bruising (hematomas).
- A week before combined facial cleansing, avoid visiting the sauna, bath, or solarium.
- After cleansing, avoid the solarium and sauna for at least 14 days. Direct sun exposure should be avoided, and baths or scrubs should not be used.
- The choice of cleansing products should only be made after consultation with a doctor.
- Patients should be warned that after manual cleansing, there may be slight redness of the skin (up to 2 days) and some discomfort.

- For a few days after the procedure, the face should be wiped with alcohol-containing tonics in the morning and evening.
- Do not apply makeup during the first 24 hours after the procedure.
- Use moisturizing creams.

During combined cleansing, side effects from both mechanical and ultrasound cleaning may occur.

Microdermabrasion of the Face

The Method:

Dermabrasion techniques emerged in the 20th century when doctors noticed that mechanical skin polishing helped its renewal. The first attempts at this method date back to the 1950s when American dermatologist Abner Curtin introduced a technique for scar removal using a rotating metal brush. Over time, the method was refined, and today modern equipment with diamond or laser tips is used.

Microdermabrasion, also known as «facial polishing,» is a type of mechanical facial exfoliation using equipment with diamond-coated tips. It is the most delicate method of mechanical peeling for the face.

Mechanism of Action:

Microdermabrasion improves the surface condition of the skin by removing the upper layer. During the procedure, keratinized skin cells are removed, stimulating the regeneration process and collagen production.

Diamond microdermabrasion is performed using tips of different sizes and hardness for different skin types and depths of exfoliation. The tips are equipped with natural diamond particles that smooth the skin and remove dead cells. During the procedure, dead cells are collected in a special container via vacuum suction.

Indications:

- Wrinkles
- Hyperpigmentation
- Uneven skin texture
- Enlarged pores
- Scars, post-acne
- Acne breakouts
- Stretch marks
- Dull complexion

Contraindications:

- Skin diseases in the exacerbation stage (psoriasis, eczema)
- Hypersensitive skin
- Keloid scars
- Herpes

- Skin integrity violations (open wounds, burns)
- Infectious diseases
- Inflammatory skin conditions
- Tendency to form scars
- Rosacea
- Pregnancy and breastfeeding
- Age under 22 years

Microdermabrasion Procedure Protocol:

1. Cleansing and Drying: The skin is thoroughly cleansed and dried.
2. Skin Tension: The skin is gently stretched with the help of the index and middle fingers, and the device is carefully moved along the facial area, performing gentle exfoliation on the face and neck.
3. Targeted Treatment: After soft exfoliation, additional treatment may be applied to areas of secondary pigmentation, acne scars, and wrinkles.
4. Removing Dead Cells: Use a cotton towel soaked in cold water to remove dead cells from the skin.
5. Toning: The skin is toned or wiped with non-aggressive antiseptics (e.g., chlorhexidine).
6. Mask: A mask is optional.
7. Post-Procedure Cream: Apply post-procedure cream with SPF 30.

Expected Results:

- Increases skin elasticity and firmness
- Accelerates cellular exchange processes
- Improves blood circulation and lymphatic drainage
- Reduces blackheads and comedones
- Removes dead skin cells
- Improves skin permeability for the subsequent application of skincare products

Doctor's Recommendations:

- Patients should be informed that mild burning or redness of the skin may occur after the procedure.
- For the first 24 hours after the procedure, avoid applying cosmetics.
- Use moisturizing creams.
- For several days after the procedure, the face should be wiped with alcohol-based tonics in the morning and evening.
- For at least 14 days post-microdermabrasion, avoid visiting the solarium or sauna.
- Avoid direct sunlight, and do not use scrubs.
- Microdermabrasion should be performed only after a consultation with a doctor and based on their recommendations.

Possible Side Effects:

- Redness and Swelling: This occurs due to mechanical damage to the upper skin layer and lasts 3–7 days.
- Skin Peeling: Resulting from active epidermal renewal, lasting up to 10 days.
- Pain and Sensitivity: Caused by the impact on deeper layers of the dermis, lasting 5–14 days.
- Pigmentation or Hypopigmentation: May occur due to improper aftercare or individual susceptibility, lasting from a few weeks to months.
- Infection Risk: Can develop with poor hygiene or a weakened immune system and may last for weeks if complications arise and require treatment.
- Scarring (Rare): Associated with deep skin damage, may be permanent.

It is important to note that the fresh complexion, smooth, glowing, and youthful skin are the results of microdermabrasion. Additionally, during the procedure, the skin's natural rejuvenation processes are activated, ensuring its youth and health from within.

3.2 FACIAL MASSAGE

Facial massage has a long history, dating back to Ancient China and India, where it was used to improve blood circulation and promote rejuvenation. In Europe, the technique gained popularity in the 18th and 19th centuries, when doctors and cosmetologists began developing special techniques for influencing the facial muscles. The famous French doctor Joseph Pierre Guerlain made significant contributions to the development of massage techniques.

Deep vacuum massage using devices has a positive effect on lymphatic activation, preventing skin tone loss, and eliminating toxins and tissue waste. It accelerates blood circulation and cellular metabolism, promoting collagen production and improving the condition of connective tissue.

Mechanism of Action:

The procedure mimics the «pumping» effect that muscles usually create in lymphatic vessels. Alternatively, pressure is reduced on the lymphatic vessels, and lymph fluid is moved toward the nearest lymph nodes. This increases lymphatic circulation, which helps remove waste products from metabolism, minimizing swelling and water retention.

Indications for Facial Massage:

- Stimulation of lymphatic drainage in the face
- Improvement of local blood circulation
- Appearance of a healthy, natural glow
- Improvement of complexion
- Wrinkles and early signs of aging

- Facial muscle spasms
- Enhancing the effects of other treatment methods

Contraindications:

- Pregnancy
- Skin diseases
- Hypersensitive skin
- Keloid scars
- Herpes
- Rosacea and fragile blood vessels
- Plastic surgery or cosmetic injections less than 2–3 weeks ago
- Skin integrity violations (open wounds, burns)

Expected Results:

- Circulatory System: Blood circulation is accelerated, allowing fresh oxygen and nutrients to reach cells more quickly. Extreme expansion of blood vessels helps combat the accumulation of capillaries and prevents erythema. Venous flow is also accelerated, preventing the development of rosacea and pink acne.
- Nervous System: Vacuum massage has a calming effect on sensory nerve endings.
- Muscle System: Accelerated blood circulation in muscles improves muscle function.
- Bone System: Enhanced circulation and nourishment of bones.
- Skin: Accelerated cell metabolism, improved complexion, softening of fat deposits, and reduced sebum production.

Result and Recovery:

The effect of one procedure lasts for 3–4 weeks. The procedure has a prolonged effect.

Doctor's Recommendations:

- After the procedure, it is recommended to refrain from using decorative cosmetics for 2–3 days and avoid scrubs.
- Deep peeling should not be performed for about 5 days (due to the risk of skin trauma).
- Use moisturizing creams.
- Avoid using scrubs.
- Vacuum facial massage should be performed only after consultation and following the doctor's recommendations.

Manual facial massage

Facial massage is one of the most well-known classic methods of basic anti-aging therapy.

Main Effects of Facial Massage:

- Activation of blood supply and lymphatic drainage of the skin and subcutaneous fatty tissue.
- Acceleration of metabolism and synthesis of elastin, collagen, and natural hyaluronic acid.
- Improvement of skin firmness, elasticity, and density.
- Elimination and prevention of wrinkles.
- Strengthening of facial muscles and contour.
- Strengthening of capillaries.
- Stimulation of the skin's local immunity.

Facial massage is an excellent form of gymnastics and part of proper skincare, suitable for people of all genders and ages. It does not require rehabilitation or anesthesia.

Results:

- Regular facial massage helps prevent skin aging effectively without medications, implants, or surgery, even contributing to the lifting of soft tissues.
- Blood and lymph circulate more actively, delivering oxygen and nutrients while removing toxins and metabolic waste.
- Skin and soft tissues gain firmness, facial contour is lifted, and wrinkles are smoothed.
- In combination with other therapies, facial massage helps eliminate pigmentation and stimulates the resorption of post-acne scars.

Contraindications:

Facial massage should not be performed on areas with:

- Moles
- Skin tumors
- Acute inflammatory processes
- Skin damage
- Hemophilia

Facial Massage Helps with:

- Age-related changes
- Wrinkles
- Contouring the face
- Skin laxity
- Dry/oily skin
- Dull complexion, dark circles under the eyes
- Acne (pimples)
- Enlarged pores
- Pigmented spots
- Scars and blemishes

Types of Massage Techniques:

- Classic Massage: Based on traditional movements like stroking, rubbing, kneading, and vibration. It improves circulation, lifts the skin, and reduces puffiness.
- Lymphatic Drainage Massage: Performed with light, smooth movements along lymphatic pathways. It helps remove excess fluid, reduce puffiness, and dark circles under the eyes.
- Myostimulation Massage: A deep massage that affects facial muscles, increasing their tone. It promotes a lifting effect and prevents skin sagging.
- Pinching Massage (Jacquet): Uses intensive pinching movements to improve microcirculation and regulate sebaceous glands. It's used for oily skin and acne.
- Japanese Massage (Zogan, Asahi): Combines deep muscle work with lymphatic drainage. Performed with attention to lymphatic pathways for rapid rejuvenation.
- Gua Sha Massage: Uses special stone or jade plates to improve circulation, relieve muscle tension, and lift the facial contour.
- Cryomassage: Uses the cooling effect of ice or liquid nitrogen to stimulate blood circulation, tone the skin, and reduce pores.
- Vacuum Massage: Uses special vacuum cups to stimulate lymphatic flow, improve skin lifting, and reduce stagnation.
- Reflex (Acupressure) Massage: Based on applying pressure to biologically active points on the face. It helps relieve tension, improves the function of internal organs, and enhances skin condition.
- Chinese Massage (Guanfa): Combines kneading, pressing, and stroking along specific energetic meridians. It stimulates blood circulation, rejuvenates the skin, and improves overall tone.

Each technique has its own features and is suitable for different skin types and cosmetic issues.

Side Effects:

For all techniques, the side effects are generally similar:

- Redness and Irritation: Caused by increased blood circulation, lasts 1–2 hours.
- Worsening of Acne: Occurs due to activation of sebaceous glands, lasts several days.
- Allergic Reactions: Occur from sensitivity to massage products, lasting from several hours to 2–3 days.
- Appearance of Spider Veins: Related to capillary damage from excessive pressure, may persist for a long time.
- Increased Oiliness or Dryness of Skin: Depends on sebaceous gland reaction, can last for several days.

Facial massages enhance the effectiveness of many other cosmetic procedures.

Cryotherapy and Cryomassage for the Face

Cryotherapy has its origins in ancient times when Hippocrates described the use of cold for healing. In the 20th century, thanks to advancements in dermatology, cryomassage with liquid nitrogen or ice became widely used for the treatment of acne, enlarged pores, and the stimulation of blood circulation. Modern technology has expanded the use of cryomassage in various cosmetic and medical procedures.

Cryotherapy involves applying cold to the skin cells, using cosmetic devices or nitrogen, stimulating cell regeneration, improving blood circulation, and enhancing tissue nourishment.

Mechanism of Action:

Cryotherapy is ideal for any abrasive treatments. The procedure soothes irritated skin, reduces redness, speeds up regeneration, and promotes skin cell rejuvenation. Cold temperatures cause blood vessels in the face to constrict, which reduces blood flow to the skin surface, thus reducing inflammation and swelling. The body then reacts by slowly increasing the flow of warm blood to the face.

Cryotherapy also helps to tighten pores, giving the skin a healthier appearance, while relaxing and toning the skin.

Indications for Cryotherapy:

- Narrowing of facial pores to prevent acne.
- Enhancing the penetration of other skin products.
- Reducing inflammation and irritation.
- Soothing the skin.
- Relaxing patients/clients.
- Reducing the intensity of wrinkles.
- Alleviating dry skin.
- Improving skin elasticity and firmness.

Contraindications:

- Pregnancy
- Cold allergy
- Skin diseases
- Hypersensitive skin
- Keloid scars
- Herpes
- Disrupted skin integrity (open wounds, burns)

Cryotherapy Procedure:

1. Cleanse the skin.

2. Apply an ultrasound gel or mask depending on skin type to the area of treatment.

3. Perform the procedure along massage lines 3–5 times, ensuring the skin remains moisturized throughout the procedure. The optimal duration of the procedure is 7–8 minutes.

Expected Results:

- Relaxes the skin: The procedure relaxes muscles, reduces stress, and increases blood circulation.
- Reduces pore size: Cryotherapy clears pores of impurities, toxins, excess oil, and bacteria.
- Increases absorption: Open pores allow the skin to better absorb nutrients, such as after applying a herbal mask.
- Smooths wrinkles: Cryotherapy tightens the skin, helping to reduce the appearance of wrinkles.
- Narrowing of pores: The «cold hammer» compresses expanded capillary blood vessels on the face caused by genetics, aging, or excessive sun exposure. This also helps retain moisture.
- Soothes the skin: The «cold hammer» helps calm irritated and sensitive skin by reducing blood flow to the affected area.

Recommendations for Post-Procedure Care:

- Avoid using makeup within the first 24 hours after the procedure.
- Use moisturizing creams.
- Do not apply alcohol-based products for several days after the procedure.
- After cryotherapy, avoid visits to tanning beds and saunas.
- Do not use scrubs.
- Cryotherapy should only be performed after consultation and recommendations from a physician.

Possible Side Effects:

- Localized redness and burning: This is a vascular reaction to the cold and usually lasts 30–60 minutes.
- Excessive dryness: Caused by pore narrowing and reduced sebum production, lasting 1–3 days.
- Peeling and irritation: A reaction to the low temperature, which can last up to 5 days.
- Frostbite: Can occur with excessive cold exposure, with duration depending on the degree of damage.
- Hypo- or hyperpigmentation: This is possible for those with skin prone to pigmentation, lasting from a few weeks to months.

Cryotherapy is an effective treatment that enhances many cosmetic procedures and can be used to address a variety of skin concerns.

3.3 ELECTROPORATION FOR THE FACE

Electroporation was invented in the 1970s in the field of molecular biology to introduce DNA into cells. In the 2000s, it became popular in cosmetology when scientists discovered that electrical impulses could temporarily open cell membranes, allowing for needle-free introduction of cosmetic products into the deep layers of the skin.

Mechanism of Action:

During needle-free mesotherapy, a serum or gel with nutrients is applied locally to the treatment area. The electrode simply massages the skin, increasing its ability to absorb beneficial substances. Electroporation facilitates microscopic «injections» into the middle skin layer at a set frequency, allowing vitamins, minerals, amino acids, and medications to penetrate to the ideal depth for the best results. The procedure helps combat free radicals, stimulates metabolic processes, improves blood circulation, lymphatic drainage, and accelerates collagen and elastin production. Vitamin C and hyaluronic acid, in particular, enhance the skin's condition, giving it a glowing and healthy appearance.

Indications for Electroporation:

- Correction of age-related changes.
- Treatment of scars on the face.
- Post-acne scar correction.
- Treatment of hyperpigmentation.
- Acne treatment.
- Treatment of chronic dermatoses.
- Treatment of vascular pathology (telangiectasia, rosacea).
- Treatment of alopecia (hair loss).
- Correction of local fat deposits.
- Pre- and post-surgical skin preparation and rehabilitation.
- Preparation for chemical and mechanical peels, laser resurfacing, and RF lifting.

Contraindications:

- Pregnancy.
- Hypersensitive skin.
- Disrupted skin integrity (open wounds, burns).
- Blood clotting disorders.
- Acute inflammatory processes in the expected injection areas.
- Exacerbation of systemic connective tissue diseases.
- Exacerbation of chronic diseases, ARD, herpes.
- Presence of long-acting gels.
- Immunodeficiency.
- Presence of a pacemaker or metal implants.
- Cancer.

Procedure Description:

1. Cleanse the skin thoroughly.
2. Fill the container with serum suitable for the patient's needs.
3. Place the grounding electrode in the patient's hand.
4. Set the device to a low intensity. Gradually increase intensity depending on the treatment area.
5. Press on the soft part of the internal container to stimulate the flow of serum onto the skin in the required amount. Move the electrode in circular motions along the lymphatic vessels.
6. Patients typically feel impulses passing through the skin and may notice a metallic taste, without any other discomfort.
7. A normal skin reaction to treatment is mild erythema.
8. Finish the procedure by applying a post-treatment cream.

Expected Results:

- Increases the formation of healthy cells.
- Significantly reduces stretch marks.
- Directly delivers nutrients into the depth of the skin cells.
- Moisturizes the skin and improves overall condition.
- Stimulates collagen production.
- Makes the skin firmer and more toned.

Doctor's Recommendations:

- Inform the patient that mild redness may appear after the procedure.
- Avoid applying makeup within the first 24 hours after the procedure.
- Use moisturizing creams.
- Avoid tanning beds and saunas for at least a week after electroporation.
- Avoid direct sun exposure and do not use scrubs.
- Use sunscreen.
- Electroporation should only be performed after consultation with and under the recommendations of a doctor.

Possible Side Effects:

- Redness and mild tingling: Occurs due to the action of the electrical impulses, usually subsiding within 1–2 hours.
- Increased skin sensitivity: Caused by stimulation of nerve endings, lasting 1–2 days.
- Allergic reactions to cosmetic products: Manifesting as rashes or itching, lasting several days.
- Mild swelling: Caused by activation of lymphatic flow, subsiding within 24 hours.
- Microburns (rare): Possible with too strong an impulse, healing within 3–7 days.

Electroporation is an effective, non-invasive procedure for introducing active ingredients into the skin, with benefits for a variety of skin conditions and rejuvenation.

3.4 OXYGEN MESOTHERAPY

Oxygen therapy developed in the 1980s when doctors noticed the positive effects of oxygen on the skin. Its cosmetic application gained popularity in the 2000s when devices were developed to deliver pure oxygen saturated with active substances, promoting improved skin color and regeneration.

This procedure enhances the effect of skincare products and activates cellular respiration. Oxygen mesotherapy is perfect for situations when a person needs to look their best in a short period, without any recovery time.

Mechanism of Action:

During the procedure, room air is filtered, combined with a special solution to create a powerful stream of low-molecular fluid with oxygen. Under high pressure, the molecules of the serum penetrate deeply into the skin, while oxygen molecules stimulate skin rejuvenation. The antibacterial properties of the procedure reduce the likelihood of skin irritation. Additionally, the procedure helps healing serums penetrate deeper into the skin layers.

The oxygen concentrator uses air as a raw material. Oxygen is separated from nitrogen at room temperature through adsorption under pressure via a high-quality molecular filter. This results in oxygen with a high level of purity.

Oxygen saturation of the skin, along with vitamins, stimulates collagen production, helping to correct facial features and restore skin elasticity and firmness. Oxygen mesotherapy also helps cleanse the skin from environmental pollutants and rejuvenates it.

Indications for Oxygen Mesotherapy:

- Reduction of wrinkles.
- Pore cleansing.
- Reduction of acne marks.
- Removal of excess oil from the skin.
- Slowing down age-related changes.
- Treatment of dry skin and skin prone to flaking.

Contraindications:

- Pregnancy.
- Hypersensitive skin.
- Disruption of skin integrity (open wounds, burns).
- Blood clotting disorders.
- Acute inflammatory processes in the expected injection areas.
- Exacerbation of systemic connective tissue diseases.
- Exacerbation of chronic diseases, ARD, herpes.

- Presence of long-acting gel.
- Immunodeficiency state.
- Cancer.

Procedure Description:

1. Thoroughly cleanse the skin.
2. Choose the necessary low-molecular serum (e.g., hyaluronic acid) for infusion and add it to the container in the oxygen gun.
3. Apply the serum along the tension lines across the entire surface of the face and neck, from the center to the periphery.
4. Repeat the procedure to achieve complete hydration of the middle and upper layers of the skin.
5. Finish the procedure by applying a post-treatment cream.

Expected Results:

- Speeds up cell reproduction.
- Accelerates regeneration, aiding the healing of scars, acne, and stains.
- Unlike other invasive anti-aging procedures like Botox or microdermabrasion, oxygen masks rarely cause side effects such as burning or redness.
- The oxygen and serum delivery process is delicate, making oxygen masks suitable for people with sensitive skin or those who prefer to avoid injections or chemical treatments.

Doctor's Recommendations:

- Do not apply makeup during the first 24 hours after the procedure.
- Use moisturizing creams.
- Avoid applying alcohol-based products to the skin for several days after the procedure.
- Avoid tanning.
- Do not use scrubs.
- Oxygen mesotherapy should only be performed after consultation with and under the recommendations of a doctor.

Possible Side Effects:

- Temporary redness: Caused by increased blood circulation, usually disappears within 1–2 hours.
- Tightness sensation: Related to the active oxygen saturation of the skin, lasting 1–2 days.
- Possible skin dryness: Occurs with insufficient hydration, which may last up to 5 days.
- Allergic reactions to cosmetic products: May occur when using active ingredients, lasting several days.

Oxygen mesotherapy is an effective, non-invasive treatment for skin rejuvenation, hydration, and improvement, offering a quick and noticeable improvement without downtime.

3.5 RF – FACE LIFTING (Radiofrequency Lifting)

Radiofrequency (RF) lifting emerged in the 1990s as an alternative to surgical facelifts. This method is based on the use of radio waves that heat the deep layers of the dermis, stimulating collagen production. Initially developed for medical purposes, the technology was later adapted for cosmetic use as a non-surgical method of rejuvenation.

Bipolar radiofrequency (RF) energy is a modern technology used with cosmetic devices for non-invasive skin tightening in the early signs of aging (looseness, loss of elasticity). RF lifting uses an electric current with a frequency range of 0.1 to 5 MHz. Pure radiofrequency energy is primarily used to treat skin laxity, particularly for tightening facial contours. This procedure is most effective for patients with mild to moderate skin sagging.

Mechanism of Action:

Radiofrequency energy works by generating heat in the area of maximum resistance within the skin. The radio waves penetrate the outer layers of the skin, transferring thermal energy to deeper layers. This energy stimulates collagen formation and causes tissue contraction. The dermis and subcutaneous layers heat simultaneously, causing collagen fibers to tighten, which in turn tightens the skin, creating an immediate effect. The metabolism of fibroblasts increases, producing new collagen fibers that last for a prolonged period.

A significant amount of RF radiation reaches the deeper layers of the skin, causing the dermis to thicken. RF lifting helps reduce the depth of wrinkles, making the skin firmer and tighter. As a result of the RF energy, collagen proteins strengthen and produce new collagen proteins.

Indications for RF Lifting:

- Skin rejuvenation.
- Reduction of cellulite (on the body).
- Reduction of scars, post-acne marks, and stretch marks.
- Skin tightening.
- Improvement of skin elasticity.
- Tightening of the double chin.
- Reduction of deep wrinkles.

Contraindications:

- Skin diseases in the acute stage.
- Hypersensitive skin.
- Keloid scars.
- Herpes.
- Disruption of skin integrity (open wounds, burns).
- Infectious skin diseases.
- Inflammatory skin conditions.

- Tendency to form scars.
- Pacemakers or implants.
- Pregnancy and lactation period.

It is recommended to undergo additional microdermabrasion or ultrasound skin cleansing before performing the RF facelift procedure to ensure better wave penetration.

Procedure Description:

1. Remove makeup and cleanse the skin.
2. Apply ultrasound gel to the cleaned skin.
3. Gradually treat individual areas of the skin, starting with a low intensity of radiofrequency to prevent burns. (The higher the intensity, the faster the specialist should move the device.)
4. Clients/patients generally feel a comfortable deep heat.
5. The session lasts between 20 and 50 minutes, depending on the area size and skin condition.
6. The average course involves 5–15 sessions, typically with 1–2 sessions per week.

Expected Results:

- A painless method with no recovery time.
- Results are noticeable faster than with monopolar RF.
- Collagen fiber contraction promotes quick skin tightening.
- Fibroblast stimulation enhances collagen and elastin production, further contributing to skin tightening.
- Stimulation and breakdown of adipocytes (fat cells) aid in cellulite treatment.

Doctor's Recommendations:

- Do not apply cosmetics during the first 24 hours after the procedure.
- Use moisturizing creams.
- Avoid applying alcohol-based products to the skin for several days after the procedure.
- Do not use scrubs.
- Avoid sauna visits for one week.
- RF lifting should only be performed after consultation with and under the recommendations of a doctor.

Possible Side Effects:

- Redness and swelling: Caused by heating of the tissues, typically resolves within 1–2 days.
- Mild pain and tingling: Due to the thermal effect on deeper skin layers, lasting for a few hours.
- Dryness or increased oiliness: Depending on individual skin reactions, may last up to a week.

- Temporary loss of sensitivity: Caused by the impact on nerve endings, typically resolves within 1–2 weeks.
- Burns or tissue overheating: Possible with improper use of the device, healing time may range from a few days to several weeks.

RF lifting is an effective, non-invasive procedure for facial rejuvenation, offering skin tightening, collagen stimulation, and a more youthful appearance without the need for surgery.

3.6 LED THERAPY (Light Emitting Diode Therapy)

LED therapy is a non-invasive cosmetic method that uses light-emitting diode radiation of various wavelengths to stimulate cellular processes in the skin.

Mechanism of Action:

This procedure improves microcirculation, activates collagen and elastin synthesis, regulates sebaceous gland activity, and promotes skin healing. Infrared light penetrates deeply into the inner layers of the skin, muscles, nerves, and bones (2–7 cm depth).

LED Therapy Wavelengths:

- Red Light – 640 nm: Helps eliminate wrinkles and stimulates collagen production to tighten the skin. It improves blood circulation to the skin tissues, thus enhancing the supply of oxygen and nutrients to the cells. Additional collagen and elastin smooth and firm the skin, slowing down the aging process, giving the skin a younger appearance.
- Green Light – 495 nm: Green light is absorbed by melanin-producing cells, slowing melanin production and gradually breaking down excess melanin. Known for its soothing effect, green light can brighten the complexion, minimizing hyperpigmentation, freckles, and age spots. It also has anti-inflammatory properties.
- Blue Light – 470 nm: Blue light in this wavelength range has potent antibacterial effects, killing the bacteria that cause acne. It is effective in treating mild to moderate acne breakouts.

Indications:

- Acne and inflammatory processes (using blue light spectrum).
- Pigmentation (green light spectrum).
- Skin laxity and age-related changes (red light spectrum).
- Skin recovery post-procedures.
- Skin sensitivity and irritation.

Contraindications:

- Epilepsy (can provoke seizures).
- Cancerous conditions.
- Acute inflammatory processes.

- Pregnancy.
- Light sensitivity or the use of photosensitizing drugs.

Procedure Description:

1. Remove makeup and thoroughly cleanse the skin.
2. Apply ultrasound gel to the required skin area.
3. Choose the light color or combination of colors that address the patient's concerns.
4. Apply post-procedure and sunscreen cream.

The effect of the procedure can be enhanced with the use of a soothing or moisturizing mask after the therapy.

Expected Results:

- Tones muscles and reduces wrinkles.
- Creates a real lifting effect.
- Improves blood circulation and capillary formation.
- Promotes lymphatic drainage.
- Stimulates collagen and fibroblast production.
- Stimulates metabolism in skin tissues.
- Helps reduce swelling on the face and body.
- Accelerates healing processes.
- Stimulates the release of total cellular energy.

Doctor's Recommendations:

- Do not apply makeup during the first 24 hours after the procedure.
- Use moisturizing creams.
- Avoid using scrubs.
- Microcurrent face therapy should only be performed after consultation and under the recommendations of a doctor.

Side Effects:

- Redness of the skin: Caused by light stimulation, typically subsides within 30–60 minutes.
- Temporary dryness: Caused by the impact of light on the skin's water balance, lasting up to 3 days.
- Possible acne flare-up: Can occur with incorrect spectrum selection, lasting for a few days.
- Headache or eye fatigue: Caused by intense light radiation, typically resolves within a few hours.

LED therapy is a highly effective and non-invasive method for addressing various skin concerns, including acne, pigmentation, and signs of aging. The treatment helps improve skin health and appearance without the need for invasive procedures.

3.7 MICROCURRENT THERAPY

Microcurrent therapy was developed in the mid-20th century. Initially used in medicine to accelerate tissue healing, improve nerve and muscle regeneration, the method began being applied in cosmetology in the 1980s for skin rejuvenation, tone restoration, and edema reduction. Microcurrent therapy is used in cosmetology, rehabilitation, and physiotherapy to stimulate muscles, improve circulation, promote lymphatic drainage, and assist tissue regeneration and recovery after injuries or surgeries.

Mechanism of Action:

Microcurrent devices stimulate weak electrical pulses, mimicking natural processes that occur within the human body. The therapy is often used for clients seeking to tighten their skin and achieve an anti-aging effect. It is a relaxing, safe, and effective procedure.

The procedure improves local blood circulation, ensuring the flow of nutrients to the treated area while also promoting detoxification. Circulation is enhanced, aiding in the formation of new capillaries and stimulating the delivery of nutrients and oxygen to skin cells, leading to healthier skin with a radiant glow.

Microcurrent therapy stimulates the lymphatic system, collagen production, and reduces puffiness under the eyes while improving skin tone. Results are noticeable after the first session.

The therapy also stimulates collagen and fibroblast production. Collagen is responsible for the skin's firmness and elasticity. By encouraging the production of collagen and fibroblasts, the procedure helps reduce wrinkles, improves skin texture, and tightens pores. Since collagen cells grow slowly, it takes time to see visible results; noticeable improvements will appear after three months of consistent treatments.

It aids in the release of cytological energy, giving cells the energy they need to optimize blood flow, oxygen, and nutrient absorption, perform detoxification, grow, and regenerate.

Indications for Microcurrent Therapy:

- Skin laxity and decreased tone.
- Wrinkles and signs of aging.
- Puffiness and dark circles under the eyes.
- Couperose and microcirculation disorders.
- Post-acne scars, uneven skin texture.
- Rehabilitation after plastic surgeries or aggressive treatments.

Contraindications:

- Pacemakers, metal implants in the treatment area.
- Pregnancy and lactation.

- Cancerous conditions.
- Epilepsy.
- Acute inflammatory skin processes.
- Infectious diseases.

Procedure Description:

1. Cleanse the skin and apply a special conductive gel for the microcurrent.
2. Use electrodes or gloves to deliver microcurrents along the facial massage lines.
3. Perform lymphatic drainage and toning movements.
4. Conclude the procedure by applying moisturizing and soothing products.
5. Duration: 20–40 minutes. The recommended course consists of 8–12 sessions.

Expected Results:

- Improved skin tone and elasticity.
- Lifting effect.
- Reduced puffiness and dark circles.
- Smoother skin texture.
- Skin rejuvenation and recovery post-procedures.

Doctor's Recommendations:

- Avoid direct sun exposure and use SPF after the procedure.
- Drink plenty of water to enhance lymphatic drainage.
- Do not use aggressive skincare products on the day of the procedure.
- Follow the recommended course of treatments for long-lasting effects.

Side Effects:

- Mild redness (subsides within 1–2 hours).
- Tingling or light numbness (temporary).
- Headache (rare).
- Allergic reactions to the conductive gel (individual cases).

Microcurrent therapy is a safe and effective rejuvenation method suitable for most skin types, offering visible improvements in skin tone, texture, and overall vitality.

23.4 Peeling

The term «peeling» comes from the English verb «to peel,» which means «to exfoliate» in Ukrainian. Currently, cleansing and exfoliating the skin is just one (and perhaps not the most important) of the many effects of peeling. It is known that in response to skin damage and exfoliation, regeneration is stimulated, and the epithelial defect is replaced by young skin cells. This phenomenon forms the basis for the rejuvenating effect of peeling. Photoaging and chronological

aging are the main indications for its use. Skin damage caused by peeling and exfoliation (down to the dermis) stimulates the synthesis of collagen and elastin fibers, slowing down aging. Peeling now rightfully occupies an important place in the treatment of diseases such as acne, keratoses (removal of hyperkeratosis), and dyschromia (removal of pigment spots).

It is used to align the skin structure (for example, in scar changes) or to restore its original appearance (such as in tattoo removal). Additionally, peeling can be an enhancer, meaning it can serve as a conductor for active substances deep into the epidermis, even reaching the dermis.

History of Peeling

The word «peeling» has entered our lives relatively recently. However, this procedure has been known since ancient times and was most widely practiced in Ancient Egypt, where great attention was paid to maintaining beauty and youth. To preserve the beauty of the face and body, various compounds were used, such as lactic products, grape and lemon juice (precursors to modern chemical peels), pineapple pulp (the precursor of enzymatic peeling), and sand (now referred to as mechanical peeling).

The end of the 19th century marked the arrival of peeling in dermatological practice. A significant role was played by the German dermatologist Unna, who developed and successfully used chemical peeling methods (specifically, the use of resorcinol, salicylic acid, and trichloroacetic acid). Initially, this technique was used to correct dermatological diseases associated with keratinization disorders. The results were so remarkable, and the demand for skin rejuvenation so strong, that this method began to be applied for anti-aging purposes as well. At the beginning of the 20th century, French surgeon Le Gassé used phenolic compounds to treat the effects of gunpowder burns on soldiers during World War I.

However, research into the scientific basis of chemical peeling began only in the 1960s, and it wasn't until 1980 that American dermatologist Obagi formulated the modern, sequential concept of performing peeling. Only by adhering to the conditions outlined below can the safety and effectiveness of the procedure be guaranteed.

Types of Peels

Currently, peeling is an integral part of skin care for both the face and body.

Peeling techniques are classified into four groups based on depth of impact: superficial (not always recognized by all authors), medium, deep, and very deep.

1. Superficial Peel – A peel for self-use at home, where only the most superficial layer of keratinized skin cells is removed.

2. Medium Peel – Works on the level of the stratum corneum of the epidermis. These procedures are carried out by cosmetologists in a cosmetic clinic. The most common type is the superficial chemical peel using acids. This group also includes methods of cosmetic apparatus such as brushing, ultrasonic

peeling, and vacuum face cleaning. A specialist with a basic medical education is sufficient to carry out these procedures.

3. Deep and Very Deep Peels – These are within the realm of dermatologists. These techniques require preparation, a rehabilitation period, special facial care products, and sometimes (due to significant peeling and erythema) temporary withdrawal from public life.

Types of Peeling Based on Origin

Peeling can also be classified by origin into mechanical, physical, chemical, and biological types:

Mechanical Peel (also called «scrub»): One of the oldest forms of peeling. Abrasives are substances of increased hardness used for mechanical processing of other materials (in this case, skin). They can be natural (mineral-based, like sand, aluminum hydroxide, or sea salt; plant-based, like crushed peach or apricot pits, coconut shells, wheat bran) or synthetic (such as polymer granules widely used today).

4.1. MECHANICAL PEELING

Mechanical peeling can be done at home using special products such as scrubs and gommas.

Indications: Skin aging and the formation of defects; acne; excessive pigmentation on the face; as a preparatory procedure; for skin treatment to enhance serum absorption.

Contraindications: Inflammatory or pustular processes on the skin, thin sensitive skin; during acne treatment with retinoids; infectious and severe somatic diseases.

Scrub – This is a cream containing abrasives (fine particles, such as crushed coconut or almond pits) for «scraping» the upper layer of keratinized skin. These particles can be large, which is suitable for oily skin. For dry facial skin, abrasives should be as small as possible since it is more sensitive. Otherwise, the scrub may cause irritation. It is recommended to use a scrub for oily skin no more than twice a week. Dry facial skin cannot handle heavy loads, so it is better to use it once every two weeks. If there are pimples or other eruptions on the face, it is better to choose another method of care. Scrubs «scratch» the face, damaging pimples and promoting the spread of infection to surrounding areas.

Gommage – A gentler facial care product that does not contain small particles; its action is based on the formation of a crust as it dries. When removed by gently rolling with fingers, the gommage comes off along with the exfoliated skin. This product is more suitable for people with very sensitive skin.

Brassage is a type of mechanical peeling. Facial care is carried out using rotating brushes. The face must be cleansed of makeup beforehand. Brassage removes the upper layer of dead skin cells and stimulates blood circulation.

Results: As a result of mechanical peeling, skin rejuvenation, an even skin tone, improved microcirculation, smoothing of fine wrinkles, delayed aging, and prevention of acne formation can be observed.

4.2. PHYSICAL PEELING

Physical peeling is performed using liquid nitrogen or dry ice, ultrasound, or lasers.

Indications: Scars, bumps, oily skin, combination skin, unhealthy complexion, enlarged pores, post-acne, acne.

Contraindications: Skin integrity violations, keloid scars, skin diseases, hypersensitive skin, herpes.

Procedure:

Liquid Nitrogen or Dry Ice (temperatures ranging from -90°C to -110°C): This peeling method is similar to chemical peeling in that it involves a «burn» from cold. However, it is painless. This method is usually not used alone, but as an additional procedure when cleansing the skin through various other methods. During the procedure, the skin is treated with ice or exposed to ultra-low temperatures. As a result, collagen production is increased, cell regeneration is activated, and microcirculation is enhanced. After cleaning the skin with a lotion or toner, a chilled tampon is used. The procedure begins by treating the forehead, followed by the chin and nose, and then the cheeks, moving from the chin to the temples. The procedure lasts between 20 and 25 minutes. An intensive course of peeling consists of 8 procedures. The effect lasts approximately 3-4 months, after which the procedure should be repeated.

Ultrasound Peeling: The skin is treated with ultrasound waves while it is moistened. This process is completely safe and painless. The advantage of ultrasound peeling over other physical facial cleansing methods is that the outer keratinized layer is exfoliated without damaging young cells. Ultrasound peeling also significantly improves blood circulation.

Laser Peeling: Laser peeling is considered a deep peeling technique and is performed exclusively at a professional level in cosmetic clinics. The procedure involves «burning» the upper skin layer with a laser, accompanied by anesthesia. The advantage of this method is that it can remove even the finest wrinkles and treat hard-to-reach areas (e.g., the skin around the eyes). Laser peeling is effective for removing scars (such as those from acne). However, the skin needs approximately a month to recover after the procedure. If a superficial laser peeling is performed, the recovery time is reduced to a few days.

Results: The complexion improves, swelling significantly decreases, the «earthy» skin tone is lightened, skin regeneration occurs, the antibacterial properties of the skin are enhanced, and metabolic processes in the skin are

normalized, leading to the formation of healthy cells. Additionally, physical peeling promotes better lymphatic drainage, blood circulation, and rejuvenates the cellular composition of tissues and fibrous structures.

4.3. CHEMICAL PEELING

During chemical peeling, the regeneration processes are actively stimulated, and the upper layers of the epidermis are shed, resulting in improved facial skin condition without the need for surgical intervention.

Indications: Chemical peeling is a radical procedure, usually performed for serious skin issues such as acne, oily problematic skin, demodicosis, wrinkles, and scars. It is also used successfully for preventing skin aging, correcting age-related cosmetic defects, eliminating hyperpigmentation, and treating keratomas.

Contraindications: Neoplasms, warts, visible skin damage and irritation, herpes, sensitive skin, allergic reactions, tendency to form keloid scars, during acne flare-ups, after recent radiotherapy, or following the use of systemic retinoids.

There are several types of chemical peels. They are classified based on the strength of the acid's effect on the skin:

- Superficial Peels (retinoic, almond, glycolic, and pyruvic acid)
- Medium Peels (TCA based on trichloroacetic acid and combined Jessner's peels)
- Deep Peels (phenol peel)

Procedure:

A cotton applicator, soaked and carefully wrung out, is used to apply the solution to the face for 30–60 minutes. The procedure's duration depends on the skin's color change. The skin is treated starting from the forehead, then the nose, cheeks, and chin. The solution is applied more thoroughly in areas with wrinkles. During the procedure, the patient typically experiences a slight burning sensation. After the treatment, swelling occurs, and the patient is unable to open their eyes for the first two days. Two layers of cotton and two layers of silk medical tape are applied to the face, making a total of four layers. This ensures that the skin retains the solution's concentration for the required duration. The entire process takes between one and two hours. The mask cannot be removed for two days, after which it will almost fall off on its own. On the second day, when the mask is removed, the skin is treated with iodine-based thymol to promote skin regeneration. This mask needs to be worn for 7 days. After 7 days, swelling reduces significantly, and the skin forms a thick crust. Then, the face is covered with a thick layer of cotton for one day, after which the cotton is removed. From this point on, the patient can care for their skin using cosmetic products. Products containing glycolic acid should be avoided,

and sunscreen with an SPF of at least 30 should be used on sunny days.

Results: The result of the chemical peeling procedure is skin rejuvenation and a renewed velvety appearance. During the peeling process, the skin is toned and regenerates. Small wrinkles are eliminated, deep wrinkles and pigmentation spots are noticeably reduced, and the skin's texture is smoothed.

Best Season for Chemical Peeling: The most favorable season for chemical peeling is autumn, as the sun is less active, and the skin is less exposed to direct ultraviolet rays. Chemical peeling has a destructive effect on the skin, and it needs time to recover, while direct UV exposure can harm the regeneration process.

Side Effects and Complications: Swelling, focal hyperpigmentation, blister formation, exacerbation of herpes lesions, and facial skin itching may occur after the procedure.

4.4 BIOLOGICAL PEELING

Biological peeling is a facial cleansing procedure that belongs to superficial treatments, acting on the granular and horny layers of the epidermis. This cosmetic procedure is performed using special enzymes that accelerate biochemical reactions in the skin.

Indications:

- Scars
- Wrinkles
- Acne treatment
- Pore reduction
- Decrease in skin oiliness

Biological peeling is primarily used for thorough surface cleansing of the face in people with oily and problematic skin, as well as for gentle correction of early signs of aging. It is not suitable for treating visible and deep skin changes. In such cases, it can only provide good hydration and cleansing.

Contraindications:

- Tendency to form scars or pigmentation spots after skin injuries
- Skin neoplasms
- Skin diseases

Procedure:

Before performing biological peeling, the skin is cleansed with a special foam or gel. Then, starting from the least sensitive areas, the cosmetic substance is evenly applied with a soft spatula. The order of application for biological peeling is: nose, forehead, chin, cheeks, neck, décolletage area, lips, and eyelids. During the action of the enzymes, you should not move, talk, or blink. The skin and muscles must remain still. After 15 minutes, you should rinse your face and gently pat the skin dry with a soft towel or tissue. Then, a moisturizing cream is applied.

The procedure takes 30–40 minutes and is performed once a week for a month. A repeat course is recommended after 2–3 months.

Post-Procedure Care:

After biological peeling, you should avoid direct sun exposure for several days and refrain from using cosmetic products containing glycolic acid.

Results:

The enzymes in the cosmetic product dissolve the accumulated dead skin cells. As a result of biological peeling, the skin starts to breathe freely, the complexion improves, cell and tissue regeneration accelerates, and noticeable skin rejuvenation occurs.

23.5 Biorevitalization

Biorevitalization is an injection technique for administering active substances that allows for rapid skin rejuvenation of the face, neck, décolletage, and body. The procedure involves the use of hyaluronic acid-based preparations, a substance naturally present in the skin. The term «bio» means natural, «re» refers to returning, and «vita» signifies life, so «biorevitalization» can be translated as «returning to life in a natural way.» This differentiates biorevitalization from plastic surgery.

History of Development:

Hyaluronic acid was accidentally discovered by American biochemist Karl Meyer in 1934. This complex carbohydrate (polysaccharide) molecule has the ability to attract 1000 times more water than its own weight. It wasn't until 40 years later that scientific research confirmed that hyaluronic acid helps retain moisture in the intercellular space and promotes skin regeneration. In 1982, hyaluronic acid was first used in cosmetics. To improve its penetration and moisture retention in the epidermis, companies began micronizing the hyaluronic acid molecules, which helped restore metabolic processes. The term «biorevitalization» was first used by Italian Professor A. Di Pietro from Milan. The first biorevitalization procedure using hyaluronic acid was performed in 2001, and its popularity has been steadily growing ever since.

Mechanism of Action:

Biorevitalization is a method of injecting hyaluronic acid, which is obtained through a special biotechnological process. This method is based on the high ability of hyaluronic acid to stimulate tissue regeneration by interacting with cell receptors. The hyaluronic acid used in biorevitalization is specially synthesized to stay in the skin and not break down as quickly as the hyaluronic acid used in mesotherapy cocktails. Biorevitalization is similar to mesotherapy, but instead of various meso-cocktails, it uses only synthesized hyaluronic acid, making it a more effective variant of mesotherapy.

Hyaluronic acid is a hydrocolloid found in the intercellular substance of the skin, responsible for its optimal hydration. However, as we age, the amount of hyaluronic acid decreases, leading to loss of skin elasticity, moisture, and the appearance of wrinkles. Biorevitalization with hyaluronic acid helps stimulate the production of collagen and elastin in the skin, which preserves smoothness, firmness, and youthfulness.

Indications:

- Aging, dry, and dehydrated skin
- Reduced skin elasticity and turgor
- Premature skin aging due to factors like smoking, stress, and sun exposure
- Skin recovery after laser resurfacing and chemical peels
- Rehabilitation after plastic surgeries
- Hyperpigmentation

Contraindications:

- Inflammatory processes in the treatment areas
- Severe chronic diseases
- Pregnancy and breastfeeding
- Allergies to the components of the preparation
- Autoimmune diseases
- Use of anticoagulants
- Increased tendency to form keloid scars
- Acute herpetic infection

Procedure:

There are two types of biorevitalization: injection and non-injection.

Injection Biorevitalization involves administering hyaluronic acid with a very thin needle. It can be considered a surface-level mesotherapy procedure that delivers the required amount of product to the desired depth. Before injections, the skin is cleansed of makeup residue, dust, and oils. The procedure takes no more than an hour and is performed using a fine needle or a special injector. The hyaluronic acid is injected intradermally until a small papule is formed. Despite the small needle diameter, the procedure may cause discomfort, so a lidocaine cream may be applied beforehand for local anesthesia if the patient has high sensitivity.

There are several main types of injection biorevitalization:

- *Papular* – hyaluronic acid is injected into the superficial and middle layers of the dermis. The needle is inserted at a 15-degree angle, and the product is injected.
- *Mound* – hyaluronic acid is injected using a 4mm needle at a 45-degree angle, targeting the middle dermal layers.
- *Linear-retrograde* – using a 13mm needle to affect the deeper dermal layers.

Non-Injection Biorevitalization uses various apparatus methods to introduce hyaluronic acid without breaking the skin's surface. This method is less effective in delivering the required concentration of hyaluronic acid to deep skin layers compared to injections. Non-injection methods include:

- *Aquaphorosis* – introducing hyaluronic acid while performing lymphatic drainage, laser therapy, and electrostimulation.
- *Ultraphonophoresis* – delivering the substance to the subcutaneous tissues using ultrasonic vibrations.
- *Oxygen-based* – the substance is delivered under pressure with oxygen.
- *Magnetophoresis* – hyaluronic acid penetrates the skin through magnetic waves.
- *Iontophoresis* – hyaluronic acid is delivered via a steady galvanic current.
- *Laser-based* – hyaluronic acid is introduced with low-intensity laser radiation.
- *Cryobiorevitalization* (cryomethod) – the acid penetrates the skin through electromagnetic waves or cold (liquid nitrogen).

Despite the invasive nature, injection biorevitalization is considered the most effective and popular method due to its deep penetration and the ability to deliver the product in the required amounts. Non-injection methods are suited for patients who want to avoid the pain and visible changes like papules and bruises caused by injections.

Types of Biorevitalization:

Preventive Biorevitalization: This is typically used to prevent skin dryness and premature aging due to an imbalance of hyaluronic acid in the skin. A typical course consists of two sessions, spaced 3–4 weeks apart. The goal is to slow down the aging process through active hydration and maintaining nutrient balance. It may include facial biorevitalization, hand biorevitalization, and lip biorevitalization.

Therapeutic Biorevitalization: This is aimed at addressing already visible skin issues related to aging. It provides intensive and deep action on the skin. Patients with loose skin and significantly reduced turgor, as well as those with dehydrated and dry skin prone to wrinkles, are ideal candidates for therapeutic biorevitalization. This course typically involves three sessions, spaced 3–4 weeks apart, focusing on combating the visible signs of aging and restoring cell nutrition by increasing the concentration of hyaluronic acid in the skin layers.

Patient Recommendations:

- Avoid visiting saunas, baths, pools, or gyms on the day of the procedure.
- Do not apply cosmetics immediately after the procedure.

Results:

Biorevitalization provides numerous benefits, including painlessness, high effectiveness, and quick results. The procedure significantly reduces wrinkles,

effectively moisturizes, smooths skin texture, increases elasticity, rejuvenates the skin, and tightens pores. It also enhances the skin's recovery from heat and sunburns, as well as from wounds and scars.

Complications and Side Effects:

- Allergic reactions
- Microhematomas (more common during menstruation, menopause, among smokers, or those taking anticoagulants)
- Pain or discomfort
- Infectious complications (pustular or herpetic eruptions)
- Nodules and changes in skin color

23.6 Mesotherapy

Mesotherapy is a technique of injecting a special intradermal cocktail at a depth ranging from 0.5 to 6 mm. This is necessary to allow vitamins, minerals, nucleic acids, and amino acids to penetrate directly into the dermis – something that topical skincare products cannot achieve. The method is used to treat wrinkles, scars, keloids, puffiness, pigment spots, and acne. Moreover, thanks to the intense stimulation of elastin and collagen production by skin cells during the procedure, issues of dry and dehydrated skin are effectively addressed.

History of Mesotherapy

Mesotherapy has been used in Europe for more than 50 years. It is especially popular in France, where it originated. Dr. Michel Pistor was treating bronchial asthma when, during one attack, he injected a pain-relieving drug subcutaneously. Not only did the patient's pain subside, but–unexpectedly–his hearing improved (he previously suffered from hearing loss). Dr. Pistor began studying the cause of this phenomenon, and this led to the development of mesotherapy. The new method of intradermal injections evolved rapidly, and in 1987, it was officially recognized by the French Academy of Medicine as part of traditional medicine, making it fully legal and accepted by the medical community.

Mechanism of Action

The active components injected during mesotherapy stimulate collagen synthesis, leading to the strengthening and smoothing of the skin. Mesotherapy also improves skin microcirculation by delivering vasodilating substances, which ensures proper nourishment of skin cells, enhances tissue oxygenation, and promotes toxin elimination – all contributing to better skin health. The injection of hyaluronic acid under the skin provides deep hydration. Many active substances used in mesotherapy are antioxidants, which neutralize free radicals caused by oxidative stress, helping to maintain youthful skin and prevent

premature aging. Mesotherapy improves skin tone and texture by stimulating cellular metabolism and encouraging the production of new cells, which reduces pore visibility, refines skin texture, and enhances overall appearance.

Classification of Mesotherapy:

- By treatment area: clinical (therapeutic) and aesthetic;
- By equipment used: manual and device-assisted;
- By type of medication: drug-free (dry mesotherapy by Pistor), with medication, electrical (combination of wet mesotherapy and physiotherapy methods);
- By type of active substances: allopathic mesotherapy, homeopathic (antihomotoxic) mesotherapy, biomesotherapy, phytomesotherapy, gas mesotherapy;
- By body effect: general, systemic, loco-regional, local;
- By injection depth: epidermal, superficial dermal, deep dermal, dermo-hypodermal, hypodermal, intramuscular, mixed.

Types of Mesotherapy

By injection method:

a) Manual – performed by hand using injections into the treatment areas with special disposable syringes and very fine, single-use needles of varying lengths.

b) Device-assisted – involves a programmed meso-injector gun, allowing large skin areas to be treated quickly, painlessly, and at a controlled depth. The gun causes less pain than manual methods.

Types of Device-Assisted Mesotherapy:

- Fractional mesotherapy: A microinjection technique based on the principle of fractional delivery—only micro-zones are treated, spaced evenly across the skin surface, covering about 20% of the total area.
- Electroporation: This procedure creates pores in the lipid membrane using an electric field. In other words, pulsed electromagnetic waves act on cell membranes, opening up channels that allow biologically active substances to enter the cells.
- Oxygen mesotherapy: Unlike standard facial rejuvenation, this method uses high-velocity jets of pure oxygen. The upper skin layers absorb oxygen directly from the air, not from the bloodstream. Increasing the concentration and pressure of oxygen increases its content in epidermal cells and the rate of oxygen exchange. This changes cell membrane characteristics, accelerating the absorption of active substances, which nourish and enrich the skin over a long period. Additionally, oxygen saturation speeds up regeneration, normalizes metabolism, and gives the skin a healthy appearance.

Indications:

Correction of age-related changes, prevention and treatment of oily and porous skin, acne, cellulite, post-chemical, mechanical, and laser peeling rehabilitation, preparation for or recovery after plastic surgeries, alopecia, atrophic and hypertrophic scars, couperose, stretch marks, striae, seborrhea, and dyshidrosis.

Contraindications:

Individual intolerance to the components of the drug; pregnancy and breastfeeding; coagulation disorders; use of anticoagulants or antiplatelet agents; acute infectious diseases or exacerbation of chronic conditions; inflammatory lesions at the intended injection sites; history of oncological diseases; diabetes mellitus; pregnancy.

Before the procedure:

It is necessary to discontinue the use of anti-inflammatory drugs or other medications that reduce blood coagulation. For patients with hypertension, blood pressure should be normalized. Mesotherapy should not be performed on the day of menstruation and should not be combined on the same day with procedures that increase blood circulation in the skin (e.g., massage, sauna, tanning beds).

After the procedure:

For 12 hours post-procedure, do not apply cream or other cosmetic products to the treated skin. Avoid gym visits, saunas, and tanning beds for 3 days. Hardware-based procedures should be performed no earlier than 3–5 days after mesotherapy.

Procedure technique:

The technique involves administering superficial intradermal injections every few millimeters across the entire surface of the treatment area.

The procedure can be performed using a specialized mesotherapy injection device or disposable syringes. Microinjections are administered in such a way that a microdose (always up to 0.1 ml) of the product is delivered into the superficial dermis with each needle insertion. The agent introduced into the epidermis does not enter the bloodstream immediately but is absorbed very slowly, thus prolonging its effect. This procedure is referred to as mesolith.

Injection techniques in mesotherapy:

a) *Intradermal injections into various dermal layers:*
   - *Nappage:* Microinjection immediately beneath the epidermis. The needle is angled at 5°, inserted to a depth of 1 mm. Dose – 0.001–0.002 ml. Papule diameter – no more than 1 mm. Distance between papules – 2–3 mm. Nappage may be superficial, external, intermediate, or deep. This is a rapid technique that stimulates the skin, requires minimal product, causes no bleeding, and can be used in any area.

- *Superficial dermal papule:* Injection into the mid-dermis. Needle angle – 15–30°. Depth – 1 mm. Dose – 0.008–0.01 ml. Papule diameter – 2–3 mm. Distance between papules – 7–8 mm.
- *Deep intradermal papule:* Injection into the deep dermis. Needle angle – 45–60°. Dose – 0.05–0.07 ml. Papule diameter – 5–7 mm. Distance – 1.5–2 cm. This technique is effective in the area of wrinkle projection.

b) *Mesoperfusion:* Subcutaneous injection lasting 2–3 seconds, delivering up to 0.1 ml of the product.

c) *Mesoinfiltration:* Administration of large volumes of the product locally.

d) *Systematic point-by-point therapy:* Intradermal injections without intervals using the "point-by-point" approach. Dosage is tailored to the specific problem area. Commonly used for wrinkles and striae.

e) *Linear-retrograde technique (tracing):* The needle is inserted into the treatment area along its full length, and during its slow withdrawal, microdoses (up to 0.005 ml) of the product are administered.

f) *Vascular axes:* Involves injecting specially selected drugs with vasodilatory or vasoprotective properties into the orthogonal projection of affected veins of the extremities, and bilaterally near areas with strong arterial pulses (e.g., carotid artery).

g) *Grid technique*: A combination of linear and papular techniques.

h) *Fan technique:* The needle is fully inserted into the skin but not withdrawn; instead, it is redirected laterally for subsequent injections. This method helps break down old collagen and form new channels.

i) *Needle-free techniques:* Indicated for patients who cannot undergo classical mesotherapy.

Equipment:

Mesotherapy requires relatively simple equipment.

- *Manual methods:* Syringes of 2, 3, and 5 ml are used for facial treatments; 5–10 ml for the body. The primary tool is the needle. Modern mesotherapy uses Labile needles. Commonly used needles: 27G and 30G, lengths of 4 and 13 mm.
- *Mechanical methods:* Offer high precision in injection depth, dosage, and rhythm. Various injectors (mesoguns) are available, including automatic and non-automatic, mechanical, electronic, or electropneumatic types.

Course:

A standard mesotherapy course consists of approximately 10 procedures, conducted once a week. Each session lasts up to 40 minutes.

Active ingredients of mesococktails may include:

- Hyaluronic acid: A key biologically active substance that regulates moisture balance and stimulates collagen and elastin synthesis, delivering rejuvenating and moisturizing effects.

- Vitamins (A, C, E, B-group): Essential for cellular enrichment with micronutrients, protection against harmful agents and free radicals, inflammation prevention, and support for tissue repair.
- Minerals (magnesium and silicon salts, potassium, selenium, etc.): Improve tissue tone and elasticity, normalize metabolism, and strengthen vascular walls.
- Organic acids and amino acids: Provide gentle exfoliation, stimulate new structural protein formation, and prevent premature aging.
- Hydrolyzed collagen and elastin: Deliver lifting and rejuvenating effects, particularly beneficial for mature skin.
- Botanical extracts (e.g., chamomile, seaweed, aloe, green tea, guarana): Soothe the skin, prevent and treat inflammation, and provide emollient properties.
- Therapeutic components (e.g., L-carnitine, thioctic acid, dihydroergotamine): Target pathological conditions and contribute to general tissue health.

Mesotherapy products can be classified as:

- Monocomponent agents (e.g., biorevitalizants based on hyaluronic acid) aimed at solving a specific problem.
- Multicomponent preparations for comprehensive aesthetic correction.
- Custom-made solutions, prepared individually by a specialist based on the patient's skin and body characteristics.

Based on their composition, mesotherapy cocktails are classified into two main groups:

1. Allopathic cocktails are designed for a wide range of applications due to their content of numerous beneficial and nutrient-rich substances for dermal tissues. These agents target specific skin imperfections, with visible results often observed after the first injection session.

2. Homeopathic cocktails consist exclusively of natural plant extracts, vitamins, and nutrients that exert a holistic effect on the entire body. The primary goal of this type of mesotherapy is to stimulate the body's internal resources to restore cellular functions and normalize their harmonious operation. All components within these cocktails are synergistically linked to deliver maximum therapeutic and rejuvenating effects.

Mesotherapy cocktails are also categorized according to their mechanism of action on the skin:

- Rejuvenating cocktails – the most in-demand group of products, which help to slow down the aging process by stimulating the synthesis of collagen and elastin necessary for rapid tissue regeneration and repair.
- Therapeutic cocktails – containing antibiotics or antiseptics, aimed at treating specific skin conditions such as acne, scarring, and rosacea.

- Lipolytic cocktails – designed to safely and effectively eliminate localized fat deposits in problem areas (e.g., facial zones, thighs, buttocks, abdominal region), thereby addressing aesthetic concerns.
- Targeted therapeutic cocktails – focused on treating specific issues such as alopecia, dark under-eye circles, etc.

Patient recommendations:

Following the procedure, temporary skin redness may occur. For the first 24 hours post-treatment, it is advised not to apply any makeup or alcohol-based products. Moisturizing creams may be used. For at least one week after the procedure, patients should avoid saunas, tanning beds, sun exposure, and the use of scrubs.

Results:

Skin rejuvenation of the face and body, lifting effect, hair restoration and nourishment, correction of skin imperfections, and cellulite treatment.

Adverse effects and complications may primarily result from pharmacological, therapeutic-cosmetic, or cosmetic agents and include:

- Allergic reactions
- Local or diffuse hyperemia
- Injection site pain
- Gastrointestinal discomfort
- Vasovagal responses (e.g., lipothymia)
- Headache
- Hepatic colic
- Other undesirable reactions (e.g., tachycardia, bronchospasm, epileptic seizures)

Adverse effects and complications due to technical errors in injection-based mesotherapy may include:

- Pain
- Infections (including those caused by atypical mycobacteria or opportunistic flora)
- Skin necrosis
- Granulomas
- Adenopathies
- Hypopigmented or hyperchromic scars and spots
- Hematomas
- Ecchymoses
- Neurological and vascular injuries

The most frequently encountered complications include: pain, erythema, ecchymoses, hematomas, allergic reactions, and exacerbation of herpesvirus infections.

Types of Mesotherapy Procedures:

- *Mesolift* – A mesotherapy technique aimed at reducing wrinkles, enhancing skin tone and elasticity, and restoring fatigued skin using vitamins, antioxidants, DMAE, glycolic acid, and other active ingredients.
- *Mesoglow* – A procedure focused on improving skin tone, radiance, and luminosity.
- *Mesosculpt* – A mesotherapy variant designed to aid in weight reduction and eliminate localized fat deposits on the face and body.

23.7 Dermal Fillers (Contouring Plastic Surgery)

Dermal fillers represent a non-surgical facial rejuvenation method involving subcutaneous injection of specialized agents based on hyaluronic acid. As a result of this non-invasive facelift procedure, dynamic wrinkles, nasolabial folds, and fine periorbital lines are smoothed out, producing a lifting and rejuvenating effect.

Historical Background:

The first attempts to compensate for soft tissue deficiency were made in the 19th century by Dr. Neuber, who used autologous fat grafts. In 1940, silicone gel was first introduced as a filler. With the advancement of medicine, various other fillers emerged and gradually became more biocompatible, minimizing adverse reactions. The use of cannulas for dermal filler injections was pioneered by French surgeon Dr. T. Herzog in 2009.

Mechanism of Action:

Dermal fillers reshape facial contours and enhance lip volume through subcutaneous injections. This procedure corrects age-related changes such as wrinkles and folds, restoring smoother and more youthful skin. The current focus in dermal filler therapy includes facial contouring, lip augmentation, and wrinkle correction using gels derived from hyaluronic acid. These are cosmetic rather than surgical procedures, yet the aesthetic results are comparable to those of plastic surgery, while being significantly more affordable.

Types of Fillers:

- *Temporary fillers* (lasting approximately 4–15 months), most commonly hyaluronic acid-based fillers.
- *Semi-permanent fillers* (lasting up to 1.5–2 years), such as calcium hydroxyapatite.
- *Permanent fillers* (lasting over 5 years).

Substances Used in Dermal Fillers:

- *Hyaluronic Acid:* Naturally present in the human body, it maintains skin hydration and elasticity. These fillers are used for wrinkle correction, lip augmentation, and sculpting the cheekbones and chin.
- *Calcium Hydroxyapatite (CaHA):* Stimulates natural collagen production, resulting in tighter, smoother skin. Commonly used for correcting nasolabial folds, the chin, and cheek volume.
- *Polymethylmethacrylate (PMMA):* Used for long-term volume correction, it contains microspheres that stimulate a collagen response, offering prolonged effects.
- *Polidocanol:* A lipolytic agent used to reduce chin volume and smooth out skin irregularities by destroying fat cells.

After entering the tissue, hyaluronic acid binds with water to form a gel. However, this effect is relatively short-lived due to the presence of enzymes in the body that degrade it. To extend its durability, the structure of hyaluronic acid is chemically cross-linked to slow enzymatic breakdown. Hyaluronic fillers are user-friendly, easy to inject, hypoallergenic, non-toxic, and generally well-tolerated by the body.

Indications:

- Expression lines on the face
- Contouring of the facial oval, cheekbones, and chin
- Lip augmentation and reshaping

Contraindications:

- Pregnancy and lactation
- Acute inflammatory skin conditions
- Open wounds in the injection area
- Acute infectious diseases (including hematological disorders)
- Severe needle phobia
- Individual hypersensitivity to hyaluronic acid

Procedure Technique:

Facial contouring is performed on an outpatient basis, takes up to 30 minutes, and is virtually painless. Fillers are injected subcutaneously using a micro-needle or a blunt cannula under local anesthesia or topical anesthetic creams. Injections are placed directly beneath wrinkles. For lip contouring, the filler is injected along the vermilion border. No visible injection marks remain on the skin. The recovery period is minimal, with visible results appearing within hours. If necessary, aesthetic results can be adjusted through additional injections or accelerated degradation using specific enzymes.

Injection Techniques:

a) *Multipoint Injection Technique:* May cause temporary swelling and discoloration, which resolves within an hour as saline is absorbed and collagen thickens. Each injection point must be massaged.

b) *Linear Threading Technique:* Ensures uniform distribution. The dermis is punctured at regular 1–2 cm intervals; injection occurs as the needle is withdrawn.
c) *Layering Technique:* Used for deeper wrinkles. Involves injecting specific fillers into the deep, mid, and superficial dermis to eliminate residual depressions. A massage is performed for 1–3 minutes following each injection type.

Post-Treatment Recommendations:

Cosmetics may be applied 2–3 days after the procedure. Avoid saunas and swimming pools for several days.

Expected Results:

Prevention and correction of signs of skin aging, enhanced lip contour and facial oval, wrinkle reduction.

Complications and Adverse Reactions:

Possible side effects include allergic reactions, hyperpigmentation, hematomas and edema (typically resolving within days), scarring, nodules and lumps, filler migration, and necrosis.

23.8 Botulinum Toxin Injections

Botulinum toxin injections hold a special place in the modern arsenal of aesthetic procedures, allowing for the immediate professional correction of wrinkles and skin folds using preparations based on botulinum toxin type A, derived from Clostridium botulinum bacteria. The use of small doses of the toxin makes it possible to employ it in aesthetic medicine as a therapeutic agent.

The ability of botulinum toxin to smooth wrinkles was accidentally discovered by ophthalmologist Dr. Jean Carruthers in 1982, during clinical trials investigating its use in the treatment of strabismus and blepharospasm, led by Dr. Alan Scott. The cosmetic effects were identified serendipitously when one of Dr. Carruthers' patients, who was undergoing regular treatment for blepharospasm, noticed a significant reduction in her glabellar lines following therapy. Dr. Carruthers discussed this observation with her husband, Dr. Alastair Carruthers, then head of dermatologic surgery at the University of British Columbia (Canada). They hypothesized that the observed effect was due to relaxation of facial mimetic muscles.

The Carruthers began studying the effects of botulinum toxin type A injected into the glabellar area and subsequently extended their investigations to lateral canthal lines (crow's feet), nasal wrinkles, and perioral folds. In 1990, their initial findings on the dermatological use of botulinum toxin were published in the *Journal of Dermatologic Surgery and Oncology*.

This concept was rapidly adopted by dermatologists and plastic surgeons in North America and Europe, leading to an expanded range of indications, including treatment of hyperhidrosis, upper and lower facial lifting, facial contouring, breast and buttock lifting, nasal tip correction, facial asymmetry correction, and the development of techniques such as "mesobotox."

In 1993, otolaryngologist Dr. Andrew Blitzer presented findings on the use of botulinum toxin type A for correcting hyperfunctional lines on the forehead and submental region. Around the same time, dermatologist Dr. Nicholas Lowe compared the clinical efficacy of two botulinum toxin preparations–Botox® (Allergan) and Dysport® (Ipsen)–and found no statistically significant differences in efficacy, duration, or side effects. The results were published in the J*ournal of the American Academy of Dermatology* in 1996.

In 1998, Dr. Henkins and colleagues at Boston University conducted a large-scale clinical study to determine the optimal dosing of botulinum toxin type A for glabellar line correction. Concurrently, methodological advancements were made. In 1998, the use of botulinum toxin became a standard adjunct in laser resurfacing protocols in the United States.

Due to its high efficacy, safety profile, rapid onset of effect, and duration, botulinum toxin therapy became extremely popular. According to Allergan, the number of botulinum toxin procedures increased more than sixfold from 1995 to 2002, and this trend continues today.

Mechanism of Action

Botulinum toxin is a neurotoxic protein that blocks neuromuscular transmission by inhibiting the release of acetylcholine at the neuromuscular junction, resulting in temporary muscle paralysis and subsequent relaxation of targeted muscles.

Available Products in Ukraine

Currently, three botulinum toxin preparations are officially approved in Ukraine:

- Botox® (Allergan)
- Dysport® (Ipsen)
- Xeomin® (Merz)

Types of Botulinum Therapy

- *Glabellar and Forehead Therapy:* Effectively smooths dynamic wrinkles and prevents formation of new ones.
- *Periocular Therapy:* Reduces lateral canthal lines ("crow's feet").
- *Neck Therapy:* Used for platysmal band treatment and "Nefertiti lift".
- *Nasal Therapy:* Corrects "bunny lines" on the nasal dorsum.
- *Perioral Wrinkle Therapy:* Treats fine lines around the mouth (lipstick lines).
- *Gummy Smile Correction:* Lowers the upper lip to reduce gum exposure.

- *Oral Commissure Lift:* Elevates the corners of the mouth to reduce a downturned expression.
- *Chin Therapy:* Targets mentalis muscle to reduce dimpling and improve chin contour.
- *Hyperhidrosis Therapy:* Reduces excessive sweating in axillae, palms, soles, and scalp.

Additionally, full-face botulinum therapy may be performed during a single session, targeting multiple facial zones.

Indications

Botulinum toxin injections are most commonly used in the glabellar area, forehead, periorbital region, and nasal bridge. These areas are well-researched and present a lower risk of complications. Indications include dynamic facial wrinkles caused by muscle activity, facial asymmetry, and functional hyperactivity of specific muscles. Botulinum toxin is not effective for static wrinkles due to skin laxity or gravitational ptosis.

Contraindications

- Myasthenia gravis and myasthenic syndromes
- Inflammation at the injection site
- Pregnancy and breastfeeding
- Acute infections
- Hemophilia
- Severe myopia
- Allergy history (especially to albumin)
- Use of medications: muscle relaxants, anticoagulants, aminoglycoside antibiotics, tetracyclines, polymyxins
- Exacerbation of chronic diseases
- Alcohol abuse
- Pronounced facial tissue ptosis, facial hernias, or edema
- Unstable psychological condition
- Unrealistic patient expectations

Procedure Technique

The needle is inserted at one end of the most prominent wrinkle. Patients are asked to frown or squint to highlight the target area. The toxin is injected while withdrawing the needle. The lyophilized product is reconstituted with saline; in some cases, a small amount of epinephrine may be added to reduce diffusion and improve precision. Antiseptics without alcohol are used to avoid inactivating the toxin. The product is injected into the hyperactive muscle or intradermally (e.g., lower eyelids, lips, neck, décolleté, or for hyperhidrosis treatment). The injection site must not be massaged post-procedure to prevent unintended diffusion. Ice may be applied locally.

Post-Procedure Recommendations

Patients should:

- Remain upright for 3–4 hours post-injection
- Avoid sun exposure, sauna, and facial massage for 48 hours
- Refrain from taking antibiotics (especially aminoglycosides and tetracyclines) and undergoing electrostimulation, microcurrent, or ultrasound therapy for at least two weeks
- Avoid repeat injections within 3 months to prevent the formation of neutralizing antibodies, which may reduce future efficacy

Results

The onset of muscle-relaxing effects depends on the preparation and typically occurs within 1–5 days, peaking at 7–14 days. The effects last approximately 4–6 months and gradually diminish, necessitating repeat treatment.

Adverse Effects and Complications

Possible side effects include:

- Allergic reactions to human albumin
- Nausea, headache, flu-like symptoms
- Pain at the injection site, ecchymosis

23.9 Redermalization

Redermalization is an effective technique for the treatment of post-acne conditions, aimed at restoring the dermis on morphological, biological, and functional levels. This is achieved through intradermal injections containing succinate and hyaluronic acid.

Mechanism of Action

Redermalization exerts potent regenerative and antioxidant effects. It addresses skin dehydration, actively neutralizes free radicals, and provides deep hydration by replenishing hyaluronic acid deficiencies within the tissue. Moreover, it enhances metabolic processes in the skin, participates in the formation of the extracellular matrix, stimulates cellular and tissue respiration, boosts ATP production, and supports both intercellular and intracellular homeostasis.

Redermalization injections improve microcirculation and stimulate the synthesis of structural skin proteins such as collagen and elastin. They also activate endogenous hyaluronic acid synthesis by significantly influencing the mitochondrial activity of fibroblasts.

Indications

- Post-acne treatment
- Age-related skin changes

Contraindications

- Pregnancy
- Hypersensitive skin
- Coagulation disorders
- Acute inflammatory processes at the planned injection sites
- Exacerbation of systemic connective tissue diseases
- Exacerbation of chronic diseases
- Acute respiratory infections
- Herpes simplex virus infections
- Immunodeficiency states
- Malignancies
- Impaired skin integrity (e.g., open wounds, burns)
- Menstruation
- Severe depression
- Atopic predisposition

Procedure Technique

Redermalization is performed under topical anesthesia. The procedure duration is approximately 1 to 1.5 hours. After cleansing the skin with non-alcoholic antiseptics and applying an anesthetic cream, the product is injected into the mid-dermal layers using a very fine needle. Injections follow Langer's lines, which correspond to the natural orientation of collagen fibers in the skin, thereby enhancing treatment efficacy.

A typical treatment course consists of 3 to 4 sessions spaced at two-week intervals. A visible improvement is usually evident after the first session and continues to increase with each subsequent treatment.

Expected Results

Redermalization leads to full functional restoration of the dermis. Improvements include more even skin tone and texture, along with narrowing of the sebaceous gland duct openings.

Post-Treatment Recommendations

Patients are advised to:

- Avoid exposure to high temperatures (e.g., saunas, steam baths, tanning beds) in the treated areas for 7 days
- Use sun protection to prevent hyperpigmentation
- Abstain from alcohol for 2 days before and after the procedure
- Avoid physiotherapeutic treatments (e.g., massage, microcurrents, phonophoresis), which may accelerate biodegradation of the product
- Refrain from applying daily cosmetic products immediately after the session

Adverse Effects and Complications

Patients may experience transient discomfort following the procedure, including mild epidermal damage such as erythema, papules, or microhematomas.

23.10 Microneedling

Microneedling is one of the most advanced techniques for skin rejuvenation and addressing various cosmetic concerns. Although this method was introduced in 2011, it is already widely used in aesthetic and dermatological clinics due to its rapid and long-lasting rejuvenating effects.

Mechanism of Action

The core principle of microneedling involves creating micro-injuries in the skin using fine needles attached to a dermaroller. These microchannels allow for deeper and more efficient penetration of active substances into the skin, enhancing their bioavailability and cellular uptake. The active ingredients stimulate collagen synthesis, tissue regeneration, and skin rejuvenation.

Additionally, the micro-needles disrupt stagnant capillaries, promoting local blood renewal and improving metabolic activity. As a result, dermal thickening and irregularities are reduced, skin tone becomes more even, and overall texture improves. The microscopic punctures close within hours, minimizing the risk of infection and significant tissue damage.

Indications

- Age-related skin changes: laxity, sagging, fine lines and wrinkles
- Senile hyperpigmentation and skin dryness
- Treatment of striae (stretch marks), scars, and hormonally induced hyperpigmentation
- Restoration of skin sensitivity and pore tightening post-chemical peels or plastic surgery
- Management of cellulite and localized adipose deposits
- Scalp treatment: stimulation of hair growth and activation of dormant hair follicles (resulting in less breakage and split ends, with improved shine and hair density)

Contraindications

- Pregnancy and breastfeeding
- Coagulation disorders
- Oncological diseases
- Known allergies to substances used during the procedure

Procedure Technique

Prior to microneedling, the target area is thoroughly cleansed to remove impurities and makeup. For patients with low pain tolerance, a topical anesthetic gel may be applied. Once the skin is prepared, an active serum or solution is evenly distributed over the area, and the dermaroller is used along the facial massage lines.

The duration of the procedure depends on the size of the treatment area and typically lasts around 30 minutes. Afterward, the skin is disinfected. For

optimal results, a treatment course of 5 to 10 sessions is recommended, which yields more pronounced and sustained outcomes.

Post-Treatment Recommendations

- Avoid applying makeup during the first 24 hours post-procedure
- Use moisturizing creams to maintain hydration
- Alcohol-containing products may be applied in the days following treatment
- Avoid tanning beds, saunas, direct sun exposure, and abrasive exfoliants for at least one week
- Use broad-spectrum sunscreens regularly

Results

Microneedling promotes cellular regeneration, accelerates collagen and elastin synthesis, provides a lifting effect, reduces visible defects, and enhances overall skin freshness and youthfulness.

Adverse Effects and Complications

Temporary side effects may include mild swelling and erythema for 24–48 hours, dryness, tightness, itching, flaking, discomfort, and increased skin sensitivity. These reactions are normal and typically resolve within six days following the procedure.

23.11 Thread Lifting (Liftface)

Thread lifting (LIFTFACE) is an innovative rejuvenation and skin-tightening technique that enhances facial definition and restores its natural contours.

Mechanism of Action

During a thread lifting procedure, biocompatible mesothreads are inserted into targeted areas of the skin using ultrafine needles. Once the needle is withdrawn, the threads remain within the dermal tissues, stimulating collagen production for 6 to 8 months. Over time, the threads naturally biodegrade into water and carbon dioxide. Due to their minimal thickness (only 0.3 mm), the threads are not visible under the skin.

Types of Mesothreads

Several types of threads are utilized in aesthetic practice:

- *Monofilament threads:* Smooth, high-quality polydioxanone (PDO) threads that promote collagen synthesis, enhance blood circulation, and improve skin elasticity.
- *Twisted threads:* Composed of two intertwined monofilaments, these threads enhance collagen and elastin formation, producing twice the effect of monofilament threads.

Based on structural characteristics, threads can be categorized as:

- *Linear threads:* Smooth, straight threads ranging from 25 to 90 mm in length, used for cheeks, periorbital and perioral regions, neck, décolletage, and facial contouring.
- *Spiral threads:* Typically 50–60 mm in length, these threads regain their original shape after tension release and do not interfere with natural facial expressions. They are commonly used to treat nasolabial folds, forehead wrinkles, crow's feet, and the chin area.
- *Barbed threads:* Equipped with notches that secure the skin in the desired position, these are inserted under local anesthesia and provide a strong lifting effect.

Indications

- Facial contour lifting
- Skin smoothing and tightening
- Neck correction (threads in the submental area)
- Forehead threading
- Eyebrow repositioning and shaping
- Body contouring (e.g., lifting of breasts, abdomen, buttocks, and arms)

Contraindications

- Pregnancy
- Oncological diseases
- Acute inflammatory illnesses with fever
- Allergies to thread components
- Use of anticoagulant or antiplatelet medications
- Autoimmune diseases
- Skin damage at the insertion site

Procedure Technique

Thread lifting requires no additional components such as vitamin cocktails. The primary tool is the bioresorbable thread, long used in surgery but now increasingly applied in aesthetic medicine. A flexible needle is used to insert the thread under the skin; the needle is then withdrawn, leaving the thread in place. Over time, the thread is completely absorbed.

Post-Procedure Recommendations

On the day of the procedure, patients should avoid saunas, baths, swimming pools, and gym workouts. The application of regular cosmetic products immediately following the procedure is not advised.

Expected Results

- Skin lifting and firming
- Reduction of fine lines and wrinkles
- Restoration of facial definition

Adverse Effects and Complications

Potential complications include swelling, hematomas, skin unevenness or nodularity, allergic reactions, and infection. In rare cases, improper technique may result in facial nerve compression, impaired facial expression, contour deformities, or subdermal thread migration.

23.12 Plasmotherapy (PRP Therapy)

PRP therapy (Platelet-Rich Plasma) is the application of blood plasma to stimulate tissue regeneration (healing and restoration). PRP therapy (plasmolifting) involves using the patient's own (autologous) blood plasma as a therapeutic or rejuvenating agent.

History of Origin

PRP therapy was first developed by hematologists in the 1970s as a treatment for thrombocytopenia. In the 1980s, PRP therapy was used in maxillofacial surgery due to its anti-inflammatory effects and its ability to stimulate cell proliferation. Over time, PRP became primarily utilized in the treatment of musculoskeletal issues, particularly sports injuries. It has also been applied in cardiology, pediatrics, gynecology, urology, orthopedic surgery, ophthalmology, and other fields. In the last two decades, PRP therapy has become widely used in dermatocosmetology for tissue regeneration, wound healing, scar treatment, and rejuvenation. Since 2006, PRP therapy has been extensively used as a highly effective treatment for alopecia.

Mechanism of Action of Autologous Blood Plasma

The effectiveness of the method is based on the biological properties of human blood plasma. It contains a concentrated mixture of water, proteins, and various mineral and organic compounds. Platelets are the key component of PRP, and their concentration in plasma is 3-5 times higher than in whole blood. Platelets are small, disc-shaped, non-nucleated cells produced by the bone marrow from megakaryocytes, with a lifespan of 7 to 10 days in healthy individuals. The main functions of platelets include hemostasis and coagulation, supported by over 1,100 proteins within platelet granules, which are modified to form more than 1,500 bioactive protein factors (immune system messengers, growth factors, enzymes, and inhibitors).

These unique properties of platelets form the basis for the broad use of PRP therapy.

Key Components in Platelet Granules:

- Adhesive proteins (von Willebrand factor (VWF), fibrinogen, thrombospondins 1 and 2 (TSP 1, 2), laminin-8)
- Growth factors (EGF, IGF-1, HGF, TGF-β)

- Angiogenesis factors (VEGF, PDGF, FGF)
- Chemokines (CCL5 (RANTES), CCL-3 (MIP-1a), CCL-2 (MCP-1), CCL-7 (MCP-3), CXCL8 (IL-8), CXCL2 (MIP-2), CXCL6 (LIX), CXCL-1 (GRO-a), CXCL5 (ENA-78), CXCL-12 (SDF-1a), CXCL4 (PF4))
- Coagulation factors and their inhibitors (factor V, factor IX, antithrombin, factor S, proteases nexin-1, nexin-2, etc.)
- Immune system mediators (complement C3 precursor, complement C4 precursor, factor D, H, C1 inhibitor, IgG)

Key Functions of PRP Components:

- PDGF (Platelet-Derived Growth Factor): Stimulates collagen synthesis, neoangiogenesis, mitogenesis, and bone tissue proliferation; activates macrophages.
- VEGF (Vascular Endothelial Growth Factor): Initiates angiogenesis, increases the size of peri-follicular blood vessels in the anagen phase, stimulates collagen type II synthesis, promotes immune cell chemotaxis, and enhances macrophage and neutrophil chemotaxis.
- EGF (Epidermal Growth Factor): Enhances cellular proliferation and epidermal cell differentiation, promotes cytokine release from epithelial cells.
- TGF-β (Transforming Growth Factor Beta): Increases collagen type I synthesis, inhibits osteoclast formation and bone resorption, enhances immune cell chemotaxis, stimulates angiogenesis.
- IGF (Insulin-Like Growth Factor): Stimulates angiogenesis and cell growth and differentiation, including osteoblasts.
- FGF (Fibroblast Growth Factor): The most active stimulator of cell division and differentiation, essential in angiogenesis alongside VEGF.

Indications for PRP Therapy:

- Treatment and rejuvenation of facial and body skin (age-related changes, wrinkles, skin sagging, enlarged pores, dark circles under the eyes).
- Hair loss treatment.
- Skin rehabilitation and enhancement of results from other cosmetic procedures, including wrinkle correction, pigmentation spots, stretch marks, acne scars, and trophic ulcers.

The efficacy of PRP in alopecia is explained by its ability to stimulate the proliferation and differentiation of stem cells in the bulge zone of the hair follicle via multiple molecular mechanisms, such as the regulation of β-catenin transcriptional activity, increased levels of bcl-2 through anti-apoptotic action, activation of Akt and ERK signaling pathways, and expression of FGF-7 in dermal papilla cells.

Plasmolifting for Soft Tissue Augmentation:

PRP can be used as a soft tissue filler, such as for deep nasolabial folds without side effects. It can also be used as an adjunct in autologous fat transplantation

procedures, improving vascularization, reducing fibrosis, and minimizing cyst formation. Combining PRP with fractional laser resurfacing can be beneficial in treating scar tissue.

PRP therapy has shown promising results in the local treatment of diabetic and other chronic non-healing ulcers (caused by stasis, impaired hemodynamics, post-trauma, and deformities) by activating reepithelialization processes.

Advantages of PRP Therapy:

PRP therapy offers several advantages, including being minimally invasive, having a wide range of applications, excellent tissue compatibility, and good patient tolerance. It can serve as an alternative to hyaluronic acid biorevitalization or be alternated with it to enhance and prolong the effect.

PRP Preparation and Procedure:

The process involves collecting venous blood from the patient, followed by centrifugation to isolate the autologous plasma. The entire procedure is conducted under strict aseptic conditions, with an anticoagulant added to prevent platelet aggregation. The PRP is then injected into the skin via mesotherapy or applied as a mask. The latter method is often used after fractional laser resurfacing. Topical anesthesia may be applied when mesotherapy is used.

The procedure is recommended in the morning, on an empty stomach, with plenty of water. The minimum therapeutic course consists of two procedures, with the recommended course being four procedures, spaced 7 days to 1.5 months apart.

Contraindications for PRP Therapy:

- Hemophilia
- Infectious and viral diseases, including hepatitis C, HIV, and AIDS
- Any form of hematologic cancer
- Conditions requiring anticoagulant therapy
- Pregnancy and lactation
- Hypersensitivity to heparin
- Mental illnesses
- Infectious or oncological skin changes at the injection site

23.13 Laser Therapy

In recent decades, the use of lasers in medicine, particularly in dermatology and cosmetology, has gained significant popularity. Due to the relative simplicity and safety of laser treatment methods, they have become widely used by both doctors and patients.

A laser is a device capable of generating coherent electromagnetic waves. The main components of the device are the laser's active medium, optical

resonator, and pumping systems (energy sources). The name of the laser device often starts with the name of the components of the active medium, which can be gaseous (argon, carbon dioxide, etc.), liquid (rhodamine solution), crystalline (alexandrite, ruby, yttrium-aluminum garnet with neodymium Nd:YAG or erbium Er:YAG), or LED-based. Using an external energy source, atoms of the laser's active medium are excited. This excited state is unstable, and electrons spontaneously return to their ground state, emitting the absorbed energy. The released energy – spontaneous emission – is emitted in the form of light quanta or photons. These photons travel along the long axis of the optical resonator and are absorbed by the activated atoms, which, when returning to their usual state, emit two photons – thus, forced emission is generated. The photons of forced emission have identical frequency and wavelength. Through a system of mirrors that guide and intensify the intensity, the photons are directed into the emitter located directly in the doctor's hand.

The radiation of any laser device is characterized by:

- *Monochromaticity* (the same wavelength of emission, depending on the active medium of the device. In pathological foci of the skin, laser emission targets, or chromophores, such as water, hemoglobin, melanin, or tattoo ink, are found);
- *Coherence* (the oscillations of the radiation coincide in frequency and phase both in time and spatially);
- *Collimation* (the laser system produces light in the form of a powerful narrow beam that can travel great distances without scattering. Collimated light can be focused on a small area, allowing precise tissue destruction).

When a laser beam strikes the skin's surface, it can be reflected, pass through, scatter, or be absorbed by different layers of the skin. A photon can interact with tissue only by transferring a certain amount of energy. Therefore, only absorbed photons cause a therapeutic effect. The absorption of photon energy leads to several effects, namely: photothermal, photochemical, and photomechanical. The photothermal effect occurs when a chromophore absorbs light of a specific wavelength, converting light energy into heat and destroying tissue. The photochemical effect is realized through natural or induced photosensitizers, which is the basis of photodynamic therapy. Photomechanical action involves tissue destruction due to the creation of sound waves through rapid thermal expansion. Photothermal and photochemical reactions are most often used in laser surgery.

The development of the selective photothermolysis theory (J. Parrish and R. Anderson) made it possible to achieve controlled destruction of affected tissue without causing significant thermal damage to surrounding healthy tissue. For selective photothermolysis, an appropriate wavelength of radiation must be selected for each chromophore or target. To reduce the negative thermal effect on healthy tissue, the doctor must choose the correct pulse duration, which should

not exceed the thermal relaxation time. The energy density of the light flux must be sufficient for target destruction within the set time. The depth of laser penetration into tissues should also be considered, as it is directly proportional to the wavelength. Thus, to ensure maximum target destruction with minimal damage to healthy tissue, the doctor must always select the correct emission parameters (wavelength, pulse duration, and energy density).

In medicine, laser radiation is used in two main directions: for nonspecific biostimulation (using low-intensity lasers) and for cutting, vaporizing, or coagulating tissue (using high-intensity lasers).

Indications for the use of lasers in cosmetology include: vascular formations, pigment disorders, tattoo removal, photo-rejuvenation, laser surgery, unwanted hair removal, hypertrophic and keloid scars, and skin resurfacing.

Laser treatment for pigment disorders: Hyperpigmentation refers to pathological changes associated with excessive pigment deposition in the skin. The color of the skin is formed by the presence of varying amounts of five types of pigments, the main one being melanin. Depending on its quantity, melanin gives the skin different shades of bronze and is produced by special cells called melanocytes, which are located in the epidermis. Melanin protects the skin from the harmful effects of ultraviolet rays. However, its synthesis is controlled by the nervous and humoral systems, which connect all elements of the human body. Any deviation from the norm in one organ leads to corresponding reactions in others. The causes of hyperpigmentation are varied. It can be caused by dysfunction of the endocrine glands (adrenal and sexual glands), pregnancy, liver and bile duct diseases, vitamin imbalances in the body (especially ascorbic acid), prolonged intoxication during chronic infections (tuberculosis, malaria, helminth infestations), metabolic disorders, the use of certain medications, and cosmetics, perfumes, essential oils, or toilet soap. There is also a genetically determined tendency to develop pigment spots. Some specialists also associate changes in a person's psychological state due to stressful situations with pigment disorders. Most benign pigment formations in the epidermis and dermis can be treated with high-energy lasers. In this case, melanin is the chromophore and can absorb a wide range of light wavelengths from 250 to 1200 nm. In the case of dermal pigment disorders, the chromophores are intracellular melanosomes or tattoo pigment particles. To eliminate pigmentation in the upper layers of the skin, it is advisable to use lasers with a short wavelength (e.g., Nd:YAG 532 nm), while for deeper pigment disorders, a laser with a longer wavelength should be used (e.g., Nd:YAG 1064 nm or alexandrite 755 nm). When removing tattoos, the chromophores are fine pigment particles absorbed by macrophages or dispersed in the dermis. The choice of parameters in this case depends on the pigment color: black pigments are best removed with the alexandrite laser 755 nm or Nd:YAG 1064 nm, blue and green pigments are better removed with the alexandrite laser, and red, yellow, and orange pigments – with Nd:YAG

532 nm. Generally, removing professionally done tattoos, compared to amateur ones, is a more challenging task for the doctor.

Despite the relative safety of this method, there are certain precautions and contraindications for its use:

- Dermatological diseases (psoriasis, vitiligo, urticaria, pyoderma, herpes);
- Malignant neoplasms (laser exposure may accelerate their growth);
- Blood diseases (immune deficiency, anemia, avitaminosis, hemophilia, leukemia);
- Diabetes mellitus;
- Severe forms of cardiovascular diseases (hypertension, ischemia, arrhythmia, varicose veins, thrombophlebitis);
- Tendency to form keloid scars;
- Pregnancy and lactation;
- Allergic reactions to light;
- Fresh suntan (interaction of epidermal melanin with laser radiation can increase the risk of scarring, hypo- and hyperpigmentation);
- Use of retinoids in the past 12 months (increases the risk of scarring and poor wound healing);
- General infections;
- Fever of unknown origin;
- Psychiatric disorders.

Procedure protocol: The patient should refrain from using creams the day before the procedure.

On the day of the procedure:

1. Thoroughly cleanse the face;
2. Apply an analgesic if the patient has a low pain threshold;
3. Apply a special light-conductive gel on the skin for better penetration of light energy into the dermis;
4. The cosmetologist selects the required parameters and begins to affect the problem areas step by step;
5. After treatment, the affected areas are treated with softening agents to minimize irritation;
6. During the procedure, the patient may feel mild discomfort;
7. In most cases, 1-5 sessions are recommended, depending on the skin condition.

Post-procedure recommendations:

- In the first hours after the procedure, there may be slight burning and tingling, and sometimes mild swelling and redness, which usually resolve on their own;
- On the second day after the session, it is recommended to start applying a cream or ointment based on dexpanthenol to prevent itching, irritation, and redness;

- For three days, avoid visiting swimming pools, saunas, and tanning beds;
- Do not apply compresses, peels, or use scrubs for skin cleaning;
- The use of anticoagulants is not recommended;
- For one month after the last session, apply a moisturizing cream to the skin to help maintain the achieved effect, and use sunscreen before going outdoors. This is because the skin becomes more sensitive to UV rays after laser exposure and is more prone to damage.

Immediately after the laser therapy session, pigmented spots may darken and scabs may form. These manifestations will subside within 10-15 days, and the skin will regain its normal tone. Laser treatment of skin pigmentation is most effective in the autumn-winter period. Persistent positive results are usually achieved by the third session (depending on the type of procedure). To achieve a stable effect, laser pigmentation removal is often recommended to be combined with various peels and skin biorevitalization.

Laser skin rejuvenation is a modern and popular cosmetic procedure aimed at reducing the size of wrinkles (both age-related and mimic), tightening the skin, and correcting scars. The effectiveness of the procedure depends on factors such as the class of equipment used, its operating modes, the type of impact (surface or deep), the treatment area, and the condition of the skin (presence of wrinkles, bags or bruises under the eyes, vascular stars). This method is characterized by simplicity, accessibility, low invasiveness, and versatility in terms of the results achieved. The essence of facial photo-rejuvenation involves heating tissues, during which powerful light pulses initiate the regeneration of epidermal cells, stimulating the internal breakdown of the old layer.

Advantages of the photo-rejuvenation procedure:

1. Versatility: Along with achieving facial rejuvenation, it helps to even out the skin tone, remove pigmented spots, acne scars, and make scars less noticeable.
2. Noticeable results: 5-6 sessions can achieve the effect of «several years younger.» The face looks natural, and the skin has a healthy appearance.
3. Minimal side effects: This is possible due to the precise laser impact on problem areas and individual selection of the light pulse length.
4. Simple rehabilitation: The recovery after the procedure takes a maximum of 2-3 days, and there is no need to drastically change skin care or lifestyle.

Indications for using the photo-rejuvenation procedure:

1. Mimic wrinkles caused by the active movement of facial muscles (laughing, crying, eye strain), mostly around the eyes and lips.
2. Loss of skin tone, causing it to sag and form unattractive folds. The laser helps fill the gaps with hyaluronic acid, accelerates collagen and elastin production, and thus tightens the skin.
3. Crow's feet – a common issue for women over 25, presenting as numerous, not very deep skin folds around the eyelids, which can make the face appear older.

4. Nasolabial folds – deep, long vertical lines that appear around the mouth, typically around the age of 35.

5. Weak skin turgor. The laser strengthens it, allowing the dermis to tighten, become firmer and more elastic, and smooth out fine lines.

6. Lip rejuvenation.

The procedure is recommended for individuals over 30-35 years old, when the first signs of aging appear. At this age, it can be used for therapeutic purposes, and for preventive purposes, it can be performed once or twice a year. The procedure is relevant for restoring skin turgor due to aging and the negative effects of environmental factors (low temperatures, sun exposure).

Contraindications and precautions are similar to those for treating hyperpigmentation.

Preparing the patient for the procedure:

- Four weeks before, it is important to exclude any cosmetic procedures and avoid sunbathing.
- Two to three days before the session, stop using decorative cosmetics.
- A day before the procedure, discontinue the use of creams.
- Before visiting the specialist, cleanse the face with soap to remove oily film and impurities.

Procedure steps:

1. The face or treated area is thoroughly cleansed.
2. For patients with a low pain threshold, a numbing agent is applied to the skin.
3. Before photo-rejuvenation, a special light-conducting gel is applied to the skin for better penetration of light energy into the dermis.
4. The cosmetologist selects the appropriate light pulse length and begins treating problem areas step by step.
5. The treated areas are treated with soothing agents to minimize irritation.
6. During the procedure, the patient may experience slight discomfort.
7. Usually, patients are prescribed one to five sessions, depending on the skin condition.

Post-procedure recommendations:

- In the first hours after the procedure, mild burning and tingling may be felt, and slight swelling and redness may appear, which usually resolve on their own.
- On the day of the procedure, you can take a shower using mild soaps.
- Within 24 hours, avoid using foundation, powder, or other cosmetics, as they can clog pores.
- On the second day after the session, it is recommended to start applying a cream or ointment based on dexpanthenol to avoid itching, irritation, and redness.

- For three days, avoid visiting swimming pools, saunas, and tanning beds.
- It is forbidden to use compresses, exfoliants, or scrubs on the skin.
- For a month after the last session, use a moisturizing cream to help maintain the results and apply sunscreen before going outside. This is because the skin becomes more sensitive to UV rays after the laser treatment.

Positive results are usually achieved after three to seven sessions, depending on the type of procedure, and they last for one to two years. The effect is achieved by reducing the size of skin stretch marks, smoothing out mimic and age-related wrinkles of various depths, increasing skin turgor, and evening out its color. In addition to rejuvenation, the patient's pores shrink, pigmented spots lighten, and scars are restored. Also, the size of the vascular network decreases, acne and couperosis marks disappear, dark circles under the eyes and bags are reduced. Patients also report the return of a beautiful glow and complexion. In combination with biorevitalization and mesotherapy, the best, even unexpected, results can be achieved.

Complications: Possible complications include pathological changes in the dermis, infection, and the appearance of keloid scars. However, these usually occur when the procedure is performed without considering existing contraindications.

Laser Removal of Vascular Lesions. Vascular removal was previously only possible through surgical methods, cryodestruction, or electrocoagulation, which resulted in skin trauma and scarring. The development of laser technology has made significant advancements in this field. The chromophore in this case is oxyhemoglobin. The most commonly used lasers for this procedure are pulsed dye lasers, diode lasers, alexandrite lasers, and Nd:YAG lasers. During the procedure, the laser beam selectively targets oxyhemoglobin, heating the blood vessels and coagulating them. The fine vascular network or individual vascular lesions are almost «sealed» from the inside under the influence of special filters, halting blood flow. A delicate laser setting is used for facial spider veins to avoid damaging the delicate skin. The effect is immediately noticeable as smaller vessels disappear instantly, and larger ones become less visible. The final result is typically visible two to four weeks after the procedure when the vessels are completely gone.

Indications: removal of vascular malformations; reduction of diffuse facial redness; treatment of rosacea.

Contraindications and precautions are similar to those for other laser procedures.

Procedure Steps:

1. Thoroughly cleanse the face or area to be treated;
2. Apply an analgesic agent if the patient has a low pain threshold;

3. Apply a special light-conducting gel to the skin for better light energy penetration into the dermis before the procedure;

4. The cosmetologist selects the appropriate wavelength and begins to treat the problematic areas step by step;

5. The treated areas are then treated with soothing agents to minimize irritation;

6. During the procedure, the patient may experience mild discomfort;

7. Typically, one to five sessions are recommended, depending on the skin condition.

Complications: Possible complications include pathological changes in dermal structure, infection, and keloid scar formation.

Post-Procedure Recommendations:

- In the first few hours after the procedure, mild burning and tingling may occur, along with slight swelling and redness, which usually resolve on their own;
- On the second day, apply a cream or ointment with dexpanthenol to prevent itching, irritation, and redness;
- Avoid swimming pools, saunas, and tanning beds for three days;
- Compresses, peels, and scrubs should be avoided;
- Anticoagulants are not recommended;
- For one month after the last session, use a moisturizing cream to maintain the results and apply sunscreen when going outdoors, as the skin becomes more sensitive to UV rays after laser treatment.

Laser treatment for vascular lesions is recommended during the autumn and winter months. Persistent positive results are usually achieved by the third session (depending on the procedure type).

Laser resurfacing methods were developed for tissue tightening, wrinkle and rhytid removal, signs of photoaging, skin lightening in superficial pigment formations caused by the sun, and treatment of dyschromia, lentigo, or actinic keratosis, and skin smoothing for atrophic scars.

CO2 laser ablative resurfacing (10,600 nm) was the only option until the mid-1990s. While effective for plastic surgeons, it had significant side effects, especially with insufficient experience. Prolonged erythema, hyperpigmentation, local sensitivity, infections, prolonged hypopigmentation, and deep scars were common issues with this method. Today, dermatologists use pulsed, CO2, and Er:YAG lasers or combined Er:YAG – CO2 lasers to minimize side effects. Ablation involves removing or vaporizing the upper skin layer to the depth of the laser beam penetration. Ablation is achieved through high-intensity laser radiation absorbed by water in skin cells, causing immediate vaporization of water and tissue. Ablative laser resurfacing can cause significant pain, which disappears after complete epithelialization. Topical anesthetics are

recommended to reduce pain and hydrate the skin, minimizing the risk of side effects. The downside is a prolonged recovery period, lasting several weeks to months.

Non-ablative laser resurfacing has several advantages over the previous method, such as minimal recovery time and no visible external tissue damage. This method increases the number of fibroblasts and collagen synthesis. Non-ablative lasers emit infrared light, targeting the dermis without affecting the epidermis. The first group of non-ablative lasers includes pulsed dye lasers (PDL) and intense pulsed light (IPL) devices, which control dermal microcirculatory damage. These lasers are indicated for rosacea, telangiectasias, and diffuse erythema. Lasers that also target melanin, such as IPL, are useful for treating lentigo, melasma, poikiloderma, and other pigmentation disorders. The second group includes mid-infrared lasers that target water in the dermis, such as 1320 nm Nd:YAG, 1450 nm Diode, and 1540 nm Er:YAG lasers.

Indications for laser resurfacing include the treatment of benign tumors (seborrheic keratoses, xanthelasmas, sebaceous gland hyperplasia, trichoepitheliomas, syringomas); precancerous conditions and malignant tumors (actinic cheilitis, basal cell carcinoma, Bowen's disease, etc.); warts; dyschromia; atrophic scars (including post-acne); signs of photoaging; rhytides and wrinkles; rosacea; telangiectasias.

Contraindications are the same as for other laser methods, with absolute contraindications including vitiligo, scleroderma, and dark skin.

Fractional photothermolysis is a relatively new procedure that involves a focused ablative effect on small areas (no more than 10% of the body surface), also known as fractions. The Er:YAG wavelength used in this method is 1540 nm with a scanning device (Fraxel).

The principle of fractional laser resurfacing involves generating powerful, high-precision microbeams. These microbeams create narrow, deep columns of coagulated tissue, which penetrate deep into the epidermis and dermis without damaging surrounding tissue. The coagulated tissue initiates a natural healing process, accelerating the formation of new, healthy tissue. The coagulated cellular debris is reabsorbed physiologically.

Indications for fractional photothermolysis include signs of photoaging, wrinkles, actinic skin damage on the face, neck, shoulders, and hands, pigmented spots, post-acne scars, hyperpigmentation, melasma, telangiectasias, and rosacea.

Side effects include erythema and swelling, which usually resolve within a few hours. Hypo- or hyperpigmentation may appear within a few days and typically resolve on their own over the course of a few months.

Contraindications for the procedure are the same as for other laser techniques described above.

Laser Hair Removal

Over the past decade, laser and light-based hair removal has become recognized as a fast, safe, and reliable method of choice compared to previous techniques, which provided only temporary results. The primary targets of laser energy in this procedure are melanin in the hair shaft, follicular epithelium, and the hair matrix.

Contraindications

Laser hair removal is contraindicated in the following cases:

- Presence of skin eruptions or large tattoos in the intimate area;
- History of abnormal wound healing;
- Chemical peeling of the intimate area within the past month or any surgical intervention in the treatment area within the past three months;
- History or presence of cancer or precancerous lesions;
- Pregnancy and lactation.

Caution is advised in patients who:

- Have previously experienced adverse reactions to laser therapy;
- Have a history of heat- or cold-induced conditions (e.g., recurrent herpes simplex) in the area planned for treatment;
- Have bleeding disorders or are on anticoagulant therapy (with the exception of low-dose prophylactic aspirin);
- Have photosensitive disorders (e.g., systemic lupus erythematosus, porphyria, or epilepsy);
- Have undergone hair removal procedures (e.g., waxing, plucking, or electrolysis) in the treatment area within the past six weeks;
- Have taken oral retinoids (e.g., isotretinoin) within the previous six months;
- Have an active medical implant (e.g., pacemaker, defibrillator);
- Have serious comorbidities such as cardiovascular disorders, poorly controlled endocrine conditions (e.g., diabetes mellitus or polycystic ovary syndrome), or immunosuppressive diseases (e.g., HIV/AIDS or current immunosuppressive therapy).

Preparation for Laser Hair Removal

- Patients must be informed that sun exposure of the treated area immediately after the session and for at least one month post-treatment can increase the risk of pigmentary changes. Therefore, sunbathing should be avoided for at least two weeks before and one month after the procedure.
- No depilatory methods (e.g., waxing, plucking) should be used in the treatment area within 14 days prior to the procedure.
- Alcohol-containing products should not be applied to the intended treatment area for at least three days prior to the session.

- Tetracycline-class antibiotics and medications that may stimulate hair growth (e.g., minoxidil) should not be used within two weeks before treatment, as they may increase the risk of burns or interfere with results.
- The skin surface of the intimate area should be carefully shaved and cleansed immediately prior to the procedure. Visible hair can become excessively heated during laser application, leading to localized thermal damage to the epidermis. In addition, shaving reduces pain by preventing superficial hair from absorbing the laser energy.

The most common side effects are erythema and swelling, which typically occur after laser treatment and resolve within 24-48 hours. Other side effects may include hyperpigmentation and hypopigmentation.

Post-Epilation Recommendations for the Patient:

- Apply antibacterial (in case of complications) and antiseptic treatments to the treated areas twice a day after laser treatment;
- On the second day after the session, apply a cream or ointment with dexpanthenol to the epilated area to avoid irritation and redness;
- For seven days, avoid visiting swimming pools, saunas, and tanning beds;
- Avoid prolonged peels and scrubbing the skin;
- For one month after the last session, apply a moisturizing cream to the skin to help maintain the results.

Recommended Treatment Course and Expected Outcome: The course of unwanted hair removal can vary in duration depending on the individual's characteristics. On average, it consists of five to ten sessions. After completing the full course of treatment, approximately 80% of unwanted hair can be removed. Since some hair remains in a «resting» phase, it is recommended to undergo a maintenance laser epilation session once or twice a year

23.14 Analysis of The Justification for Aesthetic Interventions

The epidermal-dermal response to invasive procedures significantly changes with the aging process. Despite increased protease activity in the skin of elderly individuals, the inflammatory response to injury is lower compared to younger ages. High activity of matrix metalloproteinases (MMPs) in patients over 65 years old is often combined with low levels of proteolytic inhibitors (e.g., TIMPs), which frequently leads to post-traumatic proteolytic damage to the dermis.

The evolutionary changes in the skin of many patients are associated with a deficiency of growth-stimulating factors, reduced fibroblast and epidermal

cell activity, which requires caution when performing procedures involving autologous tissues (lipofilling, plasmalifting, cell technologies, etc.). Wound healing after aesthetic and surgical interventions in patients over 60 years old is rarely complicated by hypertrophic and keloid scar formation.

Aging processes are significantly accelerated by sun exposure, which stimulates the breakdown of fibrous-vascular skin structures due to the action of free radicals. Understanding the mechanisms of photoaging helps dermatocosmetologists choose the most rational aesthetic procedures depending on the skin phototype. Physiological aging, in contrast to photoaging, occurs more slowly; the skin does not lose elastin or collagen in large quantities over a short period, and thinning, elastosis, and significant atrophic changes do not form. It is known that patients who have protected their skin from sunlight throughout life have significantly fewer pigmented neoplasms and deep wrinkles.

It is specifically UVA or UVB rays that most intensively accelerate skin aging by negatively affecting epidermal cells and the state of the fibrous dermal framework. It is important to remember that UVA rays easily pass through clouds, ordinary glass, and even clothing. People receive the most intense burns on cloudy days, especially when skiing or at the beach near water, where the «reflection effect» (from water, snow, and other objects) results in double light exposure. Therefore, the main method of preventing photoaging is limiting sun exposure and using photoprotective products with the highest level of sun protection (SPF50+).

When performing an aesthetic procedure, it is crucial not only to select its direction and scope correctly but also to understand how well it aligns with the client's wishes. The justification of the procedure performed, and, most importantly, the subsequent monitoring and assessment of its quality, should be ensured through a set of objective criteria.

Hardware methods for evaluating the quality of aesthetic interventions (EIs) and the justification of claims regarding the service provided include: dynamic photofixation, bio-instrumental skin analysis (seboanalyzer, measuring skin turgor, hydration, skin sensitivity, melanin production activity), confocal dermatoscopy, ultrasound examination, coherent tomography of the skin, and skin biopsy. Below are the devices most commonly used in European countries to assess the condition of a patient's skin before and after aesthetic interventions (see Table 23.2).

To the most accessible methods of dynamic skin condition assessment, photodocumentation can be included, which allows evaluating the skin condition during each patient visit. The generally accepted standard is to maintain consistent color tone and color field stability, which is ensured by special photographic stands. Usually, these standards are maintained with a white background, having a gray reflection coefficient of slightly over 18%.

Table 23.2
Methods for non-invasive assessment of skin condition (recommendations of the European Academy of Dermatology and Venereology 2021)

Name of diagnostic tool	Scope of use
Nova-metr	hydration
Skison	hydration
Corneometr	hydration
TEVA-metr	analysis of skin barrier function
Derma-lab	analysis of skin barrier function
Aqua-Flux	analysis of skin barrier function
Delfin VapoMeter	analysis of skin barrier function
Cutometr	elasticity and firmness
Chromametr	skin tone (erythema, radiance…)
MexaMeter	skin tone (erythema, radiance…)
Sebumetr	skin oiliness
D-squames	exfoliation, peeling
Ultrasound	analysis of fibrous skin structures
Optical Coherence Tomography	analysis of neoplasms
Confocal imaging	visualization of skin structures

Topographical fixation, complete cessation of facial activity (such as smiling, frowning, etc.), and prohibiting the use of makeup are also part of the aesthetic intervention standardization elements.

It is also important to consider subjective data – patient complaints regarding negative symptoms such as paresthesia, the sensation of a foreign body in the areas of invasion, undercorrection or overcorrection after filler injection, critical changes in appearance, etc. It is important to remember that even the appearance of visible damage in areas of invasion cannot be considered solely as the result of iatrogenic action, as it is often related to the patient's violation of the rehabilitation regimen.

An important component of photodocumentation in dermatocosmetology is the use of cross-polarization, which helps avoid glare and blurriness, enhancing the clarity of atrophic and vascular changes in the skin. In cases of dyschromia, it is advisable to use UV-filtered photo documentation, which allows assessing the area and depth of melanin deposition in the skin. When studying the degree

of skin colonization by Propionibacterium acne, UV fluorescence cameras are used. Detection of areas with high porphyrin concentration (orange-red coloring) in places where the pathogen accumulates allows increasing the effectiveness of topical agents in acne treatment.

One of the most convincing methods for assessing the depth of wrinkles and periorbital lines is light optical profilometry, which evaluates silicone rubber impressions made directly on the areas of aging skin changes. While optical profilometry is an effective and time-tested method for assessing skin aging, its use is associated with difficulties in creating silicone replicas. However, light optical profilometry remains the most effective method for assessing wrinkles based on parameters such as number, length, width, depth, and area.

An important aspect of evaluating the effectiveness of topical agents in rejuvenation programs is the use of Minolta chromometry and mixometry. These technologies allow assessing the antioxidant activity of various cosmetic products when interacting with the skin. The main evaluation criterion is the speed at which the minimum erythema dose is achieved within 5 days in fixed

Table 23.3
Instrumental analysis of photo images during cosmetic procedures according to the Stephens & Associates program (European Academy of Dermatovenereology 2019)

Analysis Area	Photography lighting	Analysis and initial parameters
Wrinkles, Fine Lines	light optical profilometry, “Raking SWIRL”	Number of wrinkles, length, width, depth
Hyperpigmentation	Cross-polarization	Areas of UV damage, number and size of age spots, total area
Pores	Cross-polarization	Number of pores, area, relative depth
Oily Skin	UV fluorescence	Percentage of areas with increased sebum secretion
Acne	Cross-polarization	
Lip Area Analysis	Light visualization “Lipwrinkle analysis”	Number, depth, localization, total area

areas where the topical agent was applied. The advantage of this method is the ability to conduct a comparative analysis across different skin areas over time and collect material to study skin cell activity, detect burn cells, levels of metalloproteinases, cytokines, p53 protein, and more (see Table 23.3).

End Stage of Aesthetic Procedure Analysis

The final stage of analyzing the documentation of aesthetic changes, particularly in the event of a conflict between the patient and doctor or when implementing new aesthetic procedures, relies on using the scientific and analytical platform Stephens & Associates. This platform allows for simultaneous assessment of a broad range of clinical skin parameters and its appendages. Photodocumentation allows the assessment of the duration of the effect after the aesthetic service is provided and helps predict the expected results. Objective evaluation of the skin condition using modern technological methods eliminates subjective evaluation from both the patient and the doctor.

23.15 Complications of Aesthetic Interventions

A practicing dermatocosmetologist may encounter complications during aesthetic interventions. While it is nearly impossible to completely avoid them, especially considering the individual characteristics of the skin structure and the vascular-neural systems in 10–15% of patients, it is advisable to study and isolate complications that are most likely to occur with specific procedures, as well as how to resolve them as quickly as possible with minimal harm to the patient. To reduce unwanted effects during aesthetic interventions, it is important to carefully analyze the patient's medical history and segregate groups of patients who have absolute or relative contraindications for any manipulation on the face and body (oncological patients, acute infectious diseases, flare-ups of autoimmune conditions).

Absolute contraindications include:

- Acute viral-bacterial infections
- Oncological diseases (active phase)
- Exacerbation of autoimmune conditions
- Exacerbation of chronic dermatoses
- Mental illnesses

Relative contraindications include:

- Retinoid therapy
- Menstruation
- Pregnancy
- Use of contraceptive agents

- Asthenia
- Endocrinopathies
- Presence of dysplastic nevi in the intervention area
- Oncological diseases (healed)
- Vasculitis in the medical history
- Presence of unverified fillers
- Use of photosensitizing drugs

Reducing unwanted effects during aesthetic procedures is possible by using certified products (fillers, botulinum toxin, professional skincare products). It is also advisable to use "test pulses" (during laser procedures) where initial interventions are performed with minimal energy load on the skin, and later transition to standard modes. It is crucial to use the settings recommended in the manufacturer's protocol (not relying on expert conclusions), taking into account the skin phototype, and limiting the use of photosensitizing products and solar exposure. Laser technologies require specially trained personnel, proper choice of manipulators, use of eye protection (glasses, reflectors), and adherence to the procedure frequency. Any additional manipulations in the treatment areas should be minimized, regardless of the type of intervention.

A dermatocosmetologist must recognize local skin changes indicating the early stages of complications from aesthetic procedures. Timely detection of undesirable effects and appropriate rehabilitation measures significantly improve the prognosis of the aesthetic procedure.

Most common undesirable effects of aesthetic interventions include:

- Hematomas
- Allergic reactions
- Infectious complications
- Soft tissue necrosis
- Embolism
- Granulomas
- Atrophic skin changes
- Hypertrophic scars
- Dyschromia
- Burns
- Paresthesia
- Paralysis
- Overcorrection
- Implant migration
- Reactive edema
- Tyndall effect
- Facial ptosis
- Asymmetry



Fig. 23.1a, 1b Upper lip hematoma that occurred during augmentation

Hematomas are limited internal or subcutaneous bleeding resulting from vessel damage of various calibers during aesthetic procedures. Hematomas most often appear directly during the procedure. It is essential for the doctor to determine if the hematoma is pulsating (to exclude the risk of damage to large arteries). To do this, the dermatocosmetologist should palpate the intervention area without significant compression. In case of arterial injury, a clear pulse wave will be felt. Initially, hematoma symptoms may present as swelling, asymmetry, pain, and subcutaneous hardening.

Hematomas:

Sometimes, the color change in the area of injury is observed significantly later than the intervention itself (2–3 days after). The most undesirable complications of hematomas include suppuration and necrosis in the area of the hemorrhage. To reduce the risk of damaging large vessels, blunt-ended cannulas should be used, and traumatic manipulations in areas with large vessels should be limited. Additionally, it is recommended to stop taking anticoagulants 1–2 weeks before the aesthetic procedure. High blood pressure can also influence hematoma formation.

There are no special treatments for hematomas; compression of the injured vessel and applying ice through a sterile bandage or gauze are generally sufficient. In more complicated cases, a hemostatic sponge or tampons with 5% aminocaproic acid can be used. If a hemangioma reaches a significant size, puncture and drainage are performed. If the hematoma persists for more than 3–5 days, heparin, troxevasin ointments, Traumeel S, or vitamin K-containing products are used. Overall, the prognosis for post-aesthetic hematomas is favorable, with a very low percentage of necrotic complications.



Fig. 23.2. Allergic contact dermatitis, reaction to topical anesthetic



Fig. 23.3. Angioedema as a reaction to the injection of filler with lidocaine

Local and Systemic Allergic Reactions:

local and general allergic reactions are common complications of aesthetic interventions, as most fillers contain animal proteins and lidocaine. The risk of allergic reactions is further increased by the growing number of unlicensed fillers in Ukraine. The first signs of such reactions are itching, erythema, and swelling. If the substances used in the aesthetic procedure (anesthetic, filler, etc.) have a systemic effect on the body, generalized allergic reactions may occur, such as toxic dermatitis, polymorphic erythema, Stevens-Johnson syndrome, toxic epidermolysis, urticaria, and others.

The treatment of allergic reactions is complicated by the prolonged action of most substances used in augmentation. In such cases, it is necessary to minimize the allergic load on the body. For example, when there is an allergic reaction to hyaluronic acid, hyaluronidase is injected. Allergic reactions to mesococktails or biorevitalizants can be blocked by administering systemic corticosteroids (only in severe cases). Most contact allergic reactions resolve with antihistamines and removal of trigger factors.

Infectious Complications:

Infectious complications are relatively common undesirable reactions during aesthetic procedures. They are not only associated with violations of aseptic and antiseptic rules but also with the poor quality of some products, improper transportation and storage conditions, or the presence of infection foci on the patient's skin prior to the procedure (such as herpes, acne, or folliculitis).



Fig. 23.4. Simultaneous streptococcal and herpesvirus complications after laser procedure in the periorbital area



Fig. 23.5. Eyelid herpes that occurred after using a laser procedure (eyelid papilloma removal)

Pyogenic Complications:

Pyogenic complications often occur at sites of direct skin injury. When the infection penetrates deep layers of the skin, zones of inflammation, swelling, abscess formation, and subsequent soft tissue necrosis develop. Staphylococcus is the most common agent responsible for the formation of abscesses and disseminated forms of skin infection. The speed of infection spread can vary depending on the condition of the immune system. More often, the affected area becomes encapsulated, forming a hardened, hyperemic area of skin. In cases of rapid progression of the infection, the lesions increase in diameter, and fluctuation and pain appear. The spread of infection on the face leads to the formation of new areas of ostefollicular suppuration. Among the most undesirable bacterial complications is suppuration directly at the site of the injected filler. In such cases, the implanted material may be rejected, leading to areas of deep necrosis, soft tissue loss, and irreversible atrophic skin changes. In such cases, the most effective treatment method is the prompt incision, removal, and drainage of the affected area, followed by antibiotic therapy.

Viral Complications of Aesthetic Procedures: Viral complications, especially those caused by herpes simplex virus (labial or other localized forms), most often arise when active symptoms of the herpes infection are overlooked and spread during various interventions. Special attention should be given to immunocompromised patients, as the rapid dissemination of the herpes infection in such cases can lead to the development of Kaposi's herpes exanthem, central nervous system involvement, and a range of ulcerative-necrotic complications.



Fig. 23.6, a, b, c. Mycotic lesion that occurred after cosmetic manipulation (a - first day of therapy, b - seventh day of therapy, c - twelfth day of therapy)

A careful medical history and prophylactic treatment with abnormal nucleotides for patients prone to herpes infection significantly reduce the risk of viral complications during and after aesthetic procedures. As a preventive measure, valacyclovir (500 mg per day) is recommended for a week prior to the procedure and for 7–10 days after the intervention.

Fungal Complications of Aesthetic Procedures: Fungal complications are relatively rare following aesthetic procedures, but they more commonly affect immunocompromised patients and individuals with diabetes. The manifestations of fungal infections can be atypical; for example, candidiasis often becomes widespread, with the most significant involvement of physiological flexural areas. Trichophytosis (ringworm) may also localize in unusual areas, such as the face or neck. These atypical presentations can sometimes make early diagnosis and treatment challenging, necessitating heightened vigilance, especially in at-risk populations.

Biofilms in Aesthetic Procedures:

Biofilms are the result of structured colonies of commensal and pathogenic microorganisms that form at the sites of aesthetic interventions, most commonly at the injection sites of biological fillers. Through metabolic and spatial interactions between microorganisms, biofilms exhibit collective behaviors that help them resist antibiotics and other treatments. The accumulation of pathogenic bacteria within biofilms leads to inflammatory reactions, which are characterized by moderate erythema, increased skin density, and sometimes pain. Diagnosis of biofilms can be confirmed using epifluorescent laser confocal microscopy in combination with pathogen culture. Unfortunately, this method is not widely accessible in Ukraine at present, but biofilm formation can be suspected based on characteristic clinical symptoms and a slow progression of symptoms.

Necrosis of Soft Tissues (NST):

Necrosis of soft tissues is the premature destruction and death of skin cells, subcutaneous tissue, and the extracellular matrix. Necrotic changes can occur through liquefaction or coagulation types. In liquefaction necrosis, there is the formation of purulent tissue dissolution, often associated with fungal-bacterial complications. In coagulation necrosis, a necrotic scab forms as a result of ischemia, commonly due to vessel occlusion. NST can also occur as a result of foreign body rejection during augmentation, where the filler is recognized as a foreign body, leading to the formation of necrotic demarcation zones, along with discomfort and pain. Autoimmune diseases, such as lupus erythematosus, necrotizing vasculitis, or neutrophilic dermatoses, which are characterized by the phenomenon of pathergy, can significantly contribute to this complication. The presence of aggressive anaerobic flora can also complicate NST. NST should not be viewed as an isolated process but as the result of secondary factors. Early signs of necrosis must be identified and treated promptly to prevent serious complications such as atrophic, scarred skin, nerve and vessel damage, or even sepsis. Treatment includes the removal of trigger factors, antibiotic therapy, proteolytic enzymes, and topical agents with antiseptic, analgesic, and necrolytic effects (e.g., Iruksol, Argosulfan, Ofloxacin, etc.).

Embolism

Embolism is a complication related to the occlusion of blood vessels by various types of emboli. These emboli may not only include fragments of the filler but also blood clots, fat tissue, necrotic masses, inert gases, and more. Embolism is a relatively rare side effect of aesthetic procedures, occurring in approximately 0.3–0.5% of cases.

The first signs of embolism are a change in skin color at the site of intervention (occlusion), usually distal to the artery's path. The affected area takes on a



Fig. 23.7. Soft tissue necrosis in the suture area as a result of unsuccessful aesthetic surgery.



Fig. 23.8. Facial artery embolism, labial branch, filler occlusion. A white area of persistent ischemia formed on the upper lip.

marbled appearance, resembling livedo. Before visual signs of occlusion, the patient experiences intense pain and a burning sensation in the embolized area. The pain occurs immediately after the occlusion and may persist for several hours to days. Livedo-like eruptions appear within 10–30 minutes after the embolism, and within hours, blue or dark purple spots form in the affected area. On days 2–3, ischemic areas begin autolysis, which leads to necrosis and scarring.

To assess the extent of the damage, a compression test (finger test) can be used. When pressure is applied to the ischemic skin, pallor persists longer than in unaffected skin areas.

Treatment:

Immediate treatment of embolism during aesthetic procedures is crucial. The first step is to identify the type of embolus. If the embolus is composed of hyaluronic acid, it is essential to inject hyaluronidase immediately. The enzyme is administered via an infiltrative method using a fine needle over the entire visible ischemic area. Ideally, 1 vial of hyaluronidase (1500 U) should be diluted in 1–2 ml of saline. After administering hyaluronidase, a gentle massage should be performed for better distribution of the enzyme. If the therapy is effective, ischemic signs should disappear within 2–3 hours. If the effect is insufficient, the procedure can be repeated after a few hours. In anatomically critical skin areas (such as near nerve bundles or large vessels), it is better to administer hyaluronidase under ultrasound guidance.

If the embolism is not related to hyaluronic acid, the use of vasodilators (e.g., sildenafil, pentoxifylline) and, if possible, oxygen therapy may be appropriate.

With timely restoration of blood circulation in the skin and subcutaneous tissue, the prognosis is generally favorable. However, prolonged ischemia usually leads to necrosis and scarring of the skin.

Granuloma

A granuloma is a localized focus of pathological proliferation of inflammatory cells (primarily neutrophils and lymphocytes), typically occurring in individuals prone to chronic purulent conditions. In aesthetic medicine, granulomatous inflammation is a relatively common complication associated with the injection of various types of fillers.

It is believed that the main causes of granuloma formation in aesthetic procedures are related to the low quality of fillers based on hyaluronic acid or polylactic acid. In contrast, procedures involving the translocation of autologous tissues are significantly less likely to result in granuloma formation.

Granuloma is essentially a reaction to chronic inflammation, which, in aesthetic medicine, is usually linked to the prolonged presence of filler material in the soft tissues of the face or other body areas. The situation worsens when multiple types of fillers are used simultaneously, as this significantly increases the risk of granuloma development.



Fig. 23.9a. Granuloma, in the area of permanent tattoo



Fig. 23.9b. Granuloma in the filler injection area that occurred a year after implantation.

In addition to poor filler quality, granulomas may be caused by individual intolerance to the substance used or violations of injection technique during the procedure.

Granulomatous reactions can also result from laser procedures in areas of permanent tattoos – and in some cases, the tattoo pigment itself can trigger the development of a granuloma.

Granulomas typically develop six months or more after the implantation of filler material. In some cases, the process may begin significantly later – even 2–3 years post-procedure. The granulomas often reach sizes of 2–3 cm. In the early stages, swelling and mild erythema appear at the affected sites. On palpation, the nodules are soft, non-encapsulated, and may exhibit interfascial extensions in the form of linear bands.

If a patient complains about a granuloma in the area of an aesthetic procedure, it is essential to identify the underlying cause – whether it is due to poor-quality filler, an individual hypersensitivity, or injection technique errors. It's also important to evaluate the extent of granulomatous involvement and determine the appropriate treatment strategy.

The most effective treatment is the removal of the implanted material that triggered the reaction. If elimination of the agent is not possible, a corticosteroid (usually long-acting) can be injected directly into the lesion. It is important for the steroid to be delivered precisely into the granuloma, which helps minimize the risk of connective tissue atrophy and bacterial complications. A typical treatment course involves 2–4 corticosteroid injections, administered every 14–30 days. With proper treatment, the prognosis is favorable. However, without timely therapy, the granuloma can persist for 3–5 years, though atrophic changes in the affected area are relatively rare.

Atrophic skin changes most often occur after aggressive procedures (e.g., deep resurfacing, ablative laser treatments, mechanical facial cleansing)



Fig. 23.10. Atrophic changes in the skin of the nose after using a neodymium laser



Fig. 23.11. Lip Overcorrection (Excessive Lip Augmentation)

or due to inadequate skin rehabilitation following aesthetic interventions. Occasionally, low-quality fillers, nerve damage, or vascular occlusion may also result in atrophy.

There have been cases of facial hemiatrophy in two women after injection with questionable-quality fillers. Unlike typical scleroderma, these cases developed rapidly over several months and had an acute inflammatory presentation, including pain and fever.

Treatment of established atrophic changes is similar to that of localized scleroderma. The best outcomes are achieved in early stages using short courses of systemic corticosteroids combined with antibacterial therapy. If the condition progresses, cytostatic therapy (e.g., methotrexate 5–10 mg/week) combined with topical tacrolimus and narrowband phototherapy may be appropriate.

Overcorrection is associated with the injection of an excessive amount of filler material during an aesthetic procedure. This complication may result either from unintentional over-injection or due to the patient's personal preferences, which are sometimes questionable from an aesthetic standpoint, especially in areas such as the lips and cheekbones.

This complication can be prevented by strictly adhering to the injection protocols and explaining to the patient the individual anatomical features that influence the expected results. Sometimes it is helpful to show the patient images of overcorrection and explain the importance of using the manufacturer-recommended filler volume.

A safe volume of implanted material is considered to be 0.1 ml per bolus area. The injection depth should be controlled with marked cannulas or visual control of the needle tip during the procedure. After injection, gentle massage of the area is performed to ensure even distribution of the filler.

Overcorrection with hyaluronic acid-based fillers can be resolved by injecting hyaluronidase at a dose of 50–100 IU per treatment site. Calcium

hydroxyapatite-based fillers can be removed using a "flushing" technique, which involves injecting warm saline directly into the overcorrected area in a volume three times greater than the amount of filler. In some cases, a puncture technique using wide cannulas or needles (14–18G) and mechanical pressure may be employed to displace the filler.

In long-standing cases of overcorrection (lasting 1 year or more), a fibrous capsule may form around the area. In such instances, a combination of enzymatic agents – collagenase, hyaluronidase, and lidase – may be used to break it down.

Implant Migration

This is a common complication of aesthetic procedures, referring to the unintended movement of the filler into undesired areas of the soft tissues. There are two types: early and delayed migration. Migration is usually due to technical errors during injection: excessive filler volume, superficial injection, or failure to reach the correct anatomical site. Additional contributing factors may include low-quality fillers, low viscosity, or post-procedure manipulation of the area by the patient (e.g., massaging, which displaces the filler).



Fig. 23.12. Implant Migration into an Unwanted Area of the Upper Lip After Augmentation

Given that the most commonly migrated material is hyaluronic acid, treatment typically involves hyaluronidase injection directly into the area of migration, sometimes repeated, in a total dose of 100–300 IU.

Reactive Edema is a relatively common complication during aesthetic procedures, especially when using laser technologies, aggressive chemical peels, mechanical facial cleansing, and similar interventions.

Reactive edema (RE) is sometimes mistaken for a purely allergic reaction, which is not entirely accurate. In this condition, the immune system perceives components of the patient's own damaged tissue as superantigens, which explains the rapid regression of reactive edema once non-viable cells are shed and the skin begins to recover.

Thus, reactive edema is more accurately described as a variant of an immune-allergic reaction. In the case of ablative laser procedures, the main trigger of reactive edema is carbonized tissue (charred skin cells) that accumulates in the skin after energy exposure. As the epidermis regenerates and damaged cells are gradually cleared, reactive edema typically resolves completely.


a


b


c

Fig. 23.13. Reactive edema after carbon laser treatment (a – on day two, b – on day five, and c – on day seven of observation)

In unfavorable cases, reactive edema (RE) may persist for over a week, which can significantly distress patients and sometimes reduce the effectiveness of the aesthetic procedure. In such cases, short courses of systemic corticosteroids are prescribed (including a possible single dose of a long-acting agent) along with epithelializing creams or fluids until the skin fully recovers.

Dyschromia – refers to persistent discoloration of the skin, caused by exogenous or endogenous factors. Dyschromia can be either hyperpigmentation or hypopigmentation.

The underlying causes are usually not related to skin cell metabolism, but are instead deeper in origin: autoimmune thyroid diseases, polycystic ovary syndrome, adrenal tumors, liver dysfunction, oral contraceptives, or certain medications, among others. Such individuals require thorough medical evaluation prior to undergoing aesthetic procedures.

During patient assessment, the dermato-cosmetologist should pay close attention to signs indicating a predisposition to dyschromia, including: hypomelanosis, leukoderma, vitiligo, ephelides (freckles), melasma, lentigines, pigmented actinic keratoses, and other pigmented lesions. These skin conditions require careful risk-benefit evaluation for each individual prior to aesthetic interventions.

Tyndall Effect (TE) – in aesthetic medicine, this complication is associated with the visible bluish tint caused by superficially placed filler. It is essentially an optical phenomenon that occurs due to light scattering as it passes through a transparent medium (the filler).

The main causes of this complication are:

- Incorrect injection technique,
- Use of high-density fillers in areas with thin skin,
- Injection of excessive amounts of filler.



Fig. 23.14. Dyschromia in the form of hyperpigmentation after laser procedures (CO2 Fraxel)



Fig. 23.15. Tyndall Effect (visualization of superficially placed filler)

The first signs of TE are usually noticed by the patient almost immediately after the procedure, and the symptoms worsen as post-procedure swelling subsides – typically within 1–2 days. Patients often describe it as a «skin translucency effect», which is most noticeable in natural daylight. The severity of the Tyndall effect depends on the injection site, most commonly observed:

- In the periorbital area,
- On the bridge of the nose.

Proper selection of filler density and injection depth significantly reduce the risk of developing the Tyndall effect. Before augmentation, it is crucial to assess skin thickness, subcutaneous tissue, and any atrophic changes.

Treatment of TE:

- If a hyaluronic acid-based filler was used, treatment involves injecting hyaluronidase.
- Calcium hydroxyapatite can be dispersed through repeated saline injections.
- In complex cases, surgical removal of the implanted material may be necessary.

Facial Ptosis (Zonal) – is the drooping of facial soft tissues associated with compression or trauma to a nerve. A specific variant of ptosis can also develop as a result of overdosage or incorrect administration of botulinum toxin.

Nerve trauma may occur:

- Directly during the aesthetic procedure (e.g., using sharp cannulas, overly aggressive injection techniques),
- Due to neglecting individual anatomical variations in the location of nerve bundles.



a b

Fig. 23.16 a, b. Zonal drooping of the right corner of the mouth (result of improper botulinum toxin injection).

Depending on the type of nerve damage, ptosis may be:

- Short-term (up to 3 days),
- Or prolonged.

Treatment approach is individualized and should primarily focus on:

- Eliminating trigger factors such as:
  - Removing filler,
  - Reducing swelling,
  - Blocking botulinum toxin effects.

Facial Asymmetry – a complication of aesthetic procedures associated with uneven injection of filler into symmetrical areas of the body (important not to confuse with ptosis).

Due to initial post-procedural swelling, this complication often goes unnoticed at first. Over time, the patient may notice uneven filler distribution, leading to the development of visible asymmetry.

In some cases, gentle self-massage of the overcorrected area may yield good results. However, most patients require corrective intervention, which may include:

- Additional filler injections to balance volume,
- Or the use of enzymes that accelerate filler degradation.

A competent specialist always informs the patient in advance about the possibility of touch-up procedures, which may be necessary due to:

- Individual anatomical variations, or
- Personal intolerance to the implanted material.

Trauma to Pigmented Skin Lesions – a fairly common complication of aesthetic procedures, especially during invasive manipulations such as:

- Chemical peels,



Fig. 23.17. Facial asymmetry as a result of unsuccessful aesthetic intervention.



Fig. 23.18. Marginal trauma of a pigmented nevus (due to hemorrhage, the lesion changed color and now resembles a venous hemangioma).

- Fractional thermolysis,
- Mechanical facial cleansing,
- Platelet-rich plasma (PRP) therapy, etc.

The degree of trauma to a pigmented lesion can vary:

- From limited surface injury to
- Complete unintentional removal or destruction of the pigmented lesion.

In such cases, the following steps are essential:

1. Thorough medical history should be collected – including:
   – Personal or family oncological history.
2. Careful dermatoscopic examination of the injured nevus.
3. Assess changes in the lesion over the past 6 months.
4. Determine whether the lesion was previously traumatized.
5. If available, preserve any remaining fragments for histopathological analysis.

Regardless of whether the trauma was partial or complete, the patient should be monitored by a dermatologist for 6–12 months.

Patients must be warned about the importance of promptly seeking medical attention if the lesion shows:

- Change in size,
- Change in shape, or
- Change in color.

In cases of partial (marginal) trauma, the following recommendations apply:

- Treat the area with non-alcoholic antiseptics.
- Avoid using iodine or other aggressive substances.
- Acceptable options include:
  – Chlorhexidine,
  – Aqueous methylene blue solution.

If there is significant trauma to a pigmented lesion (involving more than 50% surface integrity loss), it is recommended to perform complete excision followed by histopathological examination.

It is essential to calm the patient and explain that in the majority of cases, trauma to moles has a favorable prognosis. However, careful attention should be paid to any changes in pigmented skin lesions.

1. To evaluate skin lipid balance, following procedures are performed:

A. Laser Doppler flowmetry
B. Corneometry
C. Mexametry
D. Sebumetry
E. Assessment of skin electrical conductivity

2. Laser Doppler flowmetry evaluates:

A. Skin lipid balance
B. Microcirculation
C. Skin moisture balance
D. Skin topography
E. Mechanical properties of skin

3. Which of the following is not a melanin type dyschromia:

A. Vitiligo
B. Tattooing
C. Melasma
D. Kaposi's disease
E. Albinism

4. The ablation phenomenon determines high therapeutic effect, when performing:

A. Microdermabrasion
B. Deep peeling
C. Oxy-mesotherapy
D. Laser skin resurfacing
E. Lipofilling

5. The advantages of botulinus toxin Estetox involve:

A. Deep penetration
B. Convenient form of release
C. Lack of human albumin
D. Predefinite effect of lipid denervation
E. Long-term effect

6. What type is not among the base types of skin?

A. Normal skin
B. Elastic skin
C. Dry skin
D. Oily skin
E. Combined skin

7. What action physical factors do not involve:

A. Vaporization
B. Brush-peeling
C. Cryotherapy
D. Thalassotherapy
E. Pelotherapy

8. Varieties of plastic surgery are:

A. Vacuum
B. Tumescent
C. Ultrasound
D. Syringe
E. All of the above

Task 1. A 26 y.o. patient with signs of post-acne visits a cosmetologist.

a) What type of treatment is appropriate?
- **A**. Botulinum toxin
- **B**. Hyaluronic acid
- **C**. Chemical peeling
- **D**. Lipofilling
- **E**. Oxy-mesotherapy

b) What are the contraindications for the chosen treatment?

Task 2. A 27 y.o. woman visits a beauty clinic complaining of greasy skin surface. *On examination*: skin surface is oily, with coarse structure; pores are wide cone-shaped, but empty.

a) What additional research is required?
- **A**. Corneometry
- **B**. Laser Doppler flowmetry
- **C**. Vibration reoelastography
- **D**. Sebumetry
- **E**. Measurement of conductivity

b) Give practical advice on caring for this type of skin.

Answers to the questions of the first level of complexity
1 – D; 2 – B; 3 – B; 4 – D; 5 – C; 6 – B; 7 – B; 8 – E
Answers to the questions of the second and third levels of complexity
1a – B; 2a – D

Sexually Transmitted infections (Venereal Diseases)

Sexually Transmitted Infections (STI) – highly contagious infectious diseases, especially sexually transmitted diseases affecting not only the genital organs. Currently there are more than 30 different infectious diseases, pathogens of which can be transmitted from person to person, primarily sexually. According to the WHO classification, some of the diseases indicated below in the table (scabies, hepatitis B and C, genital warts) are usually transmitted asexually, and therefore are only conditionally referred to the diseases transmitted mainly sexually.

WHO classification of sexually transmitted infections	
Nosology	**Pathogen**
Classic venereal diseases	
1. Syphilis	*Treponema pallidum*
2. Gonococcal infection	*Neisseria gonorrhoeae*
3. Chancroid	*Haemophilus Ducrey*
4. Lymphogranuloma venereum	*Chlamydia trachomatis*
5. Granuloma inguinale (donovanosis)	*Klebsiella granulomatis*
Other sexually transmitted infections	
A. With a predominant damage of genital organs	
1. Urogenital chlamydiosis	*Chlamydia trachomatis*
2. Urogenital trichomoniasis	*Trichomonas vaginalis*
3. Urogenital mycoplasmosis	*Mycoplasma hominis*
4. Candidal vulvovaginitis and balanitis	*Candida albicans*
5. Genital herpes	*Herpes simplex virus*
6. Genital warts (condylomata acuminata)	*Papillomavirus hominis*
7. Genital contagiosum epitheliale	*Molluscovirus hominis*
8. Bacterial vaginosis	*Gardnerella vaginalis* and other pathogens
9. Urogenital shigellosis of homosexuals	*Shigella species*
10. Phthiriasis (pediculosis pubis)	*Phthyrus pubis*
11. Scabies	*Sarcoptes scabiei*
B. *With a predominant damage of other organs*	
1. Infection, caused by human immunodeficiency virus	*Human immunodeficiency virus*
2. Hepatitis B, C	*Hepatitis B,C virus*
3. Cytomegalovirus infection	*Cytomegalovirus hominis*
4. Amebiasis (predominantly of homosexuals)	*Entamoeba histolytica*
5. Lambliasis	*Giardia (lamblia) intestinalis*

24 TOPIC

Syphilis: general information and principles of diagnostics

Syphilis *(syphilis), synonym: lues* – is a chronic systemic infectious disease with a rhythmical undulating variable course, which is predominantly transmitted sexually and which affects all organs and systems of human body.

TRAINING AND EDUCATIONAL OBJECTS

- Understand classification of diseases, predominantly transmitted sexually
- Be oriented in history of origin and circulation of syphilitic infection in Europe and in the world
- Analyze the peculiarities of epidemiology of the indicated infection
- Compile information on the ways and the possible conditions of infection with syphilis
- Determine the incubation period and the factors influencing its course and features
- Understand the general course of syphilis and its classification

TO KNOW:

- current understanding of the etiology and pathogenesis of syphilis;
- morphological characteristics of the causative agent of syphilis – Treponema pallidum
- ways of transmission and conditions of infections, peculiarities of immunity, reinfection, superinfecting with syphilis;
- significance and clinical evaluation of serological reactions;
- general course of syphilis in the human body;
- main (most common) mistakes in the diagnosis of syphilis;
- legal and ethical aspects of venereal pathology.

TO BE ABLE TO:

- deontological properly collect general and sexual medical history of the patient suspected of having a sexually transmitted disease;
- classify the diseases, primarily transmitted sexually;
- analyze the features of the epidemiology of sexually transmitted diseases;
- during the treatment consider characteristics of the psychological and behavioral responses of people with sexually caused infectious pathology;
- analyze information on the ways and conditions of possible infection with sexually transmitted diseases.

Etiology. Syphilis is caused by Treponema pallidum (Treponema pallidum), belonging to the class of Spirochaetales, family of Treponemaceae, genus of Treponema. It received its name because of a very poor ability to paint. Treponema pallidum has the form of a thin spiral of width of 0.2 μm and a length of 5-15 μm. Its 8-12 curls are placed at the same distance from each other. They are very mobile and constantly carry out sliding (forward and backward), rotational, pendulum and contractile (wavy) movements. The small number of surface antigens (protein, polysaccharide, lipid) in Treponema pallidum determines its weak immunogenicity and helps to quite successfully counteract antibodies and lymphocytes of the human body. As facultative anaerobes Treponema pallidum finds the optimal conditions for its location and development in the lymphatic system. Treponema pallidum is unstable to drying and high temperature (at 55 °C it dies after 15-20 min.). The optimum temperature for its existence is +37 °C. **Epidemiology**. Syphilitic infection occurs only in humans. According to the WHO estimates (eng – WHO) about 15 million people in the world are infected with syphilis each year. Today, the disease is considered by experts as well as a co-factor contributing to HIV – infection.

Sources of infection. The source of infection is the sick person, especially with infectious (active) manifestations of primary and secondary syphilis.

Ways of infection. There are three main ways of infection with syphilis:

1. Contact:
   - sexual – in case of genital, anal and oral contacts;
   - professional – during surgery, instrumental examination;

2. Transfusion way – in the case of a direct penetration of Treponema pallidum in the blood, particularly during blood transfusions, medical manipulations (cutting, an injection during surgery).

3. *Transplacental* – from sick pregnant woman to the fetus through the placenta.

Immunity. True (sterile) or artificial immunity in case of syphilis in human does not exist, as there is no natural immunity. After infection only unsterile (infectious) immunity gradually develops, which is caused by an allergic changes in the body as a result of the disease-causing agent in it. When recovering infectious immunity disappears.

Reinfection – is recurrent disease of syphilis in human who had previously been sick with it, and did not fully recover from it, that manifested itself as the absence of any clinical symptoms, and persistent negative reaction of such person in all serological tests.

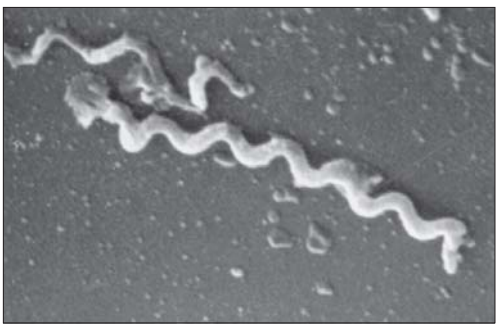


Fig. 24.1. Treponema pallidum (submicroscopy). Zooming x9000.

General course of syphilis and its classification. Syphilis infection is

characterized by the cyclical type of clinical course which is manifested by a certain sequence of occurrence of the external symptoms, the change of periods of active and latent clinical course.

In the clinical course of syphilis infection the following periods and forms are defined:

1. Incubation period – from the moment of infection to appearance of the hard chancre.

2. Primary period (*syphilis I primaria*) – stage of the disease from the moment of appearance of hard chancre to the development of secondary syphilides. It consists of:

- *seronegative (syphilis I seronegativa)* syphilis with persistently negative serological reactions in the presence of clinical symptoms;
- *seropositive (syphilis I seropositiva)* syphilis with positive serological reactions in the presence of clinical symptoms;
- *latent (suphilis I latens)* syphilis, which is characterized by the absence of specific clinical manifestations in patients.

3. Secondary period (syphilis II secundaria) – stage of the disease, which is characterized by polymorphic rash (papules, macules, pustules) on the skin and mucous membranes and their determined staging, namely:

- *secondary recent syphilis (syphilis II recens)* – period, characterized by numerous polymorphic eruptions on the skin and mucous membranes, polyadenitis, the presence of residual symptoms of the hard chancre and strongly positive serological reactions;
- *secondary recurrent syphilis (syphilis II recediva)* – period of secondary syphilis characterized by a small polymorphic grouped rash;
- *secondary latent syphilis (syphilis II latens)* – period of the disease, which is clinically latent and manifested only by positive serological reactions.

4. Third syphilis (syphilis III tertiaria) – stage, characterized by the damage of internal organs and nervous system.

5. Latent syphilis (syphilis latens). The latent syphilis includes such cases of syphilis infection, in which serological reactions are positive, but there are no clinical signs. The following variants are possible:

- premature latent syphilis (syphilis latens praecox)*, when less than two years passed from the moment of infection;*
- tardive latent syphilis (syphilis latens tarba)*, when two years and more passed from the moment of infection;*
- unspecified latent syphilis (syphilis ignorata)*, when the period of infection can not be specified.*

6. Congenital syphilis (syphilis congenita) occurs when infection with Treponema pallidum is caused by ill mother in the period of intrauterine growth. It is customary to distinguish the following types:

- *premature congenital syphilis (syphilis congenita praecox)* – syphilis of fetus and of children up to two years;
- *tardive congenital syphilis (syphilis congenita tarda)* – in children older than two years;
- *latent congenital syphilis (syphilis congenita latens)*, in case of which the clinical manifestations are absent, and laboratory parameters of cerebrospinal fluid are normal.

7. Syphilis of nervous system (neurosyphilis).

General principles of diagnostics. Diagnostics of syphilis is based on:

a) the presence of specific clinical manifestations on the skin and mucous membranes;

b) the history data – sexual contacts;

c) the positive results of laboratory tests.

If the rash elements that are not accompanied by subjective sensations are present on the skin, genitals and mucous membranes, one should think that it may be manifestations of syphilitic lesions. It is desirable to establish a patient's sexual contacts over the past few months.

Clinical observations and corresponding experimental studies have demonstrated that infection may not occur if only a negligible amount of treponemes penetrates the organism or if there is a high concentration of thermolabile treponemostatic and treponemocidal substances in human serum. These substances, upon contact with treponemes, induce immobility and, in some cases, lysis of the fragile treponemes. The ability of treponemes to convert into cysts or L-forms results in a prolonged asymptomatic course of syphilis. In cases of late latent syphilis without involvement of the nervous system or internal organs, treponemes persist in the host in the form of cysts that exhibit weakly expressed properties.

Consequently, the diagnosis of syphilis requires a comprehensive set of serological methods. Currently, serological diagnosis is performed in accordance with the Medical Care Standards "Syphilis" (approved by the Ministry of Health of Ukraine in 2023). Specifically, treponemal tests (TT) are employed, including an express test (ETS), immunochemiluminescence assay (ICLA), enzyme-linked immunosorbent assay (ELISA for IgM and IgG), treponemal antibody immunofluorescence reaction (TIF – absolute), passive hemagglutination reaction (PHAR), and immunoblot (IB for IgM and IgG). In the event of positive TT results, non-treponemal quantitative tests (NTT) are conducted, such as the microprecipitation reaction (MPR) and the rapid plasma reagin test (RPR).

1. What agent causes syphilis?

A. *Pediculus corporis*
B. *Sarcoptes scabiei varietas hominis*
C. *Demodex folliculorum*
D. *Treponema pallidum*
E. *Staphilococcus albus*

2. Which one of these diseases refers to classic veneral diseases?

A. Genital warts
B. Chancroid
C. Scabies
D. Pediculosis
E. All the above mentioned

3. Which of the following agents cause so called "classic veneral diseases":

A. *Chlamydia trachomatis*
B. *Neisseria gonorroeae*
C. *Treponema pallidum*
D. *Klebsiella granulomatis*
E. All the above mentioned

4. What types of movements can syphilis causative agent – Treponema pallidum cause:

A. Sliding (forward and backward)
B. Rotational
C. Pendulum
D. Contractile (wavy)
E. All the above mentioned

5. Which period is not defined in the clinical course of syphilis infection:

A. *Syphilis primaria*
B. *Syphilis congenita*
C. *Syphilis tertiaria*
D. *Syphilis secundaria*
E. *Syphilis nummularis*

6. Which are the ways of infection with syphilis:

A. Sexual
B. Transfusion
C. Transplacental
D. All the above mentioned

Task 1. Patient of the dermato-venereological department with a diagnosis of "primary seropositive syphilis" was treated with penicillin. 9 hours after the first injection a patient's body temperature rose to 38.2 ^{0}C, malaise, headache, and the maculopapular rash on skin appeared.

a) How can these symptoms be explained?

A. As allergic reaction
B. As toxic reaction
C. As idiosyncratic reaction
D. As infectious disease
E. As viral disease

b) Give therapeutic recommendations.

Task 2. The woman of 35 years received treatment of the secondary latent syphilis in the past.

a) How can be her complete medical treatment proved?

A. Absence of the disease manifestations
B. Birth of healthy children
C. Absence of disease relapses
D. Results of negative specific serologic reactions
E. All the above mentioned is true

b) Is the repeated infection with syphilis possible?

Answers to the questions of the first level of complexity
1 – D; 2 – B; 3 – C; 4 – E; 5 – E; 6 – D
Answers to the questions of the second and third levels of complexity
1a – B; 2a – E

25 TOPIC

Primary period of syphilis

Primary period of syphilis *(syphilis I primaria, lues primaria)* – stage of the disease from the appearance of primary sore (hard chancre) to the appearance of secondary syphilides.

TRAINING AND EDUCATIONAL OBJECTS

- Determine the overall course and clinical characteristics of the primary period of syphilis
- Get oriented in the typical and atypical manifestations of the primary period of the disease
- Determine the modern features of clinical manifestations of the primary period Study the features of filling in the medical records of patients with primary syphilis.

TO KNOW:

- factors affecting the duration and peculiarities of the incubation period of syphilis;
- clinical signs of classical hard chancre;
- atypical forms of chancres: chancre-felon, chancre-amygdala, indurative edema;
- peculiarities and clinical characteristics of lymph nodes;
- diagnostic algorithm of the primary period of syphilis;
- complications, caused by hard chancre (balanitis, balanoposthitis, phimosis, paraphimosis, mortifying, esthiomene, vulvitis, vulvovaginitis);
- personal preventive measures for this disease.

TO BE ABLE TO:

- deontologically and reasonably take a general and sexual history;
- conduct a comprehensive examination of the patient in the proper manner;
- analyze the results of laboratory tests of a patient with a primary period of syphilis;
- differentiate between the clinical manifestations of the primary period of syphilis;
- make a differential diagnosis of diseases that have similar clinical symptoms.

Incubation period – this is a period of development of a specific infection in the human body, which begins with the moment of infection and continues to manifestation of the first clinical signs of the disease. Its duration makes up an average of 3-4 weeks.

Clinical picture. Primary period of syphilis begins with a *primary syphiloma*, *or hard chancre*, and lasts for about 6-7 weeks before the onset of multiple lesions (secondary syphilides) on the skin and mucous membranes. 7-8 days after the formation of the had chancre, increase in the size of lymph nodes becomes noticeable (*regional scleradenitis or specific bubo*). This regional scleradenitis has fairly typical symptoms: tightly elastic consistency, non-inflammatory nature, focus location, absence of cohesion of nodes with skin, their considerable mobility.

Given Wasserman reaction primary period of syphilis is divided into primary sero-negative (*first three weeks*), and primary sero-positive (*following three-four weeks*).

In most cases, chancre is localized on the genitals. Chancre can appear on other areas of penetration of the agent (the area of the rectum, mammary gland, tunica mucosa of mouth).

Hard chancre –is a painless saucer-shaped ulcer or erosion, with smooth edges without visible inflammation manifestations, on the bottom of which the infiltration of the cartilaginous hardness, or tangible induration like a thin film and shine are formed. There are clinical varieties of hard chancre depending on the number of formations, the localization of process, anatomical peculiarities of lesions (single, multiple, erosive, ulceration, genital, estragenital, large and small in size).

Clinical signs of the classic hard chancre:

- morphological element in the form of erosion or ulceration;
- the bottom of the color of raw meat;
- the chancre is of regular round or oval form;
- edges are not saped, are clearly lined up, saucer-shaped and at the same level of the skin, if chancre is ulcer;
- size of 0.7-1.5 cm;
- lesion focus is painless and without inflammation swab around the periphery;
- chancre erosive surface is smooth and shiny;
- surface of the ulcer chancre has a small hemorrhage, and is sometimes covered with purulent layering;



Fig. 25.1. Erosive hard chancre.

- significant density of edges and bottom during palpation;
- skin around the elements of the rash is not changed;
- presence of concomitant regional scleradenitis;
- infiltration under erosion after its epithelization persists for several weeks, and then fully and completely resolves;
- ulcerative chancre heals without treatment in 6-9 weeks, leaving a hypochromic scar.

There are also often atypical forms of hard chancres as indurative edema, chancre-felon and chancre- amygdalitis.

Indurative edema is localized mostly on the labia – in women, as well as in the foreskin and scrotum – in men. Due to lesions of Treponema pallidum of lymphatic vessels, edema area increases significantly, is compacted, acquires a kind of pale pink or bluish-red coloration.

Chancre-felon clinically resembles an ordinary felon, is localized on the nail phalanx in the area of periungual nail wall, usually of the index finger. Finger becomes



Fig. 25.2. Ulcer hard chancre.



Fig. 25.3. Multiple ulcer hard chancre.



Fig. 25.4. Hard chancres in the area of anus.



Fig. 25.5. Hard chancres in the area of upper lip.

swollen, it swells in the shape of clubbell and has a bluish-red color. Chancre-felon often takes the form of a deep ulcer in the shape of a crescent, with rough edges and the bottom covered with a dirty-gray fur. Patients feel a sharp throbbing, shooting pain. The elbow and axillary lymph nodes that are often painful during palpation are increased.

Chancre-amygdalitis is characterized by an increase, density and hyperemia of one tonsil with formation of neither erosion nor ulceration. The border of a redness is clear, pain is slight, overall temperature reaction is missing. Regional lymphadenitis of submandibular and cervical lymph nodes is developing. The process differs from angina by the unilateral lesion, the lack of significant pain and diffuse hyperemia of the mucous membranes of the mouth, and the general condition of the patient is normal.

The clinical course of chancre can be complicated. The *vulvitis, vulvovaginitis* develops in women, in men – *balanitis* (inflammation of the epithelium of the balanus), *balanoposthitis* (balanitis in combination with inflammation of the inner layer of the foreskin), *phimosis* (narrowing of the foreskin ring).

Severe complications of hard chancre include *mortifying*.

The second clinically manifested symptom of primary period of syphilis is ***regional lymphadenitis***. It becomes apparent at the end of the first week after appearance of the hard chancre. Its localization is directly related to the place of the chancre appearance. For example, chancre in the genital area causes an increase of the inguinal lymph nodes.



Fig. 25.6. Indurative edema.

Lymph nodes gradually increase in size, become dense, they are not painful, are not connected to each other or with the skin, are mobile; external signs of inflammation are not observed. Some (package) lymph nodes increase mainly in the area close to the lesion.



Fig. 25.7. Indurative edema regional lymphadenitis (specific bubo).

4-6 weeks after the appearance of the hard chancre, symptoms indicating generalization of treponemal infection in the body appear. Almost all the lymph nodes increase, i.e., polyscleradenitis develops.



Fig. 25.8. Chancre-felon.

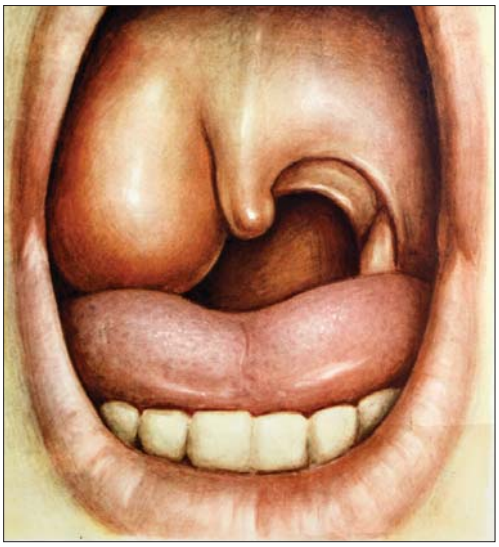


Fig. 25.9. Chancre-amygdalitis.



Fig. 25.10. Ulcerous chancre, complicated with balanoposthitis and phimosis.



Fig. 25.11. Hard chancre, complicated with balanoposthitis and phimosis.

At the end of the primary period of the disease, 15-20% of patients have other symptoms: increased body temperature, headache and other symptoms of general uneasiness.

Primary period of syphilis ends not with healing of the hard chancre, but only with the appearance of secondary syphilides.

Diagnostics. Diagnosis of primary seronegative syphilis should always be confirmed by detection of Treponema Pallidum in secret from the surface of the hard chancre. In order to confirm the diagnosis of primary syphiloma, classic serological tests of blood, which become positive 3-4 weeks after formation of primary syphiloma, are also used. It is also important to identify the patient's sexual contacts.

Differential diagnostics. In case of differential diagnostics one shall distinguish hard chancre from erosions or ulcers that occur in other diseases, and are also located primarily in the area of external genital organs. These include traumatic erosions, herpes rash, tuberculous ulcers, skin lesions in case of chancroid, balanitis and balanoposthitis, pyoderma chancriformis, erythroplasia of Queyrat, carcinoma of the skin.

Pyoderma chancriformis is most similar to an ulcer in the primary syphiloma: it has a round or oval shape, dense infiltration, is painless, can be accompanied by concomitant scleradenitis. Treponema pallidum in the serum from the ulcer surface are not detectable. Serological tests for syphilis are negative.

The itching and burning sensation in the areas of future eruptions precede *herpes simplex* 1-2 days before the disease. Herpes is characterized by the typical small grouped vesicles with serous contents, as well as surface erosions with polycyclic contours.



Fig. 25.12. Hard chancre, complicated with mortifying and esthiomene.



Fig. 25.13. Regional lymphadenitis (specific bubo; balanoposthitis).

Chancroid has a short two-three day incubation period, is characterized by the appearance of inflammatory maculo-papules, then pustules, which soon transforms into an ulcer. After the appearance of the first ulcer (parental) as a result of auto-infection, daughter ulcers appear. The edges of these very painful ulcers are swollen, bright red, saped, abundant pus is discharged. The scrapings from the ulcer or from its edges contain streptobacillus of Dyukrey-Unna-Peterson.

Erosive balanitis and balanoposthitis are manifested by the painful surface bright red erosions, without density with a thick discharge. There is no regional bubo.

Chancriform itchy ecthyma is usually multiple and accompanied by acute inflammatory signs, itching and presence of other symptoms of the scabies, the lack of a density and regional scleradenitis.

Traumatic erosion is mainly of linear form, accompanied by acute inflammatory signs, is painful and rapidly epithelialized, accompanying bubo is missing.

Carcinoma of skin mainly occurs after the age of 45-50 years; the ulcer edges are turned out, covered with small whitish nodules, the bottom is pitted, covered with necrotic decay foci, slightly bleeding, slowly progressing with no scarring.

Erythroplasia of Queyrat is manifested by the emergence of the small painless lesions on the balanus, which slowly develops, has clearly lined edges, bright red, velvety, shiny surface.

1. The incubation period of syphilis makes up:
- **A.** 3–5 days
- **B.** 2 weeks
- **C.** 3–4 weeks
- **D.** 2 months
- **E.** 3 months

2. Hard chancre resembles:
- **A.** Macule
- **B.** Ulcer
- **C.** Tuberculum
- **D.** Papule
- **E.** Pustule

3. The complications of hard chancre include:
- **A.** Mortifying
- **B.** Chancre-amygdalitis
- **C.** Large chancre
- **D.** Chancre-felon
- **E.** Indurative edema

4. Name the atypical forms of primary syphiloma:
- **A.** Balanitis, balanoposthitis
- **B.** Phimosis,
- **C.** Indurative edema
- **D.** Mortifying
- **E.** All the above mentioned is true

5. The typical hard chancre is not characterized by:
- **A.** Regular round or oval shape
- **B.** Smooth shiny bottom
- **C.** Pain
- **D.** Saucer shape with some raised edges
- **E.** Unicity

6. Primary period of syphilis is characterized by the presence of:
- **A.** Chancre
- **B.** Regional lymphadenitis
- **C.** Lymphangitis
- **D.** Positive serological tests for syphilis (treponemal and non-treponemal)
- **E.** All the above mentioned

7. Indurative edema is characterized by the following manifestations, except:
- **A.** Develops as a result of lesion of lymph capillaries of the skin on the penis and scrotum, or small and large labia
- **B.** Affected organs increase in size
- **C.** The skin of the affected organs s dense, bluish in color
- **D.** When pressing the pit does not remain, palpation is painless
- **E.** When pressing the pit remains, palpation is painful

8. The main clinical symptoms of the regional lymphadenitis include:
- **A.** The complete absence of signs of acute inflammation
- **B.** Non-cohesion of lymph nodes between each other and with the skin
- **C.** Nodes of round and oval form, the skin over the nodes is not changed
- **D.** Tightly elastic consistency, painless n case of palpation
- **E.** All the above mentioned

9. Chancre-amygdalitis (specific amygdalitis) is not characterized:
- **A.** The increase and induration of the amygdala without the formation of erosion and ulcer
- **B.** Absence of pain when swallowing
- **C.** Unilateral affection, the absence of violations of the general state of the body
- **D.** Unilateral affection of submandibular and cervical lymph nodes
- **E.** Morbidity and bilateral ffections

10. Primary period of syphilis lasts for:
- **A.** 7–8 weeks
- **B.** 14 weeks
- **C.** 3 weeks
- **D.** 4 weeks
- **E.** 6 months

Task 1. The prophylactic examination of the 37-year-old woman revealed a bilateral increase in the size of the inguinal lymph nodes, hyperemia with a bluish tint of right labia majora, which the patient has noticed about five weeks ago. *During examination*: other groups of lymph nodes are not enlarged, skin is free of rash.

a) Which is the most probable diagnosis:
- **A**. Bartholinitis
- **B**. Seropositive primary syphilis, chancre-amygdalitis
- **C**. Seronegative primary syphilis, typical hard chancre
- **D**. Seropositive primary syphilis, indurative edema
- **E**. Latent primary syphilis

b) What diagnostic researches shall be conducted?

Task 2. 35 years old patient turned to the dermatology and venereal clinic with the complaints for the increase and soreness of the penis. *Objectively*: the penis is increased in case of inflammatory edema of prepuce, outer leaflet of which has a bright red color. Balanus does not open, during palpation of prepuce from the right side, induration focus with diameter of 2 cm s detectable; purulent discharge under the prepuce is reinforced. Inguinal lymph nodes are enlarged to the size of a plum, other groups of lymph nodes are not enlarged. Serological tests are positive.

a) Which is the most probable diagnosis:
- **A**. Seropositive primary syphilis, paraphimosis
- **B**. Seropositive primary syphilis, esthiomene
- **C**. Seropositive primary syphilis, balanoposthitis
- **D**. Seropositive primary syphilis, indurative edema
- **E**. Seropositive primary syphilis, phimosis

b) What clinical consequences can develop?

Task 3. The laboratory worker of the dermatology and venereal clinic came to dermatologist for consultation in connection with finger cut with glass when doing the urinalysis of patient with secondary recurrent syphilis.

a) What clinical consequences this may have:
- **A**. The development of primary syphilis with a reduced incubation period
- **B**. Development of syphilis without a hard chancre (syphilis d'emblee)
- **C**. There will not be infection
- **D**. Development of septicemia status
- **E**. Formation of chancre-felon in the cut

b) Your therapeutic recommendations

Task 4. A 32 years old woman complaining of neck pathology turned to the otolaryngologist. *During examination*: unilateral increase of the left amygdala, which caused no pain when touching to it with a spatula. The patient can not connect this kind of pathology with anything.

a) Which is the most probable disease:
- **A**. Bartholinitis
- **B**. Seropositive primary syphilis, chancre-amygdalitis
- **C**. Seronegative primary syphilis, typical hard chancre
- **D**. Seropositive primary syphilis, indurative edema
- **E**. Catarrhal angina

b) What diagnostic researches shall be conducted?

Answers to the questions of the first level of complexity
1 – C; **2** – B; **3** – A; **4** – C; **5** – C; **6** – E; **7** – E; **8** – E; **9** – E; **10** – A
Answers to the questions of the second and third levels of complexity
1a – D; **2a** – E; **3a** – C; **4a** – B

26 TOPIC

Secondary period of syphilis

Secondary period of syphilis *(syphilis II secundaria)* – stage of the disease, which is caused by hematogenous spread of Treponema pallidum from the place of primary focus throughout the body, which is characterized by polymorphic rash (spots, papules, pustules) on the skin and mucous membranes, and determined staging of the clinical course and the possible affection of the internal organs and the nervous system.

TRAINING AND EDUCATIONAL OBJECTS

- Determine the features of the clinical course of secondary period of syphilitic infection
- Distinguish between ways and the possible conditions of infection through the persons with active manifestations of the secondary period of syphilis
- Determine the characteristic clinical features of the macular, papular and pustular syphilides of the secondary period of the disease
- Identify the features of pigmented syphilides, syphilitic alopecia and mucosal syphilides in patients with secondary period of syphilis
- Generalize clinical picture of the typical manifestations of the secondary period of syphilis

TO KNOW:

- general characteristics of the secondary period of syphilis;
- features of the clinical course of the secondary period of syphilis (recent, recurrent, latent);
- characteristics and variety of clinical manifestations of secondary syphilis on the skin – macular, papules, pustules, syphilitic alopecia, pigmented syphilides;
- clinic picture of affection of internal organs and mucous membranes in case of secondary syphilis;
- features of serological reactions in the secondary period of syphilis.

TO BE ABLE TO:

- Deontologically resonably take a general and sexual history in a patient with a secondary period of syphilis;
- analyze the results of laboratory tests of the patient and determine the right diagnosis;
- clinically examine the state of lymph nodes;
- differentiate between the clinical manifestations of the secondary period of syphilis;
- make a differential diagnostics of diseases that have similar clinical symptoms.

Clinical picture. Secondary period of syphilis begins when the hematogenous generalization of syphilitic infection is being realized. This usually occurs in 9-10 weeks after infection with Treponema pallidum or 6-7 weeks after the appearance of hard chancre. The appearance of skin rash indicates the beginning of the secondary period of syphilis. At this time roseolous rash appears on the skin and mucous membranes.

General features of clinical course of the secondary period:

- absence of subjective feelings and violation of the general condition of the patient;
- rash is highly contagious;
- the clinical manifestations are resolved independently without treatment;
- total duration of secondary syphilis – 2-4 years;
- all serological reactions are strongly positive;
- rash is presented by macular, papular, pustular and pigmented syphilides (true polymorphism), as well as syphilitic alopecia;
- rash does not occur simultaneously, but jerky, that is, within 2-3 weeks, and is at different stages of evolution (false polymorphism) in case of regression;
- rash is not acute inflammatory, its color is pale pink or brownish.

Most often at the beginning of second period (secondary recent syphilis) abundant roseolous rash appears, which is often polymorphic (roseola, papules), and is not prone to merge. The rash is symmetrical. Some have ulcerative hard chancre or the signs of primary syphiloma (pigmented secondary macule either fresh scar) and scleradenitis. After 1-2.5 months rash fades and only the positive serological reactions remain, secondary latent period begins. Later relapse of clinical manifestations of the disease with a very varied course occurs – secondary recurrent period.



Fig. 26.1. Roseolous syphilide.

Unlike the secondary recent syphilis, there is less eruptions on the skin at this stage of disease, they are larger, tend to group, are paler, more often located in large folds of skin, in trauma places, in areas with increased sweating; polyadenitis does not almost happen. Serological tests of blood are positive in 98% of patients, although the titer of Wasserman reaction is lower than in secondary recent syphilis. There are

cases of lesions of the internal organs, the nervous and endocrine systems, sensory organs, bones, joints.

Roseolous syphilide – most typical rash in case of secondary recent syphilis. It is placed symmetrically on the side of the chest, abdomen, back, front surface of the upper extremities and hips. The rash is multiple and focused. The color of roseolas varies from pink to yellow-brown. Roseolas are round with a diameter of 8-12 mm, not shelled, they do not itch and disappear at diascopy. They become more visible after intramuscular injection of penicillin (Jarish-Herxhimer reaction). Without treatment they exist for about 3-4 weeks, and then disappear. They are rare on the palms and soles, as well as on the face. In case of secondary recurrent syphilis roseolas are larger, but not so bright, often spherical, tend to group, their quality is not large.

Differential diagnostics of roseolous syphilide. During the differential diagnostics one should exclude macular rash in some infectious diseases, which are accompanied by severe general condition, high body temperature, conjunctivitis, enantemy, laryngitis, tracheitis, bronchitis.

Papular syphilide may be also in the secondary recent syphilis, but the appearance of papules is more characteristic of secondary recurrent syphilis. In the case of secondary recurrent syphilis the number of papules is smaller, they tend to group together and are found on the palms and soles. Papules size varies from 2 mm (lenticular syphilide) to 12 mm (nummular syphilide). Hypertrophic papules – *wide condylomas* appear in the places of constant friction (in the folds, on the genitals).



Fig. 26.2. Lenticular popular syphilide.



Fig. 26.3. Lenticular popular syphilide; ghonnerhea recent acute.

Typical signs of syphilitic papules:

- color is red or copper-red;
- dense, round;
- are mostly located isolated from each other;
- clearly localized from the surrounding skin, without inflammatory crown around the edge;
- cause no subjective feelings;
- in case of regression of papules, a kind of peeling, which starts from the center and extends to the periphery, leaving a Biett's horn-crown – collar is observed;
- sometimes the well-defined papules resembling corn are observed on the palms and soles;
- under the influence of maceration and friction, lenticular papules placed on the external genitals and skin folds grow and become moist and erosive. These papules are most contagious;
- due to irritation of the bottom of the erosive papules, vegetation – wide condylomas of pale pink color, resembling a cauliflower, gradually develop.



Fig. 26.4. Papular syphilide.



Fig. 26.5. Lenticular popular syphilide on sole.



Fig. 26.6. Hypertrophic papules (wide condylomas) in the area of anus.

Differential diagnostics of papular syphilides. Syphilitic papules should be differentiated from papular rash at various dermatoses: psoriasis, lichen planus, parapsoriasis, molluscum contagiosum and other.

Wide syphilitic condylomas shall be distinguished from:

- *pointed condylomas,*
- *hemorrhoidal varicose veins,*
- eruptions in case of *vegetating acantholytic pemphigus*.



Fig. 26.7. Syphilitic impetigo.

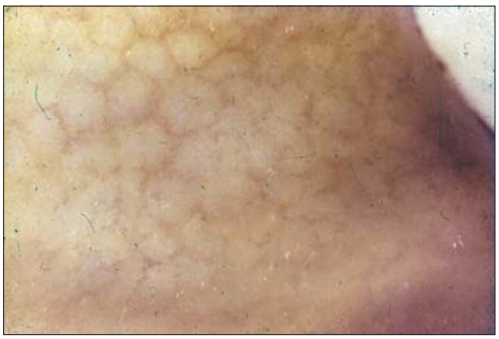


Fig. 26.8. Syphilitic leukoderma.



Fig. 26.9. Fine-focal syphilitic alopecia.



Fig. 26.10. Diffuse syphilitic alopecia.

Pustular syphilide is observed rarer. Unlike true pustules, a swab of the infiltrate, not acute inflammatory rim is placed at the periphery. Depending on the symptoms they distinguish syphilitic impetigo, acneiform syphilides (syphilitic blackheads), varioliform syphilide, syphilitic ecthyma, syphilitic rupias. Their form depends on the location of eruptions, elements size, the degree of their decomposition.

Differential diagnostics of pustular syphilide. During the differential diagnostics of syphilitic ecthyma with pyoderma one shall consider the lack of an inflammatory rim and normal pustulation, presence of the red-bluish dense infiltrative swab at the periphery, which did not break up, the presence of other symptoms of syphilis, as well as data of clinical history and confrontation.

Pigmented syphilide *(syphilitic leukoderma)* is observed in the secondary recurrent syphilis. It is vaguely demarcated, incompletely hypopigmented leukoderma. It occurs in patients who have darkly pigmented skin. Leucoderma firmly holds and disappears within 6-12 months, and sometimes even within 1.5-2 years even with the full treatment, it is often combined with syphilitic alopecia.

Differential diagnostics of pigmented syphilide. Differential diagnostics should be carried out with the secondary leucoderma after psoriasis, parapsoriasis, seborrhea, versicolor tinea. In case of all these pathologies first of all a rash appears on the skin, and change in pigmentation is a direct consequence of its evolution. In addition, serological tests for all of these pathologies are negative.

Syphilitic alopecia is observed in the secondary recurrent syphilis. Six months after infection, multiple patches of hair loss of 5mm to 20 mm in diameter appear and spread gradually on the entire scalp.

There are three types of alopecia – *fine-focal, diffuse and mixed*. It appears suddenly and progresses rapidly. It often affects the frontal-parietal and occipital areas. Hair recover and grow in 1-2 months after resolution of infiltrates.

Differential diagnostics of syphilitic alopecia. It should be differentiated from alopecia areata. ***Syphilides of mucous membranes*** are common in patients with secondary syphilis and are sometimes the only obvious symptom of this disease. Rash is macerated and eroded, and highly infectious. It affects the mucous of lips, cheeks, tongue, throat, vocal cords, straight intestine, female genitals.

Roseolous syphilides on the oral mucosa present circular red-bluish clearly delineated formations of small size – 0.5-0.7 cm. They gradually merge forming erythematous patches. They do

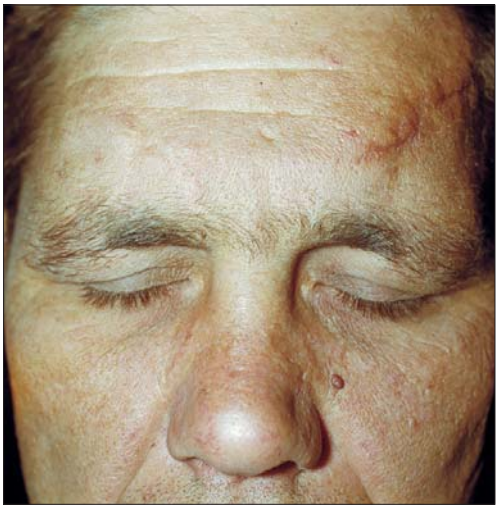


Fig. 26.11. Syphilitic alopecia of lateral brow areas.



Fig. 26.12. Papular syphilide on the tongue.

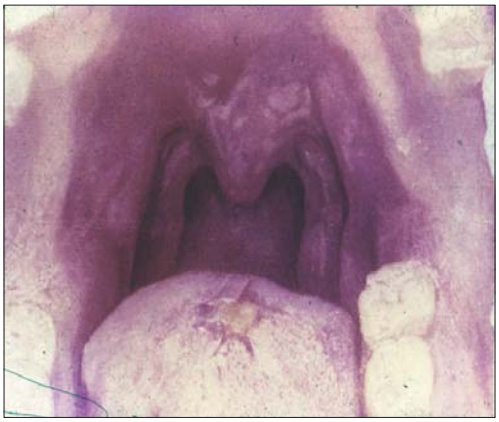


Fig. 26.13. Syphilitic erythematous angina.

not cause subjective feelings, disappear without a trace. They often affect the tonsils, the front and rear handles, the tongue and soft palate (syphilitic erythematous angina) or larynx (syphilitic erythematous laryngitis).

The most common manifestations of secondary syphilis on the mucous membranes include papular rash – flat, well-demarcated, with no peripheral inflammatory rim, of deep red color, it usually does not bother the patient.

Differential diagnostics of syphilides of mucous membranes. Ona shall differentiate papular syphilitic angina along with such diseases – angina, diphtheria, lichen ruber planus, ulcerative stomatitis, flat leukokeratosis. Standard angina is accompanied by increased body temperature, rapid swelling and hyperemia of the throat, tonsils, handles, soft palate, indeterminate limits of affection, great soreness

Ulcerative stomatitis also has acute inflammatory course.

1. Secondary period of syphilis lasts for:
- **A.** Up to three weeks
- **B.** From three weeks to two months
- **C.** Up to one year
- **D.** From two to four years
- **E.** More than five years

2. What is characteristic for secondary recurrent syphilis:
- **A.** white dermographism
- **B.** Positive test of Auspices
- **C.** Leucoderma
- **D.** Positive symptom of Asbo-Hansen
- **E.** Positive symptom of Nikolskii

3. From what diseases should be roseolous rash of secondary syphilis differentiated:
- **A.** Sycosis
- **B.** Tuberculosis lichenoid
- **C.** Versicolor tinea
- **D.** Scabies
- **E.** Lichen ruber planus

4. Which period of syphilis is characterized by the remains of hard chancre:
- **A.** Secondary recurrent
- **B.** Primary latent
- **C.** Secondary recent
- **D.** Latent
- **E.** Tertiary

5. Scaly crusts placed at the periphery of morphological elements in case of the secondary syphilis are called:
- **A.** Biett's collar
- **B.** "Necklace of Venus"
- **C.** "Crown of Venus"
- **D.** Voronov's fimbria
- **E.** Robinson-Fournier scars

6. Aggravation after the injection of penicillin in case of the secondary recent syphilis is called:
- **A.** Lukashevich-Jiarish-Herxheimer reaction
- **B.** Passive hemagglutenation reaction
- **C.** Immunofluorescence reaction
- **D.** Mantoux reaction
- **E.** Polymerase chain reaction

7. What is characteristic for papular syphilides:
- **A.** Not localized from the surrounding skin
- **B.** Do not merge with each other
- **C.** Tendency to peripheral growth
- **D.** Itching
- **E.** Smooth consistency

8. From what diseases should be papular rash of secondary syphilis differentiated:
- **A.** Pemphigus
- **B.** During's dermatosis
- **C.** Lichen ruber planus
- **D.** Versicolor tinea
- **E.** Gibert's disease

9. What is not characteristic for secondary recurrent syphilis:
- **A.** Asymmetrical localization of eruptions
- **B.** The tendency of elements of the rash to group
- **C.** The tendency of elements of the rash to merge
- **D.** Symmetrical localization of eruptions
- **E.** Lack of subjective feelings

10. Clinical varieties of secondary peri od of syphilis are:
- **A.** Roseolous syphilide
- **B.** Papular syphilide
- **C.** Loss of hair
- **D.** Syphilitic leukoderma
- **E.** All the above mentioned

Task 1. The 27 years old patient, the driver, complains for rash on the skin of the corpus, which appeared last week. Rash was preceded by the weakness, pain in the muscles and joints, worsening at night. The skin of the corpus is covered with large rash of rose-red macules with a diameter of 1 cm with clear boundaries. Elements are isolated, subjectively do not bother. Peripheral lymph nodes are moderately enlarged, are painless, of tightly elastic consistency, mobile, unconsolidated.

a) Determine the provisional diagnosis:
- **A**. Toxicoderma
- **B**. Gibert's disease
- **C**. Secondary recent syphilis
- **D**. Secondary recurrent syphilis
- **E**. Versicolor tinea

b) Carry out differential diagnostics with versicolor tinea.

Task 2. The patient went to the doctor because of a rash on the corpus and extremities without subjective feelings. On the eve she had weakness, increased body temperature. *Objectively*: small brightly colored roseolas, polyadenitis. A sexual contact with an unfamiliar man 10 weeks ago is marked in the past medical history.

a) Determine diagnosis:
- **A**. Secondary recurrent syphilis
- **B**. Toxicoderma
- **C**. Gibert's disease
- **D**. Versicolor tinea
- **E**. Secondary recent syphilis

b) What methods of examination shall be applied to determine the clinical diagnosis?

Task 3. Patient of 42 years passed a full course of treatment for secondary recent syphilis, but she was treated with the violation of treatment regimen (used alcohol). Two years later, new papules and patches of pale pink color with a tendency to group appeared on the skin of corpus. Serological tests are positive.

a) Determine diagnosis:
- **A**. Secondary recent syphilis
- **B**. Secondary recurrent syphilis
- **C**. Secondary latent syphilis
- **D**. Toxicoderma
- **E**. Moniliformis scrophulosorum

b) Carry out differential diagnostics of secondary recent and recurrent syphilis.

Task 4. Patient of 29 years, married, involved as contact of man being in the hospital for the inpatient treatment of secondary recent syphilis. *Objectively*: the papular rash on the palms and soles, hypertrophic papules without subjective feelings on the anogenital areas. Serological tests are positive.

a) Indicate, what period of syphilis this woman has:
- **A**. Primary seropositive syphilis
- **B**. Primary latent syphilis
- **C**. Secondary recent syphilis
- **D**. Secondary recurrent syphilis
- **E**. Secondary latent syphilis

b) Who was the source of infection in this case, man or woman?

Task 5. On the back and side areas of the neck the patient has hypochromic circular patches without inflammation which are placed on the hyperpigmented background like lace. Test with 2% alcohol solution of iodine is negative.

a) What diagnosis can be proposed:
- **A**. Versicolor tinea
- **B**. Secondary latent syphilis
- **C**. Secondary recent syphilis
- **D**. Toxicoderma
- **E**. Secondary recurrent syphilis

b) What methods of examination shall be applied to determine the clinical diagnosis

Answers to the questions of the first level of complexity
1 – D; **2** – C; **3** – C; **4** – C; **5** – A; **6** – A; **7** – B; **8** – C; **9** – D; **10** – E
Answers to the questions of the second and third levels of complexity
1a – C; **2a** – E; **3a** – B; **4a** – D; **5a** – E

27 TOPIC

Tertiary period of syphilis

Tertiary period of syphilis (*syphilis tertiaria), or latent syphilis (syphilis tertiaria seu gummosa),* – this is a serious chronic systemic infectious disease, in which case the destructive pathological changes with a violation of their functions develop in the affected organs.

TRAINING AND EDUCATIONAL OBJECTS

- Distinguish features of the epidemiology of the development of tertiary period of syphilitic infection
- Understand the general characteristics of clinical manifestations of the tertiary period
- Identify clinical picture of typical manifestations of nodular syphilide
- Identify clinical picture of typical manifestations of gummatous syphilide
- Determine the characteristic clinical features of Fournier's roseola
- Analyze clinical picture of affection of the mucous membranes in the tertiary period of syphilis
- Determine the main clinical signs of visceral affections and lesions of the locomotor system in syphilis
- Orient in the differential diagnostics of clinical manifestations of the tertiary period of syphilis

TO KNOW:

- etiopathogenic features of tertiary syphilis;
- factors contributing to the development of the tertiary period of syphilis;
- methods of laboratory diagnostics of tertiary period of syphilis;
- methods of test treatment as a diagnostic phenomenon and its features;
- clinical picture of typical manifestations and variations of nodular syphilide;
- clinical picture of manifestations and variations of gummatous syphilide;
- clinical manifestations of tertiary syphilitic lesions of the mucous membranes;
- principles of differential diagnostics of manifestations of tertiary period of syphilis.

TO BE ABLE TO:

- properly take medical history, including sex;
- determine the features of a specific affection of skin, mucous membranes and internal organs, locomotor system during the tertiary period of syphilis;
- determine the morphological elements on the skin and mucous membranes, the dynamics of the pathological process;
- determine the appropriate amount of the survey and its sequence (the use of physical, laboratory, including serological methods);
- interpret the results of laboratory tests;
- carry out differential diagnostics of the diseases that have a similar clinical picture.

Tertiary syphilis develops in 5–15 years after infection.

General features of clinical manifestations of tertiary period of syphilis:

1. Manifestations of tertiary syphilis have undulating clinical character, and holding for several months, spontaneously regress, followed by a period of relative calm. In the presence of clinical symptoms *active tertiary syphilis* is diagnosed, in the absence thereof – *latent tertiary syphilis.*
2. Term of existence of tertiary syphilides – months and years.
3. Manifestations of tertiary syphilis bear infectious and allergic nature.
4. Intensity of specific immunity in the tertiary period is gradually reduced.
5. All the elements of the rash do not have Treponema Pallidum due to which tertiary syphilides are noncontagious.
6. Subjective acute inflammatory feelings are missing.
7. Changes in the skin, mucous membranes and internal organs, bones and joints, nervous, cardiovascular, endocrine systems, bear organic destructive nature.
8. A small number of tertiary syphilides on the skin and mucous membranes: *nodules* are numbered in tens; *gumma* – single, *tertiary roseola of Fournier* is very rare.
9. Rash has monomorphic nature.
10. Asymmetric arrangement of rash.
11. Inflammation of tertiary syphilides with the formation of infectious granulomas, which are situated in the vital organs, break their structure and function, bear productive nature.
12. Development and regression of tertiary syphilides takes place slowly with the formation of ulcers, scars and ulerythema.
13. Serological diagnosis for suspected tertiary syphilis requires conducting a panel of treponemal tests (TP-PA, IFA for IgM + IgG, FTA-ABS, TPPA, IHA for IgM + IgG) and non-treponemal tests (VDRL and/or RPR).
14. Manifestations of tertiary syphilis respond well to regress under the influence of treatment against syphilitic infection.

Clinical picture. Manifestations of tertiary syphilis are observed on the skin, mucous membranes, the internal organs, the locomotor system.

Tertiary affections of skin are manifested by two morphological elements of rash: dermal nodules (nodular syphilide) and hypodermal nodules (gumma) – gummatous syphilide that differ only in the size and depth of affection, because in both cases anatomopathologically this is an infectious granuloma. The so-called late, or tertiary, roseola of Fournier is vary rare.

Nodular syphilide (superficial gumma, tertiary papule, syphilis tuberculosa). Morphological element of the rash is a nodule in the form of sharply outlined dense infiltrate up to 0.5–0.8 cm in diameter, embedded in the dermis. The nodules are located in limited areas of skin scattered or grouped. Nodular syphilide has elevated hemispherical surface of brownish-red or bluish-red color. First, it is smooth, and eventually it is covered with scaly crusts. Evolution of syphilitic nodules is carried out

in two ways: the nodule may dissolve and disappear, leaving a pigmented scar atrophy; and in other cases, there is a decomposition of the tissues of the nodule and the formation of sharply demarcated round painless ulcer. Further due to the presence of healthy skin between the individual small scars, the so-called star-shaped scar is formed on the place of ulcer.

There are such clinical varieties of nodular syphilide: aggregated, serpiginous (creeping), dwarf, diffuse ("platform").

Aggregated nodular syphilide (syphilis tuberculosa aggregata) is characterized by the focused placement of nodules which do not merge with each other.

Serpiginous (creeping) nodular syphilide (syphilis tuberculosa serpiginosa) is characterized by the merge of the individual nodules with the formation of specific infiltrate. The ulceration and scarring of old elements is realized along with the appearance of new nodes.

Dwarf nodular syphilide (*syphilis tuberculosa nana*, tertiary papule) – small nodules with a size of a millet or hemp seed, which are located in separate groups in a small area.

Nodular syphilide in "platform" (diffuse nodular syphilide, *syphilis tuberculosa en nappe seu diffusa*) is formed by the close adjoining of the individual nodules to one another and looks like a bottle-shaped infiltrate of 5-10 cm.

Differential diagnostics of nodular syphilide. It should be carried out with *tuberculous lupus*, which differs by a soft consistency of nodules (positive symptom of "probe"), and a symptom of "apple jelly" during diascopy).



Fig. 27.1. Nodular syphilide.

In case of tuberculoid leprosy nodules are arranged in a ring.

Basalioma is usually single, often located on the face skin, has a clear edge. The ulcer, which is not tending to scarring, unlike syphilide, is formed in the core of the focus.

Gummatous syphilide (*syphilis gummosa, gumma subcutanea, syphilis nodosa profunda*, syphilitic gumma). Gummas are presented by the clearly separated dense painless nodules that in the process of evolution ulcerate to form star-shaped scar or in the rare cases are absorbed, leaving a scar atrophy.

Gummas appear gradually as a separate dense and painless nodule with intact skin over it. Then, the skin over it gradually becomes dark red. Gumma breaks the hole with the release of the small amount of adhesive tenacious ropiness

liquid of dirty yellow color, resembling acacia gum (hence the name – gumma). Further, a dense compact mass, called gummy stem, is formed. Then, gummy ulcer with vertical edges is formed. Some time later, star-shaped scar is formed.

Differential diagnostics of gummatous syphilide. One shall differentiate syphilitic gumma primarily with *tuberculous gumma (strumoderma*), the nodule of which is from the beginning a more gentle than syphilitic, and breaks in several holes. Ulcers in this case have a soft undermining.

In case of *Bazin's disease* the nodes are usually multiple, localized symmetrically on the skin of the posterior-lateral surface of lower legs and hips.

Cancerous ulcer differ from gummy by solid iliac roll, often twisted edges, the bottom of the ulcer is nodulated, bleeds easily.

In case of *lipomas* nodules are multiple, subcutaneous, softer.

Fournier's tertiary erythema (syphilitic tertiary roseola, *erithema tertarium tardivum, roseola tardiva*), – very rare clinical manifestation of tertiary syphilis. It is characterized by asymmetric ring- and arch-shaped large macular elements of 5 to 15 cm in diameter with a wide red border.

Differential diagnostics of Fournier's tertiary erythema. It shall be differentiated from microsporia or ringworm of body.

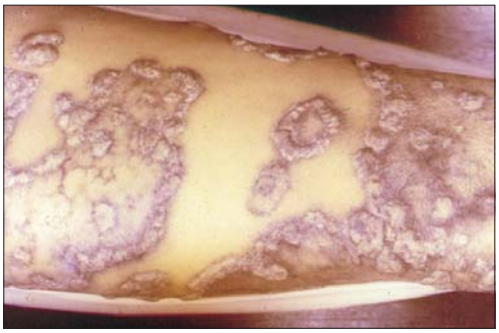


Fig. 27.2. Serpiginous nodular syphilide.



Fig. 27.3. "Mosaic" scars after evolution of nodular syphilide.



Fig. 27.4. Gummatous syphilide.

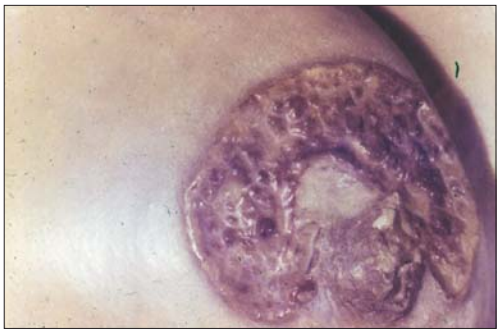


Fig. 25.5. Gummatous syphilide in the area of mammary gland.

Manifestations of tertiary syphilis in mucous membranes. They occur relatively frequently and have their own characteristics: most often found in the mucous membrane of the mouth, nose, throat, pharynx, tonsils, larynx; the predominant place of localization in the oral cavity are areas of hard and soft palate, palatine velum and kion; mucous membrane of the mouth may be the only place of clinical manifestations of tertiary syphilis, among the clinical forms of which – gummas, gummy infiltration and nodular syphilide.

Tertiary syphilides on mucous membranes have bright colors and puffiness. Formation of gummas on the oral mucosa does not differ from their formation on the skin. Gummatous process ends with ulceration with a deep and significant destruction of not only the soft tissues, but bones.

Nodular syphilide in the mucous membrane of a mouth is less common than gummatous. The nodules, as well as gummas, can be localized in any place, but more often in the mucosa of the lips, alveolar bones and palate. The nodules may be isolated or may be in the form of infiltrative focus with sharp jagged outlines. They are tightly elastic, red-brown in color, have a relatively fast flow, are treated with scar formation.

Differential diagnostics of tertiary syphilis of mucous membranes. One shall differentiate manifestations of tertiary syphilis of mucous membranes first of all from tuberculosis, cancerous ulcer and leprosy.

The decisive criterion in the diagnosis of tertiary syphilis is the result of treponemal tests (TP-PA, IFA for IgM + IgG, FTA-ABS, TPPA, IHA for IgM + IgG) and non-treponemal tests (VDRL and/or RPR) in blood and cerebrospinal fluid, as well as pathomorphological studies of biopsy specimens.



Fig. 27.6. Gummatous syphilide.

Affection of internal organs and systems in case of tertiary syphilis *(syphilis visceralis).* In case of tertiary syphilis limited nodules and gummatous infiltrates may be observed in all internal organs, and there may be a variety of degenerative processes and metabolic disorders. Most often the cardiovascular system (90-94% of cases) is affected, rarely – liver (4.6%) and other organs – lungs, kidneys, stomach, intestines, testicles (1-2%).

Affection of cardiovascular system *(cardiovascular syphilis)* makes up almost 90% of all cases of late visceral syphilis. It often affects the aorta (syphilitic mesaortitis, aortic insufficiency, aneurysm, affection of coronaria entrances), rarely – myocardium (syphilitic myocarditis).

Affection of liver in case of tertiary syphilis may have the following clinical forms: chronic epithelial hepatitis, chronic interstitial hepatitis; focal gummatous hepatitis, miliary gummatous or diffuse infiltrative hepatitis.

Syphilitic affections of the stomach, lungs, kidneys and other internal organs is accompanied by symptoms of disorders of the above-mentioned organs.

Affection of the visual organ. Affection of the visual organ occurs against a background of both a secondary and tertiary syphilis; inflammation and pupillary disorders dominate in case of eyes affection; difficulties in diagnostics occur due to the lack of alertness of physicians regarding latent forms of syphilis and its association with other infections.

By the time of the development of tertiary syphilis, eye symptoms are mainly associated with the damage of the nervous system, but the development of tarsitis, chorioretinitis and gummatous affection of various parts of the visual organ are typical for this stage.

Parenchymatous syphilitic keratitis is characterized by unilateral nature of the process, a relatively benign and is easily subjected to antisyphilitic therapy. *Deep pustule-shaped syphilitic keratitis* is characterized by persistent prolonged course and resistance to the specific therapy. *Gummatous keratitis* develops in a form of the syphilitic gumma in the corneal stroma and is always complicated by its turbidity, iridocyclitis and decrease or loss of vision.

Syphilitic neuritis of optic nerve is observed in basal meningitis, and is usually bilateral. Functions of the eye violate very early. The thorough and comprehensive examination of the patient helps diagnostics to confirm the syphilitic nature of the disease.

Affection of locomotor system in case of tertiary syphilis. The affection of the bones and joints may be the only symptom of tertiary syphilis or combined with the affection of other organs. Limited gummatous nodules or diffuse gummatous infiltration usually affect those bones of the skeleton, which are covered with small muscles and are prone to injury. The bones of forearms, clavicle, beastbone, nose, skull are rarely affected.

Differential diagnostics shall be carried out with chronic purulent osteomyelitis of tuberculosis of the bones.

Joint diseases in case of tertiary syphilis are less common than bones affection. A characteristic feature of syphilitic affection of the joints is almost complete absence of pain and possible preservation of joints function.

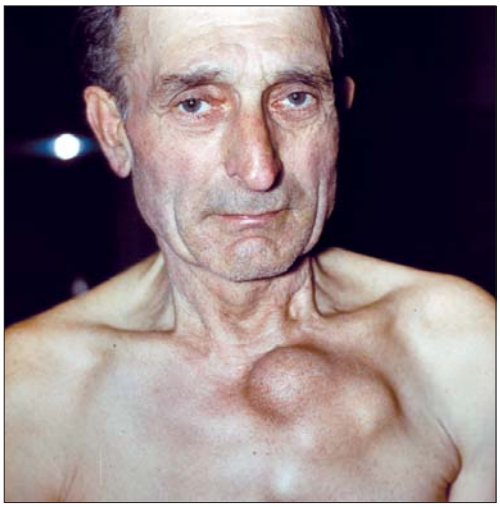


Fig. 27.7. Syphilitic aortitis. Aortic aneurysm.

1. What is not characteristic for the tertiary syphilis from the below mentioned:

A. Limited skin affection
B. Focus location of rash
C. Tendency of elements of the rash to breaking
D. Scarring at the eruption site
E. Bright color of elements of the rash

2. The main morphological elements on the skin and mucous membranes in case of tertiary syphilis are:

A. Knots
B. Nodules
C. Erosions
D. Macules
E. Vesicles

3. What is syphilitic gumma:

A. Vesicle
B. Tubercle
C. Papule
D. Nodules
E. Vegetation

4. What is the basis of tertiary syphilides:

A. Acantholysis, spongiosis
B. Spongiosis, acanthosis
C. Hyperkeratosis, papillomatosis
D. Infectious granuloma
E. Parakeratosis, keratosis

5. What from the below mentioned does not refer to the consequences of gummatous syphilides:

A. Traceless resorption
B. Scar atrophy
C. Purulent ulceration
D. Deep sclerotherapy
E. Atrophic scarring

6. What is the nature of the scars in case of evolution of syphilitic gumma:

A. Keloid
B. Hypertrophic
C. Mosaic
D. Aatrophic
E. Stellate

7. From which specific diseases one shall differentiate gummatous syphilides:

A. Tuberculous lupus, leprosy, leishmaniasis
B. Scleroderma, psoriasis, neurodermatitis
C. Scabies, lice infestation, demodicosis
D. Urticaria, leprosy, lupus erythematosus
E. Pemphigus, urticaria, eczema

8. What scars remain on the skin after regress of syphilitic nodes:

A. Mosaic
B. Keloid
C. Atrophic
D. Stellate
E. Hypertrophic

9. What from the below mentioned does not constitute variety of the nodular syphilis:

A. Grouped
B. Dwarf
C. Serpiginous
D. "Platform"
E. Striate

10. From which diseases from the below mentioned shall one differentiate nodular syphilide, except:

A. Tuberculosis lupus
B. Moist sore
C. Lepromatous form of leprosy
D. Deep mycosis
E. Microbial eczema

Task 1. After the injury of the right leg, the patient at the age of 27 years has on the outside surface of the leg the nodule, which broke with the release of a small amount of sticky yellowish liquid. There was a circular ulcer with dense smooth edges and necrotic masses at the bottom. Subjective feelings are absent.

a) Determine initial diagnosis:
A. Phlegmon of lower leg
B. Furunculosis of lower leg
C. Tuberculosis of lower leg
D. Tertiary syphilis
E. Erythema induratum
b) Make up the plan of additional examination of the patient for diagnosis confirmation.

Task 2. More than five years ago, the patient of 35 years old was treated from the secondary recurrent syphilis, the treatment was not finished. During examination: there is a rash in the form of nodules on the skin of the forehead and the nose. Serological tests (treponemal and non-treponemal) are positive.

a) What disease can be thought of:
A. Secondary syphilis
B. Lupus erythematosus
C. Tuberculosis lupus
D. Erythema induratum
E. Tertiary syphilis
b) Make up the plan of the patient's treatment.

Task 3. The patient of 63 years old went to a doctor complaining for the presence of rash on the skin of right sole without subjective feelings during two months. Disease is not connected with anything. He had never received treatment. During examination: on the heel and back of the right foot there are bluish and brown nodes, some elements are smooth, shiny, and on some – ulceration. There are new elements at the periphery of the focus. The scar atrophy and mosaic scars are present in place of the former elements. Serological treponemal tests (CLIA, FTA-ABS) and non-treponemal tests (VDRL and/or RPR) are positive.

a) Determine diagnosis:
A. Deep pyoderma
B. Deep mycosis
C. Tertiary syphilis
D. Erythema induratum
E. Indurative erythema
b) Make a treatment plan for the patient.

Task 4. Woman of 65 years old noticed nasal voice, discomfort when speaking. During examination: the tongue is increased in size, painless, dense, which impairs its movement. Submandibular lymph nodes are not enlarged. Serological blood tests (treponemal and non-treponemal tests) are positive.

a) Determine diagnosis:
A. Candidal glossitis
B. Tuberculosis glossitis
C. Syphilitic glossitis
D. Lupus glossitis
E. Herpetic glossitis
b) Determine treatment regimen

Answers to the questions of the first level of complexity
1 – E; **2** – B; **3** – B; **4** – D; **5** – A; **6** – E; **7** – A; **8** – A; **9** – E; **10** – E
Answers to the questions of the second and third levels of complexity
1a – D; **2a** – E; **3a** – C; **4a** – C

28 TOPIC

Syphilis of nervous system

Neurosyphilis *(neurosyphilis)* – common name of affections of the nervous system of syphilitic nature that occur in the absence or in case of inadequacy of previous treatment of syphilis.

TRAINING AND EDUCATIONAL OBJECTS

- Identify ways of Treponema Pallidum penetrating into the central and peripheral nervous system
- Determine general course and clinical characteristics of neurosyphilis
- Orient in the early and late manifestations of neurosyphilis
- Identify the features of the diagnostics of syphilis of the nervous system

TO KNOW:

- pathogenetic features of neurosyphilis;
- classification of syphilitic affections of the nervous system;
- features and clinical characteristics of affection in the early and late neurosyphilis;
- diagnostic algorithm for early and late neurosyphilis;
- features of additional methods of examination in case of this disease.

TO BE ABLE TO:

- Deontologically reasonably take a general and sexual history;
- properly conduct a comprehensive examination of the patient;
- clinically examine the state of the central and peripheral nervous system;
- analyze the results of laboratory tests of neurosyphilis;
- differentiate clinical manifestations of early and late neurosyphilis;
- fill out medical documentation on patients;
- carry out differential diagnostics of diseases that have similar clinical symptoms.

Pathogenesis. Treponema pallidum penetrate into the central and peripheral nervous system by hematogenous, lymphatic and perineural ways.

The main factors contributing to the development of neurosyphilis are the lack or inadequacy of treatment for early forms of syphilis, tuberculosis, HIV infection, viral hepatitis advanced age.

Classification. The basis of classification of neurosyphilis consists of clinical and morphological changes in the nervous system, according to which neurosyphilis is divided into:

- *early (mesenchymal) syphilis of the nervous system (neurosyphilis praecox*), occurring during the first five years after infection;
- *late (parenchymal) syphilis of the nervous system (neurosyphilis tarda*), developing more than five years after infection.

Clinical and diagnostic features of the early neurosyphilis. It is characterized by affection of the brain membranes and vessels with a predominance of mesenchymal reaction in the form of exudative and inflammatory, and further proliferative and inflammatory processes. Late (parenchymal) neurosyphilis is associated with damage of the neurons, the nerve fibers and neuroglia. Changes in the nervous tissue bear parenchymal nature with a predominance of degenerative processes. This division reflects only the sequence of pathological changes in the nervous system. According to clinical symptoms they distinguish syphilis of the central nervous system, syphilis of the peripheral nervous system, mental disorders in case of neurosyphilis.

Clinical manifestations of mesenchymal neurosyphilis are very diverse and can range from asymptomatic forms to an acute generalized affection of the nervous system. There are following clinical forms of mesenchymal neurosyphilis: syphilitic meningitis and its complications; meningovascular neurosyphilis; gumma of the brain and spinal cord; specific affection of the peripheral nervous system.

Hidden (latent, asymptomatic) syphilitic meningitis occurs in 10-15% of patients with primary and in 50% of patients with secondary and latent syphilis. In case of development of asymptomatic meningitis after two years from the time of infection it is called late latent syphilitic meningitis. The diagnosis of latent syphilitic meningitis should always be confirmed by the results of the liquorologic study, namely the determination of content of the protein, cellular elements and serological parameters of cerebrospinal fluid. ***Meningoneurotic syphilitic meningitis (basal meningitis)*** – a type of mesenchymal neurosyphilis detected in 20% of cases of early neurosyphilis. It is manifested by meningeal symptoms and neuritis of optic, hearing, discharge and block eye-moving nerves.

Acute generalized syphilitic meningitis is rarely observed. The disease is characterized by rapid (within 1-2 weeks) development of clinical symptoms and is manifested by meningeal phenomena

Meningovascular neurosyphilis *(lues meningovascularis)* is characterized by involvement in the pathological process of vessels of cerebral or spinal brain. Clinical picture of the disease is determined primarily by vascular affection.

Cerebral meningovascular neurosyphilis *(lues meningovascularis cerebri)* – one of the most common clinical forms of neurosyphilis.

Gummas of the brain and spinal cord *(lues gumossa cerebrospinalis)* are rarely observed. The clinical picture resembles clinic of brain tumors and is manifested by cerebral symptoms and focal neurological symptoms, in accordance with the localization of gumma in those or other parts of the brain.

Specific affection of the peripheral nervous system can be observed at the early and the late stages of syphilis, it is often combined with central nervous system, but can occur in isolation.

Clinical and diagnostic features of the late neurosyphilis. Parenchymal (late) neurosyphilis is usually manifestrf by cerebrospinal tabes, progressive paralysis, taboparalysis.

Cerebrospinal tabes *(tabes dorsalis)*. Pathomorphologic basis of disease is a specific affection of the posterior roots and stems, and spinal membranes, which lies in an inflammatory proliferation and destruction of nerve tissue, followed by sclerotherapy. The first symptoms of cerebrospinal tabes appear in an average of 5-20 years of infection with syphilis. The disease can be relatively benign with long-term duration and unexpressed clinical symptoms. The classic clinical manifestations of cerebrospinal tabes are associated with the disruption of the sensitive sector, reflexes and coordination; pupillary disorders, muscular hypotonia, disruption of the sphincter and sexual function, trophic disorders, cranial nerves affection.

Pupillary disorders represent one of the most important and the most frequent clinical manifestations of cerebrospinal tabes. They are characterized by high severity, the bilateral nature of the disorders, stability and irreversibility.

Pathognomonic for parenchymal forms of neurosyphilis (cerebrospinal tabes, progressive paralysis) is a *complex of symptoms of Argyll-Robertson* – the lack of a direct and friendly reaction of pupils for light in case of preservance of response to convergence and accommodation, which is often combined with miosis (rarely with mydriasis), the significant deformation of the pupils and anisocoria.

Muscular hypotonia is caused by fall-out from the spinal reflex from the dorsal root on the motor neuron. During the cerebrospinal tabes hypotonia is clinically manifested by weakening until the complete lack of muscle resistance to changes of static postures (posture *genu recurvatum, valgum*). Disruption of the sphincter and sexual functions – a frequent manifestation of cerebrospinal tabes.

Trophic disorders in case of cerebrospinal tabes are caused by affections of the autonomic pathways and centers, clinically manifested by different disorders of the joints, bones, skin and its appendages.

Trophic skin changes may be manifested by ulcer, which is more often localized in the middle or on the edge of the sole. The process begins with the appearance of

infiltrate or bladder with a further ulceration and deeper penetration into the underlying tissues. ***Progressive paralysis*** *(paralisis progressiva)* is caused by syphilitic meningoencephalitis. The disease occurs in 10-20 years after infection occurs with increasing disintegration of the personality and mental activity, affect and delusional disorders, neurological symptoms of parenchymatous neurosyphilis, cachexia. Disorders of liquorologic indicators are characteristic for this disease.

Taboparalysis – a combination of symptoms of cerebrospinal tabes and progressive paralysis in the patient. Such a condition can be treated as cerebrospinal tabes with elements of progressive paralysis (if the symptoms of cerebrospinal tabes are predominant) or progressive paralysis with cerebrospinal tabes elements (with the prevalence of symptoms of progressive paralysis). Late forms of neurosyphilis are often associated with cardiovascular syphilis, which shall be considered when examining patients and assigning the appropriate treatment for them.

To confirm the diagnosis of neurosyphilis, in addition to serological testing of blood serum, an examination of cerebrospinal fluid is performed, including non-treponemal tests (VDRL and/or RPR) and treponemal tests (ELISA for IgM + IgG, TPPA, immunoblot for IgM + IgG, FTA-ABS).

1. What pathomorphological changes in the nervous system are characteristic for meningovascular syphilis:
- **A.** Degenerative
- **B.** Sclerotic
- **C.** Inflammatory
- **D.** Necrotic
- **E.** All the above mentioned

2. Affection of which nerves is observed in case of meningoneurotic form of neurosyphilis:
- **A.** Intercostal
- **B.** Cranial
- **C.** Sciatic
- **D.** Cubital
- **E.** Knee

3. Which complex of symptoms is pathognomonic for cerebrospinal tabes:
- **A.** Hutchinson's triad
- **B.** Polyadenitis
- **C.** Pseudoparalysis of Parrot
- **D.** Argyll-Robertson syndrome
- **E.** All the above mentioned

4. The progressive paralysis is not characterized by:
- **A.** Loss of coordination
- **B.** Attacks of pain in the extremities
- **C.** Psychiatric disorders
- **D.** Functional apoplexy
- **E.** All the above mentioned

5. In case of progressive paralysis, change of cerebrospinal fluid:
- **A.** Is missing
- **B.** Is present
- **C.** Is associated with the stage of pathological process
- D. Is correlated with blood CSR
- **E.** None from the above mentioned

6. Study of cerebrospinal fluid is carried out for:
- **A.** IgM + IgG enzyme-linked immunosorbent assays
- **B.** Passive hemagglutination reactions (PEA)
- **C.** Immunofluorescence reactions (IFR – abs)
- **D.** Microprecipitation reactions (MPR)
- **E.** All the above mentioned is true

7. Main factors, contributing to the development of neurosyphilis are:
- **A.** Absence or inadequacy of therapy of early forms of syphilis
- **B.** Traumatic brain injury and severe physical illness
- **C.** Chronic infections, intoxications
- **D.** Immune disorders and mental strain
- **E.** All the above mentioned is true

8. What clinical form is missing in mesenchymal neurosyphilis:
- **A.** Syphilitic meningitis and its complications
- **B.** Meningovascular neurosyphilis
- **C.** Taboparalysis
- **D.** Gummas of the brain and spinal cord
- **E.** Specific affection of the peripheral nervous system

9. Parenchymal neurosyphilis is often characterized by the following clinical forms:
- **A.** Cerebrospinal tabes
- **B.** Progressive paralysis
- **C.** Taboparalysis
- **D.** Complex of symptoms of Argyll-Robertson
- **E.** All the above mentioned is true

10. The following reaction is conducted to confirm the diagnosis of neurosyphilis:
- **A.** TPPA
- **B.** FTA-ABS
- **C.** ELISA for IgM + IgG
- **D.** Immunoblot for IgM + IgG
- **E.** All the above mentioned is true

Task 1. The patient of 32 years old, who had been treated with repository penicillin preparations for secondary recurrent syphilis for four years has been sent to an eye doctor for consultation. He complains of intermittent headaches over the years, blurred vision and the appearance of dark spots before his eyes within the last month. *Objectively:* changes in the skin and mucous membranes are not detected, ophthalmoscopy defines concentric narrowing of the field of view, expansion of retinal vessels, hyperemia of the optic disc. Treponemal and non-treponemal tests in blood and cerebrospinal fluid are positive.

a) What provisional diagnosis can be determined:
- **A.** Late latent syphilis
- **B.** Basilar meningitis
- **C.** Acute syphilitic meningitis
- **D.** Latent syphilitic meningitis
- **E.** Meningovascular neurosyphilis

b) Make up the plan of additional examination of patient for diagnosis confirmation.

Task 2. A man of 36 years old with complaints of headaches, nausea, stuffy ears, numbness in the right hand and the difficulty of movements of its fingers was hospitalized to the neurological department. The disease began acutely – within a day. The reduction of tactile and pain sensitivity and paresis of the right hand were fixed during neurological examination, blood pressure – 180/100 mm. Hg. Art. *Anamnesis:* often administered antibiotics. CSR is positive at a titer 1:5.

a) What diagnosis can be thought of:
- **A.** Syphilitic neuritis
- **B.** Cerebrospinal tabes
- **C.** Basal meningitis
- **D.** Syphilitic meningomyelitis
- **E.** Meningovascular neurosyphilis

b) What additional examination shall be conducted to determine the final diagnosis?

Task 3. 42 years old woman was hospitalized with complaints of weakness, numbness in the feet, fast tiredness when walking. Not married, does not have a regular sexual partner, is abusing alcohol. During neurological examination: in the Romberg posture – unstable, slips during heel-shin test, pain hypersthesia in the breast area, tactile hyperesthesia of the soles, reduction of knee and absence of Achilles reflexes, lack of reaction of pupils to light. *Laboratory tests:* Treponemal tests (CLIA, FTA-ABS) and non-treponemal tests (VDRL and/or RPR) in blood and cerebrospinal fluid are positive.

a) What provisional diagnosis can be determined:
- **A.** Cerebral meningovascular neurosyphilis
- **B.** Syphilitic polyneuritis
- **C.** Acute generalized syphilitic meningitis
- **D.** Cerebrospinal phthisis
- **E.** Syphilitic meningomyelitis

b) Carry out differential diagnostics of the detected disease.

Answers to the questions of the first level of complexity
1 – C; **2** – B; **3** – D; **4** – C; **5** – B; **6** – E; **7** – E; **8** – C; **9** – D; **10** – E
Answers to the questions of the second and third levels of complexity
1a – B; **2a** – E; **3a** – D

29 TOPIC

Congenital syphilis

Congenital syphilis *(syphilis congenita)* results from transplacental infection during intrauterine growth of a fetus with the spirochete Treponema subspecies pallidum from the ill mother.

TRAINING AND EDUCATIONAL OBJECTS

- To name routes of mother – to – child transmission of syphilis.
- To estimate the social meaning of congenital syphilis.
- To analyze the influence of syphilis infection of pregnancy and its outcome.
- To know the classification of congenital syphilis.
- To detect clinical symptoms of the early congenital syphilis
- To detect clinical symptoms of the early congenital syphilis
- To interpret the serologic test results
- To choose the concerning syphilis diagnostic methods and therapeutic approach.

TO KNOW:

- Etiopathogenesis of the congenital syphilis.
- The influence, which syphilis exerts on pregnancy and its outcome and consequences.
- Channels of infection with the congenital syphilis.
- Classification of the congenital syphilis.
- The signs of specific lesion in the placenta and umbilical cord.
- Clinical features of the syphilis infection in fetus.
- Manifestation of the early congenital syphilis – the lesion in skin, mucous membranes, bones, internal organs, nervous system, eyes.
- Diagnostic measures, concerning early congenital syphilis.
- Symptomatic of the late congenital syphilis – probable and significant signs.
- Diagnostic criteria of the congenital syphilis.

TO BE ABLE TO:

- To obtain the anamnesis correctly from mother of the ill child.
- To make physical examination of the ill child.
- To detect the signs of the specific lesions in skin, mucous membranes, bones, internal organs, nervous system, eyes in children with the congenital syphilis.
- To identify the probable and significant symptoms of the late congenital syphilis.
- To make differential diagnosis of the congenital syphilis.

Classification and clinical signs of congenital syphilis

According to the accepted actual classification of WHO, the following types of syphilis are distinguished:

- *Early congenital syphilis (syphilis congenital praecox)* in fetus and infants under the age of two years, the symptoms of which are following: pemphigus syphiliticus, diffuse papular skin eruption, lesions of mucous membranes, parenchymal organs, bone tissue, nervous system, eyes.
- *Late congenital syphilis (syphilis congenital tarda)* with symptoms, by which the symptoms appear in children, older, than two years.
- *Latent congenital syphilis (syphilis congenital latens)* – early and late – is characterized with the absence of clinical manifestation and of the changes in cerebrospinal fluid. This disease is usually discovered by serologic tests.

Syphilis and pregnancy

The probability of intrauterine infection of fetus with Treponema Pallidum is maximal by secondary and early latent syphilis in mother and makes up 80-85 % of syphilis cases. Unspecified or late latent syphilis in pregnant woman appears in 10 % of cases to be the cause of congenital syphilis in fetus. Least of all suffer from congenital syphilis the children, born to mothers, affected with primary syphilis – less than 1,5 % of cases of the congenital syphilis. According to the data, given by WHO experts, the pregnant women with untreated early syphilis will bear infected children in 70 – 100 % of cases, in 1/3 of cases – stillborns.

Pregnancy outcome in infected women may be different: early or late spontaneous abortion (at 12th – 16th week), premature delivery, perinatal death; birth of infant with the symptoms of early congenital syphilis or with positive serological tests without clinical manifestation. There remains a probability to bear healthy child.

Placental and umbilical cord lesions

Specific placental and umbilical cord lesions precede the congenital syphilis. When the infection of placenta takes place, the late becomes hypertrophied, with areas of grayish-yellow and rosy colors – ("variegated"), crumbling, with tendency to tear very easily. Syphilis infection is characterized with the lesions in form of sclerosis of placental villi, epithelial degeneration, cell infiltration of vascular walls with their obliteration. The described histological changes occur in fetal placenta. The maternal placenta, on the contrary, remains unaltered. Typical for this kind of infection is enlarged placental mass. In comparison with normal fetal/placental mass ratio, which makes up 1:6, by syphilis infection this correlation is 1:3.

Fetal syphilis

The only channel for the fetus infection is transplacental transmission. In consequence of specific septicemia, the 75-80% of fetal death, caused by syphilis

infection, is registered in the 4th-5th, but more often – in the 5th – 6th month of pregnancy. The most commonly observed clinical symptoms are following: low fetal weight, hypoplasia or total absence of subcutaneous fat, skin rugosity, by which the folds have earthy color ("senile skin"). Specific lesions in internal fetal organs (liver, spleen, lungs) are introduced with diffuse inflammatory process – globocellular infiltration and connective tissue growth.

Early congenital syphilis

In vast majority of infants the symptoms of the early congenital syphilis arise within first three months of life. Manifestations include: pale rugous "senile" skin, saddle nose, enlarged head because of exaggeration of the frontal eminence and venous distension; permanent rhinorrhea, which causes labored breathing and difficulties during sucking.

The clinical symptoms of the early congenital syphilis are following:

- Diffuse papular infiltration of the skin (Hochsinger infiltration)
- Pemphigus syphiliticus
- Lesions of the sense organs
- Lesions in the locomotive system
- Lesions in visceral organs
- Lesions in nervous system.

Diffuse papular infiltration of the skin (Hochsinger infiltration) appears within the first three months of life, with localization on the palms, buttocks, chin, superciliary arches, scalp. The skin surface is smooth, sparkling (varnish – like), red-purple tinted. Different skin injuries lead to the formation of rhagades, which are localized radially around the mouth and form, when healing, *radial Robinson – Fournier scars*. The skin infiltration on the palms is attended with maceration, rugosity, scaled desquamation.

Pemphigus syphiliticus is observed in 11-12 % of cases at birth or within first days or weeks of life, and is typically placed on the skin of palms and feet. The Treponema pallidum is usually revealed in the blister fluid. The tent blisters, with serous content, are localized on the infiltrated skin areas and have inflammatory border. Pemphigus syphiliticus must be differentially diagnosed from neonatal impetigo, which usually begins with omphalitis along with fever. The groups of blisters are placed separately, on the skin of back and chest, and very rarely – on the areas of palms and feet. The above mentioned rash tends to the peripheral growth and perifocal inflammation.

Other alterations of skin and mucous membranes. The skin alteration fully coincides with the lesion, caused by secondary syphilis infection. The nasal mucosa is affected by *syphilitic rhinorrhea*. Much rarelier the *laryngeal mucosa is involved with the development of diffuse inflammatory infiltration*, causing the symptoms of hoarseness, dysphonia.

The skin appendages in infants can also be affected by syphilitic infection. The hair lesion is characterized with the circular and/ or diffuse hair loss.

Syphilitic rhinitis observed in 25 – 30 % of cases of the disease at birth or within first weeks of infant's life in form of syphilitic rhinorrhoea.

On the initial stage occurs the edema of nasal mucosa, which results in noisy breathing. In the sequel appear purulent discharges. While sucking, the child is often distracted to inhale deeply.

After above mentioned pathological changes occur the destructive processes, leading to the damage of cartilaginous and bone tissue of the nasal septum, followed with formation of *saddle nose*. The voice becomes snuffling. Nasal discharge contains Treponema pallidum in quantity. The alterations of the nasal septum appear in form of osteochondritis, syphilitic gummas, diffuse globocellular infiltration of nasal septum mucosa.

Lesions of the sense organs are characterized with specific eye alteration in form of conjunctivitis, chorioretinitis, iritis, optic atrophy. The ophtalmoscopy by chorioretinitis reveals pigmented fundus lesions and little light spots, producing "salt and pepper fundus". The eye alterations occur in 37 – 47 % of cases of the congenital syphilis.

Lesions in the locomotive system are the most frequent manifestation of syphilis infection and have the character of:

1. Osteochondritis (Parrot disease);
2. Periostal changes, such as periostal thickening, ossification periostosis, hyperostosis, osteophyte, osteosclerosis;
3. Destructive changes (osteoporosis, defects of joint ends of the bones, gummas);
4. Fractions and infractions.

Characteristic features of the osteochondritis are lesions in the area between epiphyseal cartilage and diaphysis. Long tubular bones are preferentially affected (humeral, femoral, forearm and shin bones).

The development of osteochondritis occurs due to the ossification disturbance, physiological cartilage resorption arrest, increased deposition of calcium salts in the cartilage, the reduction and partial disappearance of the bone trabecules followed by the formation of necrotic areas. The bone trabecules are scanty and, therefore, the separation of epiphysis from the diaphysis occurs, known as epiphysiolysis (Parrot disease).

In the case of syphilitic epiphysiolysis, the clinical picture is observed similar to flaccid paralysis of the limbs, which has nothing in common with the paralysis of spinal origin, therefore, this disease was called Parrot pseudoparalysis. Clinically, in case of Parrot pseudoparalysis, the limb l limp lies slackly on the bed, any movement is painful. Regarding the sensorium no disorders are observed.

In the case of *syphilitic periostitis* the limb bones, ribs and rarely flat bones are affected. The affection of the periosteum (periostitis) occurs as an independent phenomenon, as well as in the combination with osteochondritis. Gummas in the bones of infants are less likely than in older children. They are located in the metaphyses, less frequently in the diaphysis. *Chondrodysplasia* (chondrodystrophy) reminds osteochondritis: by the time of birth the straightening, widening, serration and increased intensity of the calcification zone are determined. Radiological Manifestations and Pathomorphological Features of Bone Involvement in Infectious Processes

When osteosclerosis affects the entire bone, radiographs reveal a homogeneous compact shadow.

Gummatous lesions of bone tissue are less common in infants than in older children. They are predominantly located in the metaphyses, less frequently in the diaphyses, forming round or oval defects. In rare cases, such lesions may lead to pathological fractures in areas of trabecular bone loss, which can occur due to minor mechanical impact, such as a slight blow or a specific limb rotation.

Involvement of cranial bones manifests radiographically as thickened hyperdense bands in the occipital and frontal bones. In the presence of a gummatous process, hypodense defects are observed. Gummas most frequently affect the parietal and frontal bones. Periosteal gummas may also occur, leading to periosteal detachment.

With increasing age, periosteal changes become more prevalent in affected children, while endochondral changes recede into the background and become exceptional beyond the second year of life.

Lesions of long bones primarily present as osteochondritis and, less commonly, as periostitis. Parrot's pseudoparalysis generally has a latent course and is observed infrequently.

Differential Diagnosis of Congenital Syphilis and Toxoplasmosis

In differentiating congenital syphilis from toxoplasmosis, it is crucial to consider that the latter is characterized by ocular and orbital hypoplasia, intraocular and intracerebral calcifications, iridocyclitis, and chorioretinitis.

Chondrodysplasia (chondrodystrophy) may resemble stage I osteochondritis. Even at birth, findings include straightening, widening, serration, and increased radiodensity in the zone of calcification. However, in toxoplasmosis, the diaphyses of long bones are markedly shortened and widened, with a clinically evident disproportion between the limbs and torso. Serologic tests are negative.

Osteochondritis of stages I–II occurs in 55–85% of cases within the first three months of life, while periostitis is detected in 10% of congenital syphilis cases.

Features of Internal Organ Involvement in Congenital Syphilis

A key feature of early congenital syphilis is gummatous involvement and periosteal changes, most commonly affecting the phalangeal bases, manifesting

as phalangitis or dactylitis. The lesions may be multiple or unilateral. The affected fingers become spindle-shaped, the process remains painless, and unlike tuberculous osteomyelitis, it does not lead to fistula formation.

Internal organ involvement in congenital syphilis is characterized by multi-organ pathology with no strictly specific clinical manifestations, which complicates diagnosis.

The liver and spleen are the most commonly affected organs (in 75–80% of cases), presenting as hepatitis and hepatosplenomegaly. These organs exhibit varying degrees of enlargement and induration while maintaining a smooth surface. Pancreatic involvement may manifest as signs of chronic pancreatitis or focal gummatous lesions.

Pulmonary involvement occurs in 10–15% of cases, manifesting as interstitial pneumonia. Less frequently, a widespread parenchymal "white" pneumonia may develop, which proves fatal for infants weakened by syphilitic infection.

Renal involvement (10% of cases) presents as glomerulonephritis and nephrosonephritis. The adrenal glands and testes are also affected relatively frequently.

Gastrointestinal involvement manifests with vomiting, profuse diarrhea containing pus, mucus, and sometimes blood, weight loss, intestinal paresis with signs of obstruction, and gastrointestinal hemorrhages.

The cardiovascular system is rarely affected, with myocarditis and myocardial dystrophy being the primary manifestations. A characteristic feature is symmetrical enlargement of the lymph nodes, particularly in the elbow region.

Peripheral blood changes in infants with early congenital syphilis include hypochromic anemia, neutrophilic leukocytosis, an elevated erythrocyte sedimentation rate (ESR) of up to 70–80 mm/h, thrombocytopenia, and prolonged blood clotting time. Secondary coagulopathies, hemolytic anemia, and hemorrhagic syndrome are also observed.

Involvement of the nervous system presents as specific meningitis and meningoencephalitis. A particularly characteristic symptom is Sisto's sign—an "unexplained" crying of the infant both during the day and at night.

Examination of cerebrospinal fluid in such children reveals high pleocytosis, positive globulin reactions, and serological tests for syphilis. Seizures, strabismus, and paresis may also occur. Hydrocephalus frequently develops in infants and may, in some cases, be congenital. Indicators of nervous system involvement include neck muscle rigidity, fontanelle tension, dilation of cranial venous vessels, seizures, hyperreflexia, and, in some cases, epileptiform attacks.

Diagnostic Criteria for Early Congenital Syphilis

Confirming or ruling out syphilitic infection in a child requires a comprehensive diagnostic approach. To avoid potential diagnostic errors, it is

essential to fully utilize all parameters that may indicate the presence or absence of the infection. These parameters include:

1. Anamnesis of the child's parents indicating a history of syphilis.
2. A thoroughly collected obstetric history and serological examination of other children in the family.
3. Presence of any stage of syphilis (including latent syphilis) in the mother.
4. Clinical and morphological findings of the placenta.
5. Examination data of the child's skin and mucous membranes.
6. Conclusions from related specialists (otorhinolaryngologist, ophthalmologist, neurologist, pediatrician, radiologist).
7. Laboratory serological tests (both treponemal and non-treponemal) conducted on the mother and child.

In the diagnosis of congenital syphilis, serological testing plays a particularly important role; however, the interpretation of serological test results must be approached with great caution.

A syphilis-exposed infant is a child born to a woman diagnosed with or suspected of having syphilis and requires medical care from birth until a definitive diagnosis is established.

Early congenital syphilis is diagnosed within the first two years of a child's life, whereas late congenital syphilis is characterized by symptom onset after two years of age. Newborns presenting with clinical signs of congenital syphilis require thorough evaluation and testing, considering the results of the mother's serological tests and her treatment history.

Timely detection and treatment of syphilis in the mother prevent congenital syphilis. Approximately two-thirds of newborns with congenital syphilis are asymptomatic at birth, though clinical manifestations may develop by the fifth week of life.

The diagnosis of congenital syphilis can be challenging, as maternal non-treponemal and treponemal IgG antibodies can cross the placenta, complicating the interpretation of positive serological test results in neonates younger than 30 days. Therefore, treatment decisions should be based on maternal syphilis status, adequacy of her treatment, presence of clinical, laboratory, or radiographic signs of syphilis in the newborn, and comparison of non-treponemal test (NTT) titers between mother and child using the same test, preferably conducted in the same laboratory.

All newborns born to treponemal-seropositive mothers and those with signs of early congenital syphilis should undergo comprehensive clinical, laboratory, and serological testing for syphilis (except in cases of false-positive maternal serology or when the mother had completed adequate treatment before the current pregnancy). The recommended evaluations include:

- Detection of T. pallidum through dark-field microscopy (DFM) and/or polymerase chain reaction (PCR) in umbilical cord blood, placental

tissue, exudates from suspicious lesions, or organ fluids (e.g., vesicular fluid, nasal discharge).

- Serological testing for syphilis using rapid plasma reagin (RPR), quantitative passive hemagglutination assay (TPHA), and IgM testing for T. pallidum via enzyme-linked immunosorbent assay (ELISA) or immunoblot (IB), preferably performed on venous blood from the newborn (rather than cord blood) on days 10–14 of life to avoid false-positive or false-negative results.
- Complete blood count, liver and kidney function markers, and electrolyte panel.
- Cerebrospinal fluid (CSF) analysis, including protein levels, RPR, and TPHA. Radiography of long tubular bones;
- Ophthalmologic and otologic evaluation as indicated.

A confirmed diagnosis of congenital syphilis is established by detecting T. pallidum using dark-field microscopy (DFM) or polymerase chain reaction (PCR) in placental tissue, autopsy specimens, exudates from suspicious lesions, or body fluids, such as nasal secretions.

A presumptive diagnosis of congenital syphilis is made in stillborn infants with positive treponemal tests (TT) for syphilis, as well as in children with a positive TT for syphilis in combination with one or more of the following:

- Persistent rhinitis, broad condylomas, osteitis, periostitis, stage II or III osteochondritis, ascites, skin and mucosal lesions, hepatitis, hepatosplenomegaly, glomerulonephritis, hemolytic anemia.
- Radiographic abnormalities of long bones indicative of congenital syphilis.
- Positive non treponemal test (NTT) in cerebrospinal fluid (CSF).
- A fourfold (or greater) increase in Treponema pallidum hemagglutination assay (TPHA) titer in the child's serum compared to the maternal serum (both samples collected simultaneously at birth).
- A fourfold (or greater) increase in non-treponemal test (NTT) titer in the child's serum compared to the maternal serum (both samples collected simultaneously at birth).
- A fourfold (or greater) increase in NTT titer in the child's serum within 3 months after birth.
- Positive anti-treponemal IgM detected by enzyme-linked immunosorbent assay (ELISA) and/or IgM immunoblot for T. pallidum in the child's serum.
- A mother diagnosed with syphilis during pregnancy who did not receive appropriate treatment either before or during pregnancy.
- A presumptive diagnosis of congenital syphilis is also made in children older than 12 months with a positive TT for syphilis, provided that household or sexual transmission has been ruled out.

Late congenital syphilis manifests between the ages of 2 and 17 years, although in some cases, it may appear even after 30 or 50 years of life. These manifestations correspond to damage of various organs and systems associated with acquired tertiary syphilis. In 60% of cases, late congenital syphilis progresses asymptomatically and is only diagnosed through the results of serological blood tests. In late congenital syphilis, there is a set of persistent, stable signs that develop as a result of syphilis contracted in early childhood, or the later impact of the specific infection on the skeletal system and other organs, which allows for the differentiation of congenital syphilis from acquired syphilis. Depending on the degree of specificity, distinct (absolute and probable) signs of late congenital syphilis are identified, as well as various dystrophies, which are most commonly observed in congenital syphilis but may also occur in other diseases.

Reliable signs of late congenital syphilis include Hutchinson's triad: parenchymatous keratitis, labyrinthine deafness, and Hutchinson's teeth.

Parenchymatous keratitis occurs between the ages of 5 and 15 years. Its clinical manifestations include evenly distributed milky-white opacity of the cornea with pericorneal vascular injection, photophobia, blepharospasm, and lacrimation. The process begins in one eye and later becomes bilateral. It is observed in 50% of patients with late congenital syphilis, and in 10–20% of cases, it presents as the only symptom of Hutchinson's triad.

Labyrinthine deafness develops between the ages of 7 and 15 years. It results from periostitis in the bony portion of the labyrinth and damage to the auditory nerve. The process is bilateral, with sudden onset of deafness, preceded by dizziness, tinnitus, and ear noise. Labyrinthine deafness is resistant to treatment and occurs in 30–38% of cases.

Hutchinson's teeth appear between the ages of 6 and 7 years (the time of eruption of permanent teeth; in children under six, these teeth do not emerge and may be detected radiologically). Clinical manifestations include dystrophy of the upper permanent central incisors in the form of a barrel-shaped or chisel-shaped form and hypoplasia of the chewing surface with a crescent-shaped indentation along the free edge. They are observed in 15–20% of patients with late congenital syphilis.

Probable signs of late congenital syphilis include various dystrophies, which have lower diagnostic value and require further confirmation. The most common of them are:

- Saber-shaped shins, characterized by a forward curvature of the tibial bones as a result of previously acquired diffuse osteoperiostitis and reactive osteosclerosis.
- Gluteal-shaped skull, which occurs as a result of the simultaneous development of limited hydrocephalus and specific osteoperiostitis of the frontal and parietal bones.

- Lorinet-like (saddle-shaped or goat-like) nose, resulting from a previous syphilitic rhinitis or nasal septum gumma.
- Robinson-Fournier scars, radial in nature, localized around the mouth after the resorption of Hochzinger infiltration.
- Axifoidia, the absence of the xiphoid process.
- Austitidys-igumenakis symptom, thickening of the sternal end of the clavicle.
- Gashé diastema, widely spaced upper incisors.
- High ("Olympic") forehead.
- Dubois-Gissar symptom, an infantile (shortened) little finger.
- Corabelli's tubercle – a fifth additional cusp on the chewing surface of the upper first molar;
- High "gothic" palate, Moon's tooth (underdevelopment of the chewing cusps of the first molars), microdontia, hypertrichosis.

A characteristic feature is the development, primarily between the ages of 7–15 years, of syphilitic gonitis (Clutton's synovitis), where the synovial membrane of the knee joints is acutely or subacutely affected without involvement of the cartilage in the epiphyses of the bones.

Criteria for Diagnosing Late Congenital Syphilis:

- Anamnesis: Information regarding the mother's syphilis history, other children in the family, and the obstetric history of the mother.
- Presence of active late syphilis manifestations combined with reliable and/or probable signs of late congenital syphilis.
- Laboratory (serological) confirmation of the diagnosis (IFA, ICHLA, RIF, RPGA, IB, RMP, RPR).
- Liquorological examination.

The diagnosis of late congenital syphilis is established based on:

Clinical signs, including reliable (parenchymatous keratitis, labyrinthine deafness, Hutchinson's teeth) and a number of probable signs of late congenital syphilis.Serological tests: initially, they may be negative in newborns infected at later stages of pregnancy and should be repeated. If the mother receives treatment during the last trimester of pregnancy, the treatment may be inadequate for the child, and congenital syphilis may still develop in the newborn. Prevention of Congenital Syphilis:

Screening of pregnant women for syphilis is conducted at the first visit for antenatal care. Testing should be repeated at later stages of pregnancy if the woman had a risk of infection after the first negative test result. In the absence of syphilis testing in the laboring woman or postpartum woman, an express test is performed with subsequent confirmation in case of a positive test result.

During the first visit for antenatal care, all pregnant women are asked about a history of syphilis, particularly when completing the "Pregnant Woman's Questionnaire."

Serological screening for syphilis in pregnant women is carried out at the first antenatal visit (preferably before 12 weeks of pregnancy) and at 20–24 weeks of pregnancy.

If necessary (for pregnant women in the behavioral risk group for syphilis infection, such as teenagers who became pregnant as a result of rape, women with unprotected risky sexual relations, or sex workers), syphilis testing is carried out as indicated.

When a pregnant woman presents for antenatal care for the first time in the third trimester (after 24 weeks), serological screening for syphilis is conducted during the visit. A second screening is performed using rapid (express) tests upon admission to the maternity hospital for delivery, followed by confirmation using treponemal and non-treponemal tests if the result is positive.

For pregnant women in behavioral risk groups for syphilis infection (such as teenagers who became pregnant as a result of rape, women with unprotected risky sexual relations, or sex workers), if the screening and repeat syphilis test results are negative, further testing for syphilis is conducted at 32–36 weeks of pregnancy or during delivery using instrumental methods or rapid (express) tests. If syphilis testing was not conducted for a woman at the time of delivery or postpartum, express testing is performed with subsequent confirmation using treponemal and non-treponemal tests if the result is positive.Serological diagnostics for syphilis in pregnant women are carried out according to Section I of these Standards

If the woman was adequately treated for syphilis and removed from the register before the current pregnancy, and there is no likelihood of re-infection, preventive treatment for syphilis during pregnancy is not carried out, and syphilis testing for the newborn is also not required.

Preventive treatment for a pregnant woman with a history of syphilis is administered if previous treatment and its results are not clearly documented, or if there are doubts about the serological cure.

For a pregnant woman with a positive treponemal test (TT), where syphilis was treated before the current pregnancy, as documented, non-treponemal test (NTT) titers are checked during the first antenatal visit. If the NTT excludes re-infection, the pregnant woman does not need further treatment.

In the case of treponemal seropositivity, the obstetrician-gynecologist refers the pregnant woman to a dermatologist-venereologist for consultation.

The general practitioner or family doctor monitors the implementation of the prescribed treatments, the schedule for visits to the obstetrician-gynecologist, and the timing for hospitalization for delivery.

A diagnosis of active syphilis at any stage in a pregnant woman, or unclear history of syphilis treatment before the current pregnancy, as established by the dermatologist-venereologist, will lead to appropriate treatment and the development of a typical delivery plan for syphilis. Pregnant women who are

socially maladjusted or who have shown non-compliance with treatment are hospitalized and provided with further treatment.

If the treatment of a pregnant woman with syphilis is interrupted for more than one day at any point during the course of treatment, the entire course must be repeated from the beginning.

In cases of a Jarisch-Herxheimer reaction during pregnancy, the treatment should be supportive, similar to that for non-pregnant women, and include the use of antipyretic medications.

Clinical and Serological Monitoring: Clinical and serological monitoring of the mother after treatment is carried out according to the criteria for serological cure. Specifically, a fourfold decrease in non-treponemal test (NTT) titers is expected in cases of early syphilis, which may occur after the pregnancy.

During clinical and serological follow-up, to assess the risk of re-infection, data regarding the pregnant woman's sexual behavior should be collected, as well as information about the treatment of her sexual partners.

1. Which symptom among the listed below does not refer to the main skin and mucosa affections in the case of congenital syphilis:

A. Diffuse skin infiltration
B. Papular eruption
C. Syphilitic rhinitis
D. Syphilitic pemphigus
E. Keratosis follicularis

2. The pathognomonic symptom of early congenital syphilis is:

A. Long bones periostitis
B. Long bones osteochondritis
C. Long bone osteoperiostitis
D. Flat bones osteoperiostitis
E. Knee joints arthritis

3. In the case of early congenital syphilis the following occurs:

A. Parrot pseudoparalysis
B. Third stage osteochondritis
C. Second stage osteochondritis
D. Osteoperiostitis
E. All mentioned above is correct

4. What changes occur in the bone tissue in the case of early congenital syphilis:

A. Osteochondritis
B. Periostitis
C. Exostosis
D. Ostitis
E. Arthritis

5. Fetal/placental mass ratio in the absence of pathology makes up:

A. 1:5 or 1:6
B. 1:3 or 1:4
C. 1:7 or 1:8
D. 1:2 or 1:3
E. 1:9 or 1:10

6. Fetal/placental mass ratio in the case of syphilitic lesion of placenta makes up:

A. 1:5 or 1:6
B. 1:3 or 1:4
C. 1:7 or 1:8
D. 1:2 or 1:3
E. 1:9 or 1:10

7. In the case of syphilitic lesion of placenta the significant alterations are observed:

A. In maternal placenta
B. In fetal placenta
C. The significant alterations are not observed
D. All mentioned above is correct
E. All mentioned above is false

8. Which of the following does not refer to the probable signs of the late congenital syphilis:

A. The shortcut little finger
B. Parenchymatous keratitis
C. The absence of xiphoid process
D. Dental dystrophies
E. "Olympian" forehead.

Task 1. An infant, with the weight of 2400 g, was born to infected with syphilis mother, and had the following symptoms and signs: hypoplasia of hypodermis tissue, macrocephaly, swollen abdomen, hepatomegaly, splenomegaly.

a) Form a diagnosis:
- **A.** Premature newborn
- **B.** Congenital pathology
- **C.** Congenital syphilis
- **D.** Congenital toxoplasmosis
- **E.** Ectodermal dysplasia.

b) Which changes can be revealed during examination and with the help of different diagnostic methods?

Task 2. An infant, with the weight of 3500 g was born to infected with syphilis mother. No pathological signs were revealed during the physical examination. In three weeks appeared the laboured breathing, attended with snuffling. Thereafter occurred serous discharges, followed with purulent one's; the process of sucking became difficult. Blood tests: RPHA, ELISA, IHL, RPR are positive.

a) Form a diagnosis:
- **A.** Adenoviral rhinitis
- **B.** Syphilitic activity
- **C.** Congenital adenoids
- **D.** Congenital toxoplasmosis
- **E.** Herpetic infection.

b) Name the stages of congenital syphilis.

Task 3. Soon after the nine months infant started to walk, occurred the fracture of the right leg. Roentgen examination revealed symmetric lesions in the shinbones of both legs. The epiphyseal line between epiphysis and diaphysis was 5 mm wide. Both mother and child have given positive Wassermann reactions. Serological blood reactions: treponemal (ELISA, CLIA, TPPA) and non-treponemal (VDRL, RPR) tests in the child and mother are positive.

a) Form a diagnosis:
- A. Syphilitic osteochondritis
- B. Parrot's [syphilitic] pseudoparalysis
- C. Syphilitic periostitis
- D. Syphilitic ostitis
- E. Syphilitic osteoperiostitis

b) Choose the therapeutic approach.

Task 4. A 10 weeks old infant, which was born to the infected with syphilis mother, had erythema on the skin of palms and feet, followed with skin infiltration. Surface of the thickened skin is smooth. The skin itself is tense, of low elasticity, with solitary fissures. Wassermann reaction, IF – test, Treponema pallidum immobilization reactions are positive.

a) Form a diagnosis:
- **A.** Palmar psoriasis
- **B.** Pemphigus syphiliticus
- **C.** Atopic dermatitis
- **D.** Diffuse syphilitic skin infiltration
- **E.** Neonatal pemphigus.

b) What other signs of early congenital syphilis are distinguished?

Answers to the questions of the first level of complexity
1 – **E**; 2 – **B**; 3 – **E**; 4 – **C**; 5 – **A**; 6 – **B**; 7 – **B**; 8 – **B**
Answers to the questions of the second and third levels of complexity
1a – **C**; 2a – **B**; 3a – **A**; 4a – **D**

30 TOPIC

Diagnostics of syphilis

At the current stage, the diagnosis of syphilis in Ukraine is carried out in accordance with the medical care standard «Syphilis» (approved by the Ministry of Health of Ukraine in 2023). This standard was developed based on the principles of evidence-based medicine and modern international recommendations reflected in clinical guidelines, namely: the UK National Guidelines on the Management of Syphilis (2015) and the European Guideline on the Management of Syphilis (2020).

Diagnostics of syphilis is based on the data of anamnesis, clinical and laboratory study. The diagnosis of syphilis is determined only after laboratory confirmation – revealing Treponema Pallidum and/or relevant data of serological tests.

TRAINING AND EDUCATIONAL OBJECTS

- Determine the information content of the methods of laboratory diagnostics of syphilis in different periods of its clinical course
- Justify the appointment of bacterioscopic studies on the identification of Treponema pallidum
- Analyze the features of the clinical material for the study
- Identify the basic methods of serological tests for syphilis, and the indications for their use
- Orientate in the methods of modern diagnostics of syphilis
- Analyze the mistakes introduced by the doctors of different specialties in the diagnostics of syphilis

TO KNOW:

- methods of laboratory diagnostics of syphilis – microscopic and serological (rapid diagnostic methods, standard and highly specific reactions for syphilis);
- rules for material sampling for laboratory detection of the presence of Treponema pallidum;
- rules of blood sampling and taking cerebrospinal fluid for the serological confirmation of the diagnosis of syphilis.

TO BE ABLE TO:

- learn the technique of collection of material for microscopic study to detect Treponema pallidum;
- conduct a study of Treponema pallidum in the dark field of view;
- differentiate Treponema pallidum from other treponema;
- interpret the results of microscopic examination;
- conduct blood sampling for serological examination of a patient for syphilis;
- assess the serological tests for syphilis and interpret their results;
- isolate treponemal and non-treponemal tests, determine the parameters for their use, clinically interpret the results;
- make a differential diagnostics of false-positive and positive serological tests.

Syphilis can be detected at various stages of the disease, and depending on this, the patient may require different examination methods. In diagnosing syphilis, a multidisciplinary approach should be used, involving specialists in dermatovenerology, obstetrics and gynecology, neonatology, pediatrics, ophthalmology, neurology, general practice – family medicine, and other specialists as needed.

A full clinical examination (neurological, ophthalmological, and otorhinolaryngological) is recommended for every patient with positive serological tests for syphilis.

The diagnosis of syphilis is based on epidemiological, clinical, and laboratory criteria (microscopic, serological, and, if necessary, histomorphological methods).

A mandatory part of the diagnosis is the collection of the patient's medical history, which includes:

Sexual history:

- For primary syphilis – all sexual partners from the last 3 months.
- For secondary and early latent syphilis – all partners from the last 2 years.
- For late syphilis – according to the history and previous serological tests for syphilis.
- Additional information on previous syphilis cases:
- Year and location of diagnosis.
- Treatment received (medication, route of administration, duration).
- Results of previous serological tests (if needed, contact the healthcare facility where treatment was conducted).

Results from prior syphilis testing (including screening tests used at the time):

- Antenatal screening.
- Blood donation.
- Sexual health screening.
- Previous infection with non-venereal treponematoses and living in endemic zones or countries.
- For women, obstetric history should also be collected if necessary, including:
- Unfavorable pregnancy outcomes (related to or characteristic of syphilis).
- Presence of children who may have late congenital syphilis.

The clinical examination includes looking for signs of syphilis in areas where infection is likely, as well as the most typical lesions of organs and systems affected by the disease.

- For early syphilis (primary or secondary), the examination will focus on the skin and visible mucous membranes of the genitals, trunk, palms and soles, and the hairy part of the head, as well as Oral cavity, eyes, and neurological examination should be conducted if neurological symptoms are present.

For symptomatic late syphilis (including suspected late congenital syphilis), the clinical examination should be carried out according to the patient's complaints, paying attention to the following:

- Skin and mucous membranes.
- Musculoskeletal system (for congenital syphilis).
- Cardiovascular system (in the presence of ultrasound signs of regurgitation in the aorta).
- Nervous system (presence of general paresis: dysarthria, hypotonia, intentional tremor, and abnormal reflexes; spinal syphilis (tabes dorsalis): pupil abnormalities, changes in reflexes, impaired vibration sensation, and joint deformities, sensory ataxia, and optic nerve atrophy).

Among the laboratory diagnostic methods for syphilis, the priority ones include:

- Bacterioscopic examination.
- Serological blood tests.
- Cerebrospinal fluid (CSF) diagnosis.

Bacteriascopical study. The most convincing evidence of treponemal nature of syphilis is the direct visualization of Treponema pallidum. For this purpose the method of dark field microscopy is widely applied. The material for the study can be presented by the tissue fluid from the surface of the chancre and punctate from lymph nodes, in case of the secondary syphilis – tissue fluid from the surface of a chancre remains on the skin and mucous membranes, tissue fluid from the surface of erosive and ulcerative elements (papules, large condylomas), the content of exudative elements (pustular syphilide), punctate of lymph nodes; in case of congenital syphilis – amniotic fluid, umbilical cord tissue fluid; placenta, and erosive and ulcerative elements on the skin and mucous membranes; the content of bullous elements in the syphilitic pemphigus of infants.

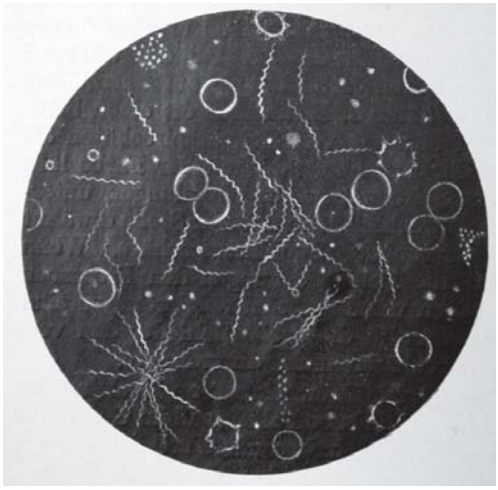


Fig. 30.1. Sketch of Treponema pallidum (microscopic study in the dark field of vision).

Methodology of material collection for microscopic study of Treponema pallidum. Surface of erosion, ulcers, erosive papules on the skin and mucous membranes is cleaned with gauze soaked in isotonic sodium chloride solution. Then the surface of erosions and ulcers is slightly annoyed by the loop until the appearance of tissue fluid, which is put by the same loop on a clean glass slide where there is a drop of saline, and is covered with a cover slip. If

one fails to get a tissue fluid by the above indicated method, one shall squeeze syphiloma with a hand in a rubber glove from the edges until the appearance of tissue fluid on its surface. In case of negative results, the study is carried out several times.

Puncture of the lymph node is carried out in primary and secondary periods of syphilis in the cases when the study of tissue fluid from the surface of the hard chancre or ulcer and erosive elements did not reveal Treponema pallidum. If the technique of puncture is performed in the proper manner, Treponema pallidum is detected in 80-85% of cases.

The study in the dark field of vision uses special devices to conventional microscope – parabaloid-condenser or kardoid-condenser. Passing through it, the light rays are directed obliquely through the side slot and are concentrated at a sharp angle at the location of a drop of tissue fluid, thus, in fact, a proper study in the dark field of vision is achieved. Illumination should be intense enough during the study. The agent is tested immediately. In the dark field Treponema pallidum have the shape of thin light spirals that forming between 8 and 12 uniform curls. Treponema pallidum move slowly, pendulumlike, around their axis, and in the rotational way and bending. An important differential feature is the flexure of the microorganism in the middle part, which differentiates Treponema pallidum from other saprophytic treponema.

In case of chancre the localization on the genitals, Treponema pallidum may be confused with Treponema crassus, and on the mucous membrane of the mouth – with Treponema bucalis, which are thicker, have wider grooves of different sizes, cut edges and are moving more chaotic and lively. Detection of specific microorganisms with characteristic morphology, motility and antigen specificity allows determining diagnosis of syphilis in the primary, secondary, recent congenital syphilis without serological tests.

The absence of microorganisms in typical lesions does not exclude the diagnosis of syphilis. This may be due to the prolonged existence of the focus, the previous treatment of the patient or unsatisfied technique for material sampling and its study.

Serological diagnostics of syphilis. Serological diagnosis of syphilis is used to confirm the clinical diagnosis, establish the diagnosis of latent syphilis, monitor the effectiveness of treatment, serve as a criterion for cure in syphilis patients, and detect immune disorders in the body in response to the pathogen.

For serological testing and obtaining reliable results, blood should be taken at least 4 hours after eating. The patient should avoid fatty foods, alcoholic beverages, and medications 3–4 days before the test. To prevent false-positive results, testing should only be conducted under normal body temperature conditions and under the following circumstances:

- Not earlier than 12–15 days after a high fever illness.
- At least 20 days after the administration of long-acting penicillin.

- After 7 days for water-soluble penicillin, erythromycin, tetracycline, etc.
- A week after menstruation.

It is not recommended to test blood immediately after vaccination, injuries, surgical procedures, or during menstruation. For newborns, testing should only be done after ten days of life.

The blood sampling technique for serological testing involves using a sterile needle and syringe to draw blood from the cubital vein on an empty stomach or at least 4 hours after eating. Blood collection from infants can be performed from the vein on the temples or from an incision on the heel. The syringe and needle are sterilized and rinsed with saline solution. Distilled water, alcohol, acids, or alkalis should not be used to prevent hemolysis. The collected blood (5–7 cm^3) is poured into a dry, sterile test tube and left at room temperature for 2–3 hours to clot, after which it is sent to the laboratory. Serum should not be tested earlier than 24 hours after blood collection. For long-distance transportation, the «dry drop» method is used. After one day, the serum is separated from the clot. One milliliter of serum is transferred using a sterile graduated pipette and spread onto paper in the form of two separate circles. The patient's full name and blood collection date are noted on the free area of the paper. A shiny dark glass-like film forms on the paper after a day. It is packaged like pharmaceutical powder and sent to the laboratory with the suspected diagnosis and the reason for the test.

Serological tests are classified into two groups: treponemal and non-treponemal.

For confirming early and congenital syphilis, direct methods for detecting T. pallidum under dark-field microscopy (DFM) (except for oral mucosal ulcers) and molecular tests such as PCR (Polymerase Chain Reaction) from exudates or tissue samples from affected areas are used.

To establish a syphilis diagnosis, two laboratory serological tests should be performed: a treponemal test, such as an express test (ET), ELISA (IgM + IgG), Passive Hemagglutination (RPGH), Immunofluorescence (RIF-abs), Chemiluminescent Immunoassay (ICLA), and Western Blot (WB for IgM + IgG), as well as a non-treponemal test, such as Rapid Plasma Reagin (RPR) and/or Venereal Disease Research Laboratory (VDRL) test.

The syphilis serological diagnostic algorithm follows these steps:

- The first screening test should be a treponemal test (TT).
- For individuals with a positive screening TT, a confirmatory quantitative (titer determination) non-treponemal test (NTT) should be performed.
- If the NTT result is negative, testing with another TT (usually RPGH) should be done.
- If the second treponemal test (TT) is positive (e.g., positive IFA, negative RPR, and positive RPGH), individuals with a history of complete treatment do not require further treatment, provided there is no suspicion

of re-infection. In this case, a repeat non-treponemal test (NTT) and physical examination should be performed 2–4 weeks after the exposure to assess for early infection.

- If the second TT is negative (e.g., positive IFA, negative RPR, and negative RPGH), and the epidemiological risk and clinical likelihood of syphilis are low, no further evaluation or treatment is necessary.

Further serological testing for syphilis should be conducted:

- 2–4 weeks after the appearance of symptoms in patients with negative DFM (dark-field microscopy) and PCR (Polymerase Chain Reaction) results and ulcerative lesions that could be caused by syphilis.
- 6 and 12 weeks after a high-risk contact (unprotected oral, anal, or vaginal sex with a male partner, multiple partners, anonymous sex, sex with a sex worker, or with a partner from a country with high syphilis prevalence).
- Every 3 months for individuals at persistent risk due to frequent «high-risk» contacts (key population groups) as part of routine STI (sexually transmitted infection) screening, especially for HIV.

Results of serological reactions for syphilis may be considered false positive in the following cases:

- If low titers of NTT (<1:4) are found, the individual should undergo a repeat test with the same NTT and a treponemal test (TT).
- If low titers of TT (especially those requiring visual assessment, such as RIF-abs, RPGH) and negative NTT results are found, the patient should undergo IFA or immunoblot testing for IgG antibodies to T. pallidum.

Clinical and instrumental examination of a syphilis patient is conducted based on indications, particularly when there is a well-founded suspicion of late-stage syphilis:

- If there are symptoms or signs of cardiovascular system involvement, a complete cardiovascular examination is performed;
- If there are symptoms or signs of nervous system involvement, a neurological examination is conducted. If necessary, brain imaging methods such as computed tomography (CT) or magnetic resonance imaging (MRI) are performed. The results should be analyzed before performing a lumbar puncture (LP);
- Performing a lumbar puncture (LP) with the evaluation of cerebrospinal fluid (CSF) is indicated for patients with clinical evidence of neurological, ophthalmological, or otological disturbances, regardless of the disease stage, as well as for tertiary syphilis (cardiovascular, gummatous).
- Before a lumbar puncture (LP), ophthalmoscopy should be performed. CSF (cerebrospinal fluid) analysis should include determination of total protein, mononuclear cell count, and both treponemal (TT) and non-treponemal (NTT) tests.

- It should be noted that in neurosyphilis, the CSF protein level may be normal
- Also, in neurosyphilis – especially in parenchymatous neurosyphilis (tabes dorsalis, general paresis) – the CSF mononuclear cell count may be normal; conversely, a high mononuclear cell count may be observed in various conditions, including HIV infection in the absence of syphilis. In the event of pathological CSF changes (elevated protein and/or pleocytosis), a repeat CSF examination should be performed after treatment (from 6 weeks to 6 months later)
- CSF evaluation is not indicated in early syphilis (regardless of HIV status) if there are no neurological, ophthalmological, or otological symptoms.
- The decision to perform a CSF examination in patients with latent syphilis is based on the results of serum NTT titers, and it is also indicated in late syphilis when there is a clinical suspicion of neurosyphilis or ineffective treatment.
- The diagnosis of a syphilitic gumma is based on the clinical and laboratory (histology, PCR) picture of typical nodules/plaques or destructive ulcers, in the presence of serological confirmation of syphilis.

General causes of false-positive serological reactions include infectious diseases whose pathogens exhibit antigenic similarity to pale treponemes (e.g., framboesia, bedjil, pinta, leptospirosis, inflammatory diseases caused by saprophytic treponemes in the oral cavity and on the genital organs), physiological states (pregnancy, childbirth, menstruation in women, consumption of fatty foods and alcohol), and pathological conditions (gout, typhoid fever, malaria, pneumonia, leprosy, endocarditis, diffuse connective tissue diseases, myocardial infarction, concussion, oncological diseases, poisoning with lead, phosphorus, chlorophos, ingestion of sodium salicylate, digitalis, etc.), which lead to alterations in metabolism – especially lipid metabolism – as well as technical errors during the performance of the reactions. Numerous studies have demonstrated the possibility of both acute and chronic false-positive reactions. Acute false-positive reactions are unstable, with spontaneous negativation occurring within 4–6 months.

The causes of acute false-positive reactions include pregnancy (especially during its final weeks and the first 10 days after delivery), pneumonia of mycoplasmal etiology, enterovirus infection, measles, infectious mononucleosis, vaccination, drug abuse, and alcohol consumption; rarely – active tuberculosis, scarlet fever, viral pneumonia, brucellosis, leptospirosis, and malaria, protein malnutrition; sometimes – severe trauma, concussion, fractures, myocardial infarction; and technical errors during the performance of serological reactions.

Chronic false-positive reactions may be observed in patients with leprosy, systemic lupus erythematosus, rheumatism, nodular periarteritis, liver cirrhosis, sarcoidosis, generalized scleroderma, cryoglobulinemic purpura, oncological

diseases, diabetes mellitus, hematological disorders, hypertension, chronic alcoholism, and drug addiction. The frequency of false-positive reactions increases with age. In women, these reactions are observed 4.5 times more frequently than in men. In some cases, the causes of false-positive reactions remain unclear, accounting for 0.03–0.25% of cases. Most often, they are weakly positive, and if positive, they exhibit low titers. Elevated titers may be seen in conditions such as lymphomas, chronic lymphocytic leukemia, rheumatoid arthritis, and liver cancer; however, with repeated testing in these conditions, the titer decreases. In syphilis, the titer either remains stable or increases.

1. The most common screening serological test for syphilis is:

A. Enzyme immunoassay for IgM + IgG
B. Immunoblot for IgM + IgG
C. Passive hemagglutination reaction
D. Immunochemiluminescence assay
E. Treponemal rapid test

2. Which serological reactions are considered treponemal tests for syphilis?

A. Immunoblot for IgM + IgG
B. Enzyme immunoassay for IgM + IgG
C. Immunochemiluminescence assay
D. Passive hemagglutination reaction
E. All of the above

3. For what purpose are serological treponemal and non-treponemal tests used?

A. To confirm the diagnosis in active forms of syphilis
B. To determine the effectiveness of syphilis treatment
C. To detect latent forms of syphilis
D. To determine the criteria for cure of syphilis
E. All of the above are correct

4. Which of the listed serological tests is primary for determining the possibility of a syphilitic infection in a patient?

A. Treponemal rapid test
B. Immunochemiluminescence assay
C. Enzyme immunoassay for IgM + IgG
D. Immunoblot for IgM + IgG
E. Passive hemagglutination reaction

5. Which laboratory methods are used to confirm the diagnosis of primary syphilis?

A. Microscopic examination for pale treponema in sample material from an erosion or ulcer on the external genitalia
B. Microscopic examination for pale treponema in sample material from a puncture of a regional lymph node
C. Treponemal rapid serological test
D. Enzyme immunoassay for IgM + IgG
E. All of the above are correct

6. Which reagent is used for cleaning the surface of a solid chamber during the examination for the presence of pale Treponema?

A. 2% boric acid solution
B. 0.02% furacilin solution
C. 0.9% sodium chloride solution
D. Chlorophyllipt solution
E. Chlorhexidine solution

7. Which laboratory methods are used to confirm the diagnosis of fresh secondary syphilis?

A. Treponemal rapid test
B. Enzyme immunoassay for IgM + IgG
C. Immunochemiluminescence assay
D. Rapid plasma reagin test
E. All of the above are correct

8. Which serological reactions are performed to confirm early or late latent syphilis?

A. Enzyme immunoassay for IgM + IgG
B. Immunoblot for IgM + IgG
C. Immunochemiluminescence assay
D. Rapid plasma reagin test.
E. All of the above are correct

Task 1. A 60-year-old patient has long suffered from liver cirrhosis. Upon hospitalization in the therapeutic department, a serological study revealed a positive treponemal rapid test.

a) Which additional serological tests should be performed to confirm or rule out the presence of late acquired syphilis in the patient?
- **A.** Passive hemagglutination reaction
- **B.** Immunoblot for IgM + IgG
- **C.** Enzyme immunoassay for IgM + IgG
- **D.** Rapid plasma reagin test
- **E.** All of the above

b) Assuming all the respective tests are positive, determine the strategy for further treatment of the patient.

Task 2. A 42-year-old patient presented to the doctor with complaints of a rash on the genital organ without any subjective sensations. The rash has been present for one week. On examination, remnants of a hard chancre were observed on the glans of the penis. Polyadenitis is noted. On the skin of the torso, there is a fine, numerous, roseola-like rash. The preliminary diagnosis is fresh secondary syphilis.

a) Which laboratory tests should be performed to confirm the diagnosis?
- **A.** Treponemal rapid test
- **B.** Enzyme immunoassay for IgM + IgG
- **C.** Passive hemagglutination reaction
- **D.** Rapid plasma reagin test
- **E.** All of the above are correct

b) Perform the differential diagnosis of the condition.

Answers to the questions of the first level of complexity
1 – E; **2** – E; **3** – E; **4** – A; **5** – E; **6** – C; **7** – E; **8** – E
Answers to the questions of the second and third levels of complexity
1a – E; **2a** – E

31 TOPIC

Principles of treatment and prevention of syphilis

TRAINING AND EDUCATIONAL OBJECTS

- Identify the principles of treatment of patients with syphilis
- Characterize the types of treatment with anti-syphilitic drugs
- Analyze the non-specific treatment of syphilis
- Identify the principles of prevention of syphilis

TO KNOW:

- principles of treatment of patients with syphilis;
- essential medicines for the treatment of syphilis;
- reserve antibiotics used to treat patients with syphilis;
- basic principle of observation of patients with syphilis;
- criteria for curability of syphilis;
- set of preventive measures in case of syphilis.

TO BE ABLE TO:

- take past medical history relatively tolerance of antibiotics;
- make up plan of the treatment of patient with syphilis;
- test the tolerance of penicillin.

Treatment of patients with syphilis is carried out taking into account the stage of the disease, individual characteristics, contraindications, and the results of tolerance testing for the medications. Depending on these factors, different treatment methods may be required. In order to prevent the spread of infection, treatment is initiated as soon as possible.

For the treatment of syphilis, treponemicidal antimicrobial agents are prescribed, such as penicillins, ceftriaxone, and doxycycline. Numerous studies have demonstrated a lower efficacy of macrolides in the treatment of syphilis.

In the event of the possible unavailability of registered penicillin-group drugs in Ukraine that are effective for syphilis treatment (e.g., benzathine benzylpenicillin, procaine benzylpenicillin as monotherapy, probencid), there are certain restrictions on their use for treating syphilis. According to Article 44 of the Law of Ukraine "Fundamentals of Ukrainian Health Legislation", unregistered medicinal products may only be used in the interest of curing a patient provided that written consent is obtained and the patient or their legal representative is informed about the objectives, methods, side effects, potential risks, and expected outcomes of the treatment.

General Principles of Therapy

The following types of treatment for syphilis patients and their contacts are provided:

1. Specific Treatment: This is administered only to patients with a confirmed diagnosis of syphilis.

2. Preventive Treatment: This is performed for the purpose of syphilis prophylaxis in individuals who have had sexual or close household contact with patients with infectious forms of syphilis, provided that no more than three months have elapsed since the contact. Individuals who had such contacts more than three months ago should undergo a full clinical and serological examination, and if the results are negative, treatment is not indicated.

3. Prophylactic Treatment: This is conducted to prevent the occurrence of congenital syphilis: (a) In pregnant women who previously received specific therapy for syphilis, if such individuals did not achieve serological negativation of blood test results before the onset of pregnancy.(b) In newborns if they are born to mothers infected with syphilis before delivery who did not receive complete specific and prophylactic treatment, provided that there are no clinical or serological signs of syphilis in these children.

4. Trial Treatment is administered when there is a suspicion of specific involvement of internal organs, the nervous system, sensory organs, or the musculoskeletal system, in cases where the diagnosis cannot be confirmed by convincing laboratory data and the clinical picture does not allow the exclusion of the development of a syphilitic infection (in cases of suspected late forms of syphilis).

At the current stage, the treatment of syphilis in Ukraine is carried out in accordance with the "Syphilis" standard of medical care (approved by the Ministry of Health of Ukraine in 2023), which was developed taking into account the requirements of evidence-based medicine and current international recommendations reflected in the clinical guidelines, namely: the UK National Guidelines on the Management of Syphilis (2015) and the European Guideline on the Management of Syphilis (2020).

Treatment According to Epidemiological Indications (Preventive Treatment)

Combined drug preparation of benzathine benzylpenicillin + procaine benzylpenicillin – 1.5 million IU intramuscularly, twice a week, for a course of 2 injections, if benzathine benzylpenicillin is unavailable.

In case of allergy to penicillin, procaine, or inability to undergo parenteral treatment:

Doxycycline – 100 mg orally twice daily for 14 days.

Early Syphilis (Including primary, secondary, and early latent syphilis, i.e., acquired <2 years ago)

Combined drug preparation of benzathine benzylpenicillin + procaine benzylpenicillin – 1.5 million IU intramuscularly, twice a week, for a course of 5 injections, if benzathine benzylpenicillin G is unavailable.

In case of intolerance to procaine:

Benzylpenicillin – 1 million IU intramuscularly every 4 hours for 21 days.

In case of coagulation disorders:

Ceftriaxone – 1 g intravenously, daily for 10 days (if there is no anaphylaxis to penicillin).

Doxycycline – 200 mg per day, or 100 mg twice daily, orally for 14 days.

In case of penicillin allergy or inability to undergo parenteral treatment:

Doxycycline – 200 mg per day, or 100 mg twice daily, orally for 14 days.

Syphilis with an Unestablished Time of Infection, Late Latent Syphilis

(i.e., acquired ≥2 years ago), as well as cardiovascular and gummatous syphilis, and additional treatment in patients with serological resistance:

Combined drug preparation of benzathine benzylpenicillin + procaine benzylpenicillin – 3 million IU intramuscularly, as a single administration given as two injections of 1.5 million IU each into each buttock on days 1, 8, and 15 of treatment, if benzathine benzylpenicillin is unavailable.

In case of intolerance to procaine:

Benzylpenicillin – 1 million IU intramuscularly every 4 hours for 28 days.

For patients with penicillin allergy or inability to undergo parenteral treatment:

Doxycycline – 200 mg per day (or 100 mg twice daily) administered orally for 21–28 days.

For all treponemicidal antibiotics used in cardiovascular syphilis, adjunctive glucocorticoids should be administered: Prednisolone 40–60 mg once daily for 3 days, starting 24 hours prior to the antibiotics.

Neurosyphilis, ophthalmologic, and auricular involvement in early syphilis

First-Line Therapy:

Benzylpenicillin – 3–4 million IU intravenously every 4 hours (totaling 18–24 million IU per day) for 10–14 days.

Second-Line Therapy (if hospitalization and administration of benzylpenicillin are not possible):

Ceftriaxone – 1–2 g intravenously once daily for 10–14 days (provided there is no anaphylactic reaction to penicillin).

With all treponemicidal antibiotics in neurosyphilis, adjunctive glucocorticoids should be given: Prednisolone 40–60 mg once daily for 3 days, starting 24 hours before antibiotic administration.

Syphilis in HIV-Positive Individuals:

Treatment is according to the stage of the infection. HIV-positive patients should receive the same treatment regimens as HIV-negative patients.

Prophylactic Specific Treatment in Pregnant Women:

Combined drug preparation of benzathine benzylpenicillin + procaine benzylpenicillin – 1.5 million IU intramuscularly, twice a week, for a course of 4 injections, if benzathine benzylpenicillin is unavailable.

In case of intolerance to procaine:

Benzylpenicillin – 1 million IU intramuscularly every 4 hours for 14 days.

For patients with coagulation disorders:

Ceftriaxone – 1 g intravenously daily for 10 days (provided there is no anaphylaxis to penicillin).

Early Syphilis (primary, secondary, and early latent, i.e., acquired <2 years ago) in Pregnancy:

Combined drug preparation of benzathine benzylpenicillin + procaine benzylpenicillin – 1.5 million IU intramuscularly, twice a week, for a course of 5 injections, if benzathine benzylpenicillin is unavailable.

In case of intolerance to procaine:

Benzylpenicillin – 1 million IU intramuscularly every 4 hours for 21 days.

Alternative Treatment Methods:

Ceftriaxone – 500 mg intramuscularly daily for 10–14 days.

Erythromycin – 500 mg orally four times a day for 14 days

Syphilis with an Unestablished Time of Infection, Late Syphilis (latent, cardiovascular, and gummatous syphilis) in Pregnancy

Combined drug preparation of benzathine benzylpenicillin + procaine benzylpenicillin:

3 million IU intramuscularly, as a single administration given as two injections of 1.5 million IU each into each buttock on days 1, 8, and 15 of treatment, if benzathine benzylpenicillin is unavailable.

In case of intolerance to procaine:

Benzylpenicillin – 1 million IU intramuscularly every 4 hours for 28 days.

Alternative Treatment Methods:

Erythromycin: 500 mg orally four times a day for 30 days.

For all treponemicidal antibiotics in cardiovascular syphilis, adjunctive glucocorticoids should be administered: Prednisolone 40–60 mg once daily for three days, starting 24 hours before antibiotic administration.

Neurosyphilis in Pregnancy

Benzylpenicillin: 3–4 million IU intravenously every 4 hours (totaling 18–24 million IU per day) for 14 days.

Alternative Treatment Methods (if hospitalization and intravenous administration of benzylpenicillin are not possible):

Ceftriaxone: 2 g intramuscularly (diluted with lidocaine) or intravenously (diluted with water for injections, NOT with lidocaine) for 10–14 days (provided there is no anaphylaxis to penicillin).

With all treponemicidal antibiotics in neurosyphilis, adjunctive glucocorticoids should be given: Prednisolone 40–60 mg once daily for three days, starting 24 hours before antibiotic administration.

Congenital Syphilis

Benzylpenicillin: 150,000 IU/kg/day intravenously, administered once daily (divided into six doses every 4 hours) for 10–14 days. Intravenous therapy is recommended for children (this is the first option listed here) due to the pain associated with intramuscular injections.

Prophylactic Specific Treatment of Newborns

Benzylpenicillin: 100,000–150,000 IU/kg/day intravenously in a single dose of 50,000 IU/kg every 12 hours during the first 7 days of life (twice daily), and from the 8th day onward, every 8 hours. The injection should be administered over 15 minutes, with a treatment course lasting 8 days.

Adverse Effects and Complications

Penicillin Group Agents: May cause side effects and complications such as urticaria, chills, arthralgias, angioneurotic edema (Quincke's edema), polymorphic erythema, exfoliative dermatitis, anaphylactic shock, stomatitis, and glossitis.

Macrolides: May cause nausea, vomiting, abdominal pain, flatulence, diarrhea, and rarely allergic reactions, neutropenia, or transient increases in transaminase activity.

Cephalosporins: May cause diarrhea, anorexia, nausea, vomiting, candidiasis, headache, and confusion sleepiness, allergic reactions (drug-induced chills,

skin rashes, itching, eosinophilia, allergic nephritis, anaphylactic reactions), neutropenia, leukopenia, reversed hypoprothrombinemia, and transient elevation of hepatic transaminase activity. With tetracycline use, possible adverse effects include nausea, vomiting, anorexia, glossitis, esophagitis, allergic reactions, angioneurotic edema, photosensitization, neutropenia, eosinophilia, hemolytic anemia, candidiasis, and dysbiosis.

A specific manifestation of anti-syphilitic therapy in patients with syphilis is the Jarisch-Herxheimer reaction. This reaction most commonly occurs in patients who have begun treatment for early syphilis (primary seronegative, primary seropositive, and fresh secondary syphilis). The reaction develops within the first 12 hours after the initiation of therapy. The main clinical symptom is a sharp increase in body temperature up to 39 °C, and sometimes even higher. The peak hyperthermia is observed 6–10 hours after the start of treatment; it lasts for 8–10 hours and gradually subsides by 18–24 hours. Other symptoms of the reaction include the exacerbation of existing clinical manifestations of syphilis, general malaise, and headache. The reaction is attributed to the massive death of treponemes induced by antibiotic therapy, which is accompanied by a significant release of their endotoxins.

To prevent possible allergic reactions, it is recommended to perform a tolerance test for penicillin-group drugs, and 30 minutes before the first injection, administer one tablet of an antihistamine. During treatment, clinical blood and urine tests should be performed at least once a week. The therapy must be comprehensive, combined with the treatment of concomitant diseases, and accompanied by the use of agents that enhance the body's resistance to infections and activate immunological defense mechanisms. In the event of a pronounced Jarisch-Herxheimer reaction, penicillin therapy should not be discontinued; instead, intramuscular corticosteroids should be administered at a dose of 0.5 mg of prednisolone per kilogram of body weight. If the exacerbation reaction does not subside after 6 hours, the corticosteroid injection should be repeated. The consumption of alcohol and smoking are prohibited. Nutrition should be regular, with a balanced diet that provides an adequate amount of proteins, carbohydrates, and vitamins while limiting fats. Physical overexertion, mental trauma, and sleep disturbances adversely affect treatment outcomes.

Specific therapy should be combined with non-specific stimulatory therapy, especially in the late stages of syphilis and in cases of nervous system involvement.

Non-specific Therapy

Non-specific therapy in patients with syphilis is prescribed to stimulate immunological reactivity, enhance the body's resistance, activate the reticuloendothelial system, improve blood and lymph circulation at the sites of lesions, and increase the effectiveness of specific therapy. The need for non-specific therapy arises in cases of latent and late forms of syphilis, neurosyphilis

and involvement of internal organs, congenital syphilis, in the presence of accompanying pathology, slow serological negativation, serological relapses, or seroresistance. It is also advisable to prescribe non-specific therapy in cases of secondary recurrent and early latent syphilis, and, when indicated, even in its fresh forms. Non-specific therapy should be prescribed only after a thorough examination of the patient, taking into account the indications and contraindications for specific medications. Various methods of non-specific therapy are employed.

Biogenic stimulators (e.g., aloe, FIBS, placental extract, plasmol) are also indicated; these are administered daily or every other day at a dose of 1–2 mL per injection, up to 20 injections per course. Vitamins are taken both in tablet form and as injections. Ascorbic acid, B-group vitamins, and antioxidants (such as Triavid, "Tri-V-Plus," etc.) are used. In late forms, multivitamin complexes containing folic acid, calcium pantothenate, vitamins A and E, and trace elements are prescribed. In the comprehensive therapy of syphilis patients, adaptogenic agents (e.g., pseutropin, ginseng tincture, lemon balm, etc.) are utilized. Immunocorticosteroid therapy is administered in cases of a "malignant" course of the disease, in the presence of concomitant conditions developing against a background of immunodepression, and in patients with chronic alcoholism. Such therapy is recommended to be conducted under the control of an immunogram. Agents from this group include methyluracil, T-active, timalin, kagoce, and others. For individuals suffering from alcoholism, piroxap is recommended. Hepatoprotective agents (e.g., Hepabene, Essenciale, Karsil, Glyceran, etc.) are indicated, as well as medications that improve microcirculation and metabolic processes.

Criteria for Quality Treatment of Syphilis Patients and Subsequent Clinical-Serological Monitoring

- When treating patients with syphilitic infection and during subsequent clinical-serological follow-up, a number of criteria must be strictly observed:
- In the treatment of syphilis, preference should be given to penicillin-group agents.When choosing a treatment regimen, it is necessary to ensure that a treponemicidal concentration of the antibiotic is achieved in the serum, and in the case of neurosyphilis—and specifically in the cerebrospinal fluid (CSF)—penicillin levels should exceed 0.018 mg/L. The appropriate treponemicidal level of antimicrobial agents must be maintained for at least 7 days.
- If, during the treatment of syphilis, the administration of the drug is interrupted for more than one day at any point during the treatment course, the entire course must be restarted from the beginning.
- During neurosyphilis and cardiovascular syphilis, glucocorticoids are prescribed alongside all treponemicidal antibiotics to prevent potentially serious complications.

- Clinical monitoring of patients following antibiotic injection is performed for 30 minutes.
- Resuscitation equipment must be available in the healthcare facility where syphilis treatment is administered.
- After treatment for syphilis, clinical-serological follow-up and evaluation of therapy effectiveness are carried out to detect any possible relapse or re-infection.
- Control clinical and serological examinations using non-treponemal tests (NTT) should be performed at 3, 6, and 12 months, and thereafter, as indicated, every 6 months until either NTT negativity is achieved or seroresistance is established.
- All repeat clinical and serological examinations must be clearly documented to avoid unjustified repeat treatment.
- A discharge summary detailing the diagnostic and treatment outcomes should be provided to the patient.
- If, after complete treatment of early syphilis, the NTT titers do not decrease fourfold within 12 months, this is noted as seroresistance, prompting a cerebrospinal fluid (CSF) examination and repeat treatment.
- Treatment failure or re-infection is established when NTT titers increase fourfold or more.
- In cases of syphilis re-infection or relapse, screening of sexual partners and their epidemiological (preventive) treatment is indicated.
- For HIV-infected patients, treatment should follow the same regimens recommended for HIV-negative individuals.
- In cases of HIV infection, lifelong annual seromonitoring for syphilis is required, and if syphilis is detected, testing should be repeated every 6 months (simultaneously with periodic HIV examinations).
- Other sexually transmitted infections (including HIV) and related disorders in syphilis patients are managed in accordance with the relevant sectoral standards.

Quality Criteria for the Treatment of Syphilis-Exposed Children and Subsequent Clinical-Serological Monitoring

The treatment of children with confirmed or suspected syphilis is carried out in accordance with the medical care standard «Syphilis.» If the child's mother was treated with macrolides during pregnancy, benzylpenicillin is prescribed for the treatment of early congenital syphilis.

All syphilis-seropositive children or those born to seropositive mothers during childbirth undergo clinical-serological monitoring after treatment. All newborns with positive non-treponemal tests (NTT) must undergo a thorough clinical examination and serological testing of NTT initially at one month and then every three months. NTT titers should decrease by three months of age and become negative by six months if the child was uninfected or adequately treated.

If an NTT test is negative at six months, no further examinations or treatment are required. If the NTT test remains positive, the child is likely infected and requires treatment.

For newborns who were not treated due to a low likelihood of congenital syphilis, non-treponemal antibody titers should decrease by three months of age and become negative by six months. This indicates that the positive test result was due to passive transplacental transmission of maternal IgG antibodies. Passive transmission of maternal treponemal IgG antibodies may persist for more than 15 months after birth.

Newborns with negative NTT whose mothers were seropositive at birth should be re-examined at three months of age to rule out seronegative congenital syphilis at birth.

For treated newborns whose titers remain stable or increase after 6–12 months from birth, a cerebrospinal fluid (CSF) examination should be performed.

Children with abnormal CSF findings during the initial examination should undergo repeated CSF testing every six months until the indicators normalize. A repeated CSF examination is not required if their NTT titers are negative after six months of age. Persistent titers and CSF abnormalities should be treated after consultation with a specialist.

Children aged ≥1 month with abnormalities in the first CSF test do not need a repeat CSF test if their NTT titers do not increase fourfold after 12–18 months. If NTT titers increase over a two-week period or do not decrease fourfold after 12–18 months, a repeat CSF test should be conducted. Persistent abnormal CSF findings that cannot be attributed to other comorbidities indicate neurosyphilis and require treatment with a 10–14 day course of parenteral penicillin following expert consultation.

Treponemal tests (TT) should not be used to assess treatment effectiveness, as they provide qualitative results, and passive transmission of maternal treponemal IgG antibodies may persist up to 15 months of age.

A positive TT result after 18 months of age may indicate congenital syphilis. In such cases, an NTT should be performed. If the NTT is negative, no further examination or treatment is needed. If the TT is positive at 18 months of age, the child should undergo a full examination and treatment for syphilis.

1. Name methods for syphilis treatment:

A. Specific antibiotic treatment
B. Prevention treatment
C. Prophylactic treatment
D. All the abovementioned

2. Choose the reserve group of the drugs for the treatment of syphilis:

A. Bicillin-3
B. Macrolides
C. Benzylpenicillin -G
D. Bicillin-5

3. What antibiotics are used for the treatment of pregnant women with syphilis:

A. Doxycycline
B. Erythromycin
C. Penicillin
D. Rocephin
E. Fromilid

4. Name the duration of clinical and serological monitoring of the patient with the infection with syphilis of more than a year:

A. 6–12 months
B. 12–24 months
C. 24–28 months
D. 24–30 months
E. 30–34 months

5. Indicate frequency of observation with the use of complex of serological reactions (CSR) of patient with the infection with syphilis of up to six months:

A. One time in 6 months
B. One time in 3 months
C. One time in 12 months
D. One time in 2 months
E. One time in a month

6. Treatment of patients with tertiary syphilis is carried out in accordance with the scheme of:

A. Primary seronegative syphilis
B. Secondary recurrent syphilis
C. Late latent syphilis
D. Recent latent syphilis
E. Secondary recent syphilis

Task 1. In the hospital the woman who was previously sick with syphilis and received a full and specific preventive treatment during the second half of pregnancy, gave birth to a child without clinical symptoms of syphilis and with negative serological results.

a) What is the tactics of child maintenance:
A. Consultation of related experts
B. X-Ray examination of long bones
C. Conducting Serological Treponemal Tests in Dynamics
D. Clinical supervision for a year
E. All the abovementioned is true

b) Shall this child be prescribed prophylactic treatment?

Task 2. The woman in labor, treated from the secondary recurrent syphilis in the second half of pregnancy was admitted to the hospital. She received a full course of specific therapy. She did not pass prophylactic treatment. The delivery went well. The baby was born weighing 3100 g with no external manifestations of syphilis, the IFT is negative.

a) What tactics with respect to the child shall be used:
A. Prescribe prophylactic treatment.
B. Conducting Serological Treponemal Tests in Dynamics
C. Consultation of related experts
D. X-Ray examination of tubulous bones
E. All the abovementioned is true

b) Provide therapeutic recommendations.

Task 3. A child in the age of 1,3 year received proper treatment with respect to congenital syphilis.

a) What is necessary for termination of the dispensary observation:
A. Consultation with a pediatrician and neurologist
B. Consultation with an otorhinolaryngologist
C. Conducting serological treponemal tests (RIF, ELISA, IB)
D. Conducting serological non-treponemal tests (RPR and/or VDRL)
E. All of the above are correct

b) How is the congenital syphilis classified?

RECOMMENDED LITERATURE LIST

I. Main Educational Literature

1. Dermatology: A Handbook / David J. Hawkroger, Michael R. Ardern-Jones. (Translation of the 7th English edition). Scientific editor of the Ukrainian translation: V.I. Stepanenko. – Kyiv: VSV «Medicine», 2023. – 175 pages.
2. Practical Dermatology and Venereology: A Training Manual / V.I. Stepanenko, A.I. Chobotar, S.O. Bondar. – Kyiv: VSV «Medicine», 2018. – 360 pages.
3. Fundamentals of Practical Dermatocosmetology: A Handbook / S.O. Galnykina, Yu.V. Boyko, B.V. Vitienko. – Kyiv: Ukrmedkniga, 2006. – 176 pages.
4. Dermatology, Venereology in Questions and Answers: A Training Manual / under the general editorial guidance of O.O. Sizon. – Lviv: Kameniar, 2017. – 180 pages.
5. Pharmaceutical Cosmetology: A Handbook / S.O. Klymyshyna, A.V. Tsysnetska, L.V. Rachkevich. – Ternopil: Volya, 2009. – 368 pages.

II. Additional Educational Literature

1. Collection of Test Tasks in Dermatovenerology for Control and Self-Control: A Training Manual / O.Y. Turkievych, O.O. Sizon, O.A. Bilinska, et al. – Lviv: Nova Zorya, 2010. – 198 pages.
2. Report on Plastic Surgery Statistics. ASPS National Clearinghouse of Procedural Statistics in Plastic Surgery. American Society of Plastic Surgeons; 2020. Google Scholar
3. Olejnik A, Gościańska J, Nowak I. The Role of Hyaluronic Acid in the Cosmetic Industry and Aesthetic Medicine. Chem. 2012; 66(2): 129-135. CAS Google Scholar
4. Vronovska L., Rodak I. Assessment of Women's Awareness of the Skin Aging Process and Treatment Options in Cosmetic Salons. Aesth Cosmetol Med. 2020; 9(3): 319-328. Google Scholar

III. Methodological Literature

Methodological foundations for preparing and conducting educational sessions for higher medical education students according to the topic, developed in higher educational institutions in accordance with the «Regulations on the Department».

Answers to the questions of the first level of complexity
1 – D; **2** – B; **3** – C; **4** – D; **5** – B; **6** – C
Answers to the questions of the second and third levels of complexity
1a – E; **2a** – E; **3a** – E

32 TOPIC

Gonorrhea

Gonorrhea is a human contagious disease, caused by Gram-negative aerobic diplococcus *Neisseria gonorrhoeae*, which is predominantly sexually transmitted.

TRAINING AND EDUCATIONAL PURPOSES

- To distinguish main morphological peculiarities of gonococci
- To define the principles of their clinical laboratorial diagnostics
- To define the clinical classifications of gonorrheal lesions
- To explain peculiarities of various clinical symptomatology of indicated urogenous lesions
- To define the possible conditions of introduction of infection and preventive measures of gonorrhea
- To determine typical clinical complications of gonorrheal infection
- To prescribe etiotropic, pathogenetic or topical treatment for gonorrhea patients

TO KNOW:

- Etiopathogenesis and epidemiological features of gonorrhea;
- Clinical forms and the course of this disease;
- The criteria of gonorrhea diagnostics and its complications;
- The principles of medical and preventive measures and medical examination of gonorrhea patients.

TO BE ABLE TO:

- Deontologically and purposefully collect sexual history of gonorrhea patients;
- Perform a set of diagnostic measures for making etiological and topical diagnosis;
- Make a differential diagnostics with the diseases with the similar clinical presentation picture;
- Appoint appropriate treatment for gonorrhea patients;
- Recommend rational prophylactic measures of gonorrhea.

Historical information. The modern term «gonorrhea» was firstly used in the II century AD by Galen, who mistakenly took discharge from the urethra of men as seminal fluid (from Greek, *gonos* is semen, *rrhoea* is discharge). The inflammatory process in gonorrhea is usually limited to urinogenital organs, accompanied by release and subjective disorders. The possible are also gonococcal lesions of mucous membrane of the rectum, moth cavity, nose, throat, tonsils, and conjunctiva and very seldom by generalization of infectious process.

Etiology. The causative agent of gonorrhea is Gram-negative aerobic diplococcus *Neisseria gonorrhoeae*, discovered by A. Neisser in 1879. Gonococcus belongs to the family *Neisseriaceae*, to the genus *Neisseria*. Coccus has got the shape of coffee beans, with concave surface facing each other, with the length of 1.25 to 1.6 microns and 0.7–0.8 microns across. Gonococcus is a complex organized prokaryotic cell, with cell wall, cytoplasmic membrane, cytoplasm, consisting of ribosomal and poly-somal complexes and nucleoid. The outer three-layer membrane of gonococcus is composed of lipooligosaccharides, pili and three types of proteins. Gonococcal pili are essential for the attachment of the bacteria to the surface of various cells, such as spermatozoa, erythrocytes, mucosae epithelium. Electron microscopy studies of gonococcus ultrastructure revealed the presence of capsule substance, which prevents intracellular digestion of gonococcus and promotes incomplete phagocytosis. Gonococci stain well with all aniline dyes and discolor provided the use of Gram's stain (they are Gram-negative), what distinguishes them from the other diplococci.

Pathogenesis. Gonococci parasitize only in human organism and affect predominantly the cells of columnar epithelium of urogenital tract, rectum, and eyes. Due to pili gonococci are quickly fixed on the surface of epithelial cells, within 24-28 hours penetrate into the intercellular gaps, and then into the subepithelial tissues, where they form microcolonies. Due to the destruction of the epithelium gonococci have got access to the superficial lymphatic and blood vessels of the genitals. In the result of canalicular and lymphatic dissemination, new sections of mucous membranes of genitals are gradually involved into the inflammation. Gonococci do not proliferate in stratified squamous epithelium and in the acidic vaginal environment, so vulvovaginitises are more common in girls and women after the onset of menopause. The possible are the lesions of rectal mucosa,



Fig. 33.1. Ultrastructure of Neisseria gonorrhea (electron microscopy). Magnification x90000.

conjunctiva and pharyngonasal cavity. The skin seldom is involved into the pathological process. The interaction of gonococcal infection and mucous membranes of various organs is determined by different anatomical, physiological, immune and hormonal characteristics of the organism associated with the age and sex. Gonorrhea, like other sexually transmitted infections, is an anthroponotic infection. The causative agent quickly dies outside the human body. Introduction of infection occurs primarily through sexual contacts. Contagiousness of gonorrhea for women is much higher than for men, and makes 60-70%.

The period, which is necessary for the development of the inflammatory response, is usually called the incubation period. On average the incubation period of gonococci is 3-10 days, but its duration may vary within wide limits. Then there appear the clinical signs of the disease, the main manifestation of which is purulent discharges from the urinogenital organs. Phagocytic reaction in gonorrhea depends on the reactivity of the organism and the intensity of the production of endotoxin by gonococci. The course of the infection process is defined by the ratio of complete and incomplete phagocytosis. In the phagocytic reaction the polymorphonuclear leukocytes PMNL, macrophages, lymphocytes and epithelial cells are involved. Acute gonorrhea is characterized by incomplete phagocytosis involving predominantly polymorphonuclear leukocytes. Between them (PMNL) and macrophages there exists the co-operation, in which the partially lysed gonococci together with the broken ones are captured by macrophages, which carry phagocytosis to completion. After the disease a true post-infectious immunity does not appear. After the recovering, in case of new contact with gonorrhea sufferer, the reinfection is possible. In addition to reinfection, superinfection is possible, which usually appears in the presence of encysted lesion focus.

Recurrence of gonorrhea usually occurs in the period of the first two weeks or during one month after the end of the treatment. Gonococci are located predominantly inside the cell and have a tendency to transformation. Reinfection occurs most frequently in 2-3 months after the end of the treatment and is accompanied by acute or subacute inflammatory process.

Epidemiology. According to WHO data, the incidence of gonorrhea in the world is about 65 million cases per year. High incidence of the disease is contributed by the characteristics of the modern course of the disease, such as increased number of asymptomatic, oligosymptomatic and chronic forms, accompanied by immune disorders and various complications. Currently, the course of gonorrheal infection is complicated by a number of peculiarities, in particular, the growing number of penicillinase-producing strains of gonococci and reducing sensitivity of the pathogen to antibacterial drugs, an increased frequency of mixed infection. Social meaning of gonorrhea is defined by the high level of morbidity and the rapid development of complications.

The source of the infection is patients with gonorrhea often with the asymptomatic or low-symptom forms of the disease. The main way of infection is sexual. Infecting

through sexual partners, in case of oral-genital contacts leads to the development of gonorrheal tonsillitis, and in case of genital-anal contacts leads to gonorrheal proctitis. Nonsexual infection is possible through direct contact (in the result of entry of discharge onto the mucous membrane of the eyes, mouth cavity and rectum when passing through the birth canal, the issue on possibility of intrauterine infection is under discussion). Indirect nonsexual infection occurs in case of very close household contact of a small child with a sick mother via a common bed and hygienic or toilet articles.

Classification. In the domestic clinical practice classification of gonorrhea is based on the duration of the disease. Distinction is made between *recent gonorrhea* with the duration of the pathological process of up to two months, and *chronic gonorrhea* with duration of more than two months. Depending on the severity of the clinical manifestations the recent gonorrhea is divided into *acute, subacute* and *torpid*. There is also latent gonorrhea (gonococcal carriage), in which the presence of the pathogen in the mucosa does not cause any inflammatory reaction. When infection gets into the blood circulation disseminated gonococcal infection may develop.

According to the International Classification of Diseases (ICD-10) there are different forms of gonococcal infection with indication of the localization process:

- gonococcal infection of the lower parts of the nephrogonoduct without abscess formation of periurethral or accessory glands;
- gonococcal pelvic peritonitis;
- gonococcal infection of the eye;
- gonococcal infection of the musculoskeletal system;
- gonococcal pharyngitis;
- anorectal gonococcal infection;
- other gonococcal infections;
- unspecified gonococcal infection.

Clinical manifestations of gonorrhea in men. Gonorrhea in men occurs predominantly in the form of destruction of urethra that is urethritis. The clinical signs of the disease are characterized by the appearance of pain during urination and suppurative discharge from the urethra of different degree of intensity. Depending on the clinical manifestations urethritis can be *acute, subacute, torpid* and *chronic*.

***Recent acute gonococcal urethritis*.** Acute inflammation of the urethra is characterized by edema and hyperemia of the urethral sponges, abundant purulent yellowish green discharge from the urethra during the whole day, lancinating pains during urination. *Acute anterior gonorrheal urethritis* is characterized by the inflammatory reaction of the mucous membrane of the distal part of the urethra, pain appears at the beginning of urination, and in case of *acute total urethritis*, when inflammation covers the whole urethra, pain increases at the end of urination (this is the sign of urethrocystitis). Total urethritis is often accompanied by the frequent urgency of urination (up to 15-20 times a day), painful erections and emissions. In the case of pronounced inflammation, the purulent discharge becomes bloody, there appears hemospermia. With time acute inflammation without treatment can move into

the *subacute stage* or initially urethritis can be characterized by moderately pronounced clinical signs. In this case, the swelling and hyperemia of urethral sponge are weakly pronounced. Discharge in the form of moderate or insignificant purulent or serous-purulent release occurs mainly in the morning after overnight break in urination. Feeling of pain during urination is characterized as insignificant. Manifestations of *torpid (asymptomatic) urethritis* follow the subacute stage, and can also appear at the beginning of the disease.

If the patient does not consult a doctor in time, if he did not receive appropriate treatment or the therapy was irrational, if he self-medicated, drank alcohol and ate spicy food, did not interrupt sexual contacts, then inflammatory process becomes chronic.

Chronic gonococcal urethritis. Clinical signs of chronic urethritis are mild itching during urination, insignificant discharge, which occurs in the morning or when pressing on the urethra. Chronic gonorrheal urethritis, as well as the recent one, can be *anterior* and *posterior*, though it is rare limited by the anterior urethra and has got usually a total character. As a rule there are no complaints in chronic gonorrhea, the possible is a slight itching or burning sensation in the urethra. In the morning if pressing at the external opening of the urethra a small drop of yellowish or turbid discharge can be seen. The discharge often is so insignificant, that it does not form a drop, but dries up and agglutinates the sponges of the external opening of the urethra. In many cases the discharge has such a viscous consistency that it stays in the cannel and can be found in the form of filaments only during visual examination of urine. Chronic gonorrhea generally has a torpid course with periodic exacerbations.

Clinical manifestations of gonorrhea in women. Gonorrhea in women is characterized by the oligosymptomatic course and multifocal lesions. These features are associated with the anatomical features of female genitourinary organs. In women, gonorrhea affects the cervical canal, urethra, vulvovaginal glands and rectum, in girls, vulvovaginitis develops, the development of proctitis is possible in the result of leakage of purulent discharge from the vagina. Gonococcal lesions in women can appear at the same time in several places (urethritis, endocervicitis, etc.) and be not accompanied by significant subjective sensations.



Fig. 32.2. Recent acute gonococcal urethritis.

There are the following clinical varieties of gonorrheal infection in women:

- *gonorrhea of the lower genitourinary tract*, these are urethritis, bartholinitis, vestibulitis, vulvitis, vaginitis, endocervicitis;

- *gonorrhea of the upper genitourinary tract or ascending gonorrhea* – gonococcal endometritis, salpingitis, oophoritis, pelvioperitonitis.

Depending on the duration of the disease there are recent and chronic gonorrhea, and on the activity of the clinical symptoms there are acute, subacute, torpid and latent gonorrhea.

Gonorrhea of the lower genitourinary tract. Gonorrheal urethritis in women in its clinical manifestations reminds the same disease in men and is characterized by pain and a burning sensation during urination. With the spreading of the infection along the urethra there appear the symptoms of urethrocystitis, dysuria in the form of frequent and painful urination. Intensity of symptoms in women can be quite variable, but it is observed that the incidence of *torpid* and *asymptomatic* forms is significantly higher than in men. In the setting of *recent acute gonorrheal urethritis*, the urethral sponges are hyperemic and swollen, after the massage of the urethra a drop of matter is discharged from its external opening. In case of recent torpid and chronic *gonorrhea*, the hyperemia and edema can be absent; during palpation the infiltration is discharged along the urethra.

Vaginitis (vulvovaginitis) occurs in girls, pregnant and menopausal women in the setting of the corresponding hormonal features. In adult women the phenomenon of vestibulitis and vaginitis can develop in presence of acute gonorrhea in case of the overlay of secondary infection (Staphylococcus, Escherichia coli). There occurs a lesion of squamous epithelium with desquamation and erosion of mucosa, resulting in the observed clinical manifestations. Acute process is characterized by the presence of heavy discharge, pain, burning sensation and itching. The walls of the vagina are edematous, hyperemic and painful. With torpid and chronic course of vulvovaginitis the clinical manifestations can be less pronounced or absent.

Bartholinitis is inflammation of the large vestibular glands. The process typically occurs on both sides. The clinical picture is determined by the degree of dissemination of inflammatory process. The lesion can be limited by excretory duct, cover completely the gland, fall outside its bounds. In case of disorder of outflow of gland secretion, the false abscess can be formed, which does not cause abnormality of general condition and breaks spontaneously after some time. In case of joining of the secondary infection there is meltdown of the gland wall with the spreading of inflammation over the surrounding tissue and with the formation of true abscess. This condition is accompanied by the appearance of symptoms of intoxication, disorder of the general condition, sharp painfulness of lesion focus.

Endocervicitis is an inflammation of the mucous membrane of the cervical canal. Columnar epithelium lining the cervical canal is affected in the first place. With acute and subacute process, the purulent discharge from the cervical canal promotes maceration of the stratified squamous epithelium of the vagina, which leads to the appearance of leucorrhea. On examination in mirrors hyperemia and edema of the vaginal part of the cervix, the erosion of the external os, purulent discharge from the cervical canal are determined. In the case of a chronic course of the process, the discharge is minor or

absent, the cervix can be deformed, there are erosions on the surface of the cervix at the external os, while taking the material the bleeding is not rare.

Gonorrhea of the upper genitourinary tract. Ascending gonorrhea in women can have the following clinical forms:

- G*enital*, these are endometritis, salpingitis, salpingoophoritis, pelviperitonitis;
- *Extragenital,* these are proctitis and pharyngitis.

Endometritis is a consequence of an ascending infection from the cervical canal, leading to the lesion of the mucous membrane of the body of uterus. In the case of an acute process the colicky lower abdominal pains appear, the body temperature raises to 39 ° C, there are abundant sanies, and disrupted menstrual cycle. In chronic process, there are dull lower abdominal pains, periodic spotting, gaping cervix and scanty, mucopurulent discharge.

Salpingitis is an inflammation of the uterine tubes. During the dissemination of the inflammatory process over the ovaries, there occurs salpingoophoritis. Acute inflammation in this area is characterized by the pronounced lower abdominal pains amplifying at movement, urination and defecation. There are symptoms of intoxication, temperature rise up to 39 ° C, disruption of the fecal masses formation, menstrual irregularities, and more frequent urination. The chronic process is accompanied by moderate pain in the iliac region, menstrual irregularities, and scanty mucous secretions. Salpingoophoritis can cause infertility due to the blockage of uterine tubes, the development of connective tissue in the result of the inflammatory process in the area of the appendages. Chronic inflammatory process of this localization can cause ectopic pregnancy.

Pelviperitonitis is a serious complication of gonococcal infection associated with inflammation of the pelvic peritoneum. It is characterized by sharp colicky lower abdominal pains. There appear dyspeptic phenomena, constipations, bloating, and disorders of urination. The body temperature is increased up to 39 ° C, there are symptoms of intoxication, anterior abdominal wall is tense in palpation, and there is positive Blumberg symptom, in a clinical analysis the EST is increased with normal amounts of leukocytes of blood.

Gonorrheal proctitis and *pharyngitis* are the forms of extragenital gonorrhea. Gonorrheal proctitis occurs in girls and women in case of leaking of purulent discharge from the vagina or in anal variant of sexual contacts in people of both sexes. Acute gonorrheal proctitis is characterized by pains during defecation, itching in the anus area. In the case of the formation of erosions and cracks blood can appear in the feces. The anal area is hyperemic, in the folds the matter is accumulated. There can be no complaints in recent torpid and chronic forms, and the signs of the inflammation in the form of hyperemia, swelling and erosion of the mucous membrane of the rectum are only detected in rectoscopy. Gonococcal pharyngitis and tonsillitis occur as the consequence of oral-genital contacts and have not got the characteristic differences from other inflammatory processes of this localization. The diagnosis is set only on the basis of the results of bacteriological examination.

Gonorrhea in girls results from the nonobservance of hygienic norms in time of direct contact with adults with gonorrhea or through transferring infection by means of household items. The girls of older age can catch a disease at attempt of sexual contact. A distinctive feature of the inflammatory process, associated with anatomical and physiological characteristics of the girls, is the simultaneous lesion of external genitals, vagina, urethra, and often rectum as well.

Disseminated gonococcal infection occurs in the case of penetration of the agent in a blood channel, favored by the destruction of the mucous membrane of the primary focus of infection. Gonococci in blood usually die under the influence of factors of natural immunity. However, in some cases, getting into the blood stream, gonococci are able to multiply and enter in various organs and tissues, causing lesions of joints, endocardium, liver, meninges, skin. The course of disseminated gonococcal infection does not depend on the nature of the primary site and the virulence of the organism. Dissemination occurs in case of long-lasting undetected infection, improper treatment, immunedeficiencies of different nature, menstruation, pregnancy, lesions of mucous membrane at instrumental manipulations and sexual contacts.

Disseminated gonococcal infection has severe and mild form. Severe form occurs with pronounced signs of intoxication, such as fever, chills, tachycardia. Polyarthritis is typical with the purulent joint effusion; in case of skin lesion there are predominantly vesicle-hemorrhagic rashes with necrosis. With severe form, sepsis can develop, followed by endo-, myo- and pericarditis, meningitis, hepatitis. With mild form the lesion is limited predominantly to knee-articular syndrome. *Gonorrheal arthritides* in their clinical manifestations are similar to other bacterial inflammatory lesions of the joints. The presence of the primary site of infection and detection of gonococci in the articular cavity confirm the diagnosis.

Gonococcal eye lesions are frequent manifestation of gonococcal infection in adults, which develops as a result of mechanical transfer of the pathogen from the genital organs to the conjunctiva. Gonococcal conjunctivitis, iridocyclitis, gonococcal ophthalmia in neonates occurs during infection when passing through the birth canal, or in utero. The cases of transmission of infection from the medical personnel are casuistical. The incubation period lasts from 2 to 5 days. In case of intrauterine infection the disease is pronounced in the first day of life. Gonococcal conjunctivitis is characterized by edema and hyperemia of eyelids, photophobia, and abundant purulent discharge from the eyes. In the absence of treatment the process



Fig. 32.3. Gonorrheal blepharoconjuctivitis.

extends to the cornea, causing swelling, infiltration, turbidity and ulceration. Neonatal ophthalmia occurs in the case of penetration of infection in the area of the inner shells of the eye. The occurring ulcer with subsequent cicatrization can lead to blindness.

Modern peculiarities of gonococcal infection lie in the fact that gonorrhea occurs predominantly as a mixed infection. With that the clinical manifestations, periods of incubation can change, complications can develop, etc.

Complications of gonococcal infection. The characteristics of anatomy of the urethra in men lead to a number of peculiar morphological changes caused by the migration of lymphocytes, neutrophils, and plasma cells in lesion focus. As a result an inflammatory reaction develops that is clinically manifested in the formation of subepithelial cellular infiltrate. The formation of urethra infiltration causes destruction of elastic tissue. Destruction of elastic fibers starts quite early and develops in proportion to the intensity of inflammation. With chronic gonorrheal urethritis the further development of changes occurring in the acute stage is observed. It is not always possible to provide a clear pathologicoanatomic demarcation between acute and chronic inflammation, because the transition from one process into another is slow and gradual. The epithelium of the urethra is subjected to the further metaplasia and gets the tendency to keratinization. Inflammatory cellular infiltrate in the mucosa and submucosa of the urethra tissue acquires a pronounced focal character and is gradually replaced by connective tissue. Depending on the degree of cellular infiltration and the presence of connective tissue in the focus of inflammation there are two pathohistological groups of urethrides.

The first group includes gonorrheal urethritis, characterized by prepotency of cellular infiltration (soft infiltrate) in the presence of insignificant amount of connective tissue.

The second group consists of urethritis with a solid infiltrate, in which the predominant element is the connective tissue. Such infiltration is observed in cases of chronic gonorrhea. Along with the changes in the mucosa and submucosa of the urethra, there are also significant changes in the urethral glands and crypts in the form of deposition of connective tissue in or around the crypts and littritis gland.



Fig. 32.4. Gonorrheal tysonitis.

Complications of gonococcal infection include:

Littritis is inflammation of alveolar tubular glands located in the urethra. When overlapping the opening of the glands by inflammatory infiltrate they can take the form of dense painful knots (pseudo abscesses), perceptible on palpation. Sometimes pseudo abscess

reaches a considerable size, the periurethral abscess can appear in case of purulent dissolution.

Morganite is an inflammation of the Morgagni's lacunae, as well as littritis, is a complication, which occurs most frequently in gonorrhea and has got similar clinical manifestations.

Tysonitis is an inflammation of Tyson glands located on both sides of the penis frenulum. They are defined as inflammatory nodules on palpation. While squeezing the glands there can be the purulent discharge from the excretory ducts. Also, abscess of gland is possible, in case of ductal blocking.

Parauthretitis is an inflammation of the paraurethral cannels, which in the acute phase is masked by manifestations of urethritis. Isolation of the pathogen in the paraurethral canals can cause a recurrence of gonorrhea. Parauretrit manifests itself as infiltration in the projection of paraurethral duct and hyperemia of the ostium of discharge opening. When closing openings the lacunar abscess can be formed.

Periurethritis develops as a result of penetration of gonococci in the periurethral tissue and the corpus cavernosum of urethra. Periurethritis looks like infiltrate with indistinct contours, which can cause abscess formation, the curvature of the penis, urination disfunction with the subsequent formation of urethral strictures.

Colliculitis appears during the propagation of the inflammatory process in the area of seed tubercle and manifests itself as a painful syndrome of different severity, radiating to the lumbar region, hips, lower abdomen, and genital organ. Colliculitis is often accompanied by sexual disorders in the form of premature or late ejaculation. There are catarrhal, interstitial and atrophic colliculitis.

Cowperitis is an nflammation of the bulbourethral glands. The clinical picture of acute process is characterized by throbbing pain in the perineum, increasing during defecation, movement and pressure, more frequent or difficult urination. Fever up to



Fig. 32.5. Gonorrheal orchiepididymitis.



Fig. 32.6. Gonorrheal balanoposthitis.

38 ° C and chilly sensation is typical from the general phenomena. Chronic cowperitis is characterized by heaviness and aching pain in the perineum, increasing during prolonged sitting, periodic discharge from the urethra, mainly in the morning.

Prostatitis is the most common complication of gonorrhea. Prostate infection occurs in lesion of the posterior urethra by gonococci. Catarrhal prostatitis appears in case of limited lesion of the prostate ducts. With involvement of lobules gland in the pathological process the follicular prostatitis develops, and in the case of the dissemination of the pathological process in the parenchyma, there occurs parenchymatous prostatitis.

Vesiculitis is an inflammation of the seminal vesicles, often combined with prostatitis. The acute form is not frequent and is characterized by the common occurrences of intoxication, fever, haematuria and haematospermia. The more frequent is chronic vesiculitis, which can be asymptomatic and is revealed at clinical and instrumental examination. During exacerbation there appear pelvic pains radiating to the urethra, perineum, rectum, painful pollutions, haematospermia and premature ejaculation.

Epididymitis is an inflammation of testicular appendage. Typically, the process is of unilateral nature. Gonococcal infection is the most common cause of this condition. Antiperistaltic movements of deferent ducts promote the development of epididymitis. Along with the appendage the deferent duct (deferentitis appears) and the tissue surrounding the spermatic cord (funiculitis) are involved in the inflammatory process. Acute process is characterized by the development of the common phenomena of intoxication, fever, increasing temperature up to 39-40 ° C. In the setting of the pain syndrome there appear hyperemia and edema of the corresponding scrotal half. At the same time there are the clinical signs of acute total urethritis with the presence of discharge and dysuric phenomena. The increased and painful appendage of testis in the form of a helmet is detected on palpation, which covers testis over its back and bottom surface. At the beginning, the inflammatory process is localized in the tail of the epididymis (testicular appendage), and only then spreads to the body and head of the epididymis. With that the testis itself can remain unaltered. It is often that epididymitis initially has subacute or torpid course without common phenomena and with indistinct clinical picture. Chronic epididymitis is a final phase of acute inflammatory process. Epididymoorchitis leads to fibrosis and cicatrization. This can result in cicatricial obstruction of deferent duct and the formation of obstructive infertility.

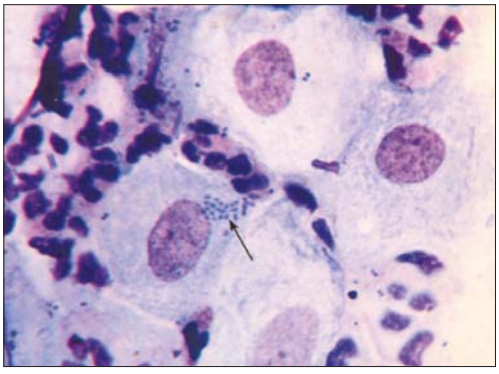


Fig. 32.7. Intracellular placing of N.gonorrhea in smears of urethral discharge. Methylene blue staining, microscopy, amplification x1000.

Balanoposthitis and phimosis occur more frequently in the presence of a long and narrow foreskin. The clinical manifestations of these complications do not differ from the similar in case of disease of non-gonococcal etiology.

Diagnose. Clinical diagnostics includes history and complaints taking, inspection and collection of material for laboratory examination.

When taking history and complaints, it is necessary to clarify the period since the sexual contact with supposed source of infection to the appearance of subjective symptoms, as well as whether the sexual partners were examined by the specialist and what diagnose is set to them. *Visual examination* includes the inspection of the skin and visible mucous membranes, hair part of the head, neck, trunk, extremities, genitals and perianal area for excluding skin diseases and other infections, mainly sexually transmitted. It is necessary to palpate all groups of superficial lymph nodes, such as submandibular, supraclavicular, inguinal, popliteal, for excluding regional lymphadenitis. In women the abdomen, greater vestibular and paraurethral glands, urethra are palpated, a bimanual gynecological examination is carried out. In men it is necessary to palpate the urethra, the prostate gland (prostate massage is contraindicated in acute process), bulbourethral Cowper's gland and organs of scrotum. Palpative examination is performed to exclude associated pathology and for clinical assessments of the affected organs. For establishing the diagnosis of gonorrhea the laboratory data are of decisive importance.

The etiological diagnosis is established on the basis of *bacterioscopic and bacteriological methods of examination*. The material for the study can be discharge of urethra, cervical canal, conjunctiva, the secretion of sexual glands, swabs from the rectum, the lacunae of tonsils, back of the throat. Discharges for the analysis are taken by the Volkmann's small spoon or a special bacteriological loop. Sampling from the different foci is aimed to the efficiency and specificity of diagnostic methods. At urethral inspection the material is taken no earlier than 4 hours after urination, otherwise discharge can be rinsed off by urine. Taking into account the prevalence of mixed forms of infection the diagnostics of other sexually transmitted infections must carried out concurrently.

For *microscopic study* the discharge of urethra, cervix, cervical canal is taken by the Volkmann's small spoon or special bacteriological loop and placed it onto the glass slide. Two preparations are to be prepared simultaneously for the two staining methods; these are the Gram's stain and methylene blue method. At this, it is necessary to take into account that Gram's stain has the basic differential diagnostic meaning. Gonococci are discolored during the Gram's staining (Gram-negative), that distinguishes them from other diplococci. At the same time it is necessary to make cultural research. Given the high sensitivity of gonococci to drying and thermal exposure, it is recommended to seed immediately to the culture medium for the isolation of gonococci. The stained preparations are placed under microscope with immersion. The characteristic location for gonococci is inside the white blood cells (endocytobiosis), especially in case of acute forms of gonorrhea; in case of chronic gonorrhea, the agent can be both intracellular and extracellular.

When establishing the diagnosis of gonorrhea in pregnancy, teenagers and children, as well as in case of sexual violence the cultural research is obligatory irrespective of the results of the microscopic examination.

Modern nonculture methods of identification of gonococci, such as nucleic acid amplification methods have high sensitivity and specificity, with allows using them for screening in the study of clinical materials obtained by non-invasive methods. But, in the case of detection of *N. gonorrhoeae* by these methods in any clinical materials the culture diagnostics must be carried out with identification of agent, which allows determining the sensitivity to antibiotics. With this, molecular-biological methods of research allow to carry out diagnostics of several sexually transmitted infections simultaneously.

Serological methods in diagnosing of gonorrhea have got no significance. Complement fixation reaction (Bordet-Gengou test) becomes positive after 3-4 weeks since the onset of the disease and can be positive during 10 years, which excludes its use for the diagnostics of gonorrhea and recent forms of gonorrhea and in case of control of healing.

Topical diagnostics is performed to determine the localization of the inflammatory process. Two-glass Thompson's test, urethroscopy, the prostate and seminal vesicles status examination with microscopy of their secretion, ultrasonography are applied in men. *The Thompson's test* is a simple and quite informative method for differentiating variants of urethral lesions and diagnostics of complications. Turbidity of the first portion of urine and of transparency of a second portion indicates the presence of anterior urethritis. More total urethritis is characterized by the turbidity of both portions of urine. The change of the second portion of urine may also be a sign of the disease of the prostate, seminal vesicles. The exact topic diagnostic of inflammatory changes in the urethra is carried out with urethroscopy. This methodology is used only for chronic forms of the disease and torpid course of gonorrhea, as in case of acute forms there exists the risk of ascending infection. With help of urethroscopy the presence of soft or hard infiltrate in the urethra, the presence of littritis, morganite and colliculitis is established, and the necessity and scope of topical treatment is considered.

In women, changes in the cervix and vagina are determined by means of colposcopy, in order to avoid damage of the uterus and appendages *bimanual and ultrasound examination* is performed, rectoscopy is carried out in case of indications.

Treatment. The success of treatment of gonorrhea patients depends mainly on the correct etiological and topical diagnosis and timely started therapy. The scope and duration of etiological treatment depend on the period of the disease and the presence of complications. When choosing a medication the possible presence of mixed infections must be taken into account.

For the last decades the urgent became the problem of the resistance of N. gonorrhoeae to antimicrobial medicines. Antibiotic, which is prescribed for the

treatment of gonorrhea, should ensure clinical efficacy in single dose against all strains of pathogens.

The preparations of group of Penicillin are known as the first highly effective treatment of various forms of gonorrhea. Until recently, the preparations of this group were recommended as the antibiotics of choice in the causal therapy of gonorrhea. At the current stage due to increasing prevalence of strains of N. gonorrhoeae, which are resistant to penicillin and its derivatives, the therapeutic use of medicines of this group is possible only in case of proven sensitivity of gonococcus to a particular medicine.

Currently, the first-line drugs in the causal treatment of different forms of gonorrhea are antibiotics of cephalosporin group. Antibiotics, tetracyclines, macrolides, and azalides are also widely used in the treatment of gonorrhea, particularly in combination with other urogenital infections (gonococci + Chlamydia, myco- and ureaplasma). At the same time, the relevant antibiotics belong to the backup group and are applied only in the case of proven resistance of N. gonorrhoeae to penicillins and cephalosporins or in case of their intolerance.

Treatment of the patients with localized recent acute and subacute uncomplicated gonorrhea with involvement of the lower genitourinary tract is performed on an outpatient basis with use of antibiotic therapy only. Treatment of the patients with recent torpid or chronic gonorrhea, as well as any other forms of gonorrhea in the presence of complications, is conducted in specialized medical institutions of dermatovenereological profile. Therapy of these forms of the disease, in addition to a causal treatment may include the appointment of immunotherapy, topical treatment, physical therapy after corresponding topical diagnostics. Prior to the administration of antibiotics the serological testing for syphilis of gonorrhea patients must be performed. In case of impossibility of such examination of sexual partners, the serological testing is to be repeated after three months.

For the treatment of localized gonococcal infections of the lower genitourinary tract, the following medications are appointed: sodium (potassium) salt of benzyl penicillin (6 million units of activity by intramuscular injection 3 million units in each buttock), novocain salt of benzyl penicillin (4.8 million units single dose), procaine penicillin G (6 million units single dose), ceftriaxone (1.0 g single dose), cefotaxime (1.0 g once by intramuscular injection), ciprofloxacin (500 mg single dose orally), ofloxacine (400-800 mg single dose orally), spectinomycin (2.0g single dose).

In the cases of mixed gonococcal and trichomonal infection the simultaneous treatment of gonorrhea and trichomoniasis is recommended. In combination of gonorrhea with clamidiosis and mycoplasmosis, the antibiotic therapy is initially performed, aimed at the elimination of N. gonorrhoeae, in particular by benzyl penicillin and then anti-chlamydial and anti-mycoplasma preparations are appointed.

Patients with torpid and chronic forms of gonorrhea are recommended medicines stimulating the increase of specific and non-specific reactivity of the organism in infection fighting. Gonococcal vaccine is applied as specific immunotherapeutic preparation, and for stimulating non-specific resistance of the organism the

preparations are applied, which activate a number of cellular and humoral factors of immune system, such as pyrogenalum, prodigiosanum, methyluracilum and others.

The local treatments are combined with other forms of therapy, sometimes they are used to increase the metabolic processes in the affected organs, to enhance the permeability of tissues in the lesion focus, for some aggravation of inflammatory process, and before the appointment of the etiotropic therapy as well.

In chronic urethritis, the urethral instillations are carried out with 0.25% silver nitrate solution or 2.1% sodium Protargolum, 2% oil solution of clorophylliptum, for the treatment session of 6-10 procedures. Vaginal washings are carried out with warm (37-38 ° C) solution of potassium permanganate (1:8000), camomile infusion and other medical means by douching 4 times a day at regular intervals. The vaginal baths are also applied. 20-30 ml of 2.1% solution or Protargolum or Collargolum is poured through the gynecological speculum, introduced into the vagina.

Urethral bougienage is mainly recommended for the treatment of infiltrates located on the mucous membrane of the urethra, the lesion of its glands, narrowing (strictures). For this purpose the metal (curved and straight) and elastic bougies are applied. The procedures are carried out every other day for the treatment session of 10-12 procedures. Ultrasonic bougienage is the most effective in the treatment of urethral strictures.

In the treatment of chronic gonorrhea and its complications paraffin-ozokeritotherapy, diathermy, inductotherapy, ionophoresis, mud therapy and other are widely used.

Therapy of gonococcal pharyngitis is conducted with the participation of the otorhynolaryngologist. One of the following medicines is recommended: ceftriaxonum (1.0 g by intramuscular injection single dose) or ciprofloxacinum (0.5-1.0 g orally single dose), or ofloxacinum (400-800 mg orally single dose). Treatment of gonococcal conjunctivitis is carried out with the assistance of the ophthalmologist. The application of ceftriaxonum (1.0 g by intramuscular injection single dose) is recommended. For topical application 1% silver nitrate solution or 1% tetracycline or 0.5% erythromycin eye ointment is prescribed.

In the treatment of complicated gonococcal infections of the upper and lower parts of the urogenital tract, gonococcal peritonitis, gonococcal infection of the musculoskeletal system one of the following treatment schemes is used: ceftriaxonum – 1.0 g by intramuscular or intravenous injection every 24 hours, cefotaximum – 1.0 g by intravenous injection every 8 hours, spectinomycinum – 2.0 g by intramuscular injection every 12 hours, ciprofloxacinum – 500 mg every 12 hours. Intravenous or intramuscular administration of one of these preparations must be continued no less than seven days. After negativation of clinical symptomatology, the therapy is continued for 24-48 hours, after that the oral administration of ciprofloxacinum or ofloxacinum is appointed. The treatment is carried out during the period of 14 days; the extension of therapy should be strictly reasoned. Selection of the above-mentioned medicines is carried out considering the data from medical history

(allergies, idiosyncrasy), the study results of gonococcus sensitivity to antimicrobial drugs, the patient's age etc.

Treatment of pregnant women is carried out at any stage of pregnancy with antibacterial medicines taking into account their possible toxic effects on the fetus.

Treatment of children is carried out with the obligatory assistance of pediatrician.

Treatment of neonates born by mothers with gonorrhea is performed with the assistance of neonatologists. For the treatment of gonococcal conjunctivitis of neonates antibiotic ceftriaxonum is used in a unit dose 25-50 mg per 1 kg of body weight intramuscularly or intravenously. The maximum dose is 125 mg. Neonates with gonococcal conjunctivitis must be hospitalized and examined for the revealing of the signs of disseminated gonococcal infection, particularly sepsis, meningitis, arthritis. The treatment of neonatal ophthalmitis is administered with the assistance of neonatologist, ophthalmologist and neuropathologist. It is recommended to provide preventive treatment even if they have no symptoms of gonococcal infection. Ceftriaxonum should be prescribed very carefully to neonates, especially to prematurely born and infants with hyperbilirubinemia due to an increased risk of developing kernicterus. For the treatment of uncomplicated gonococcal vulvovaginitis, endocervicitis, urethritis, proctitis and pharyngitis in children weighing less than 45 kg ceftriaxonum is used intramuscularly in a dose of 250 mg unitary. Treatment of gonococcal infections in children weighing more than 45 kg is administered according to the scheme for adult patients. Selection of the medicines is carried out considering the data from medical history (allergic reactions, idiosyncrasy), as well as the study results of gonococcus sensitivity to antibiotics.

Criteria of gonorrhea cure. Control tests are carried out 10-15 days after the end of treatment. The obligatory bacteriascopical and cultural examination of discharge of material is conducted, a great attention is paid to determining the amount of leukocytes. In case of absence of clinical manifestations and with negative results of laboratory research, the patients are left on the medical observation at and the similar tests are repeated after 1-1.5 months. In women, the material for laboratory examination should be collected 1-2 days after menstruation, during 2-3 menstrual cycles. If after repeated gonococcal test, the results are negative and gland state is normal, patients are removed from dispensary registration.

Prevention. Basic principles of prevention of gonorrhea are the timely treatment, the identification of sexual contacts and sources of infection, family members' workup, and cure control. Preventive maintenance must be carried out among the patients with gonorrhea in order to prevent sexual contacts during the infectious period, and it must also be aimed at the reducing probability of re-infection among patients and people with past gonorrhea. For the success of preventive maintenance the close relationship of dermatologists with urologists and gynecologists is required. Explanatory talks and lectures, conducted by the medical staff, the presence of available literature on the prevention of gonorrhea and other infections mostly sexually

transmitted in medical institutions are of great concern. Preventive measures lay also in educational work among the persons of the risk groups, pregnant women, care workers. In the maternity hospitals for the prevention of neonatal ophthalmitis all children immediately after birth the eyes are instilled twice with 30% solution of sulfacyl sodium.

In the preventive maintenance of gonorrhea the important is the ability of a doctor to collect history of the patient sexual life, to properly conduct educative activities, to make recommendations for the prevention of sexually transmitted infections.

1. Which pathogen causes gonorrhea?

A. *Staphylococcus aureus*
B. *Pelobacter acidigallici*
C. *Lachnospira multiparus*
D. *Neisseria gonorrhea*
E. *Trichomonas vaginalis*

2. What is the average incubation period in case of gonorrhea infection?

A. 24 hours
B. 3–10 days
C. 2–4 weeks
D. 2 months
E. 1 month

3. What method of staining is used for microscopic diagnosis of gonorrhea?

A. Schick's stain
B. May-Grunwald-Giemsa stain
C. Gram's stain
D. Romanovsky-Giemsa stain
E. Hematoxylin and eosin stain

4. Specify the possible variants of the course of gonococcal urethritis in men:

A. Recent acute gonorrheal urethritis
B. Recent subacute gonorrheal urethritis
C. Chronic gonorrheal urethritis
D. Asymptomatic gonorrheal urethritis
E. All the above

5. Which sign is typical for the clinic of acute anterior gonorrheal urethritis in men?

A. There is no discharge
B. Discharge is insignificant
C. Discharge is purulent in large amount
D. Appearance of drops of blood at the end of urination
E. Pain at the end of urination

6. What type of urethritis is characterized with that result of two-glass test (Thompson's test), when urine is turbid only in the first portion:

A. Recent acute posterior gonorrheal urethritis in men
B. Recent acute anterior gonorrheal urethritis in men
C. Chronic gonorrheal urethritis in men
D. Recent torpid anterior urethritis in men
E. Chronic gonorrheal urethritis in women

7. Bacterioscopic study of patients with acute gonorrhea reveals:

A. Extracellular arrangement of gonococci, a small amount of leukocytes
B. Streptococci, staphylococci, yeasts, squamous epithelium
C. Intracellular and extracellular arrangement of gonococci, a large number of leukocytes
D. Trichomonads, a small amount of N. gonorrhoeae in trichomonads, a small amount of leukocytes
E. Leukocytes, yeast, epithelium

8. Clinically, chronic gonorrheal urethritis in men is characterized by:

A. Insignificant serous-purulent discharge in the morning of the external urethral
B. Purulent discharge in large number
C. Frequent urgencies for urination
D. Absence of discharge
E. Serous discharge in large number

9. What of the following is not the complication of gonorrhea in men?

A. Balanoposthitis
B. Colliculitis
C. Vaginitis
D. Epididymitis
E. Vesiculitis

10. Which of the indicated preparations is not applied for treatment of gonorrhea?

A. Ceftriaxonum
B. Benzylpenicillin
C. Ciprofloxacinum
D. Ofloxacinum
E. Trichopol

Task 1. A pregnant woman with a pregnancy of 20 weeks consulted obstetrician-gynecologist. At examination she was diagnosed with gonorrhea.

a) What should be the medical tactics in this case:
- **A**. Treatment with antibiotics in the third trimester of pregnancy
- **B**. Treatment with antibiotics after delivery
- **C**. Urgent treatment with sulfanilamidums
- **D**. Urgent treatment with benzylpenicillin
- **E**. Urgent treatment with tetracycline

b) Define the criteria of cure.

Task 2. The patient addressed to venereologist with complaints about painful urination, abundant purulent discharge from the urogenital organs. She considers herself to be ill during a week. She associates the disease with the casual sexual contact about 3-4 weeks ago. The preliminary diagnosis of acute gonorrhea of the lower genital tract is confirmed.

a) At the bacterioscopic research of discharge they will detect:
- **A**. Proteus vulgaris
- **B**. Mycoplasma
- **C**. Trichomonads
- **D**. Gram-negative diplococci
- **E**. Gram-positive diplococci

b) What treatment should be appointed?

Task 3. A patient at the age of 27 is complaining about lower abdomen pains, painful urination and purulent discharge from vagina. The patient is on outpatient treatment at the gynecologist. At microscopic examination of vaginal discharge, Gram-stained, the white blood cells occupy the entire field of vision, gram-negative diplococci are located intra- and extracellularly.

a) What is the probable causative agent, which led to the appearance of this pathology:
- **A**. Trichomonads
- **B**. Chlamydiae
- **C**. Colibacillus
- **D**. Gonococcus
- **E**. Staphylococcus

b) What is necessary to clarify from the medical history?

Task 4. A patient at the age of 18 had a casual sexual encounter with an unknown woman. On the second day he paid attention to the frequent urination, burning sensation and itching in the urethra appeared on the third day. On the fourth day there was purulent discharge from the urethra. Urethral sponges are swollen and red.

a) Which diagnosis could be considered as preliminary:
- **A**. Candida urethritis
- **B**. Mycotic urethritis
- **C**. Gonorrheal urethritis
- **D**. Chlamydial urethritis
- **E**. Noncpecific bacterial urethritis

b) Which examinations must be performed to confirm the diagnosis?

Task 5. Patient visited a doctor with complaints about painful urination and urethral discharge. He is sick about a week. At examination: the urethral sponges are hyperemic, swollen, discharge is purulent. Urine in the first glass of two-glass test is diffuse and turbid. Bacterioscopic method revealed in the smears an increased number of leukocytes – up to 100 in the field of vision, diplococci are arranged in couples.

a) Which diseases must be considered:
- **A**. Recent acute posterior gonorrheal urethritis
- **B**. Recent acute anterior gonorrheal urethritis
- **C**. chronic gonorrheal urethritis
- **D**. Recent torpid anterior urethritis
- **E**. Asymptomatic gonorrheal urethritis

b) Make a scheme of treatment.

Answers to the quiz of the first level of complexity
1 – D; **2** – B; **3** – C; **4** – E; **5** – C; **6** – B; **7** – C; **8** – A; **9** – C; **10** – E
Answers to the quiz of the second and third levels of complexity
1a – D; **2a** – D; **3a** – D; **4a** – C; **5a** – B

33 TOPIC

Non-Gonorrheal Contagious Diseases

A group of **non-gonorrheal contagious diseases** includes Genitourinary and extragenital lesions caused by Trichomonas, Chlamydia, Mycoplasma and Gardnerella, *Candida* species and some other pathogens.

TRAINING AND EDUCATIONAL OBJECTS

- To distinguish between main morphological properties of chlamydia, trichomonas and other agents of genitourinary pathology;
- To define the principles of clinical and laboratory diagnostics of non-gonorrheal contagious diseases;
- To explain the characteristics of various clinical symptoms of genitourinary lesions;
- To deontologically carefully and purposefully collect both general and especially sexual anamnesis of patients;
- To analyze the results of clinical examination of patients;
- To single out inherent clinical complications of non-gonorrheal contagious diseases;
- To feature common clinical manifestations of prostatitis of venereal origin;
- To analyze options for the use of combination therapy of genitourinary infections given the etiology, nature and duration of inflammation.

TO KNOW:

- The etiology and pathogenesis of non-gonorrheal genitourinary tract contagious diseases;
- Epidemiological features of these diseases;
- Their clinical forms and course;
- The criteria for the diagnostics of non-gonorrheal genitourinary tract contagious diseases and their complications;
- Prophylactic measures and principles of clinical examination at non-gonorrheal genitourinary tract contagious diseases.

TO BE ABLE TO:

- Properly collect patient's history of non-gonorrheal genitourinary tract contagious disease;
- Conduct a complex of diagnostic procedures to establish etiologic and topical diagnosis;
- Prescribe appropriate treatment for patients with non-gonorrheal genitourinary tract contagious disease;
- Share rational prophylaxis of these diseases.

Genitourinary Trichomonasis

Genitourinary trichomonasis *(trichomonasis)* is wide spread inflammatory disease of human genitourinary tract, which is, mostly, sexually transmitted and is caused by Trichomonas vaginalis.

Etiology. The causative agent of genitourinary trichomoniasis is Trichomonas vaginalis (*Trichomonas vaginalis*) – a microorganism that has adapted through evolution to parasitism in human genitourinary system. *T. vaginalis* belongs to the genus of Trichomonas, which also includes intestinal *T. hominis (intestinalis)* and oral cavity *T. tenax (elongate)* saprophytes. The colonization of genitourinary system with oral and intestinal species of Trichomonas does not lead to the development of pathological process. *T. vaginalis* is the only pathogenic species of Trichomonas for humans that does not cause disease in animals and cannot exist outside the human body.

T. vaginalis is the simplest single-celled organism from flagellates (*Flagellata)* class, belonging to *Trichomanadidae* family of *Trichomonas* genus. There is only one form (or stage) of the development of vaginal trichomonas i.e. trophozoite. The causative agent, preferably, has oval pear-shaped nucleus. At the front end of the body of Trichomonas there are four free flagella extending from basal corpuscle. The fifth flagellum goes back to about one third of length of the body, thus forming an undulating membrane. There is an axostyle all along the cell. Dimensions of Trichomonas fluctuate significantly depending on the growth conditions and characteristics of the strain. Average sizes of *T. vaginalis* are 10-30 мм in length and 5 мм in width. All the elements of Trichomonas vaginalis structure are detected by special staining methods, while in usual diagnostic tests specialists are guided by the size, shape and mobility of cells. Trichomonas is actively moving by means of free flagella and undulating membrane. Under certain conditions, they form pseudopodia, which ensure amoeboid movement.

The main method of reproduction of Trichomonas is division of a cell into two daughters, but sometimes there is schizogony type of division into 8-24 cells. Multiple fission occurs more often under adverse conditions of existence, and Trichomonas do not form cysts, which explain their rapid death outside the human body. Today there are known three morphological forms of *T. vaginalis* i.e. pear-shaped (flagellar), amoeboid and round (spherical). At the outbreak of chronic inflammation Trichomonas are often round-shaped resembling the nucleus of epithelial cells, making it difficult for the microscopic identification of pathogen. Trichomonas feed themselves endosmotically and by phagocytosis. The optimal pH for the existence of *T. vaginalis* is 5.2-6.2. Trichomonas on artificial media develop at 36.5-37 ° C. *T. vaginalis* culture, unlike other cultures, is not capable of hemolysis, plasma-coagulation, it cleaves glucose, maltose, starch well, but lactose – weak, it does not form a hydrogen sulfide and indole. Being out of human body, Trichomonas die quickly because of drying. Direct sunlight, a solution of carbolic acid (1%) and chloramine B (1%) are detrimental for *T. vaginalis*. Trichomonas are resistant to low temperatures and can remain viable at -10 ° C up to 22-45 min. and for 95-115 minutes at 1-4 ° C temperature.

Epidemiology. Based on WHO data, more than 180 million cases of genitourinary trichomoniasis are registered each year all over the world. Trichomonas infection occurs through an infected person, most often it happens during sexual intercourse. So far, the epidemiology of genitourinary trichomoniasis has been studied badly, but the prevalence of infection is increased in older age groups, unlike gonorrhea and chlamydia, which are most common for those aged 19-29 years. In women with inflammatory diseases of pelvic organs, Trichomonas are identified in 5,6-20,6% of cases, in pregnant women – in 0,98-32%, while in patients with infertility – in 19.5% cases, in men with inflammatory diseases of genital area – in 0,2-8,5% cases. There is a connection between genitourinary trichomoniasis and premature birth and low birth weight of newborns.

In recent decades, the incidence of genitourinary trichomoniasis has remained high. The infection occurs as a result of close household contacts. *T. vaginalis* may also be the etiologic agent of pneumonia in neonates and such children may die if untreated with specific drugs. Perinatal trichomonas infection occurs in about 5% of infants born from infected mothers and *T. vaginalis* may stay in the child's body from 3 to 9 months or more.

Classification. Depending on the duration and intensity of organism's reaction to the presence of *T. vaginalis* there are the following forms of trichomoniasis:

1) *recent trichomoniasis* (with disease duration of up to two months), which, in its turn, is divided into *acute, subacute and torpid (oligosymptomatic)*;

2) *chronic trichomoniasis*, which is characterized by torpid course and duration of the disease for more than two months;

3) *trihomonas-carriage*, when in the presence of Trichomonas no any subjective and objective symptoms of the disease exist.

Clinical presentations. The incubation period of genitourinary trichomonias infection is from 3 days to 3-4 weeks (usually 7-10 days). Colonization of genitourinary tract with *T. vaginalis* leads to the development of mucosal, skin and affected organs sub-epithelial tissue inflamation. Morphological changes of epithelium are characterized by degeneration, desquamation, proliferation, metaplasia and formation of inflammatory infiltrate consisting of lymphoid elements, histiocytes and plasma cells with a mixture of leukocytes.

Often genitourinary trichomoniasis runs subjectively, without any manifestations of symptoms. More than 30-40% of women and 60-70% of men with *T. vaginalis* do not have any complaints. In pregnancy, postpartum or post-abortion period, with excessive sexual activity on the background of alcohol drinking and reduction of immunological reactivity, inflammatory process may manifest. Asymptomatic genitourinary trichomoniasis is a serious danger to the sexual partners of patients who did not know about the disease, continue to lead normal life and, thus, become a source of further infection.

Clinical manifestations of trichomonas infection depend on the location and severity of inflammatory process.

Clinical manifestations of trichomonas infection in women. In women the inflammatory process may involve vulva, vagina, urethra, lacunar channels, cervix, uterus and its appendages, large vestibular gland, bladder and renal pelvis.

In women, in 95-99% of cases, clinically genitourinary trichomoniasis manifests by affection of the lower region of genitourinary system, vaginitis, which is often combined with an infection of urethra, paraurethral ducts and large vestibular glands. Based on literature data, sometimes Trichomonas could be found in the cavity of the uterus, remote fallopian tubes and rectum. Trichomonas infection in women may be asymptomatic, but in a third of these patients clinical manifestations of genitourinary trichomoniasis develop within six months.

The inflammation of large vestibular glands of trichomonas etiology is characterized by the appearance of painful formation in the lower third of the labia majora. Clinical manifestations of Trichomonas vestibulitis are similar to those of gonococcal.

In the course of colposcopical examination in a small number of patients with vaginitis (5.2%) there are single-point hemorrhages comparable with strawberries or wild strawberry – a symptom of "strawberry" ("wild strawberry") cervix uteri defined on the mucous membrane of the vagina and vaginal cervical with iodine-negative lesions when stained with 3% Lugol's solution. Clinical signs of the disease appear cyclically and are more pronounced before and after menstruation.

Clinical manifestations of trichomonas infection in men. In men the inflammatory process involves urethra, prostate, seminal vesicles, bladder and renal pelvis. Thus, *T. vaginalis* spread throughout urethral mucosa, penetrating into its glands and lacunae. Trichomonas urethritis in men is often short-lived, transitory, apparently, due to unfavorable conditions for the existence of parasites in male urethra. In about 40% of case Trichomonas urethritis is complicated by prostatitis, which may run subjectively and without any symptoms for years. In a number of observations *T. vaginalis* causes inflammation of epididymis with tubular degeneration and infiltration of sub-epithelial and interstitial tissue, clinically, running like other non-specific epididymitis. Epididymitis is usually accompanied by trichomonas vesiculitis and/or cowperitis that occur with minimal clinical manifestations. The invasion of prostate with Trichomonas is usually asymptomatic; rarely do they register clinical inflamation in the form of catarrhal inflammation or parenchymal prostatitis. Dissemination of infection from primary lesion (urethra) is usually by transtubular way.

As a rule, *T. vaginalis* colonize organs of genitourinary system, but they also can cause ulcers and erosions on the balanus skin in males and vulva mucous membrane in women, hence there is a need for differential diagnostics with other diseases with erosive and ulcerative elements that are characteristic of syphilis, herpes etc.

Clinical manifestations of trichomonas infection in children. In children, before puberty, genitourinary trichomoniasis is rare. The classic manifestation of genitourinary trichomoniasis in girls is in the form of vulvovaginitis; rarer occur urethritis and cervicitis.

Clinical picture is characterized by profuse vaginal discharge, often of frothy nature, accompanied by intense itching and formation of erosions, not only on the mucosa of anogenital region, but also on the inner thighs. Often the course of trichomonas infection is latent, thus the frequency of the child's examination and the use of effective methods of laboratory identification of *T. vaginalis* are of great importance.

Complications of genitourinary trichomoniasis:

In women – salpingitis, salpingo-oophoritis, pyosalpinx, endometritis in various combinations;

In men – prostatitis, orchiepididymitis.

Diagnostics of Trichomoniasis. The diagnosis of trichomoniasis is set by means of identification of causative agent in biological materials. Today there is microscopic, culture, immunological and molecular and biological methods for the identification of *T. vaginalis*.

Microscopic method involves the study of native preparation and smears stained with methylene blue and by Gram's (to simultaneously identify *N. gonorrhoeae*) or Romanowsky-Giemsa method. When examining men, they prepare a smear of discharge from urethra or the sediment of centrifuged urine, while with women – they take discharge from posterior vaginal fornix. In chronic inflammatory process the agent can be localized in prostate gland, which requires microscopic examination of its secret. Negative results of microscopic examination should not be regarded as final; the survey should be repeated in 2-3 weeks. On the other hand, epithelial cells, leukocytes and macrophages present in the smears are often perceived as a modified form of *T. vaginalis*, which leads to over-diagnosis of trichomoniasis.

Immunological methods combine the methods of direct and indirect immunofluorescence (DIF and IIF).

Molecular and biological techniques involve polymerase and ligase chain reaction (PCR and LCR). They have a high specificity and sensitivity, simple and easy to use and allow detecting in one sample such bacteria as *T. vaginalis, Candida spp., Gardnerella vaginalis*, which is essential in case of co-infection of genitourinary tract.

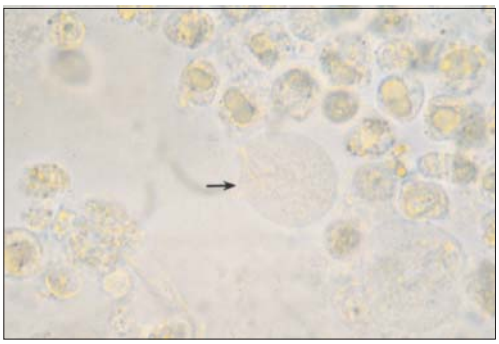


Fig. 33.1. *Trichomonas vaginalis* in microscopy of native preparation (urethra discharge). Microscopy, enlargement x1000.

Treatment. The treatment shall be applied to persons who were found positive for *T.vaginalis* regardless of clinical manifestations of the disease and patients who were negative for this type of bacteria, but their sexual partners were positive. The only group of drugs that are effective against *T. vaginalis* is derivatives of 5-nitroimidazoles, the antiprotozoal activity of which had been proved yet in 1956. It was in 1960 when

Metronidazolum was first applied to treat trichomonas infection. In the following decades there were synthesized analogues of metronidazole and a series of new drugs in this group with high activity against protozoa and anaerobic bacteria has been developed. These drugs include Ornidazole, Nimorazolum, Secnidazole.

Based on modern international guidelines on selection of single-dose and course antiprotozoal drugs to treat patients with trichomoniasis, the preference is given to single oral administration of Metronidazolum or Tinidazolum at a dose of 2.0 g

Alternative techniques involve prescription of Metronidazolum 500 mg orally two times a day for 7 days or Tinidazolum 500 mg orally two times a day for 5 days;

Methods of treatment of patients with genitourinary trichomoniasis proposed in Ukraine are as follows:

Metronidazolum (Trichopol etc.) 250 mg 2 times a day for 10 days or 250 mg three times a day for the first 4 days and 250 mg 2 times a day for the next 4 days;

- or 500 mg 2 times a day – in the first day, 250 mg 3 times a day – on the second day and 250 mg 2 times a day – on the fourth and fifth days; or 500 mg 4 times a day for 5-7 days (recommended for chronic or complicated trichomoniasis);
- or 750 mg 4 times a day – in the first day, 500 mg 4 times a day – on the second day (recommended for recent trichomoniasis with a small disease duration);
- or Metronidazolum 500 mg in 100 ml of intravenous solution (by drop infusion) 3 times a day for 5-7 days (recommended for chronic continuous course, frequent relapses, complications of trichomoniasis);
- 2.0 g single dose of Tinidazolum;
- Ornidazole 500 mg 2 times a day for 5 days.

After inflammation relief you should conduct local treatment that must be justified by uretroscopic survey. Male urethra is washed with solutions of potassium permanganate (1:1000-1:6 000) Rivanolum (1-1 000), Furacilin (1:5 000) Gibitanum (1:5000).

Women patients with genitourinary trichomoniasis are prescribed local antitrichomonad drugs in the form of vaginal suppositories or vaginal tablets (Trichopol, Tergynan). Tergynan preparation (vaginal tablets) includes: ternidazol, neomycin sulfate, nystatin, prednisolone. Respective components of Tergynan preparation determine its pharmacological properties. Ternidazol has trichomonicidal, also it is active against anaerobic bacteria, including gardnerellas. Neomycin sulfate is a broad-spectrum antibiotic of aminoglycoside group. Nystatin is an antifungal antibiotic from polyenes group and it is active against *Candida* fungi. Prednisolone is a glucocorticoid with anti-inflammatory action. The indications for use of Tergynan drug (vaginal tablets), except for trichomoniasis, include bacterial vaginitis that is caused by simple pyogenic organisms; vaginitis caused by *Candida* fungi; vaginitis caused by mixed infection (Trichomonas, anaerobic infection, yeast-like fungi).

Pregnant women patients with genitourinary trichomoniasis should be prescribed antiprotozoal systemic therapy not earlier than the end of the II – III trimester. In case of diagnosing genitourinary trichomoniasis in women in early pregnancy, you should

prescribe specific (antiprotozoal) local treatment by applying vaginal suppositories or vaginal tablets (Trichopol, Tergynan), 1 per day for 8-10 days.

Follow-up examination. Follow-up examination shall be carried out 7-10 days after the end of treatment; further examination is carried out twice at an interval of one month.

Sexual partners should be treated. Patients should be advised to avoid sexual contact until the end of the treatment and control of laboratory tests.

Prevention. Preventive measures for trichomoniasis are similar to measures for gonorrhea. These include the earliest possible detection and treatment of trichomoniasis, identifying and bringing to examination and treatment of persons who are the source of infection, as well as preventive health screening and health communication among people.

Genitourinary chlamydia infection

Genitourinary chlamydia infection is now the most common among the diseases that are transmitted mainly via sexual contact. The world is witnessing a constant increase in the incidence of chlamydia, particularly among young people who had just entered the period of sexual activity. The prevalence varies widely among different age groups in different regions of the world, but everywhere the disease is much more common than gonorrhea. Slow development of symptoms and often a complete lack of them results in late request of patients for specialized medical care.

Medical and social importance of chlamydia infection is conditioned by high incidence of morbidity and complications that significantly affect the demographics, because Chlamydia infection is the most common cause of male and female infertility.

Etiology. Genitourinary chlamydia infection is caused by *Chlamydia trachomatis*, a representative of *Chlamydiales* order, which includes 4 families, 6 genera and 13 species. Modern classification of microorganisms involves the use of strict criteria of genosystematics to describe various levels of taxonomic groups. The presence of 95% homology of nucleotide sequences of 16S and 23S rRNA genes is the basis for unification of all representatives into generum. Based on phylogenetic analysis of 16S and 23S rRNA genes, substantiated by genetic and phenotypic traits, *Chlamydia trachomatis* belongs to *Chlamydiales* order, *Chlamydiaceae* family of *Chlamydia* genus.

Based on new classification, *C. trachomatis* is an obligate human parasite responsible for a wide range of diseases, i.e.: trachoma, genitourinary infections, some forms of arthritis, conjunctivitis and pneumonia of newborns. The structure of chlamydiae cell wall is similar to the structure of gram-negative microorganisms. All chlamydiae are similar in morphology, they share genus-specific antigen presented by lipopolysaccharide (LPS) of the outer membrane of cell wall and a variety of species-, subspecies-and type-specific antigens that are protein in nature and characterized by thermolability.

Chlamydia elementary bodies are surrounded by tight rigid cell wall, which is separated from plasma membrane by electronically non-transparent periplasmatic space. The cell wall of chlamydiae has typical of gram-negative bacteria two-layer structure: it is composed of proteins, phospholipids and lipopolysaccharides. Unlike other prokaryote, chlamydiae cell wall doesn't contain peptidoglycan that is necessary to maintain its rigidity. Protein components of the outer membrane of chlamydiae consist of cysteine-rich proteins Omp1, Omp2 and Omr3 (Omp – *Outer membrane protein*). The rigidity of chlamydiae cell wall is caused by a large number of disulfide cross-links between proteins.

Approximately 60% of the total weight of membrane protein makes Omp1 – the major outer membrane protein (or MOMP – *Major Outer Membrane Protein*). Molecular weight of MOMP varies depending on the serotype from 38 to 42 kDa.

MOMP protein is a dominant antigen of *C. trachomatis*, which determines its serotype. This protein comprises four variable domains (*variable domain, VD*), disposed approximately equidistant from each other. Immunogenic properties of variable domains depend on their superficial location. In variable domains there are areas described as antigenic determinants. Chlamydia of one and the same genitourinary serovar may contain more than one serovarspecific epitope. Until recently chlamidiae have been defined using monoclonal antibodies. Using this technique, 18 servovars of *C. trachomatis* were identified and their connection with clinical manifestations of infection was shown. Thus, LI, L2, L2a and L3 serotypes found in lymphoid tissues are infectious agents of Lymphogranuloma venereum. A, B, Ba, and C serotypes cause trachoma development. D-K serotypes are causative agents of genitourinary infections and lead to the development of cervicitis, endometritis and salpingitis in women and urethritis both in men and women. Thus, chlamydia serotypes or serovars are usually divided into lymphogranuloma, trachoma and genitourinary. Recently, however, trachoma serovars were found in the genitourinary tract.

At the current stage, as an alternative for determination of chlamydiae, it is proposed to use the analysis of polymorphism of DNA restriction fragment length. This method was called genotyping and serotypes were called genotypes. This analysis allows detecting new subtypes of known serotypes. Serotype F is often associated with damage to the upper genital tract and pronounced clinical symptoms. E serotype is associated with asymptomatic infection or mild clinical signs of infection. Identification of genotypes of more virulent and capable of causing serious diseases of the upper genital tract, may serve a prognostic indicator of complications.

The life cycle of chlamydiae has been studied well enough. It provides for the change of two forms of pathogens – metabolically inactive extracellular elementary corpuscles (ECs) and metabolically active non-infectious reticular corpuscles (RC). ECs are adapted to extracellular survival. They are the carriers of specific signs of chlamydiae and at the same time represent highly infectious form of the parasite. These are tiny spherical cells 200-300 nm in diameter with electron-dense nucleoid and protoplast, which gives resistance to environmental factors. A characteristic feature of

unmodified ECs is their ability to stimulate their own endocytosis of sensitive cell and inhibit the fusion of lysosomes with the vacuole-containing chlamydiae. RC is a form of existence of intracellular pathogen 400 to 1000 nm in size that ensures reproduction of microorganism by binary fission. Transitional forms that exist in the development cycle are defined as transient corpuscles (TC). There are also persistent forms that are considered to be a deviation from normal development cycle. These forms decrease the synthesis of all major structural components that give a special strength to the cell wall. On this background, there is a continuous heat shock protein synthesis. This protein plays a key role in the development of immunopathological processes and maintaining constant inflammatory response. Thus, in particular, heat shock protein having antigenic similarity with same human protein, causes cross-autoimmune response. During the first phase, which lasts for 7 to 10 hours after infection, ECs penetrate into the cytoplasm of epithelial cells and start forming small cytoplasmic inclusions. Within 2-8 hours ECs turn into RCs. At this time there occurs attenuation of disulfide bonds between MOMP and other outer membrane proteins, which leads to increased permeability of membrane, increased transport of nutrients and increased metabolic activity. After 2 hours after penetration into the cell, expression of some genes (recA, rpoB, rpoD, groEL etc.) begins. When staining with acridine orange ECs become red, indicating the presence of RNA therein. The synthesis of chlamydiae antigens begins when host cell DNA synthesis is inhibited. During the second phase (14-22 h) mainly large RCs are observed. Within this period chlamydiae RNA and proteins are synthesized continuously. The synthesis chlamydiae DNA, as shown by greenish orange glow after acridine orange staining, begins after 14 hours. Approximately in 18 hours after infection with chlamydia cells, there begins differentiation of RCs into ECs. One may observe recondensation of chlamydia chromosome and expression of histoprotein Hcl and some outer membrane proteins. In the shell there are cysteine-rich proteins that ensure its rigidity through disulfide bonds. After 20-22 hours, new ECs able to infect new host cells appear. During the third phase (after 24-30 hours), in cytoplasmic inclusions there are mainly ECs. Cytoplasmic inclusions are colored in green, which speaks of the presence of DNA. The life cycle of chlamydia end up with decomposition of cells or exocytosis. New ECs are released into the extracellular space and infect new host cells.

Outside the cells metabolic activity of chlamydiae is very weak. The reason for this is that they are incapable of producing their own ATP and depended upon host cell energy, therefore sometimes they are called "energy parasites". Now it is known that under certain conditions, an infection caused by *C. trachomatis* is developed via persistence. In this case, the normal cycle is disturbed as all the conditions for chlamydiae transition to the persistent form has not yet been fully explored.

Epidemiology. The source of infection with genitourinary chlamydia is a person with an acute or chronic form of the disease. The main routes of transmission are sexual, contact-household. Given the common ways of transmission of sexually transmitted infections, chlamydia often occur in association with other organisms, such as gonorrhea, trichomonas, mycoplasma, ureaplasma etc.

Pathogenesis. Chlamydiae are profoundly responsive of columnar epithelium that covers mucous membrane of urethra, cervix canal, rectum, conjunctiva and the nasopharynx. The ability to infection is attributed only to EC chlamydiae. The experiments on cultivation of chlamydiae in cell culture have defined that susceptible to infection only those cells whose membrane due to the action of certain factors has lost mechanisms preventing adhesion and intrusion of EC.

ECs adhesion on cell membrane and their inside penetration are the first step in the interaction between cells and chlamydiae. By penetrating into the cell, chlamydiae inhibit fusion of lysosomes with phagocytic vacuole. EC penetrate into the cell by pinocytosis, being protected from destruction by phagosome membrane. A few ECS can be present in the cell at the same time, i.e. some groups of chlamydia microcolonies can happen to be in the cytoplasm of cells. Being in the cytoplasmic vacuoles (endosome), ECs consistently across the stage of TC (transitional corpuscles) are transformed in the RCs, which, in their turn, are subject to binary fission. At the end of fission period RCs are subject to reverse transformation into ECs. Newly formed ECs go out the cell, destroying it and infecting new cells.

Complete intracellular cycle of development under *in vivo* study continues to 48-72 hours, its duration depends on a number of factors, in particular a strain of chlamydiae, the nature of cells and medium conditions. Outside the organism chlamydiae lose their infectious properties after 24-36 hours at room temperature, are killed by ultraviolet radiation, boiling and disinfectants action. The contaminated material can keep its infectious properties for up to two days at a temperature of 18-19 ° C.

The study of immune responses to this infection showed that a lot of complications are combined with severe destructions of immune regulation. Immune response in chlamydia infection is diverse and is characterized by production of secretory Ig of A, M, G classes, inflammatory mediators (cytokines), such as IFN, IL-1, IL-4, IL-6, tumor necrosis factor etc. The type of disease course depends on human immunity, the massiveness of infection, pathogenicity and virulence of the pathogen, and many other reasons. Complications of genitourinary chlamydia infections are often combined with severe disorders of immune regulation, in particular, with a reduction in the concentration of T-lymphocytes, T-helper cells, lowered IFN-status of the patient.

Clinical picture. There are the following peculiarities in the course of chlamydia infection in men, women and choldren.

Clinical picture of genitourinary chlamydia infection in men. In vast majority of cases, chlamydia infection in men is oligosymptomatic. The most common form of the disease in men is urethritis.

Based on clinical classification similar to gonorrhea classification there are three forms of urethritis:

- *recent urethritis* (with disease duration of up to two months), which may occur *acutely, subacutely and torpidly*;

- *chronic urethritis* (with disease duration of more than two months, or with unknown duration of illness), runs torpidly, with exacerbations by type of acute or subacute urethritis;
- *latent chlamydia urethra infection* (singled out by some authors).

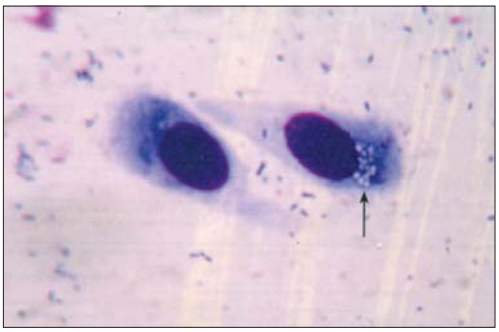


Fig. 33.2. Chlamydiae reticular corpuscles in columnar epithelium cell. Romanovwsky-Giemsa stained. Microscopy, enlargement x 1000.

Recent and chronic urethritis are divided into *anterior*, when inflammatory process is limited to the anterior segment of urethra, and *total*, when inflammatory process is spread proximal to the external urethral sphincter.

Acute urethra inflammation is rare, and the patients are concerned with serous or seropurulent urethral discharge, painful and frequent urination. Even without treatment within a few days or weeks acute urethritis symptoms subside, and the inflammation becomes subacute or torpid. In *recent torpid chlamydia urethritis* inflammation, in most cases, is limited to the defeat of the anterior segment of urethra. In practice, the more common are subacute or torpid courses of urethritis, when patients do not complain at all and chlamydiae detection occurs by accident, or complain of a little itchy in the urethra and meager discharge. When examining, you may notice slight swelling and redness of urethral lips.

During exacerbation of *chronic chlamydia urethritis* patients' complaints and clinical picture are consistent with recent acute and subacute urethritis, and lesions totally cover the anterior and posterior segments of urethra. Exacerbation occurs after consumption of alcohol, spicy food, sex, exposure to cold or other factors that reduce protective properties of the microorganism. Ureteroscopy in chronic chlamydia urethritis reveals mucosal changes that are consistent with the picture of soft, transitional or solid infiltrate.

In *latent chlamydia infection* objective and subjective symptoms are absent; the diagnosis is set on the basis of detection of chlamydia in urethra scrapings. There is possible transformation of latent infection into clinically apparent disease, the cause of which may be associated with concomitant diseases of genitourinary tract with other etiologies.

Genitourinary complications. The spread of infection on to above areas of genitourinary tract leads to the development of complications, among which a special place is occupied by an inflammation of prostate gland.

Prostatitis in most cases occurs as primary chronic process. There are four symptoms of this complication – a *painful, dysuric, sexual, reproductive*. Each of these symptoms may be the only symptom or manifestation of primary disease.

Pain is localized in the perineal area, and irradiation may be in the rump, anus, suprapubic area, urethra, testicles. The intensity of pain varies from paresthesia to the

feeling of heaviness and pressure followed by severe pain. Pain may increase with prolonged sitting, bumpy ride, defecation etc.

Dysuric symptoms include pollakiuria, dysuria, nocturia, sluggish stream of urine, sometimes strangury. Given the fact that all of these symptoms can be observed in BPH, it is necessary to carry out differential diagnostics of this disease in men aged 45 years and older. Dysuria with prostatitis is often caused not only by urethra inflammation, but also it involves bladder neck in the process.

The emergence of sexual dysfunction in some patients with changes in the prostate depends on the involvement of adjacent organs (seed tubercle, seminal vesicles) into inflammation process. In this case, even the most minor infractions as rapid ejaculation and certain unpleasant feelings can cause neurotic disorders in the patient, which, in its turn, closes the circle of neurotic symptom complex. Sometimes, chronic prostatitis is latent, when there are no symptoms for years, and the disease manifests itself in copulatory and reproductive dysfunctions or only one of them. This can occur on the background of genetically determined congenital hypoandrogenism. It may however be caused by prolonged inflammation in prostatic acini.

Common symptoms of chronic prostatitis include fatigue, weakness, low-grade fever, which is probably due to intoxication and hormonal disorders. Long-term course of the disease, the presence of multiple symptoms, excessive focus on existing problems lead to the development of neurotic disorders. Vegetative local and general reactions lead to the appearance of paresthesias in patients, anorectal itching, perinea sweating.

Prostatitis is characterized by alternation of active phases with periods of remission. Without treatment, chronic chlamydia prostatitis can continue for an indefinite period of time. The result of this process depends on its form, state of macroorganism and therapy effectiveness. At a superficial inflammation of the prostate and early treatment a patient can recover with full restoration of function, while in case of late treatment parenchyma is replaced with scar tissue.

The spread of contagious agent from the back of urethra through spermduct to the epididymis leads to the development of *epididymitis*. *Acute epididymitis* is manifested by intense pain in the corresponding part of the scrotum, the skin of which is congested, swollen and hot to the touch. The body temperature rises to 39 ° C. When examining epididymis by touch it is defined as a helmet, covering the bottom and the back surface of the testis. The appearance of serous effusion in the egg shell (*periorchiepididymitis*), involvement of testis into the process (*orchiepididymitis*) result in palpation of scrotum organs as a single conglomerate, in which it is difficult to distinguish the egg from epididymis. Spermduct can also be involved into pathological process (*vasitis*), which is palpable in the form of a painful cord. Spread of inflammation to the surrounding tissue of spermatic cord leads to its inflammation (*funiculitis*). Without treatment, within 2-3 days, all the painful events are increasing, and in the next 2-3 weeks they gradually subside, the effusion between shells resolves, but may remain scars in the tail of epididymis, which disrupts the patency of

ductuli efferentes. However, impairment of fertility is not always associated with mechanical causes. Immune mechanisms of self-aggression may play one of the important roles in development of infertility.

Extragenital complications. Among the most frequent extragenital complications are ophtalmochlamydia infection, reactive arthritis that form the symptomatic complex of Reiter's disease, to include pharyngitis and proctitis.

A serious complication of chlamydia infection is Reiter's syndrome (*syndromum urethrooculosynoviale*). The disease develops in individuals with a genetic predisposition; it often affects HLA B27antigen carriers. Men suffer 20 times more often than women. The disease is characterized by combined lesion of urinary organs (genitourinary prostatitis, xerotica balanitis), eyes (conjunctivitis), joints – by type of asymmetric reactive arthritis and skin (psoriasiform rash, keratoderma of palms and soles). The disease usually occurs with repeated attacks and remissions. *C. trachomatis* or its antigens are found in synovial fluid samples obtained from diseased joints.

Clinical picture of genitourinary chlamydia infection in women. Chlamydia infection in women is associated with impaired reproductive function and infectious complications in the form of inflammatory diseases of pelvic organs, tubal infertility and ectopic pregnancy. Clinical manifestations of genitourinary chlamydia infection vary from expressed inflammation events to asymptomatic carriage. They single out the affection of the lower region of genitourinary tract (endocervicitis, urethritis, paraurethritis and bartholinitis) and ascending infection (endometritis, salpingitis, salpingoophoritis, pelvioperitonitis, perihepatitis). The spread of chlamydia from foci located in the lower genitourinary tract, promote abortion and other operations, including extragenital. Often, the process becomes complicated and manifests by the development of infertility. Chlamydia infection is multifocal. In the vast majority of cases, the process is asymptomatic or with poor clinical symptoms and is often associated with other genitourinary infections. In women cervical canal is most often affects than urethra.

Urethritis in women occurs less often than in men, and due to their anatomy, it is accompanied by less severe symptoms, including slight leukocytosis in microscopy of scrapings from urethra.

Bartholinitis is an inflammation of large vestibule glands. It is often manifested in the form of catarrh with lesions on mouth ducts only. The development of an acute process with a fever, severe pain and formation of abscess in big vestibule gland, is possible only with concomitant infection with gonococci and pyogenic microbes.

Colpitis is rare as chlamydia do not breed in the stratified squamous epithelium, and outside the cells, they are sensitive to vagina acidic reaction. Primary colpitis is possible only in case of change in endocrine profile, in women of post-menopausal period, pregnant women and girls.

C. trachomatis can cause urethral syndrome, characterized by dysuria, pain in the urethra, and sometimes pain in the lower back. Often chlamydia cervical lesions, morphologically, are characterized as follicular cervicitis and erosive affection of cervix.

Endocervicitis is frequent, the most typical and common manifestation of genitourinary chlamydia infection in women, it is its most common clinical form. However, chlamydia can attack vulva in newborn girls, and vaginal vault in women who have undergone hysterectomy.

Chlamydia cervicitis is the main source of infection for men and children. Clinical manifestations of cervicitis occur in about 3-4 weeks after infection and are accompanied by dysuric disorders. Some women complain of itching and burning in the perineal area, whites and lower abdominal pain. Cervicitis runs with scant mucous purulent discharge, the appearance of inflammatory halo around the external os to form a peculiar lymphoid follicles in the external os (*follicular cervicitis*) and light vulnerability of this site. The discharge from cervical canal macerate stratified squamous epithelium of vaginal part of cervix, thus causing its partial desquamation. The cervix becomes edematous and so-called hypertrophic ectopia appears. A kind of an infected cervix can vary from clinically normal to erosive, with thickened edematous mucosa and lots of mucous purulent discharge.

Likewise in other genitourinary infections, genitourinary chlamydia infection in women, besides cervix, affects urethra and paraurethral ducts, to include rectal mucosa. *Proctitis symptoms* develop less than urethral syndrome. Proctitis is characterized by rectal bleeding and absence of diarrhea. Approximately in two thirds of women proctitis is caused by passive dissemination of vaginal discharge, and in a third – because of anogenital contact. Bartholinitis of chlamydia etiology occurs relatively rare.

Characteristic of *chlamydia cervicitis* symptoms that can be minimally expressed include: cervical contact bleeding, mucous-purulent discharge from the cervix and pseudoerosions.

Due to the close connection of cervical duct and uterine, inflammatory lesions of cervix are almost always accompanied by the appearance of processes covering the endometrium. *Chlamydia endometritis* may occur in acute and chronic forms, when the latter is accompanied by uterine bleeding. Chlamydia endometritis develops slowly. Postpartum and post-abortion periods contribute to the emergence of chlamydia endometritis. Chronic chlamydia endometritis in its pure form is rare; it is often accompanied by chronic salpingitis or salpingoophoritis.

Among all of chlamydia genital lesions *salpingitis* attracts due to the frequency of the disease and pronounced clinical symptoms.

Acute salpingitis is a severe systemic disease. Clinical diagnosis of acute salpingitis is relatively simple – it is established on the basis of severe pain in the abdomen, pain on palpation, increased body temperature, high leukocytosis, accelerated erythrocyte sedimentation rate.

Inflammatory diseases of pelvic organs are a group of independent clinical entities, witnessing of the presence of bottom-up process including any combinations of endometritis, salpingitis, oophoritis, tubo-ovarian abscess and pelvic peritonitis.

The spread of chlamydia infection in the peritoneal cavity leads to the development of perihepatitis known as Fitz-Hugh-Curtis syndrome. Peritonitis and

perihepatitis complicate genitourinary chlamydia infection predominantly in young women. The onset of the disease is sudden; there are sharp pains in the abdomen and in the right upper quadrant extending into the right shoulder blade and shoulder, positive peritoneal signs, fever and intoxication. Fitz-Hugh-Curtis syndrome can occur after such interventions as hydrotubation.

Genital chlamydia infection can also occur in pregnant women. The likelihood of adverse pregnancy outcomes and fetus affection in pregnant women depend on the severity of genitourinary chlamydia infection, duration of the disease and the adequacy of treatment. Clinical picture of genitourinary chlamydia infection in pregnant women is the same as that of non-pregnant.

Clinical picture of chlamydia infection in children. A common clinical form of chlamydia in newborns is conjunctivitis (so called *conjunctivitis with inclusions*), non-severe disease, which does not cause much anxiety in neonatologists. The disease is characterized by diffuse conjunctival hyperemia, bonding of eyelids after sleep, no copious purulent discharge. However, in line with conjunctivitis or later in infancy, there appear other clinical forms of chlamydia infection acquired before birth or during the passage via birth canal. These include pharyngitis, pneumonia, vulvitis and vulvovaginitis, urethritis, which are asymptomatic in most cases.

Diagnostics of chlamydia infection. *Laboratory Diagnostics* of chlamydia infection is of paramount importance because clinical manifestations are non-pathognomonic and much common are atypical and asymptomatic forms of the disease. The development of laboratory methods for diagnostics of genitourinary chlamydia infection is directly associated with understanding of biological characteristics of chlamydiae, their antigenic structure, the pathogensis of infection process caused by this agent, to include the overall progress in the field of diagnostics of infectious diseases.

The quality of diagnostics of genitourinary chlamydia infection depends on the correctness of taking clinical material, the compliance with terms of its delivery to the laboratory and use of high-quality diagnostic tests. To isolate chlamydiae you should investigate biological materials from different sources, often scrapping smears from men's urethral mucosa and women's cervix and urethra. With the introduction of molecular biology techniques it became possible to study non-invasive clinical samples, such as the first portion of freely released urine in men and vaginal discharge in women. If necessary, study material is taken from the rectum, nasopharynx and lower eyelid conjunctiva. In children you should explore the discharge from lower lid conjunctiva, the rear wall of pharynx, vulva in girls. Based on clinical signs, you may study biopsy and surgical materials.

Such methods of diagnostics as culture, immunofluorescence test, PCR, ELISA test are used to study materials obtained from the cervix, urethra, rectum, nasopharynx, conjunctiva, biopsy and surgical materials. To study the first portion of urine and vaginal secretions only PCR is used.

Cytoscopical method of diagnosing genitourinary chlamydia infection involves the study of Romanowsky-Giemsa stained biological materials using light microscopy. The criterion for detecting chlamydiae in this case is the presence of Halberstadt-Provazek corpuscles in the cytoplasm of infected cells. Light microscopy makes it possible to find large blue-violet vegetative forms (RC) and small pink infectious forms (EC). Cytoscopical method is widely available, but is effective only for acute forms of infection and requires qualified assessment of cytological picture. In genitourinary chlamydia infection the frequency of detection of Halberstadt-Provazek corpuscles in scrapings from urethra and cervix usually does not exceed 10-12%.

Immunomorphological methods (Immunofluorecsence test, ELISA test) are based on detection of chlamydia antigenic substance in the epithelium and other tissues. The sensitivity of immunofluorecsence test is 80-90%, while specificity – 98-99%. According to various researchers, the sensitivity of ELISA test ranges from 60 to 80%. Immunofluorecsence test and ELISA test are not suitable for the study of materials obtained from rectum, nose, throat, and urine samples.

One of the most objective methods of chlamydia infection laboratory diagnostics is the isolation of the pathogen from affected tissues in McCoy cells culture (*culture method*). This method is labor intensive, besides from 1 to 4 weeks is required to get the response. It has been recognized as gold standard all over the world and has one hundred percent of specificity. It should be stressed that, being the gold standard for specificity, the culture method is inferior to the rest by sensitivity. The sensitivity of this method in the study of a sample from cervix makes 75-80%.

Amplification tests aimed at identifying nucleic acids of chlamydiae, such as polymerase chain reaction (PCR), have a sensitivity of at least 93-96%.

Now the most promising and highly sensitive are molecular and biological methods chlamydiae detection i.e. PCR, hybridization reaction, RNA detection, SDA, NASBA, etc.

Serological studies relate to the subsidiary methods of diagnostics of genitourinary chlamydia infection. They can detect IgM, IgA, IgG in the serum, which is especially important for chlamydia detection in children, in complicated process in adults when the use of other methods of detecting the pathogen or its antigen is impossible, and in mass epidemiological studies.

Thus, it should be noted that today there are many different methods for chlamydia infection diagnostics. It is important to choose the most reliable, allowing setting correct diagnosis and to timely carry out and monitor the specific therapy.

Treatment. The treatment of patients with genitourinary chlamydia infection is subject to general principles of management of infectious patients. The therapy should be integrated and etiologycally, pathogenetically and symptomatically differentiated according to the clinical form of inflammatory process, the nature of affection, the severity and duration of illness.

Causal treatment of genitourinary chlamydia infection must meet a number of requirements, in particular to high degree of penetration of antichlamydia drug into the cell, its accumulation and to the ensurance of inhibitory concentration at the point where the agent is localized.

To treat patients with chlamydia infection they use such antibiotics as tetracyclines, macrolides and fluoroquinolones.

The *group of tetracyclines* includes antibiotics that are congenial by chemical structure, antimicrobial spectrum and mechanism of action and that are assigned according to the following schemes:

Tetracyclinum and Oxytetracycline orally after meals, 500 mg 4 times per day for 7 or 14 days;

Metacyclinum – 300 mg four times a day for 7-10 days;

Doxycyclinum – 100 mg 2 times a day for 7-14 days.

Macrolides are broad-spectrum antibiotics, which are characterized by the presence of macrocyclic lactone ring in their molecule. There are known natural (Erythromycinum, Oleandomycinum, Josamycinum and Spiramycinum) and semisynthetic (Azithromycin, Roxithromycine, Clarithromycin etc.), macrolide antibiotics that are assigned according to the following schemes:

- Erythromycinum – 500 mg four times a day for 7-10 days;
- Azithromycin – 1000 mg once daily;
- Azithromycin – 500-1000 mg a day, 3000 mg per course;
- Josamycinum – 500 mg 2-3 times a day for 7-10 days;
- Clarithromycin – 250 mg 2 times a day for 10 days;
- Spiramycinume – 3 million IU 3 times a day for 10 days.

Such drugs as Azithromycin Josamycinum, Clarithromycin penetrate well into the various tissues and biological fluids, thus creating high and stable concentration of the drug, which is much higher than in serum. Macrolides are referred to the safest antibiotics due to a minor number of possible side effects.

Fluoroquinolones are fluorinating derivatives of nalidixic acid, the spectrum of activity of which involves mainly the action of gram-negative bacteria.

Treatment for pregnant women. In compliance with applicable guidelines, the following treatment is proposed: Erythromycinum 500 mg orally four times daily for 7 days; Erythromycinum 250 mg orally 4 times a day for 14 days; Amoxicillin 500 mg orally 3 times a day for 7 days; Azithromycin 1,0 g orally once; Josamycinum 750 mg orally 2 times a day for 7 days.

The approaches to local treatment of genitourinary chlamydia infection should meet the following principles:

a) selection of an adequate dosage form for optimal use in a particular patient (ointments, gels, suppositories etc.);

b) multivectoral action of drugs that should have bactericidal or bacteriostatic effect, as well as anti-inflammatory and anti-allergic effects, improve microcirculation, promote phagocytosis, restoration, etc.

Standard local measures traditionally involve washing, douching (of urethra, vagina) with a solution of potassium permanganate (1:8000) in alternation with instillation of 1.2% Protargolum solution, 1-2% Collargolum solution during 10-15 days.

Officinal local media that have antichlamydia activity include vaginal suppositories and Betadine cream as well as Erythromycinum and Tetracyclinum ointment.

Follow-up examination. After the treatment of patients with genitourinary chlamydia infection follow-up examination should be carried out not earlier than in 3-4 weeks. PCR study examination conducted earlier than 10-14 days after antibiotic therapy, can give false positive results. To control the cure it is desirable to use two methods (culture in combination with PCR or immunofluorescence test in conjunction with PCR), when, at the same time, you may use RT-PCR method and real-time NASBA.

Detection of chlamydiae one month after the treatment requires the appointment of a repeated course of therapy with other groups of drugs, the duration of which shall not exceed 7-10 days.

Prevention. Prophylaxis of chlamydia infection is not significantly different from prophylaxis of other sexually transmitted diseases. First of all prophylaxis shall involve comprehensive and timely treatment of patients, elimination of infection in asymptomatic carriers of the pathogen, detection and qualitative examination of patients -sexual partners, administration of prophylactic treatment, use of condoms, health education of the population and especially high-risk groups.

Genitourinary mycoplasmosis

Genitourinary mycoplasmosis is a group of diseases caused by mycoplasma and proceeding with affection of human genitourinary system. Mycoplasmosis plays an important role in the onset of inflammatory diseases of genitourinary organs such as: urethritis, cystitis, pregnant women, fetuses and infants pathology and may be a cause of infertility.

Etiology. Mycoplasma is a group of diverse in shape (spherical, annular, coccobacillus, filamentous, branching), gram-negative organisms of small size (150-200 nm). They do not have a dense cellular wall; they are coated with cytoplasmic membrane and do not take the most dyes. Mycoplasmas are intermediate between bacteria and protozoa. Mycoplasmas multiply in several ways – binary fission, the release of elementary bodies formed in the threads and budding. Grow well in specific cell-free artificial media, forming colonies with a dark center and a lighter periphery (in appearance like a fried egg).

Mycoplasmas comprise urease, which splits urea to ammonia.

Mycoplasmas belong to *Mycoplasmataceae* family being a member of *Mycoplasmatales* order of *Mollicutes* class. This class is divided into two genera – *Mycoplasma*, which includes about a hundred of species, and *Ureaplasma*, which has only three species. Now there are five species of mycoplasmas causing human

disease. These are *M. pneumoniae, M. genitalium, M. hominis, U. urealyticum, M. incognita*. A group of urea-mycoplasmas that is associated with genitourinary infections includes *M. genitalium, M. hominis, U. urealyticum*. Among all mycoplasmas the most pathogenic properties are assigned to *M. genitalium*.

Epidemiology. Infection with genitourinary mycoplasmosis often occurs through sexual contact. It is also possible to infect via contact-household way, especially for women and girls. Infection can penetrate through various household items (bedding, a pot) or medical instruments in obstetric and gynecological and urological offices, unless disinfection rules are complied. There has been defined the possibility of intrauterine infection of the fetus and infant exposure when passing through an infected birth canal.

Epidemiology. Genitourinary mycoplasmosis takes one of the first places in the pattern of diseases that are predominantly sexually transmitted. Mycoplasmosis is detected with trichomonal (in 40-69% of cases), gonococcal (in 22-30% of cases) and chlamydia (int 6-15% of cases) acute and chronic inflammations of genitourinary tract. *M hominis, U. Urealyticum* are found in no less than 50% of sexually active men and women, the most vulnerable are people aged 30-40 years. In clinically healthy persons mycoplasmas are detected in 5-15% of cases. Some researchers consider this fact as asymptomatic infection (carriage) that may be activated during pregnancy, childbirth, exposure to cold, stress and lead to abortion or sepsis.

There are certain factors that activate the development of mycoplasma infection in genitourinary tract. These include infection of a different nature – bacterial, viral, chlamydial, fungal, etc.; hormonal changes and some other changes in physiological and immune status.

Genitourinary mycoplasmosis incubation period (the duration of which is still unclear) can range from 3 days to 5 weeks, and this period in patients with an acute course of the disease during is shorter than in patients with prolonged or subacute forms of the disease.

Clinical presentations. Classification of genitourinary mycoplasmosis is based on the topics of affection. Specialists single out mycoplasmosis in men, women and children, which also includes: mycoplasma urethritis, balanitis, prostatitis, epididymitis, cervicitis, bartholinitis, endometritis, salpingitis etc.

Genitourinary mycoplasmosis in men. The affection in genitourinary mycoplasmosis is characterized by a variety of clinical manifestations – from acute to oligosymptomatic and torpid. There is recent mycoplasmosis (with acute, subacute and torpid course) for a term of up to two months of illness and chronic mycoplasmosis with more than two months process duration. In men, mycoplasmosis affects urethra, lacunar ducts, prostate, seminal vesicles, epididymis and urinary bladder.

Clinical picture of genitourinary mycoplasmosis does not differ significantly from the lesions of other etiologies. However, attention is drawn to a higher percentage of torpid and subjectively asymptomatic forms and mycoplasmocarriage. Mycoplasmas

can persist for a long time in lacunar ducts, causing disease recurrences and spread of infection. Lacunar ducts are primarily or secondarily infected from urethra.

Most often infection penetrates into the prostate and seminal vesicles. There are several forms of prostatitis occurring torpidly with a variety of subjective feelings.

With mycoplasmal epididymitis, which is characterized by unilateral affection, inflammation often spreads to the tail and body, rarely to the head of the epididymis. In most cases of mycoplasma epididymitis develops gradually, torpent, symptoms are vague, sometimes in the form of uncertain pulling pain in the groin, perineum and in the relevant part of the scrotum. The pain that gradually increases is not too pronounced. In 1-2 days, the inflamed epididymis increases and becomes dense. Changes in the scrotal skin are slightly expressed. Often the affection of epididymis occurs on the background of low grade or normal body temperature.

There is possible balanitis and balanoposthitis in which patients complain of a slight itching and discharge out of the foreskin, where often mycoplasmas are found. Affected areas of foreskin may be hyperemic, edematous, eroded.

Genitourinary mycoplasmosis in women. There is mycoplasmosis of external and internal genital organs. The affection of external genitalia occurs predominantly without subjective sensations. Mycoplasmas affect vagina, lacunar ducts, urethra, vestibule of vagina, small and large vestibular glands and cervix. New forms of the disease occur rarely. They are characterized by short-term poorly marked itching and minor transient watery discharge from vagina and urethra. During chronic process, patients complain of periodic itching, minor discharges that periodically disappear. In some women, genitourinary mycoplasmosis is asymptomatic.

Pathogens can affect upper region of female reproductive organs and lead to the development of endometritis, salpingitis, oophoritis, adnexitis, pelvioperitonitis, which clinically occur the same way as other genitourinary infectious diseases.

The frequency of mycoplasma detection in pregnancy varies widely. During pregnancy, there activate asymptomatic and latent forms of genitourinary mycoplasma, which often end in miscarriage, stillbirth or baby birth with low birth weight. The condition of post-abortion and post-natal women suffering from mycoplasmosis may be complicated by fever, endometritis, salpingitis, adnexitis.

The role of mycoplasma infection in the development of infertility has not been finally established. Judging by the results of several studies, mycoplasmas are equally found in normal and infertile couples. At the same time, in men with *U. urealyticum* it is possible to detect morphological changes of sperm using electronic microscope.

Genitourinary mycoplasmosis in children. Newborn babies are infected during passage via birth canal. Detection of *M. hominis* in infants is often associated with premature and early discharge of amniotic fluid, fever during labor and postpartum period in their mothers. Affected children may develop pneumonia, abscesses, meningitis, vulva, encephalitis, in which mycoplasmas are isolated in the lesions. In some time after the birth mycoplasmas disappear in a part of children. It is assumed that the pathogen also plays a role in causing birth

defects. This point of view is due to frequent detection of mycoplasma in children with disabilities.

Diagnostics. Customary for detection of mycoplasma is bacteriological research method. Study material is a discharge from affected organs of genitourinary system. *M. hominis* is cultured on liquid and solid media. 200-300 microns size colonies resemble a fried egg. *M. hominis* cleaves arginine amino acid to form ornithine and ammonia, which makes the medium more alkaline and leads to the change of color of indicator added to the medium. Ureaplasmas grow on agar medium supplemented with urea in the form of fine dark brown or brown-black colonies 15-30 microns in diameter. Ureaplasma indication is based on their ability to decompose urea into carbon dioxide and ammonia, that causes a change in medium reaction from acidic into alkaline and, accordingly, in the indicator's color (bromothymol blue) from lemon yellow to green or blue, depending on the height of titres.

Among serological methods of study they use complement fixation test (CFT) with glycolipid antigens and f passive hemagglutination test (PHT) with tannin sensitized red blood cells, indirect (IIF) and direct (DIF) immunofluorescence test.

Treatment. Causative treatment of patients with genitourinary mycoplasmosis is conducted with antibiotics active against mycoplasmas. The most effective are tetracyclines and macrolides.

Tetracyclinum is administered orally at a dose 500 mg 4 times per day, while Doxycyclinum 100 mg 2 times a day for 10-14 days; Erythromycinum 500 mg 4 times per day for 10-14 days; Azithromycin 1.0 g (4 capsules) on the first day orally once, then 500 mg (2 capsules) per day per one time for 4 days.

Follow-up examination. In determining the recovery of patients with mycoplasmosis in 7-8 days after the course of treatment you should re-investigate discharges from dufferent lesions – urethra, lacunar ducts, vagina, cervix, etc., and in men – discharge from prostate, seminal vesicles and ejaculate. Of critical importance is the monitoring of patients after completion of treatment for mycoplasma during 2-3 months.

Prevention of genitourinary mycoplasmosis is the same as with other genitourinary infections. An important component of prevention is health communication with specification of different forms and courses of mycoplasma infection symptoms, ways of its distribution and possible consequences of the disease.

Bacterial vaginosis

Bacterial vaginosis is one of the most common diseases of genitourinary system, which is often diagnosed in association with other pathogenic and opportunistic microorganisms.

One of the causative agents of bacterial vaginosis is *Gardnerella vaginalis*.

Gardnerella vaginalis is immovable gram-negative bacillus devoid of capsule (however, there are often gram-variable variants can be met), up to 2 microns in length and from 0.7 to 0.9 microns in diameter.

Epidemiology. The main mode of infection transmission is sexual. A newborn can be infected when passing through the mother's birth canal; intrauterine infection of the fetus is also possible.

Pathogensis. The pathological process may involve all departments of genitourinary system in both men and women. The infection may cause the development of severe inflammation in infants (meningitis, pneumonia) and obstetric complications.

Clinical presentations. The incubation period of the disease in average is 7-10 days, but it can range from 3 days to 5 weeks. Women suffer from vaginitis and ecervicitis.

If *acute course* the patients note discomfort in the genital area, itching, vulva burning, vaginal discharge. Objectively, there is hyperemia of the mucous membrane of vulva, vagina and abundant thick turbid discharge with "fishy" odor, which accumulate in the posterior vaginal fornix or coat vagina and cervix with thin film. Urethral lips are hyperemic, edematous. After massage there is a slight discharge from urethra. Vaginal portion of cervix is hyperemic, there is scant discharge from cervical canal resembling vaginal discharge.

In *torpid course* there is short-term itching in the area of external genital organs, scant periodic discharge from vagina or urethra. In typical cases, the discharge is slight, grayish-white, watery, with unpleasant "fishy" odor as a result of the collapse of amines produced by anaerobic bacteria that are actively multiplying in Gardnerella vaginitis.

Diagnosis. Study material is taken out of urethra, the posterior vaginal fornix and cervix.

Microscopic examination:

- native speicements show flat epithelial cells, to the surface of which gardnerella are attached, thus making characteristic "peppered" form; such cells were named "key cells" (pathognomonic sign of gardnerellosis);
- Gram stained smears show individual leukocytes, a considerable amount of fine, usually negative, occasionally gram-positive bacilli located on epithelial cells;

Bacteriological examination:

The optimal medium to culture gardnerellas is blood agar. The culture is incubated in an oxygenfree environment. Colonies of up to 0.5 mm in diameter are transparent, convex, with a grayish bloom and zones of hemolysis. In smears they reveal gardnerellas i.e. bacilli with twisted ends, located singly or in short chains.

They carry out the test with 10% KOH solution (vaginal content in the amount of one droplet is mixed with one drop of 10% KOH solution). If there is a positive reaction a smell of "rotten fish" caused by abnormal amines appears.

The diagnosis should be set on the basis of the following criteria:

- the presence of "key" cells (vaginal epithelial cells covered with small gram-variable bacilli);
- additional sign – low white blood cell count in the material;
- positive test with 10% KOH solution.

The differential diagnostics is carried out with gonorrhea, trichomoniasis and chlamydia infection.

Treatment. There are common and local therapies.

Antibacterial therapy may include tetracyclines, semi-synthetic tetracycline, macrolides and fluoroquinolones.

Genitourinary Candidiasis

Genitourinary candidiasis is a chronic, often relapsing disease caused by yeast-line fungi of *Candida* genus. Etiology, clinical manifestation and treatment has already described in the chapter 7.

1. A group of non-gonorrheal contagious diseases includes lesions caused by:
- **A.** Trichomonas vaginalis
- ***B.*** *Chlamydia trachomatis*
- **C.** Candida
- **D.** Gardnerella vaginalis
- **E.** All the aforementioned is true

2. The affection of which organs is not typical of trichomoniasis, chlamydia infection and mycoplasmosis:
- **A**. Prostate
- **B**. Seminal vesicles
- **C**. Kidney
- **D**. Testicular
- **E**. Epididymis

3. Gardnerella vaginalis is:
- **A**. Mycoplasma
- **B**. Gram-negative bacilli
- **C**. The spirochetes
- **D**. Gram-positive diplococcic
- **E**. All of the above is true

4. To diagnose genitourinary chlamydia infection they apply:
- **A**. Inoculation on Saburo medium
- **B**. Pathogen isolation on meat-peptone agar
- **C**. Pathogen isolation on McCoy cells
- **D**. Inoculation on blood agar at 37 ° C under anaerobic conditions
- **E**. All of the above is true

5. To diagnose trichomoniasis in women they use:
- **A**. Urethra discharge
- **B**. Urine "threads"
- **C**. Perianal surfaces smear
- **D**. Posterior vaginal fornix discharges
- **E**. All of the above is true

6. Reiter's disease pathogens are:
- **A**. Chlamydia trachomatis
- **B**. Trichomonas
- **C**. Gram-positive diplococcus
- **D**. Gram-negative diplococcus
- **E**. Gardnerella vaginal

7. There are the following methods of trichomoniasis diagnostics:
- **A**. Microscopic
- **B**. Culture
- **C**. Immunological
- **D**. Molecular biology
- **E**. All of the above items are true

8. To treat urethritis caused by Candida fungi, it is advisable to apply:
- **A**. Polymyxinum
- **B**. Kanamycinum
- **C**. Ofloxacinum
- **D**. Itraconazolum
- **E**. Penicillin

9. To treat genitourinary trichomoniasis they use:
- **A**. Metronidazolum, Ornidazole
- **B**. Metacyclinum, Doxycyclinum
- **C**. Medrol, Itraconazolum
- **D**. Macropen, Erythromycinum
- **E**. Benzylpenicillin, Amoksiklav

10. Causative treatment of patients with genitourinary mycoplasmosis includes the following group of drugs:
- **A**. Doxycyclinum, Tetracyclinum, Erythromycinum
- **B**. Ofloxacinum, Ciprofloxacinum
- **C**. Trihopol, metronidazole
- **D**. Itraconazolum, Fluconazole
- **E**. Penicillin, Bicillin

Task 1. The doctor was appealed by the patient complaining of slight discharge from urethra, pain in the perineum, which is stronger during defecation, weakening of erection and ejaculation. From history we know that the patient after casual sex often imposes self-treatment with large doses of antibiotics. In smears and crops of discharge from urethra no any gonorrhea, trichomonas or any other bacteria were detected.

a) What disease can be anticipated?
- **A.** Candida urethritis
- **B.** Trichomonas urethritis
- **C.** Gonorrheal urethritis
- **D.** Chlamydial urethritis
- **E.** Gardnerella urethritis

b) What other additional studies are needed to accomplish?

Task 2. 30 years old woman, married, with a child of three years old, appealed to the doctor in 10 days after a single sexual encounter with a stranger complaining of vaginal discharge that smell like "tainted fish".

a) Put the preliminary diagnosis:
- **A.** Mycoplasmosis
- **B.** Gardnerellosis
- **C.** Gonorrhea
- **D.** Chlamydia infection
- **E.** Trichomoniasis

b) Determine doctor's tactics as referred to the patient's husband and child.

Task 3. The patient is 25 years old, single, have multiple sexual partners. In the last three months noticed slight mucoserous discharge from urethra; subjectively – intermittent itching or burning sensation in the ureter. Two months ago there was a pain in the knee joint. At the same time the patient neither got hurt, nor supercooled. A week ago, he felt discomfort in the eyes – watery eyes, itching.

a) Which probable pathogen has caused the disease?
- **A.** *Trichomonas vaginalis*
- **B.** *Chlamydia trachomatis*
- **C.** *Candida*
- **D.** *Gardnerella vaginalis*
- **E.** *Neisseria gonorrhoeae*

b) Determine the tactics of the patient's treatment.

Task 4. A woman complains of constant itching of moderate intensity in vulva that worsens before menses and subsides after its completion. *On examination*: mucous membranes are stagnant hyperemic, infiltrated, lichenificated. Whitish plaque resembling cottage cheese found on the surface of large and small labia minora.

a) Which infection led to the emergence of this disease?
- **A.** *Trichomonas vaginalis*
- **B.** *Chlamydia trachomatis*
- **C.** *Candida*
- **D.** *Gardnerella vaginalis*
- **E.** *Neisseria gonorrhoeas*

b) What studies are required to confirm the diagnosis?

Task 5. 24 years old patient appealed to family medicine clinic with complaints of pain in the knee joints, fever up to 37.7 C, pain during urination and a feeling of sand in the eyes. The patient has been sick for the past 6 weeks. Has no regular sexual partner. *Objectively*: the affected joints are swollen; movements are painful and somewhat limited. Feet hyperkeratosis. Blood test: WBC – 9.3 x 109 / l, ESR – 32 mm / hour. Rheumatoid factor test is not available.

a) What kind of infection is possible in this case?
- **A.** Trichomonas
- **B.** Chlamydia
- **C.** Candida
- **D.** Gonococcal
- **E.** Staphylococcal

b) Put the preliminary diagnosis and determine the ways of its specification.

Answers to the quiz of the first level of complexity
1 – E; **2** – C; **3** – B; **4** – C; **5** – D; **6** – A; **7** – E; **8** – D; **9** – A; **10** – A
Answers to the quiz of the second and third levels of complexity
1a – D; **2a** – B; **3a** – B; **4a** – C; **5a** – B

Infection caused by human immunodeficiency virus (HIV/-infection) Skin and mucous membranes affection with AIDS

34 TOPIC

Infection caused by human immunodeficiency virus (HIV) is a new contagious disease, which spreads rapidly and is characterized by the staging of the course. The final stage of the disease is Acquired Immune Deficiency Syndrome AIDS.

TRAINING AND EDUCATIONAL OBJECTS

- To form the skills to purposefully and deontologically thoroughly collect medical history, to specify the duration of the incubation period, to find out the data about the alleged source of infection and subsequent sexual contacts
- To assess the objective data of the clinical picture of HIV infection and to generalize their results
- To demonstrate the ability to determine AIDS-defining diseases
- To orient in the dermatological manifestations of AIDS (infectious dermatoses, neoplastic dermatoses, ordinary dermatoses with malignant or generalized course in AIDS)
- To know the clinical classification, to determine the general course and to establish the diagnosis of HIV infection in an individual patient
- To select the appropriate laboratory methods to confirm the diagnosis of HIV infection (IFA, PCR etc.)
- To correctly interpret the obtained results of clinical and laboratory studies to confirm the diagnosis of HIV infection in adults and children
- To make a comprehensive plan of treatment of patients with HIV infection
- To carry out the prevention of HIV infection, using national, public and individual preventive measures in health facilities

TO KNOW:

- The features of general course of HIV infection, its classification and variants of the course of the terminal stage of HIV infection (AIDS);
- AIDS-defining diseases;
- The characteristics of most frequent skin lesions in HIV/AIDS and peculiarities of their course;
- The structure and life cycle of HIV, immunopathogenesis and epidemiology of HIV infection;
- High risk groups of HIV infection;
- Methods of laboratory diagnostics of HIV infection (IFA, PCR etc.);
- Methods of laboratory diagnostics of HIV infection in children;
- Methods of laboratory diagnostics of AIDS-defining diseases;
- Methods of laboratory diagnostics of immune system disorders;
- The principles of treatment of HIV patients;
- Prophylactic HIV infection measures.

TO BE ABLE TO:

- Put questions to HIV patients, clear up the complaints, collect medical history, general and sexual anamnesis, demonstrating a particular delicacy in regard to clarifying the circumstances of infection, sexual contacts etc.;
- Carry out examination, palpation and vitropression in HIV-patients.

Historical information. As individual disease HIV-infection was first registered in 1981 in the United States. Patients were young homosexual men who were diagnosed with pneumonia, caused by opportunistic Pneumocystis. Such form of pneumonia has been observed earlier in neonates with immunodeficiency and in adults in the setting of immunosuppression caused by the organ transplantation or radiation therapy with administration of cytostatics in patients with malignant neoplasms. At the same time, attention was paid to the homosexuals with an aggressive course of Kaposi's sarcoma, which quickly led to death. Immunological studies have helped to established that immunity suppression lays in the basis of pathogenesis of new disease. The term AIDS was introduced in 1982 to designate this disease.

The works to clarify the etiology of HIV infection, conducted simultaneously in 1982-1983 in the United States (a group led by Robert Gallo) and in France (a group led by Luc Montagnier), were successful. The virologists from the group led by Gallo isolated from the lymphocytes of AIDS patients retrovirus – the pathogen of the disease, having called it HTLV-III *(human T-lymphotropic virus)*. Retroviruses HTLV-I and HTLV-II were discovered earlier by these researchers. The first retrovirus was isolated from the lymphocytes of T-cell leukemia patients, and the second one was isolated from the lymphocytes of hairy cell leukosis patients.

Etiology. The causative agent of AIDS, which is a human immunodeficiency virus belongs to the family of retroviruses having a reverse transcriptase, which is an enzyme providing synthesis of DNA copies with RNA-virus and their integration into the genome of the cell. HIV penetrating the cell of host organism is combined with its genetic material, resulting in a life-long infection.

A viral particle of spherical shape (its diameter is 80-200 nm) has a complex structure. The outer shell of the virus consists of a two-layer membrane with numerous thickenings and protrusions in the form of pins. An eccentrically located elongated cone-shaped core is a typical morphological feature of HIV. The membrane types are two linked glycoproteins: gp41 with a molecular weight of 41and gp120 with a molecular weight of 120.

Lipoprotein envelope of HIV is coated on the inner side with a layer of the protein p17, which, penetrating the viral particle and linking its structural elements in a single complex, is an isometric matrix.

The core of HIV contains nucleocapsid with a viral genome and nucleocapsid proteins p7, p9 and p13. HIV genome is eccentric, it is presented by two molecules of RNA associated with the nucleocapsid proteins. Nucleoid containing the molecules of reverse transcriptase, integrase and protease, is rolled into a tight spiral and is enclosed inside the core.

As up to the present moment there are three genotypes of causative agent of human immunodeficiency, these are HIV-1, HIV-2 and HTLV-IV. HIV-2 was isolated from the blood of patients from and infected mainly in West and Central Africa. HTLV-IV, according to experts, is a form of HIV-2. HIV-1 is more common genotype in comparison with other ones, and it is considered to be a conventional

causative agent of human immunodeficiency. HIV-1 in the literature is traditionally denoted just as HIV without index.

HIV lives in humans only. It is found in many cellular elements and fluids of the patients and infected persons. The predominant location of the virus is blood and semen fluid. There are processes in the blood, leading to the suppression of immunity as a major pathogenetic mechanism of HIV infection. Blood also is an important factor in the transmission of HIV. HIV is mainly found in lymphocytes and in small amount in the plasma and its fractions. Helper T-cells are the basic and massive reservoir of the virus in organism of HIV/AIDS patients. Sperm is also of great concern in the transmission of HIV. The question of detection of the virus in semen (in a free state or linked with lymphocytes and secretion macrophages) has not been conclusively solved. HIV is in vaginal and cervical secretions, and probably in the menstrual blood. The presence of HIV in saliva, tears, sweat, breast milk and cerebrospinal fluid is proven. The quantitative content of the virus in body fluids is not finally found out, it is probably insignificant. It should be noted that saliva contains a special inhibitor of HIV, which suppresses lymphocytes infection. It is believed that the infection does not occur through saliva, even in case of bite and oral-genital contact. However, some researchers admit the possibility of such infection. Of the above mentioned bodily fluids, breast milk only can transmit HIV-infection during prolonged breastfeeding.

Outside the human body HIV is weakly stable. At a temperature of 56 °C it dies in 30 minutes. In the dried state, the virus remains viable for a few (4-6) days at a temperature of 22 °C. It is insensitive to ultraviolet and ionizing radiation and is highly sensitive to the action of preparations containing chlorine, hydrogen peroxide, acetone, ether, etc.

The development of HIV infection is a result of penetration of the virus in the blood. It is possible to be infected with the virus that causes AIDS only from an infected person or virus carrier. HIV is more frequently transmitted through sexual route (especially in case of homosexual relationship, in which the micro-traumas with bleeding are often), with blood at its direct getting into the bloodstream (through transfusion of blood and its products, organ and tissue transplantation, the use of unsterilized needles, syringes and other instruments contaminated with infected blood), during artificial insemination of women, and from infected mother to child.

Homosexuality, sexual promiscuity and drug addiction was and is of great importance in the spreading of HIV infection. About 75-80% of AIDS patients become infected during sexual intercourses, mostly homosexual. Homosexuals, predominantly passive, make the first in significance risk group. Active homosexuals are also at risk of infection, but not to such degree as the passive ones.

At the current stage of the HIV infection spreading, the heterosexual transmission of the virus is increased. Some authors believe that during heterosexual infection transmission, the possibility of sexual partner infection is mutually equal and does not depend on the fact who is infected primary either man or woman; while others believe that a man is more often the source of infection than a woman is.

The second in size risk group is made by the drug addicts who use for the injectable (mainly intravenous) administration of drugs shared non-sterile needles and syringes. The percentage of drug addicts in the structure of AIDS incidence ranges in different countries from 11 to 25%. Women make about 20% of drug addicts, AIDS patients. It should be noted that homosexual drug users simultaneously belong to both infection risk groups. As it is known, many drugs (cocaine, amphetamine, ethyl chloride, etc.) cause T cell immunodeficiency, thus worsening the course of HIV infection. Possibly, it can promote active character of asymptomatic course of the disease.

The third group consists of people with hemophilia, which is typical to men only. Infection mostly occurs via antihemophilic globulin (factor VIII) and plasma component of thromboplastin (component IX), which are delivered in the form of concentrate or cryoprecipitate. Greater is the probability of infection, during administration of concentrate because it is prepared from the blood of 2-5 thousand of donors, whereas cryoprecipitate is made of blood of 20 donors only.

The fourth group is children born by HIV-infected mothers. Transplacental infection occurs during the passage of the fetus through the birth canal, through the milk during breastfeeding. It is believed that HIV, unlike other retroviruses, is not transmitted to the offspring in the form of insertion into the genome.

The transfusion of blood and its components is one of the possible ways of infection. The blood plasma and preparations made from it can be safely decontaminated by HIV inactivation, but the preparations of the cellular forms (packed red blood cells, white blood cells, platelets) and bone marrow from infected donors don't take such decontamination.

HIV infection can be transmitted during transplantation of organs and artificial insemination of women. There are cases of children infection with HIV in the hospital in the result of reuse of unsterilized syringes with the replacement of sterile needles only.

Pathogenesis. HIV infection is determined by the cumulative defect of predominantly cellular immunity due to lymphopenia, as well as functional disability of lymphocytic cells and their altered polyclonal activation. These immunological changes are especially pronounced in the last phase of HIV-infection, AIDS stage. Lymphopenia develops mainly as a result of lysis of T-helper cells, which are the main targets of HIV action. The number of T-helper cells of HIV-infected patients is suddenly decreased. If normally it amounts to 1 000-2 000 in 1 mm^3 of blood, then in the setting of AIDS it drops to 300-200 in 1 mm^3 and less. In this result there is ratio distortion of T-helpers (defined by monoclonal antibodies OKT4) and T-suppressors (defined by monoclonal antibodies OKT8): normally the ratioOKT4/OKT8 is greater than unity (1.9-2.4), and in the setting of AIDS it is less than unity (0.5 or less). Reduction of the number of T-helper cells and the ratio OKT4/OKT8 is one of the characteristic signs of HIV-infection, the impact of which causes the violation of normal regulation of the immune response with the predominance of the process of suppression over the process of activation /induction, V-system is re-affected and the

cytotoxic reactions depending on antibodies are violated. As the result of the destructive impact of HIV subpopulation of T helper cells does not occur. This creates favorable conditions for the activation of relatively pathogenic flora and development of opportunistic infections. Due to the exclusion of T-helper cells from the immune response, the organism loses the protection against neoplasms. HIV-infected T-cells and macrophages, circulating in the body, play a crucial role in the generalization of HIV-infection. In a lesser degree HIV affects B lymphocytes, platelets, endothelial cells of blood and lymph vessels, epithelial cells, and glial cells of the nervous tissue and neurons, which are also involved in the development of pathological process.

It is presently believed that the pathomorphological changes in the cerebrospinal axis may arise not only in connection with an immune deficiency, but also as a result of direct impact of HIV.

Clinical presentations. The characteristic features of HIV infection are connected with the peculiarity of causative agents, life-long virus infection carriage state, prolonged symptoms silence, specificity of pathogenesis and clinical findings, associated by progressive decrease in immunity, lethal outcome. Concerning the duration of the incubation period of HIV infection there is no generally accepted opinion, as there is no first of all a single principle of its calculating. The end of the incubation period is determined from the beginning of seroconversion and generalized lymphadenopathy, and AIDS-related complex, and AIDS. Duration of incubation period from the moment of infection to the development of clinical manifestations of the terminal stage of AIDS varies widely, from three months to ten years or more.

The assumption that pronounced form of AIDS develops in a small proportion of infected persons is found to be unjustified. According to the literature, 3-5% of HIV-infected patients get AIDS during a year.

The course of HIV infection is staged and is characterized by the alternation of relapses and remissions. In the final stages of the disease the remissions are short and the relapses are long and severe; the final stage AIDS ends lethally. All stages of the disease are observed not always. A certain sequence of transition from one stage to another is not obligatory.

In the course of HIV infection five stages are distinguished, these are initial (acute), asymptomatic, generalized lymphadenopathy, AIDS-related complex, and AIDS.

The initial stage develops about in half of the patients in 2-8 weeks after infection. The duration of this phase of the disease is 3-14 days. Clinically, the initial stage of HIV infection has acute course. In the acute stage the generalized lymphadenopathy is usually observed, accompanied by temperature rise, sickliness, sore throat, diarrhea, Banti's syndrome, generalized roseolous rash (appearance of round and oval spots ranging in size from a pinhead to a lentil and more), which resembles a syphilitic roseola. In acute HIV infection hemorrhagic rash is described, as well as ulcers of the mouth and esophagus. In this period there are the cases of acute encephalopathy, epileptiform fits. Lymphopenia is characteristic.

The listed symptoms are unstable and rapidly vanishing. Swelling of the lymph nodes only remains, but it also often disappears.

The development of antibodies occurs in the initial period. Seroconversion appears in this period not always.

Asymptomatic stage (stage of virus infection carrier state) occurs after the acute stage, if it took place. This latent period continues for months and years (5-6 years and more, and 3,5 years on average in homosexuals), without any symptoms. The general state of the patients remains satisfactory for a long time.

The definition of asymptomatic stage is attended with great difficulties; it can be achieved only with use of laboratory methods for the isolation of viruses, recognition of antigen and antibodies to it, and the study of immune indices. The method of virus isolation is a complex and expensive research, which is not performed in practical healthcare facilities. Immunological methods are not always informative and strictly specific. Usually the recognition of antibodies is made by means of serological reactions.

The duration of period between infection and production of antibodies is not precisely established. The earliest dates of detection of antibodies to HIV are 2-7 weeks from the date of infection. Seroconversion can occur in 3-5 months after infection as well. Specific antibodies can be not detected for a very long time because of the time-lapse immune response or a low concentration of antibodies. The possible also is latent persistent viremia in the absence of antibodies; probably, HIV antibodies are formed not always or they quickly enter the complex with viral antigen and thus are not revealed.

Some researchers believe that certain virus carriers remain, probably, healthy. However, for validation of such opinion long-lasting follow-up of the HIV-infected persons is required.

Stage of generalized lymphadenopathy is observed in the vast majority (90%) of the HIV-infection cases. For this stage persisting lymphadenopathy is characteristic. All the peripheral lymph nodes may be affected, but mostly the nodes of arms, neck, face. Enlarged lymph nodes have tight elastic consistency, are mobile, unpainful, the skin over them is not altered.

Lymphadenopathy has long lasting course with remissions and exacerbations and can be the only objective clinical symptom of HIV infection over many years.

AIDS-related complex usually develops in the presence of generalized lymphadenopathy and is formed in 1-3 years after its appearance. Sometimes the complex can occur without prior lymphadenopathy. AIDS-related symptom complex is characterized by a combination of numerous and diverse symptoms of common disorders and lesions of different organs, such as general weakness, headache, loss of appetite, lethargy, fever, arthralgia, weight loss, lymphadenopathy, splenomegaly, diarrhea, amenorrhea, neoplasms and other. Dermal diseases are often observed (pyoderma, candidiasis, herpes, etc.), the possible are ulcerative lesions of the mucous membranes of the mouth. The opportunistic diseases may occur, but they are less pronounced than in the terminal stage of AIDS.

Laboratory changes include leukopenia, lymphopenia, thrombocytopenia, anemia, decrease in the number of T-helper cells (<400/mm3), increased levels of immunoglobulins.

At first the described pathological conditions and disorders are moderately pronounced and may even regress. This does not concern the loss of body mass, which is constantly progressing. With the course of the disease the patient's state worsens, the severity of clinical symptoms increases and in severe cases, the terminal stage of AIDS can occur. The development of AIDS is possible even without the preliminary stages of the disease.

Acquired immune deficiency syndrome (AIDS) is a final stage, which is the most severe form of the disease having lethal outcome. At this stage there are opportunistic infection developping, and malignant tumors or lymphoproliferative diseases. AIDS has got no specific clinical manifestations, however, it is characterized by a range of «marker» diseases, such as pneumonia caused by *Pneumocystis carinii*, Kaposi's sarcoma, infectious mononucleosis, intestinal amebiasis, candidiasis, atypical forms of tuberculosis and other.

Categories A3, B3, C1, C2, and C3 are determinant for the AIDS cases and are subject to follow-up in the USA as AIDS patients.

Table 34.1
Classification of stages of HIV infection and expanded definition of AIDS cases in adults and adolescents (CDC, 1993)

	Clinical categories		
Immunological categories by the number of CD4+ T-lymphocytes (c/mm^3)	**A2** Asymptomatic acute (primarily) HIV-infection or persistent generalized lymphadenopathy	**B3** Symptomatic states, which do not belong to category A and C	**C4** AIDS-defining diseases
(1)>500	A1	B1	C1
(2) 200–499	A2	B2	C2
(3)<200	A3	B3	C3

Category A includes one or more of the following conditions in adolescents and adults (at age of 13 and more):

- asymptomatic HIV-infection;
- persistent generalized lymphadenopathy;
- acute (primarily) HIV-infection with clinical manifestations or acute HIV-infection in anamnesis.

Category B includes the following conditions:

- bacillary angiomatosis;

- oropharyngeal candidiasis;
- vaginal candidiasis (persistent or poorly responding to treatment);
- cervical dysplasia (moderate to severe), cervical carcinoma in situ;
- fever up to 38,5 ^{0}C, diarrhea for more than a month;
- hairy leukoplakia;
- herpes zoster, recurrent or with lesions of more than two dermatomes;
- listeriosis;
- pelvic inflammatory disease, especially complicated by tubo-ovarian abscess;
- peripheral neuropathy.

Category C includes AIDS-defining diseases, such as:

- candidiasis of bronchi, trachea, or lungs;
- esophageal candidiasis;
- generalized or extrapulmonary coccidioidomycosis;
- extrapulmonary cryptococcosis;
- chronic intestinal cryptosporidiosis (lasting more than one month);
- cytomegalovirus infection with visceral involvement, excluding liver, spleen or lymph nodes;
- cytomegalovirus retinitis with loss of vision;
- HIV-associated encephalopathy;
- herpes infection, that is chronic ulcer (ulcers) lasting more than a month;
- bronchitis, pneumonitis or esophagitis;
- generalized or extrapulmonary histoplasmosis;
- chronic intestinal isosporiasis (lasting more than one month);
- Kaposi's sarcoma;
- Burkitt's lymphoma;
- immunoblastic lymphoma;
- cerebral lymphoma (primary);
- infections caused by *Mycobacterium avium* complex or *M. kansassi*, generalized or extrapulmonary;
- infections caused by *Mycobacterium tuberculosis*, of any localization (extrapulmonary or pulmonary);
- infections caused by other or unidentified species of mycobacteria, generalized or extrapulmonary;
- pneumonia caused by *P. carinii*
- recurrent pneumonias;
- progressive multiple leukoencephalopathy;
- recurrent salmonella septicemia;
- cerebral toxoplasmosis;
- wasting syndrome due to HIV.

Skin and mucous membranes affection in AIDS

Skin and mucous membranes lesions due to their frequency and peculiarity of the clinical picture can be the earliest sign of HIV infection.

In the initial stage, when the disease develops according to the type of infectious mononucleosis, pink and red round spots can appear on the skin, not exfoliative, with a pronounced peripheral growth. They resemble to some extent the clinical findings of toxicoderma and quickly disappear spontaneously.

Viral, bacterial and fungal infections with the manifestations on the skin and mucous membranes can be activated in AIDS patients. The high frequency and atypical course of viral skin lesions in AIDS stand out.

Herpes simplex in AIDS patients develops 40-50 times more frequently and is observed in 22-87% of AIDS cases. The rash usually is multiple, recurs periodically, exulcerates, prone to prolonged duration, is often complicated by candidiasis.

Herpes zoster is characterized by a frequent generalization of the process, and the rash necrotizes relatively quickly, exulcerates, is accompanied by severe persistent neuritis and may recur and become complicated by pyogenic infection.

In children suffering from AIDS, *varicella* manifests as generalized vesicular and pustular rash, elements of which can necrotize, exulcerate. Skin lesions can acquire protracted course and be accompanied by severe general reaction.

Often men with AIDS in the area of coronal sulcus of the penis, on the inner layer of the foreskin and in the perianal region have got multiple, enlarged, subject to ulcerations and resistant to therapy *peaked condylomas*, having relapsing course.

The multiplicity and the prevalence of pathological process are characteristic for *vulgar warts* and *molluscum contagiosum*. Individual elements acquire considerable dimensions. Typical localization of warts of molluscum contagiosum is the skin of the palms and plantae, genitals and perianal area.

11-25% of AIDS patients have got in the lateral surfaces of the tongue *hairy leukoplakia* appeared, accompanied by the formation of whitish plaques with villous surface and, probably, associated by the invasion of papillomatous virus, Epstein-Barr virus and herpes.

Mycotic infection is rather often activated in AIDS. Patients in most cases have *pityriasis versicolor* and *erythrasma* appeared. Tinea versicolor is very common and often affects the skin of the face.

There is high level of manifestations, tendency to generalization and relapses of rubromycosis (lesion of nail plates, white nails), and other superficial mycosis of skin. Candidal lesions are found in 47-50% of HIV-infected patients. The mucous of the mouth and esophagus is most often damaged in men, in women – the mucous of genitourinary tract. In the pathological process the large and small skin folds are involved, as well as periungual walls, nail plates, mucous of nasal cavity, esophagus, stomach, intestine, lung, kidneys, and brain. There are descriptions of cases of candidal sepsis. The development of chronic generalized granulomatous candidiasis with the formation of numerous infiltrative foci with ulcers, vegetations and crusts is

possible. Generalized candidiasis of skin is generally combined with candidal pneumonia and colitis. The identification of a high titer of agglutinins to Candida antigens is of great importance for the diagnosis of visceral candidiasis. The development of chronic candidal conjunctivitis is possible.

Patients often have got *cryptococcosis* (deep blastomycosis of Busse-Buschke), *histoplasmosis* (Darling's disease), *aspergillosis* and other deep mycoses, which are characterized by the lesions prevalence and the severity of the pathological process. The characteristic manifestation of AIDS, such as *seborrheic dermatitis* is quite often registered. On the skin of the scalp, trunk, face, neck, bends of elbow and popliteal spaces there are hyperemia and infiltration of the skin, psoriatic exfoliation and severe itching, which are resistant to glucocorticoid creams and ointments. A large number of yeast-like organisms are revealed in the scales of lesion foci.

The pyogenic infections, such as staphylo- and streptodermae are often activated on the skin of AIDS patients, these infections are characterized by a prolonged course, a multiplicity of lesions, tendency to relapses, and resistance to therapy.

On the sites where there were *folliculitis*, the infiltration of bluish-red color remains for a long time, the small scars remain, multiple painful *furuncles* develop with the spread of infiltration over the entire dermis and partially over the hypodermis with the following necrotization of tissues.

Carbuncles are often formed with the possible development of facial vein thrombophlebitis and sepsis, the treatment of which is often ineffective.

Young people suffering from AIDS can have *acne,* more often indurative and conglobata, *acne-like folliculitis*, occurring not only on the skin of face, upper chest and back, but also on the buttocks and perineum, after which the scars remain, keloids sometimes. Sycosis can be observed in AIDS, which is characterized by the extraordinary resistance to the treatment and the pronounced aggressiveness of the course.

The characteristic features of impetigo (more common in older persons) are a significant prevalence of the process, the aggressiveness of the course and pronounced resistance to treatment. The increased contagiousness of streptococcus strains stands out.

Chancriform pyoderma is localized in the genital area, and formed at the base of ulcer infiltrate is beyond its borders, which is a characteristic sign of this disease in case of AIDS. The ulcerous skin defect is slightly raised above the surface of the surrounding tissues. Telangiectasias are generated resembling the changes of vascular pattern in some skin diseases. The patients with chancriform pyoderma in AIDS, may have a positive Wassermann reaction, whereas the TIT (treponemal immobilization test) and IFT (immunofluorescence test) are negative.

Erysipelatous inflammation in patients with AIDS can be located at any sites of the body (arms, trunk, face, genitals, etc.; classical localization is on the lower legs

predominantly), it is characterized by clinical poverty, the lack of temperature reaction, rapid swelling of the skin in the lesion foci, resistant to treatment and preservation of lesion asymmetry.

There are the foci of *chronic atypical pyoderma*, which proceeds by ulcerative, vegetating and absorbent type.

People with AIDS often have *urticaria* (usually papular form), alopecia (multiple focal lesions with a distinct trend of transfer in the diffuse form), ichthyosis, thrombocytopenic purpura, leukoplakia and eosinophilic pustular folliculitis. The course of psoriasis and eczema becomes much more complicated. In patients with psoriasis, Reiter's syndrome is observed, and in patients with eczema varioliform pustulosis Juliusberg-Kaposi is observed.

The most common pathognomonic form of skin lesion in AIDS is Kaposi's sarcoma (KS). According to the WHO classification (1994), it is classified to the group of vascular tumors (angioreticuloendothelioma). The etiology of the disease is unknown. It is supposed to have viral origin (HHV-8-type); great importance is attached to the genetic factors. Undoubted is the connection of the diseases with immunodeficiency of any nature. There are *sporadic* (classic) Kaposi's sarcoma, *immunosuppressive* (appears in the setting of immunosuppressive therapy after organs transplantation), *associated with AIDS* (fulminant, malignant). According to the manifestations on the skin and pathomorphological changes last three forms are similar to sporadic KS.



Fig. 34.1. Herpes zoster in AIDS.

Sporadic KS occurs predominantly in men and starts with the gradual development of spots, nodes, infiltrate plaques, multiple nodes or tumors, often symmetrical, of reddish-bluish, dark-brown or purple-black, usually on the skin of the lower extremities, trunk, face, on the oral mucosa. Tumors and nodes are of



Fig. 34.2. Hairy leukoplakia in AIDS.

spherical shape the size of a hazelnut significantly protruding above the level of normal skin. Their surface is smooth, rough, glitters and resembles orange peel, has a tight elastic consistency and a bluish-brownish color. Due to destruction of the nodes deep sharply painful ulcers of irregular shape are formed, their edges are kind of turned out. The bottom is uneven, covered with bleeding gangrenous secretions. The rash can appear on the palms, plantae, fingers; sometimes it merges and is scleroid. Venous and lymphatic stasis may develop on the extremities, the regional lymph nodes are endured and enlarged.

Depending on the course and severity of the process there are chronic (less malignant) form of the disease, which lasts 15-20 years, malignant subacute, lasting up to 2-3 years, and acute (very rare), similar to KS in AIDS.

Subacute form of KS is observed in 10-12% of cases, is characterized by common manifestations, rapid development of lymphostasis, multiple lesions of the lymph nodes and internal organs. Epidemic and immunosuppressive KS according to clinical picture and course is close to subacute form.

KS in AIDS patients is observed in 30-35% of cases and is an early dominant symptom of the disease, is often combined with pneumocystic pneumonia. It develops mainly in men aged 20-50 years. The course is acute. The rash appears quickly, often has infiltrative-plaque or knotty nature, it is multiple, the rash elements are succulent of bright coloring, are located on the upper extremities, face, mouth and genital mucosae, in the perianal region. The bigger areas of the skin are soon involved in the pathological process. With the localization of KS on anticnemions, there are pronounced edemas. The rash can dissolve with the formation of generalized ulcers. Suddenly, in the setting of pronounced general reaction there can be the generalized and persistent lesion of peripheral lymph nodes, especially the cervical, axillary, cubital, inguinal, femoral ones, which manifests as symptoms of tumor damage to internal organs (stomach, liver, kidneys, brain, etc.)

The lethal outcome occurs rapidly (from several weeks to 4-6 months). The cause of death is pneumocystic pneumonia or sepsis. The primary lesion of the internal organs and lymph nodes is possible in the intact skin. One of the peculiarities of KS in AIDS is its resistance to cytostatic therapy. The diagnosis of KS should be confirmed histologically.



Fig. 34.3. Candidiasis of the mucous membranes of the mouth and tongue in AIDS.



Fig. 34.4. Seborrheic dermatitis in AIDS.

In the affected areas there are accumulations of newly formed blood and lymphatic vessels, spindle cells, hemorrhage, hemosiderosis and fibrosis. The plasma cells are often found in the infiltration.

Among the other tumor diseases *lymphomas* (of skin and brain) and *squamous cell carcinoma* are observed in 3-4% of AIDS patients.

In different regions of the world, there are certain clinical manifestations of AIDS. In the USA and Europe the clinical picture of AIDS is dominated by lymphadenopathy and at least two concurrent infections caused by Pneumocystis (71% of cases), cytomegalovirus (40%) and herpes simplex virus (29%), as well as Kaposi's sarcoma. In African countries the key features are weight loss (99%), fever (75%), and diarrhea (76%). This triad has been described as a disease of weight loss, generalized lymphadenopathy, cryptococcosis with signs of meningoencephalitis and other opportunistic infections. In several African countries, along with frequent gastrointestinal lesions central nervous system often suffers, and Kaposi's sarcoma is diagnosed less frequently, but it differs by an aggressive course.

Diagnostics. Clinical and laboratory diagnostics of HIV infection has three directions:

1. Establishment of the fact of HIV infection.
2. Determining the stage of the disease and the identification of opportunistic diseases.
3. Prognosis of the clinical course of the disease and laboratory control of treatment effectiveness.

Diagnostics any viral infection is based on the detection of the virus, its DNA or RNA, viral antigens, as well as specific antibodies. HIV infection is characterized by that the macroorganism steadily produces antiviral antibodies. They are determined by the *indirect* and *competitive (direct) methods* and *immunoenzyme agglutination techniques* as well. Immunoenzyme techniques are aimed at the detection of antibodies in blood serum.



Fig. 34.5. Kaposi's sarcoma in AIDS.



Fig. 34.6. Kaposi's sarcoma in AIDS.

For diagnostics of HIV infection immunoenzyme assay is predominantly used, these are test systems, first developed and introduced into clinical practice with the participation of R. Gallo (1985). Since then, all donor blood, its components and transfusion products are carefully examined for the presence of antibodies to HIV. Today there are several generations of test systems for the detection of antibodies to HIV.

Diagnostics, based on the competitive test systems, requires less time and is characterized by high sensitivity. However, there exist difficulties during their production and storage. In the laboratories research with a small volume of researches the express systems are applied by means of which testing and investigation of one serum lasts from 5 to 40 minutes.

The majority of these diagnostic test-systems along with high sensitivity and specificity have low predictive index. Therefore, the confirmation of the primary positive results of diagnostics is required. All positive results of the previous research are subject to checking with use of another test-system, and then immunoblotting (this method supposes the study of the structural and intermediate proteins of HIV-1/HIV-2 on the polyacrylamide gel with help of electrophoresis). The positive results of immunoblotting are based on the determination of diagnostic strips staining. The sensitivity of this method is enhanced by the possibility to detect all the structural and intermediate proteins of HIV.

To confirm the initial positive results the modern way of laboratory diagnosing HIV infection is developed. It consists of the combination of such test systems:

1) three different immunoenzyme test-systems;

2) immunoenzyme and non-immunoenzyme tests;

3) a combination of three non-immunoenzyme tests.

Simple methods of agglutination diagnosing HIV infection as to their sensitivity and specificity are highly competitive with immunoenzyme methods. Their advantages are technological availability, low price and possibility of visual monitoring of the research results.

Method of indirect immunofluorescence allows defining antibodies against HIV-1 and detecting early immune response to HIV. Determination of protein p24, which is a major component of HIV-1 nucleocapsid, helps to verify the infection in adults and children at the early stages of the disease. Thanks to polymerase chain reaction antiviral DNA and genomic RNA is determined.

With regard to diagnostics of HIV infection in children, here exist objective difficulties, as in the blood of neonates and children up to 12-15 months there can be maternal IgG antibodies. There is no HIV replication in the children of the first month of life, and consequently neither virus nor its genome is detected. In babies up to a year HIV is determined by *polymerase precipitation reaction,* verification of HIV in cell culture; the positive results are confirmed by determination of p24 protein. After reaching a year method of choice is immunoenzyme assay, the positive results of which should be confirmed by immunoblotting.

Treatment. The basic principles of therapy of HIV infection are prevention of disease progression, saving the state of chronic infection, the use of antiviral therapy and treatment of opportunistic infections.

The modern medications administered for HIV infection can be divided into *etiotropic, pathogenetic* and *symptomatic*.

The basic etiotropic therapy directed at the suppression of HIV reproduction is active antiretroviral therapy.

Preparations applied for antiretroviral therapy are:

I. Nucleoside inhibitors, these are thymidine analogs such as Zidovudinum (Retrovir, Thymazide), Stavudine (Zerit), cytidine analogues such as Zalcitabin (Hivit), Lamivudine (Epivir), adenine analogues such as Didanosine (Videx), guanine analogues such as Abacavir (Ziagen), a combination of drugs, such as Zidovudinum + Lamivudine (Combivir).

II. Non-nucleoside inhibitors, these are Nevirapine (Viramune), Delavirdine (Rescriptor), Efavirenz (Sustiva, Stocrin).

III. The protease inhibitors – Indinavir (Crixivan), Nelfinavir (Viracept), Ritonavir (Norvir), Saquinavir (Invirase, Fortovase), Amprenavir (Agenerase), Lopinavir (Kaletra).

Strategy and tactics of complex therapy provides the primary and secondary prophylaxis for opportunistic infections. Immune deficiency requires the primary prophylaxis, the etiotropic preparations are appointed when number of CD4 lymphocytes is less than 200 in 1 uL. Secondary prevention is performed by means of etiotropic medicines to prevent relapses of opportunistic infections.

More effective treatment will be with using a combined etiotropic therapy, as:

a) the use of several drugs suppresses the viral life cycle more significantly;

b) it is possible to reduce the dose of preparations, as well as reduce their toxic effects on the macroorganism;

c) various medications have different ability to penetrate into the tissues (liver, kidney, brain);

d) a combination of preparations slows down the development of resistance to them.

There are many different treatment schemes for patients with HIV infection. Simultaneously with a combined antiviral therapy it is necessary to apply medicines for the treatment of AIDS-related opportunistic infections. Early detection, treatment and prevention of the secondary opportunistic infections increase life expectancy of HIV-infected patients. Despite the high cost, the treatment of HIV/AIDS patients does not only prolongs the life of patients, but also improves its quality.

Answers to the quiz of the first level of complexity
1 – A; **2** – A; **3** – D; **4** – A; **5** – B; **6** – E; **7** – B; **8** – E; **9** – B; **10** – C
Answers to the quiz of the second and third levels of complexity
1a – E; **2a** – A; **3a** – A; **4a** – B; **5a** –B

1. Indicate the causative agent of HIV-infection:
A. RNA-retrovirus
B. Herpes-virus
C. DNA-retrovirus
D. Herpes-virus of the 8th type
E. Cytomegalovirus

2. The largest epidemiological risk concerning HIV infection belongs to:
A. Blood, sperm, vaginal secretion
B. Saliva
C. Breast milk
D. Cerebrospinal fluid
E. Sweat, urine, feces

3. According to the classification of SDS (1993) AIDS diagnosis is set to persons with the level of CD4 lymphocytes:
A. Above 500 in 1 ml of blood
B. Below 1000 in 1 ml of blood
C. Above 2000 in 1 ml of blood
D. Below 200 in 1 ml of blood
E. Above 200 in 1 ml of blood

4. What are the stages of HIV infection according to the WHO classification (1994)?
A. Acute stage of disease, asymptomatic stage, stage of generalized lymphadenopathy, AIDS-related complex, AIDS
B. An incubation period, asymptomatic stage, stage of generalized lymphadenopathy, AIDS-related complex, AIDS
C. Asymptomatic stage, stage of generalized lymphadenopathy, AIDS-related complex, AIDS
D. Acute stage of disease, stage of generalized lymphadenopathy, AIDS-related complex, AIDS
E. Acute stage of disease, asymptomatic stage, stage of generalized lymphadenopathy, AIDS

5. What are the most likely routes of infection by immunodeficiency virus?
A. Fecal-oral
B. Sexual, vertical, parenteral
C. Contact-household
D. Transmissible
E. Droplet spread

6. Specify the AIDS-defining diseases:
A. Candidiasis of the esophagus, trachea, bronchi and lungs
B. Generalized Kaposi's sarcoma in patients under 60
C. Infection caused by the herpes simplex virus, which manifests as ulcers on the skin and/or mucous membranes, persisting more than one month
D. Pneumocystic pneumonia
E. All of the above

7. Which of these reactions is screening for HIV infection?
A. Polymerase chain reaction (PCR)
B. Method of immunofluorescent assay (IFA)
C. Immunoblotting (IB)
D. Immunofluorescence test (IFT)
E. Hybridization analysis (HA)

8. The signs of immunodeficiency are:
A. A reduction in the numbers of CD4 and a decrease of the index of differentiation of lymphocytes SD4/SD8 in the blood.
B. Increasing of the level of the circulating immune complexes
C. Increasing of the concentration of immunoglobulins of the IgA and IgG classes
D. Decrease of the concentration of immunoglobulin of IgM class
E. All of the above

9. What changes in the clinical analysis of blood are seen in patients with HIV infection?
A. Eosinophilia
B. Lymphopenia
C. Neutrophilia
D. Thrombocytosis
E. Hematocrit increase

10. Name the preparations used for antiretroviral therapy:
A. Lamivudine
B. Stavudine
C. Nevirapine
D. Ritonavir
E. All of the above

Task 1. When performing spinal puncture of HIV-infected patient, the cerebrospinal fluid gets into the nose, the eyes and the mouth cavity of doctor who made a puncture.

a) What measures are to be done to prevent HIV infection:
- **A**. To rinse oral cavity with 70% solution of ethyl spirit
- **B**. To inject into the nose 30% solution of Albucidum
- **C**. To wash eyes with water with clean hands, rinse eyes with a solution of 30% Albucidum
- **D**. To inject into the nasal cavity 0.05% solution of potassium permanganate
- **E**. All of the above

b) Make a plan of survey of the sufferer.

Task 2. A patient attended a stomatologist with complaints about tongue lesion. It is known that the patient is injection drug user with promiscuous sexual activity. On examination: mucosa on the lateral surface of the tongue is thickened, wrinkled, ash-white, covered with hairs due to filariform enlargements of up to 1 cm.

a) What disease can be suggested by the stomatologist:
- **A**. Villous leukoplakia
- **B**. Oral candidiasis
- **C**. Lichen planus
- **D**. Herpetic stomatitis
- **E**. Leukoplakia

b) Suggest the plan of examination and the treatment scheme of this patient.

Task 3. A HIV-infected patient attended a dermatologist with complaints about rash, accompanied by painfulness. It is known from the patient's medical history that he has already had a similar eruption after which the scars left. On examination: there are the groups of close spaced vesicles with hemorrhagic content, erosions and ulcerations on hyperemic skin in the area of waist and trunk along the nerve trunks.

a) Which disease in the setting of HIV-infection can be suspected:
- **A**. Herpes zoster
- **B**. Pemphigus
- **C**. Duhring's dermatosis
- **D**. Allergic dermatitis
- **E**. Eczema

b) Make a plan of patient's examination and treatment.

Task 4. A HIV-positive patient at the age of 30 attended a doctor with complaints about rash on the skin of face. On examination: there are about 20-25 dense, a little shiny semicircular nodules of yellowish-white color up to 1 cm in diameter on the skin of face. There is umbilication in the center of nodules; of which when squeezing the nodules with forceps the whitish grout is released.

a) What disease can be suspected:
- **A**. Warts
- **B**. Molluscum contagiosum
- **C**. Acne
- **D**. Sycosis
- **E**. Cutaneous tuberculosis

b) Perform the differential diagnostics of this disease.

Task 5. A patient visited a doctor with complaints of recurrent rash on the penis. The disease began with grouped small vesicles on hyperemic and slightly edematous mucosa. Earlier, the disease regressed, but during last time the permanent course is observed. The patient is HIV-positive. On examination: in the area of penis balanus there is an ulcer with diameter of 2 cm with a moist polycyclic bottom, very painful, which continues to increase in size and does not heal.

a) Which disease has a doctor suspected:
- **A**. Syphilis
- **B**. Genital herpes
- **C**. Cancer
- **D**. Chancriform pyoderma
- **E**. Soft chancre

b) Set the full clinical diagnosis and appoint treatment.

Ulcus molle, lymphogranuloma venereum, granuloma inguinale (donovanosis)

35 TOPIC

According to the WHO classification of sexually transmitted infections, the subgroup of nosologies united under the name "Classic venereal diseases", except for syphilis and gonococcal infections, also includes ulcus molle (chancroid), lymphogranuloma venereum and granuloma inguinale (donovanosis).

TRAINING AND EDUCATIONAL OBJECTS

- To orientate oneself in the peculiarities of etiology and epidemiology of ulcus molle, lymphogranuloma venereum, granuloma inguinal;
- To identify ways and probable conditions for infection with these diseases;
- To determine an overall course and modern features of ulcus molle, lymphogranuloma venereum, granuloma inguinal clinical picture;
- To orientate oneself typical and atypical manifestations of these diseases;
- To characterize the principles of treatment of patients with ulcus molle, lymphogranuloma venereum and granuloma inguinal.

TO KNOW:

- The peculiarities of etiology, epidemiology and course ulcus molle, lymphogranuloma venereum, granuloma inguinale incubation period;
- Clinical signs of the diseases;
- Clinical characteristics of atypical forms of ulcus molle;
- Clinical forms of granuloma inguinale (ulcerative, verrucous, blooming, necrotic and mixed);
- Clinical features of lymph nodes affection in ulcus molle, lymphogranuloma venereum, granuloma inguinale;
- Diagnostic algorithm for ulcus molle, lymphogranuloma venereum, granuloma inguinale;
- The complications of ulcus molle (balanitis, balanoposthitis, phimosis, paraphimosis, vulvitis, vulvovaginitis);
- Therapeutic and personal prophylactic measures in ulcus molle, lymphogranuloma venereum, granuloma inguinale.

TO BE ABLE TO:

- Deontologically and carefully assemble sexual history with ulcus molle, lymphogranuloma venereum, granuloma inguinale;
- Correctly examine patients with these diseases;
- Clinically examine lymph nodes status in these diseases;
- Analyze the results of respective laboratory tests for lymphogranuloma venereum, granuloma inguinale;
- Differentiate clinical manifestations of ulcus molle, lymphogranuloma venereum, granuloma inguinale;
- Conduct differential diagnostics with diseases that have similar clinical picture;
- Assign causal and pathogenetic therapy to patients with ulcus molle, lymphogranuloma venereum, granuloma inguinale according to the applicable recommendations.

Ulcus molle

Ulcus molle *(urcus molle)*, the ***synonum: chancroid*** is a contagious disease transmitted primarily via sexual contact. It is characterized by acute clinical course with formation of specific ulcers on the skin and mucous membranes in areas of pathogen penetration. A typical feature of chancroid is also regional lymphadenitis (bubo).

Etiology. The causative agent of ulcus molle is *Haemophilus Ducrey* bacillus, which is former Ducrey-Unna-Petersen streptobacillus. For the first time chancroid causative agent was described by *Ferrari* in 1885 and independently by O.V. Peterson in 1887. Detailed study of this pathogen had been carried out by J. Ducrey in 1889 and M. Unna in 1892

In smears, taken from specific lesions, chancroid agents have the form of gram-negative bacillus arranged in parallel rows like a flock of fish. The length of chancroid bacillus is from 1.5 to 2 мm, the width – 04-0,5 microns, they have rounded ends and constricted in the middle. Chancroid bacillus are unstable to high temperatures (they die at above 40 ° C), but low temperatures are tolerated well. These microorganisms are fairly resistant to various chemicals: 0.25% formalin solution gives detrimental effect on them after 40 minutes, while 05% Chinosolum solution – within a few minutes.

Disease transmission path. Infection usually occurs via sexual contact. Skin or mucous membranes injuries contribute to infection. It is also possible to get infected via non-sexual way; in particular, there are few reports about the infection of children and health care workers.

Epidemiology. Chancroid in Ukraine and CIS countries is rare. This disease is endemic in Africa, Southeast Asia, Central and South America. Chancroid has also been recorded in the UK, Portugal, Italy, France, the United States and other countries.

Men suffer more than women. There is no durable immunity after ulcus molle.

Clinical picture. Incubation period usually lasts 2-3 days. However, there are literature reports which indicate that incubation period for chancroid is 7-10 days and even 2-5 months. Initially, on the place of pathogen penetration there appears a bright red spot, which is rapidly increasing in diameter and slightly elevates above the skin due to edema. In a day in the center of the spot there appears acute-inflammtory papule, and then – pustule. On the third day the pustule reveals, thus forming a painful ulcer, which is rapidly increasing in diameter (1-1.5 cm). On the fourth, fifth day of the onset of clinical manifestations of the disease he ulcer has an irregular oval shape, undermined soft edges surrounded by inflammatory aureole. Ulcer bottom is soft, covered with yellowish-gray necrotic plaque. There is pus coming out of the ulcer. After 2-3 weeks, the process stops progressing, the pus, inflammatory changes, pain gradually decrease, ulcers become filled with granulation. Healing with scar formation occurs in 1-2 months.

Ulcus molle is manifested mainly in the form of numerous painful genital ulcers with jagged edges, purulent discharge and lymphangitis. Regional lymph nodes are enlarged and painful. In men, ulcers are more often localized in the inner layer of the foreskin, on penis bridle, on the lips of external urethral opening, while in women – in small and large labia, in clitoris, pubic areas, inner thighs, perineum and around the anus.

Along with typical clinical forms of chancroid there is also the variety of its forms, namely, *gangrenous chancroid*, which results from complications caused by anaerobic infection and is characterized by deep gangrenization of ulcer bottom; *esthiomenous* – differs from the gangrenous by lack of demarcation line, the progression of gangrene in depth and at the periphery, accompanied by fever and septic manifestations; *funnel-shaped* – is characterized by the formation of deep ulcer located on the neck of glans penis; *impetigo* – clinically is similar to impetigo; *diphtheroid* – ulcers are covered with greenish-gray fibrous plaque, which is conditioned by the accession of infection by Bacillus pseudodiphtheriae; *serpiginous* – an atypical form of chancroid in which ulcer heals from one side, while on the other side it continues its peripheral growth; *follicular* – an atypical form in which there are numerous small ulcers with slightly raised edges and deep bottom, that is caused by pathogen penetration into the ducts of sebaceous glands and hair follicles; *mixed* – observed in simultaneous infection with syphilis and chancroid, when the ulcer, characteristic for chancroid, later acquires the characteristics of a chancre.

The size of chancroid ulcers ranges from a pinhead to the palm size and more. The ulcers are very painful and bleeding. There are usually multiple, fused together ulcers. Sometimes primary chancroid ulcers can be placed extragenitally. In most cases, primary extragenital chancre is associated with homosexual and oral-genital sex. There are also secondary extragenital chancroids, which are formed a s a result of pus inflow from ulcers located on the genitals to the inner thighs skin areas or other areas of the body distant from genital organs. This phenomenon is observed in the case where the infection is transferred to corresponding portions of the skin by the hands of the patients.



Fig. 35.1. Ulcus molle ulceration.

In the event of the accession of secondary infection, chancroid in men may be complicated by balanitis, balanoposthitis, phimosis and paraphimosis. Women with chancroid may also experience acute-inflammatory complications caused by concomitant pyococcus infection, trichomonas and other pathogenic microorganisms.

Specific complications of chancroid include lymphangitis and lymphadenitis, the occurrence of which is conditioned by penetration of the disease causative agents into lymph nodes. Lymphangitis in men occurs more often in the back of the penis, while in women – on the outer surface of the labia majora. It is placed under the skin, not soldered thereto, detectable in the form of non-uniform thickness of dense painful cord. The skin over it is hyperemic and swollen. Sometimes, along this painful inflammatory cord there are inflammatory nodes that can fester, and then turn into bubonulae (*Nisbet's chancre*).

A typical feature of chancroid is a regional lymphadenitis (bubo) that appears on the 2-4th week of the disease due to the penetration of the disease causative agents into the lymph nodes. In case of localization of chancroid on the genitals, inguinal, sometimes femoral lymph nodes increase. Regional lymphadenitis is mostly one-sided; it is usually acute and involves one or more lymph nodes, forming a conglomerate. There is a spike of lymph nodes with the skin, which becomes edematous and hyperemic. Corresponding changes are accompanied by pain and fever.

Then, there may be festering of a node, which is soon broken off with a significant amount of pus and ulceration. Within 3-4 weeks the ulcer is filled with granulation and forms a scar. At the same time, opportunely started treatment may cause bubo disappear.

Diagnostics. Chancroid diagnostics is based on anamnesis data, clinical presentation of the disease, confrontation and bacterioscopically confirmed identification of the causative agent. In order to detect chancroid bacillus ulcer's surface is cleaned with isotonic sodium chloride solution. Then, study material is taken from ulcer edges with a sharp spoon. The scrapping is smeared on a glass slide. It is most appropriate to perform Romanowsky-Giemsa staining . The causative agent of chancroid is usually placed in the form of chains with 20-30 short gram-negative bacilli. Chancroid causative agent can also be found in the pus of regional lymph node (bubo). In doubtful diagnostic cases they apply cultures. The pathogen is also isolated by inoculating discharge from the lesions onto the "chocolate" agar with 1% Izovitalex solution and 3 мg / mL of Vancomycin.

Differential diagnostics. Ulcus molle (Chancroid) should be distinguished from a chancre, herpes simplex, erosive and gangrenous balanoposthitis, genital diphtheria and tuberculosis ulcers.

Diagnostics is hindered in cases of co-infection with syphilis and chancroid. In patients with mixed (soft and hard) chancre it is quite difficult to find chancroid bacillus in ulcers scrapings. For the early diagnosis of mixed chancre



Fig. 35.2. Ulcus molle multiple ulceration.

it is mandatory to study scrapings from ulcers and lymph nodes on the subject of pale treponema, as well as to hold serological blood tests.

Treatment. Causal treatment of chancroid involves the use of antibiotics and sulfanilamides. When selecting antibiotics, the preference is given to drugs that do not effect on pale treponema. From this viewpoint, it is advisable to treat with aminoglycoside antibiotics (Gentamycinum, Kanamycinum etc.). Aminoglycosides have pronounced activity against chancroid causative agent and do not erase the clinical picture of syphilitic infection, if it accompanies chancroid. The course of treatment is 7-10 days. The causal treatment of chancroid also involves application of tetracycline antibiotics (Tetracyclinum, Oxytetracyclinum etc.). However, the application of tetracyclines in the treatment of chancroid should take into account their action against treponema. Sulfanilamides (Sulfadimethoxinum, Biseptol etc.) are also quite effective in chancroid treatment. The course of treatment is 10-14 days.

The great importance in the treatment of chancroid is given to local therapy, which is carried out simultaneously with causal therapy. Usually they assign daily warm bath with a solution of potassium permanganate (1:500). After the rejection of necrotic material from the bottom of ulcer lesions are smeared with 5% Emulsion Streptocidi and then by 5-10% Dermatol or 5-10% Methyluracil ointment.

Prophylaxis of ulcus molle (chancroid) should be carried out with due account for common principles of preventing infection with contagions that are transmitted mainly via sexual contact.

Lymphogranuloma venereum

Lymphogranuloma venereum (*lymphogranulomatosis inguinalis*), synonyms: inguinal lymphogranuloma, venereal lymphogranulomatosis, poradenitis is an infectious disease transmitted almost exclusively through sexual contact and is characterized by the appearance on the external genitals of painless erosion that is rapidly epithelialized, with subsequent development of regional lymphadenopathy, the collapse of lymph nodes, formation of bleeding ulcers and multiple fistulas.

Historical information. Clinical manifestations of the disease were first described in 1912 by *Rost*. Original name "poradenitis" was offered by *Nicolas* and *Favre* in 1913 due to the similarity of histology of affected lymph nodes with histology of lymph nodes in Hodgkin's disease.

Etiology. Lymphogranuloma venereum pathogen belongs to *Chlamydia trachomatis* species, particularly to L1-L3serotypes, which are the most virulent representatives of chlamydia. It primarily affects humans, found in the genitals and is able to multiply in the cells of various tissues.

Disease transmission path. The causative agent is transmitted via sexual contact. The reservoir of infection is chronic patients in whom the disease is asymptomatic.

Epidemiology. Fairly high incidence of lymphogranuloma venereum is registered in tropical and sub-tropical areas, particularly in South and South-East Asia, Central and South America. However, the intensification of communication links increases the risk of spread of the disease in other parts of the world.

Clinical picture. The incubation period ranges from 3 to 30 days. The clinical course of the disease involves three stages – the emergence of primary manifestations of infection, affection of lymph nodes, severe clinical symptoms of the disease.

Primary manifestations of infection in men occur mainly at the head of the penis, less – in the urethra or on inguinal areas skin, while in women – often in the vagina and labia, less – on the cervix. These primary manifestations may be in the form of papules, pustules and erosions.

After two weeks from the onset of primary manifestations, lymph nodes are increasing, fuse and become painful. The topography of lymph nodes affection depends on the location of initial infection. Usually, inguinal lymph nodes are affected first. The skin over these nodes becomes hyperemic, the nodes gather and pus comes out of multiple fistulas. At the stage of acute lymphadenitis one may observe general symptoms i.e. headache, fever, rash, arthralgia, signs of meningeal lesions. The inflammatory process may also be anemic (like chronic adenopathy) for many months with periodic sharpening.

Without special treatment the disease moves to the third stage, during which there are severe destructive changes not only in lymph nodes, but also in the surrounding tissues and organs. There may be deep infiltrative ulcerative and sclerofibrous process with the evidences of elephantiasis in the region of external genitalia, perineum, anus and rectum. The scarring of these ulcers can cause severe complications, including stricture of urethra and rectum etc.

Diagnosis. Due to the diversity of clinical picture in lymphogranuloma venereum, anamnesis data (staying in endemic regions) as well as identification of the causative agent of the disease by microscopy study are of great importance. The material for study is pus and biopsy of affected lymph nodes. The staining for the corresponding microscopy studies is carried out by Romanowsky-Giemsa method. For diagnostic purposes, they apply complement fixation test (CFT). This reaction to chlamydial antigen is sensitive enough, but its specificity may be restricted due to cross-reactions. For diagnostic purposes they use immunofluorescence test (however, you should keep in mind that antibodies have the ability to cross-react with other chlamydia) and intradermal test reaction (Frei's test).



Fig. 35.3. Lymphogranuloma venereum.

Differential diagnostics. Lymphogranuloma venereum should be differentiated from chancroid, syphilis, granuloma inguinal, axillary lymph node tuberculosis and deep mycosis.

Treatment. Causal treatment is performed using tetracycline antibiotics, macrolides and sulfanilamides. The course of treatment with antibiotics and sulfonamides ranges from 15 to 30 days. Causal treatment is quite effective, especially at early stages of the disease. In severe clinical symptoms of the disease, along with causal therapy, they prescribed pathogenetic and symptomatic agents. Locally, they apply anti-inflammatory absorbable drugs. In advanced forms of the disease with destructive changes, surgical treatment is recommended.

To prevent the spread of lymphogranuloma venereum, timely identification of infection sources, as well as conduct of early specific treatment is of great importance.

Granuloma inguinale

Granuloma inguinale *(granuloma venerum),* ***synonims: donovanosis, granuloma venereum*** is an infectious disease transmitted primarily via sexual contact and is characterized by the formation of granulomatous ulcers on the skin and subcutaneous tissue mainly in the genital and perineum.

Etiology. The causative agent of granuloma inguinale is *Calymmatobacterium granulomatis*, first described by Charles Donovan in 1905. Therefore, sometimes these bacteria are called Donovan's corpuscles. These are polymorphic bacillus with 1-2 мм in length and 0.5-0.7 мм in width and with rounded ends. The bacillus are usually surrounded by a capsule, they infest mainly in macrophages.

Disease transmission paths. Infection occurs primarily via sexual contact, much less via household way. The pathogens penetrate into the body via damaged areas of the skin or mucous membranes.

Epidemiology. The disease is fairly common in Central and South Africa, India, and southern provinces of China, Indonesia, Burma, Vietnam and also in some countries in South America, particularly in Brazil, Mexico and several others.

Clinical picture. Incubation period lasts from a few days to 3-6 months and longer. Most often on the edea (balanus, prepuce, labia, cervix), in anus perineum, rarely on the face, arms, torso there appear acute-inflammatory papules, pustules, papulovesicles, 14 mm in diameter, which later ulcerate with formation of painless bright red ulcers with grainy surface and soft texture. Ulcers' edges are irregular and elevated; the discharge is serous-purulent or blood-tinged with an unpleasant odor. Ulcers are characteristic of peripheral growth and affection of adjacent skin areas. Infection is transferred to other parts of the body by contaminated hands. The reaction of regional lymph nodes is less pronounced or absent.

The clinical course of granuloma inguinale depends on the form of the disease. There are several clinical forms of granuloma inguinale i.e. ulcerative, verrucous, blooming, necrotic and mixed.

Ulcerative form. There appears vegetation; ulceration with growth and spread to the edea, inguinal folds and anus area occurs. The pathological process proceeds by ulcerative-vegetating, serpiginous-ulcerative and scar- keloid type.

Verrucous form. Pale pink, minor painful, verrucous, slightly bleeding, covered with serous-bloody crusts growths appear at the bottom of ulcers. In this form of the disease they single out papulohypertrophic, condilomatous and eleohantious types of granuloma inguianl.

Blooming form. Painful bright red juicy granulations with an exudation and serous-purulent discharge with an unpleasant odor appear on the edges and on the bottom of ulcers.

Necrotic form. Secondary infection joins; tissue necrosis with the growth of ulcers on the periphery deep to the fascia, muscles and bones occurs, even with destruction of genitals and the development of rectovaginal fistula. General body condition worsens; toxicity increases; sepsis can occur.

Mixed form. This form is characterized by simultaneous presence of several clinical forms of the disease in one patient.

Diagnosis. The diagnostics is performed by microscopy study of material taken from ulcers' edges. Smears are stained by Romanowsky-Giemsa method. Bacterioscopy s involves identifying the causative agent of granuloma inguinale i.e. *Calymmatobacterium granulomatis* (Donovan's corpuscles).

Differential diagnosis. Granuloma inguinale should be differentiated from syphilis, chancroid, lymphogranuloma venereum and genital tuberculosis.

Treatment. Causal treatment involves the use of sulfanilamides (Bactrim, Biseptol-480) for 10-14 days, or tetracycline antibiotics and macrolides for 14 days. Along with the causal therapy, they perform local treatment with an application of lotions and powders for ulcers, as well as creams and ointments with antibiotics.

Prophylactic measures are the same as for other sexually transmitted diseases.

1. The infection with ulcus molle (chancroid) often occurs via:

A. contact with sick animals
B. Sexual contact with a sick person
C. Contact with soil, which contains pathogens
D. Contact with some insects, which are mechanical carriers of infection
E. All of the above is true

2. In atypical course of chancroid there are/is no:

A. Multiple ulcers with irregular edges and purulent discharge
B. Enlarged painful regional lymph nodes
C. Regular round or oval ulcers with smooth shiny bottom
D. Very painful and bleeding ulcers
E. Festering lymph node and its break through with significant amount of pus and ulceration

3. The varieties of chancroid do not include:

A. Seborrheic
B. Funnel-shaped
C. Gangrenous
D. Diphtheroid
E. Follicular

4. What complication does not occur in men in the event secondary infection joins ulcus molle (chancroid)?

A. Balanitis
B. Balanoposthitis
C. Phimosis
D. Paraphimosis
E. Vulvovaginitis

5. The causative agent of lymphogranuloma venereum is:

A. *Treponema pertenue Castellani*
B. Gram-negative *Haemophilus Ducrey* bacillus
C. M type *Treponema pallidum*
D. *Chlamydia trachomatis*
E. *Calymmatobacterium granulomatis*

6. Lymphogranuloma venereum clinically is characterized by:

A. Transfer exclusively via sexual contact
B. The appearance of papules, pustules, erosions on the edea
C. The development of regional lymphadenitis
D. The collapse of lymph nodes with formation of bleeding ulcers and multiple fistulas
E. All of the above is true

7. Which method is not used to diagnose lymphogranuloma venereum?

A. Bacterioscopic study with appropriate staining of smears by Romanowsky-Giemsa method
B. Inoculation of discharge from the lesions onto the "chocolate" agar containing 1% Izovetalex solution and 3 mcg / mL of Vancomycin
C. Complement fixation test (CFT)
D. Immunofluorescence test
E. Intradermal test reaction (Frei's test)

8. What clinical forms are singled out in granuloma inguinale?

A. Verrucous
B. Blooming
C. Mixed
D. Necrotic
E. All answers are correct

9. Differential diagnosis of granuloma inguinale is not carried out with:

A. Syphilis
B. Chancroid
C. Tinea cruris
D. Lymphogranuloma venereum
E. **Genital tuberculosis**

10. Causal treatment of granuloma inguinale involves the use of (optionally):

A. Sulfanimides (Bactrim, Biseptol-480) for 10-14 days
B. Tetracycline antibiotics for 14 days
C. Macrolides for 14 days
D. All of the above is not true
E. All of the above is true

Task 1. 35 years old patient addressed to Venereal Diseases Dispensary complaining of a rash in the penis. The anamnesis showed that initially, on the site of the lesion there was swollen bright red spot, three days after sexual contact with an unfamiliar woman while in vacation in Africa, which rapidly increased in diameter. A day after, in the center of the spot there appeared a bundle, and then – an abscess, which broke on the third day with the formation of painful skin defect. The dermatological examination revealed ulceration at the inner layer of the foreskin 1.5 cm in diameter, of irregular oval shape with soft undermined edges surrounded by inflammatory areola. Ulcers' bottom is soft, covered with yellowish-gray necrotic plaque. Pus releases from ulcers. Regional inguinal lymph nodes are enlarged and painful.

a) What is the most probable diagnosis in this case?
- **A.** Primary course of frambesia
- **B.** Primary course of pint
- **C.** Primary course of syphilis
- **D.** Ulcus molle (chancroid)
- **E.** Early course of bejel

b) What additional diagnostic methods should be used?

Task 2. 37-year-old woman appealed the dermatologist complaining of a rash on the genitals, increased size of inguinal lymph nodes, pain and body temperature growth. *Objectively*: on the external genitals you may observe numerous painful ulcers with irregular edges, purulent discharge and lymphangitis. The pathological process involves several inguinal lymph nodes on the right, forming a conglomerate, soldered to the skin. The skin over the altered lymph nodes is swollen and hyperemic. The patient underwent scraping of the lesions on genitals, followed by staining of test material by Romanowsky-Giemsa method.

a) What is likely to show up at bacterioscopic study?
- **A.** The pathogen is in the form of short chains with 20-30 gram-negative bacilli, which are generally extracellular
- **B.** The pathogens are polymorphic bacillus, 1-2 мм in length and 0.5-0.7 мм in width, with rounded ends, surrounded by a capsule and parasites inside macrophages
- **C.** The pathogen belongs to *Chlamydia trachomatis* species, particularly to L1-L3 serotypes
- **D.** Tissue parasite having a shape of a thin spiral, 0.2 мм in width, 5 – 15 мм in length and 8-12 curls, placed equidistant from each other
- **E.** All of the above is not true

b) Give therapeutic recommendations to the patient.

Task 3. 35 years old patient addressed Venereal Diseases Dispensary complaining of soreness and increased penis, which developed over two weeks. The patient associates these signs of the disease with casual sex. The patient undertook self-treatment. *Objectively*: the penis is increased as a result of inflammatory edema of prepuce, the outer layer of which is of bright red color. The balanus does not open, prepuce palpation detects a 2 cm hardening. Copious purulent discharge from the prepuce is observed. Inguinal lymph nodes are enlarged to the size of plums, and soldered together with the surrounding tissues, painful. The skin over them is hyperemic, edematous. Serological tests are negative.

a) What is the most probable diagnosis in this case?
- **A.** Chancroid, paraphimosis
- **B.** Seropositive syphilis, phagedaenismus
- **C.** Seropositive syphilis, phimosis
- **D.** Chancroid, balanoposthitis
- **E.** Chancroid, phimosis

b) What clinical implications may arise?

Task 4. The patient appealed the dermatologist complaining of a rash in the genital area, the increase in the inguinal lymph nodes, their tenderness. According to the patient's data primary symptoms of the disease appeared nearly a month ago after returning from East Asia on the labia in the form of nodules and

pustules, which later turned to erosion. Independently, she applied Furacuinum lotions. After two weeks from the onset of primary manifestations, left-side inguinal lymph nodes grew and merged into a single conglomerate. The skin over these nodes is hyperemic. On the eve of visit to the clinic the general condition of the patient deteriorated: appeared headache, fever, arthralgia; pus started to release from multiple fistulas on lymph nodes.

a) What is the most probable diagnosis in this case?

A. Primary course of frambesia
B. Lymphogranuloma venereum
C. Primary course of pint
D. Chancroid
E. Granuloma inguinale

b) Which period of the disease this clinical picture corresponds to?

Task 5. The patient after accidental exposure in China (4 months ago) noticed a rash on the external genitals, about which he asked for an advice from venereologist. *Objectively*: on the balanus, prepuce, perineum one may observe acute-inflammatory papules, pustules, papulovesicles, 1-4 mm in diameter, which sometimes ulcerate to form a painless bright red ulcer with grainy surface and soft texture. On individual ulcers there appears vegetation that grows and spreads to external genitals, inguinal folds and anus region. Ulcers' edges are irregular and raised. The discharge is serous-purulent with an unpleasant odor. Regional lymph nodes are not enlarged.

a) Put a preliminary diagnosis:

A. Blooming form granuloma inguinale
B. Mixed form granuloma inguinale
C. Ulcerative form granuloma inguinale
D. Verrucous form of granuloma inguinale
E. Necrotic form of granuloma inguinale

b) What other diseases are needed to make a differential diagnosis?

Answers to the quiz of the first level of complexity
1 – B; **2** – C; **3** – A; **4** – E; **5** – D; **6** – E; **7** – E; **8** – E; **9** – C; **10** – E
Answers to the quiz of the second and third levels of complexity
1a – D; **2a** – A; **3a** – E; **4a** – B; **5a** – C

36 TOPIC

Tropical treponematoses: yaws, bejel, pinta

Tropical treponematoses feature a significant share in the overall morbidity of the population of most countries in Asia, Africa and Latin America. Currently, tropical treponematoses include several diseases. From clinical and epidemiological point of view, yaws, bejel and pinta are most interesting cases. These treponematoses differ from each other both clinical manifestations and epidemiological characteristics. At present, the Ukrainian tourism industry is actively developing. Economic cooperation with many countries of the world grows, thus expanding business contacts. In this connection, the problem of tropical treponematoses is relevant in virtue of possible cases of the diseases, which may occur in patients that come from tropical countries.

TRAINING AND EDUCATIONAL PURPOSES

- Be conversant in the range of problems of the diseases that belong to a group of tropical treponematoses (yaws, bejel and pinta)
- Analyze the features of the epidemiology of tropical treponematoses
- Compile information on the ways and probable conditions of infection with tropical treponematoses (yaws, bejel and pinta)
- Determine the incubation period and factors that affect the characteristics of the overall flow of tropical treponematoses
- Identify the characteristics of diagnosis, differential diagnosis and treatment of patients with the pathology

TO KNOW:

- modern views on the etiology and pathogenesis of tropical treponematoses (yaws, bejel and pinta);
- morphological features of the causative agents of yaws, bejel and pinta, as well as and the ways to identify them;
- transmission paths, conditions of infection and immunity in regard to these diseases;
- general course of infection in humans with yaws, bejel and pinta;
- features and clinical characteristics of the lesions in tropical treponematoses (primary, secondary, tertiary periods of yaws and pinta; early and late forms of bejel);
- significance and clinical evaluation of serological tests in tropical treponematoses;
- basic errors in the diagnosis of tropical treponematoses (yaws, bejel and pinta);
- features of the treatment of tropical treponematoses.

TO BE ABLE TO:

- Collect a proper deontological general and sexual history of a patient with suspected tropical treponematoses;
- conduct a proper survey of the patient;
- analyze the features of the epidemiology and transmission routes of tropical treponematoses (yaws, bejel and pinta);
- timely identify the features of the clinical course of this infectious disease (primary, secondary, tertiary periods of yaws and pinta; early and late forms of bejel);
- identify the causative agents of tropical treponematoses (yaws, bejel and pinta) under a microscope;
- analyze the results of a patient's laboratory tests;
- carry out a differential diagnosis of yaws, bejel and pinta with the diseases that have similar clinical symptoms.

Yaws

Yaws (*pian, framboesia tropica*), synonyms: tropical syphilis, which is an infectious disease that resembles the clinical course of syphilitic infection; characterized by the formation of a chancre primary affect, followed by the formation of secondary efflorescence, its spread to the entire skin, lesion of mucous membranes, bones and joints.

Etiology. The causative agent of yaws is *Treponema pertenue Castellani*, first discovered in 1905 in Ceylon. This movable spiral treponema features the length of 7-20 microns and has 8-20 curls. First, its culture was obtained by *Noduchi* in 1911. Microscopic examination in the native form or in a stained preparation shows that *Treponema pertenue Castellani* is not very different from the causative agent of syphilis, which is *Treponema pallidum,* in its morphological and biological properties. Numerous studies of the degree of identity of these treponemes, as well as researching the difference between them, have not provided significant results. According to Ovchinnikov M.M. and Delektorskiy V.V. (1974), who studied the structure of these treponemes in the electron microscope, *Treponema pertenue Castellani* is only characterized by a double-layer shell and a single-layer cytoplasm membrane, whereas *Treponema pallidum* features a three-layer membrane and a two-layer cytoplasm membrane. The antigenic properties of *Treponema pertenue* and *Treponema pallidum* are very similar, which explains the cross-immunity between syphilis and yaws.

Epidemiology. The countries of South America (Brazil, Colombia, Venezuela, Peru, Bolivia, etc.), as well as Central Africa, Southeast Asia and Oceania are considered epidemic.

Transmission. Most often, infection occurs through the contact with soil that contains the causative agents of yaws. Infection may also occur within a direct contact with a patient (sexual, close household). It is believed that the spread of infection is significantly enhanced by certain insects, which are mechanical carriers of the infection. Children are subject to the infection most frequently. The highest degree of lesion is observed in children aged 3 to 16 years. In these age groups, passive immunity is gradually weakened, while active production of protective antibodies is formed rather slowly. At puberty, the degree of active immunity increases. Therefore, the incidence within the period 16-20 years is somewhat reduced. Thus, children remain the main reservoir of infection, while adults are infected by sick children. Microtraumas of skin and mucous membranes are s gateway for infection.

Clinical features. In clinical course, yaws is similar to syphilitic infection. It is characterized by the primary affect (chancre) and subsequent formation of secondary efflorescence with the spread to the entire skin, lesion of mucous membranes, bones and joints. Unlike syphilis, the lesion of internal organs and nervous system are absent.

Yaws is characterized by a cyclical flow. After an incubation period of 3-4 weeks, primary period of the disease develops, followed by secondary and tertiary periods.

Primary period. It begins with the appearance of ulcer formation – chancre, which is formed at the site of penetration of *Treponema pertenue Castellani*. Typically, yawsn chancre is localized to the lower limbs, hands, mouth, on the red border of lips, vulva. First, a papule of pink color is formed; it is eroded within 1-2 days, and then a red oval ulcer is formed (non-painful, undensified at palpation). The chancre is gradually increased in size, reaching a diameter of 5 cm or more. The bottom of the ulcer is covered by vegetations and papillomatous growths that resemble raspberries. Hence the name of the disease goes, that is yaws (from Fr. *framboise* – raspberry). Around the chancre, small papules can appear. This phenomenon is called chancre pianomization. There occurs a regional lymphadenitis. Lymph nodes are non-painful, feature dense-elastic consistency, not soldered to each other and surrounding tissues, feature no abscess. After 2-5 months, chancre is healed with the formation of atrophic scar.

Second period. On average, the second period begins 2-4 months after the onset of the disease. Manifestations of the second period include: single or multiple papillomatous vegetating lesions, which are gangosae (yaws), on the skin of scalp, areas of skin folds and around the orifices. Gangosae are characterized by the appearance of vesicle pustules, on the bottom of which vegetations are developed (papillomatous growths that resemble raspberries). They non-painful, the surface is covered with hemorrhagic exudate or crust. Sometimes yaws are grouped to form rings and arcs. When localized on soles and palms, the areas of hyperkeratosis appear; they resemble psoriatic rash. In the areas of hyperkeratosis, deep cracks are formed. In yaws, mottled squamous small hyperkeratotic papules may appear, called pianides. They tend to group to form a ring.

Tertiary period. This period begins in the absence of immediate treatment right after the second period, or in a few years. In clinical manifestations, the period is similar to the Tertiary syphilis. It is manifested with the formation of gummas, followed by further ulceration. Ulcers feature a round or polycyclic form, infiltrated along the edges. Ulcer healing occurs with the formation of scars.

The characteristic manifestation of the Tertiary yaws involves bone affection. With the gummy process localized in the central facial area, there occurs the destruction of nasal bones and hard palate. Other manifestations of the tertiary period include anterior bowing of tibia and deforming monodactylism. Unlike syphilis, yaws damages no internal organs, while a congenital form of the disease is also absent.

Diagnosis and differential diagnosis. The diagnosis is based on a clinical picture of the disease; laboratory diagnosis is not different from the diagnosis of syphilis infection. For microscopy study, the material from ulcer formations (chancres) or papillomatous rash of the second period (pianomas) is collected to identify the causative agent of *Treponema pertenue Castellani*. In addition, a serological survey is carried out.

Yaws should be differentiated from other treponematoses: syphilis, bejel, pinta, as well as cutaneous leishmaniasis and leprosy.

Treatment. Treatment of yaws involves the use of the drugs of etiotrop action, aimed at eradication of the pathogen. Penicillin or its repository drugs are prescribed (bitsillin). Other antibiotics are also used, in particular tetracyclines or cephalosporines. Individualized symptomatic and topical therapy is carried out.

Bejel

Bejel, synonyms: endemic syphilis, syphilis Arabic is an infectious disease characterized by the lesions of skin, mucous membranes, bones and joints, with no visceral and neurological disorders.

Etiology. The causative agent is *Treponema pallidum* type M (TPHA Type S is the causative agent of syphilis). In biological and morphological (including electron microscopic studies) properties, the pathogen of bejel is non-different from that of yaws. On that ground, a concept of identity of yaws and bejel is proposed. The diseases differ with insignificant clinical manifestations, explained by the influence of climate and racial characteristics of the population of endemic areas.

Epidemiology. The disease was first described in 1928 among Arab nomads, the inhabitants of Syria. At the present stage, bejel is registered mainly in the Middle East, particularly Syria, Yemen, Jordan, Iraq, Iran, Saudi Arabia, as well as in a number of African countries.

Transmission. The source of infection is a sick man. Infection occurs through nonsexual direct contacts with patients, as well as household items (dishes, linens, etc.). Children are affected most frequently. The spread of the disease is enhanced by low hygienic standards of people, especially some of the nomadic tribes.

Clinical features. The clinical course of bejel is similar to that of syphilis, while there are no primary chancre, visceral manifestations and congenital forms. There exist early and late periods of bejel.

Early period of the disease. Incubation period ranges from 2 to 6 weeks. Primary chancre appears at the site of the pathogen's penetration and is accompanied by slight inflammatory manifestations in the form of rapidly vanishing papule-vesicle. Lymphangitis and lymphadenitis are absent. There appears papular rash: erosive papules located mainly on mucous membranes of mouth, genitals and around the anus. Rash elements feature a circular or oval shape, bleed, are covered with a grayish film. On erosive surfaces, papillomatous growths are developed. Skin rash of erythematous-vesicular nature (forming arcs or rings) may appear. All of the early clinical manifestations of bejel are contagious. Rash reveals a large amount of pale treponemes.

Bones are affected, more often long tubular. Osteitis and osteoperiostitis are casual. As with early yaws, bone symptoms disappear tracklessly, with no destructive changes.

Late period. Clinical manifestations of the late period of bejel appear several years after the onset of the disease. The later period is preceded by a long-term latency period with no clinical manifestations. In this period, the only sign of infection

is presented by positive serological reactions. Clinical symptoms of late bejel resemble the symptoms of tertiary syphilis. Cuspal and gummy rash may appear. In bejel, cuspal rash features psoriasiform hyperkeratosis on the surface. There appear osteitis, periostitis, and gummy bone disease, followed by destruction. Nervous and cardiovascular systems are not affected.

Diagnosis. Bejel is diagnosed based on clinical manifestations, bacterioscopic microscopy to identify the disease causative agent and positive serological reactions.

Treatment. Clinical management of bejel is the same as that of yaws.

Pinta

Pinta (*mal del pinto, pinta*) is an infectious disease characterized by the lesion of skin and mucous membranes with no involvement of internal organs, bones and joints.

Etiology. The causative agent of pinta is *Treponema pintaum*, which was first discovered by *Kerrejon* in 1927. In morphological and biological properties, Treponema *pintaum* is similar to *Treponema pallidum* (syphilis), and *Treponema pertenue Castellani* (yaws). *Treponema pintaum* features a corkscrew shape with 10-15 swirls, the length of 7 to 20 microns, and pointed ends. It can be easily painted by Romanovsky-Giemsa method.

Epidemiology. The disease is registered mainly in South and Central America (Venezuela, Mexico, Colombia, Ecuador, Peru, Brazil, Paraguay, Argentina, Chile, Honduras, Panama, Nicaragua, and Guatemala). Very frequently, pinta is found in some countries in Africa and Asia.

Transmission. The causative agent of pinta is present in soil and tropical plants. Penetration in the human body occurs through damaged skin or mucous membranes. Infection by means of some insects is also proved. However, a direct and indirect contact with a sick person remains the main route of infection. Most often, children are infected.

Clinical features. Incubation period lasts from 1 to 4 weeks.

Primary period of the disease begins with the appearance of an inflammatory papule (mainly on face, neck, legs) with a diameter of 0.5-1 cm at the site of Treponema penetration. Within several weeks, the papule is transformed into an eritemato-squamous spot, surrounded by a cushion. Subjectively, mild itching in the rash area is reported. Over 3-7 months, new spots gradually appear (pintids). This occurs due to the generalization of infection on the background of the primary eritemato- squamous focus or its remnants. The spots can be placed both around primary tumor and throughout the body. The appearance of this eruption shows the disease switched to the second period.

Secondary period is characterized by the appearance of achromatic and hyper-chromatic spots. Peculiar rash promotes leukomelanodermia. The emergence of

dyschromias is explained by the fact treponemes are localized in the cells of malpighian layer, with subsequent disappearance of melanocytes from the areas of skin lesions. The development of fresh eruption gradually stops, while the disease enters into latent period, which lasts for several years. In the future, pinta enters the *tertiary period*, which is characterized by the appearance of small areas of atrophic surface. Most often, these lesions are observed on the upper and lower extremities. Dyschromias remain for a lifetime. Internal organs are not affected, congenital forms are absent.

Diagnosis. Characteristic clinical manifestations, results of microscopy studies to identify the disease causative agent and results of serological reactions are considered.

Treatment. Treatment is carried out by means of penicillin or the repository drugs.

1. The causative agent of yaws is:

A. *Treponema pertenue Castellani*
B. *Treponema pintaum*
C. *Treponema pallidum type M*
D. *Treponema pallidum type S*
E. None of the above

2. Infection with yaws often occurs through:

A. Contact with soil that contains pathogens
B. Sexual contact with a sick person
C. Close household contact with a sick person
D. Contact with some insects, which are mechanical vectors of the infection
E. All of the above is true

3. What is non-typical for yaws?

A. Incubation period
B. Lesion of internal organs and nervous system
C. Primary period of the disease
D. Secondary period of the disease
E. Tertiary period of the disease

4. The similarity of the antigenic properties of the causative agents of tropical treponematoses with *Treponema pallidum* promotes formation of cross-immunity between:

A. Syphilis and yaws
B. Syphilis and bejel
C. Syphilis and pinta
D. All answers are correct
E. All of the above are wrong

5. At the present stage, bejel is registered mainly in the countries of:

A. South America (Brazil, Colombia, Venezuela, Peru, Bolivia, etc.)
B. Central Africa, South Asia, Oceania
C. Middle East (Syria, Yemen, Jordan, Iraq, Iran, Saudi Arabia)
D. Central America (Venezuela, Mexico, Colombia, Ecuador, Peru, Guatemala)
E. None of the listed

6. Clinical picture of bejel is characterized by the absence of:

A. Primary chancre
B. Visceral manifestations
C. Congenital forms of the disease
D. Negative results of serological tests
E. All of the above is true

7. What clinical manifestations are absent in the later period of bejel?

A. Long latency period with no clinical manifestations
B. Seropositive tests
C. Characteristic formation of cuspal and gummy rash
D. Formation of ostitis, periostitis, gummy bone disease
E. Lesions of nervous and cardiovascular system

8. What clinical signs are absent in the primary period of pinta?

A. Development of an inflammatory papule with a diameter of 0.5-1 cm mostly on face, neck and legs, which is transformed into an eritemato-squamous spot within several weeks.
B. Formation of small areas of surface skin atrophy
C. Moderate itching in the rash area
D. Development of new spots (pintids) as a result of the generalization of infection on the background of primary erythematous-squamous focus or its residues
E. All of the above are not true

9. Second period of pinta is characterized by:

A. Development and dissemination of achromatic and hyper-chromatic spots, followed by leukomelanodermia
B. Amalgamative populous elements
C. Development of small areas of surface skin atrophy
D. Involvement of internal organs, bones and joints into a pathological process
E. All of the above is not true

10. Treatment of tropical treponematoses involves the application of:

A. Dexamethasone or Prednisolone
B. Ketokonazole or itraconazole
C. Nerobolum or Retabolil
D. Penicillines (Bicillin)
E. Naklofen or Diclofenak

Task 1. A mother of a 12 y.o. son visited a dermatologist. A young man complains of a rash on the upper limbs, which appeared the fourth week after he returned from Colombia. Mother says the illness started from the appearance of a pink nodule on the right hand, which turned in ulcer formation within 1-2 days. Dermatological examination showed that the dorsum of the right hand features an oval-shaped red ulcer, non-painful, non-callous by palpation, the diameter is 5 cm. The bottom of the ulcer is covered with papillomatous growths that resemble raspberries. Around the ulcer, small papules are observed. Regional lymphatic nodes are non-painful, feature dense-elastic consistency, not soldered between each other and surrounding tissues.

a) What is the most likely diagnosis?
- **A**. Primary period of yaws
- **B**. Primary period of pinta
- **C**. Secondary period of yaws
- **D**. Primary syphilis
- **E**. Early period of bejel

b) What additional diagnostic methods must be applied in this case?

Task 2. A female STI clinic laboratory assistant applied to a dermatologist. She complains of a finger cut with a glass when performing a scraping test taken from erosive papillomatous lesions in a patient with a primary period of bejel.

a) What clinical effects may occur in this case?
- **A**. Primary syphilis
- **B**. Felon chancre
- **C**. Infection will not occur
- **D**. Septicemia
- **E**. Primary period of bejel

b) Provide therapeutic recommendations.

Task 3. After a two-month stay in Yemen, a patient noticed a nodule in the area of genitals. A man received no treatment for 2 weeks. Dermatological condition worsened, while the patient applied to a dermatologist. At the time of examination, erosive papules located mainly on mucous membranes of mouth, genital area and anus were detected. Rash features an oval shape, bleeds, is covered with a grayish film. In some areas, papillomatous growths are developed on erosive surfaces. Primary chancre and visceral manifestations are absent. Lymphangites and lymphadenitis are not detected. An MRI examination found the osteitis of the left tibia.

a) Put a preliminary diagnosis:
- **A**. Yaws
- **B**. Pinta
- **C**. Bejel
- **D**. Syphilis
- **E**. Warts

b) Which period of the disease is characterized by the mentioned eruption?

Task 4. The examination of a 15 y.o. patient found malaise, weakness, lethargy, pain in bones and joints, intensified at night; rash on the lower extremities. The disease history says a patient was bitten by insects in Brazil 3-4 weeks ago. At the site of the bite, leg skin got covered with rash, which eventually started looking like raspberry. Regional lymphatic nodes are non-painful, feature dense-elastic consistency, not soldered between each other and surrounding tissues. Lesions of the internal organs and nervous system are absent.

a) What is the most likely diagnosis?
- **A**. Warts
- **B**. Yaws
- **C**. Syphilis
- **D**. Pyoderma chancriformis
- **E**. Pinta

b) Determine the tactics of treatment.

Task 5. A 24 y.o. female patient applied to a dermatologist. A woman complains of a rash on the lower limbs. The disease is associated with a holiday stay in Mexico. The history says the pathological cutaneous process began with the appearance of an inflammatory papule

with a diameter of 1 cm in the inner surface of the right foot. Within three weeks, the papule transformed into an erythematous-squamous spot, surrounded by a cushion. In the area of lesions, mild itching is observed. Over four months, new spots gradually appeared on the background of the remnants of the primary erythematous-squamous focus. The spots are located around the primary focus and throughout the whole body. Dermatological examination revealed numerous achromatic and hyper-chromatic spots on the lower limbs. Internal organs are not affected.

a) Put a preliminary diagnosis:

A. Primary period of yaws
B. Primary period of pinta
C. Secondary period of yaws
D. Second period of pinta
E. Late period of bejel

b) With diseases a differential diagnosis should include?

Answers to the questions of the first level of complexity
1 – A; **2** – E; **3** – B; **4** – Д; **5** – C; **6** – E; **7** – E; **8** – B; **9** – A; **10** – D
Answers to the questions of the second and third levels of complexity
1a – A; **2a** – E; **3a** – C; **4a** – B; **5a** – D

Medical Ethic and Duty, Deontology

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TOPIC

The Concept of Medical Ethics

It should be noted that the concepts of «ethics» and «aesthetics» are difficult to define. They cover a boundless amount of phenomena both in static and in historical (evolutionary) terms. In modern dictionaries, the concept of «ethics" (Latin *ethica* – character, habit) is provided with the following definitions:

- a doctrine about morality, virtue as a form of social consciousness, its essence, class content, laws of historical development and role in public life;
- a system of rules of moral behavior of people, their social responsibilities, obligations to their people, class, family and each other.

Medical ethics is an integral part of medical deontology. According to Tsaregorodtsev G.I., medical ethics, as a form of professional ethics, is a set of regulatory principles and norms of behavior of health workers caused by the specifics of their activities, as well as value and position occupied in a society.

Doctoring must fully realize the principles of the universal humanism: -love of the patient, complete performance of a medical debt near a patient's bedside, care of a patient, responsiveness and principles not deluded by any profit motives.

Only true practice of medicine provides the unity of opinions and actions, that is practical application of the principles of universal humanism.

Medical ethics is a historically formed moral canons, rules, commandments, codes, principles and rules to govern a doctor-patient relationship, as well as the relationship of physicians between each other. Medical ethics is a part and a concrete manifestation of social morality, adapted to the peculiarity, value and conditions of a doctor's medical practice.

Doctor's moral rules and regulations require a behavior aimed at maintaining a patient's health and life. Here we deal with the evaluation of a physician from ethic or immoral position as to whether his actions conform to the rules and regulations, as well as the summarization of these parameters in a special medical ethical representation system.

Along with the interdependence of work, morality and ethics, a certain independence of medical ethics, in accordance with the nature of activities in an immediately tangible form, as well as the concepts to reflect these moral senses are to be considered. Medical ethics considers no individual actions of a doctor, but the similarities and patterns of behavior common to all members of this profession.

Medical ethics is the doctrine of social responsibilities of a physician, in connection with the laws of development and formation of medical ethics, its role and place among other social phenomena, as well as the relation towards general rules and principles of social morality.

Medical ethics studies the characteristics of development and dependence of medical ethics on the conditions of medical practice, specific manifestations of general requirements of morality in medical practice.

Professional ethics is a unity of personal, professional and civic principles, connected with one another. Typically, people of high professional duty possess the

best personal and human qualities, in particular, such as moral purity, boundless dedication and selflessness. This is clearly manifested in medical ethics, which consists in the fact that medical profession requires a certain rejection of personal interests and dedication.

Teaching professional ethics allows one to create the ability to the most prolonged and difficult heroism, which is daily routine work.

About medical duties

Medical profession is a difficult choice. It requires self-sacrifice, purity of heart and intentions.

Medical debt, sympathy and attention to a sick person, unselfish help: these most important principles of medical ethics can and should be fully implemented in our society.

The feeling of medical debt is an integral part of a doctor's moral character. Unmistakably, it can be argued that the concept of medical debt includes all the basic elements of medical ethics, that is, everything that relates to the execution of a medical debt, will benefit the society, and therefore is ethical.

The concept of medical debt is very wide: from an honest and diligent execution of daily medical work to the onset of high courage in extraordinary circumstances, as well as willingness to sacrifice oneself for the sake of the rescue of people or a scientific experiment to prevent an epidemic of a dangerous infectious disease. The history knows striking examples of such medical feats, including those of domestic doctors, who threw themselves into the focus of pneumonic plague and other terrible diseases, often sacrificing themselves.

Life resists to diseases and death, while doctors are to deal with them. A doctor has no limitations for office hours. In practical and scientific activity, a physician should not work on a schedule. Sometimes, circumstances require a deviation from narrow standards, since medical debt involves thinking about the patient both during and after a working day. Doctor is obliged to learn for a lifelong. Otherwise, he will be unable to work successfully.

Medical Deontology

The term of «deontology» (from Greek *deon* – necessary and *logos* – teaching) was introduced in the early twentieth century by an English philosopher, Bentham, as the name of a science to study human professional behavior. Medical deontology is a part of the overall ethics, which studies the principles of behavior of medical personnel that are intended to maximize the relevance of treatment and avoid errors in medical practice. In addition, medical ethics represents a system of relationships established in between doctor and patient in the course of treatment.

Within each medical specialty, the content of ethics has its own characteristics.

Medical profession requires unique ethical demands, very complex and filled with psychological doctor-patient relationship nuances. Permanent responsibility to the

patient and his relatives, understanding that a physician's experience and skills influence a person's life, necessity to consider a patient's characteristics, ability to perfectly keep calm in dramatic situations: all this characterizes a doctor's daily work. Quite often, a physician has to be a witness to great patient's suffering with no possibility to stop pain, be aware of an imminent patient's death and find strength to inspire him of a speedy recovery. The word of a doctor has a miraculous power. On the one hand, a lot of iatrogenic diseases are caused by a carelessly thrown word; on the other hand, psychotherapy can sometimes be an important and powerful pathogenetic treatment. The word is also related to complex aspects and problems of confidentiality and manifestation of complete openness and a patient's trust in intimate matters.

Over a hundred years ago, a Moscow doctor, Haas F.P., proclaimed medicine as the queen of sciences, since health is a prerequisite for all the great and wonderful in the world. This «holy doctor», as called by patients, vividly conveyed the grandeur of medical profession: «The surest way to happiness lies not in a desire to be happy, but make others happy. For this, one should listen to the needs of people, worry about them not being afraid of work, helping them in word and deed. In short, a doctor is to love patients, while the more often he expresses such love the stronger it becomes.»

No wonder the grave of Haas F.P. features the inscription of «Hasten to Do Good.»

A famous Dutch physician of the seventeenth century, Nicholas Van Tulp, offered a burning candle to depict the medical emblem and symbol: «Aliis inserviendo ipse consumer», which means «I burn myself while lighting to others.» A prominent scientist and physician of the Middle Ages, Abu Ali ibn Sina, better known as Avicenna (980-1037 yrs.), provided a poetic description of a physician's personality: «he must have the eyes of a falcon, the hands of a girl, wisdom of a serpent and the heart of a lion.»

For many centuries, the understanding of diseases, medical tactics and methods of treatment improved. In order to truly serve people, modern physician must be knowledgeable in different issues of medical science, as well as a number of related disciplines: psychology, education, sociology, etc. At the same time, the science of humanology is the most important. It is ever new and versatile, and knows no borders.

Modern medicine requires a doctor to be a comprehensively educated professional with high cultural level and wide range of knowledge that goes beyond the specialty. Ancient Chinese sages said the knowledge that is not being improved and used is diminished every day. A Polish scholar and physician, Kelanovsky T., wrote a doctor that fails to look into a book is to be avoided even more than the disease itself.

In addition to acquisition and accumulation of the experience and knowledge in the field, formation of clinical thinking is one of the most important tasks in the course of preparation and improvement of doctors of different specializations.

For the whole life, a physician is to be enriched with new information and knowledge on how to improve the art of treatment. Struggling with death and

diseases, he consolidates strength, invincibility and the everlasting joy of life. A physician must be aware of this and help a patient to overcome fear and sense of hopelessness that arise in most difficult moments.

The medical profession will continue to exist as long as humanity exists. Social significance of a doctor's work is huge, since it involves self-sacrificing struggle for human health, carried by means of all accumulated by theoretical and practical medical science and acquired through personal experience. This requires constant insistent self cultivation for a better human present and future.

The image of a wise doctor was described by a French writer, Antoine de Saint-Exupery: «I believe the day will come when a sick person would give himself into the hands of physicists ... Not asking for anything, these physicists will take his blood, determine some constants and multiply one to another. Then, using the table of logarithms, they will cure a patient with a single pill. And yet, if I get sick, I will then turn to some old rural doctor, he will look at me out of the corner of his eyes; feel my pulse and stomach, then listen to my breathing. Then he will hoop, lit his pipe, rub his chin and smile to me to better relieve pain. Surely, I admire science, but I also admire wisdom.»

Most patients believe these and other positive traits are to be inherent to a doctor whom people trust the most precious thing of all that he has, which is health.

The introduction of the advancements of modern science and technology into clinical research and treatment (which, of course, is very important) features a downside. It involves the fetishization of technical means and poses the threat of dehumanization of medical science. Physician is often connected with a patient only through complex technical and laboratory testing, while test results tend to overshadow a patient himself.

The estrangement in a doctor-patient relationship comes in contradiction with the nature of healing. People began to appreciate those doctors that see the motto of «Closer to the sick person» proclaimed by a famous Kiev clinician, Professor Theophilus Gavriilovich Janowski, in the beginning of the last century as the «symbol of medical faith.» Such doctors give each patient a few hours, communicate with a person closely, carefully consider a patient's medical history, as well as the results of clinical and laboratory studies, while comparing them to establish the correct diagnosis.

One of the founders of the Russian clinical medicine, Mudrov M.Y., wrote there exist «spiritual medications to treat the body.» Regardless of specialty, every physician is to study the characteristics of a patient's lifestyle, the nature of his complaints and responses to them. At the present stage, psychotherapeutic techniques firmly entered the practice of various branches of medicine. In addition to psychoneurology, they are used in clinics of physical profile for diseases of visceral organs, endocrinology, dermatology, obstetrics and gynecology, dentistry, etc. In some cases, psychotherapy is used with medical treatment, physical therapy and other manipulations. In other cases, it is of great importance.

Clinical picture of various diseases may feature secondary neurotic disorders or neurosis-like symptoms. Manifestations of anxiety-depressive and phobic-depressive symptomatology with different sorts of fears, anxiety, state of worry and confusion are quite common in many diseases of skin, especially in patients with psoriasis, eczema, acne, rosacea, lupus, sycosis, etc. For such states, the application of various methods of individual and group psychotherapy, suggestive method and autogenous training can help achieve a positive effect.

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DERMATOLOGY VENEREOLOGY

Textbook

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Друге видання підручника (перше вийшло у 2012 р.) підготовлено співробітниками кафедри дерматології та венерології з курсом косметології Національного медичного університету імені О.О. Богомольця та провідними дерматовенерологами однопрофільних кафедр закладів вищої освіти України під загальною редакцією член-кореспондента НАМН України, професора В.І. Степаненка.У підручнику на сучасному рівні викладено погляди на етіологію й патогенез захворювань шкіри і її придатків та інфекцій, які передаються переважно статевим шляхом. Представлено клінічну картину й перебіг ряду дерматозів та інфекцій, які переважно передаються статевим шляхом, а також новітні методи діагностики, лікування та профілактики їх. Підручник укладено відповідно до Закону України «Про вищу освіту» (2014 р.), Стандарту вищої освіти зі еспеціальностей «Медицина», «Педіатрія», «Стоматологія», де визначено обсяг теоретичних знань, умінь, авичок та інших компетентностей для досягнення визначених результатів навчання , відповідно до концепції освітньої діяльності та освітніх програм за спеціальностями «Медицина», «Педіатрія», «Стоматологія», що базується на відповідних галузевих стандартах.

Підручник включає обов'язкові для засвоєння теми з урахуванням тематичного плану лекцій і практичних занять. У ньому представлено також ряд інших розділів дерматології та венерології, знання яких потрібне для

проведення диференційної діагностики нозологічних форм шкірної патології. Окрім цього, підручник включає теми елективних курсів «Медична косметологія» та «Новоутворення шкіри». У тексті використано ілюстративний матеріал, заснований на клінічних спостереженнях співавторів підручника, зокрема, співробітників кафедри дерматології та венерології з курсом косметології НМУ імені О.О.Богомольця, а також окремі ілюстрації навчальних ексклюзивних експонатів музею муляжів цієї кафедри. У розділі «Медична косметологія» представлено ілюстративний матеріал клінічних спостережень співавторів цього розділу співробітників профільної кафедри Одеського національного медичного університету. Для здобувачів вищої медичної освіти закладів вищої освіти України, лікарів-інтернів, практикуючих лікарів.

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