ОГЛЯДИ

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Helicobacter pylori and its role in the pathogenesis of diseases of the digestive system

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Helicobacter pylori is a gram-negative bacterium that is quite common among the world's population. To date, the pathogenetic mechanisms of the bacterium's influence on gastroduodenal ulcers and gastric cancer have been most deeply studied. However, there is a growing number of sources devoted to the association of Helicobacter pylori with the occurrence of many extra-gastric diseases. These data are quite contradictory and controversial. Given the close anatomical and functional relationship of the digestive system (digestive tract and digestive glands), it is quite natural that the bacterium Helicobacter pylori, which persists in the antrum of the stomach, has a pathological effect on this system, causing the development of a number of diseases and their complications. The purpose of this study is to analyze the current state of the problem of the role of Helicobacter pylori in the pathogenesis of diseases of the digestive system. This review presents the latest data on the pathogenetic mechanisms of gastroduodenal ulcer and gastric cancer. The persistence of the bacterium in the pancreatic-biliary system causes cholecystitis, and gallstone disease, including cholelithiasis, acute and chronic pancreatic inflammation, non-alcoholic fatty liver disease, and liver cirrhosis. Various mechanisms of carcinogenesis of tumors of the liver, gallbladder and bile ducts, and pancreas, in which Helicobacter pylori is directly involved, are highlighted. Further study of the role of the bacterium as a predictor of the development of diseases of the digestive system and their complications is promising and relevant.

Key words: Helicobacter pylori; digestive system diseases; liver; gallbladder; pancreas; stomach.

INTRODUCTION

Helicobacter pylori (H. pylori) is a gram-negative bacterium that infects about 4.4 billion people worldwide [1, 2]. The pathogen possesses various mechanisms that improve its ability to move, adhere, and manipulate the gastric microenvironment; this makes it possible to colonize the organ with a high acidity lumen [3]. However, its prevalence varies in different geographic regions and is up to 90% in developing countries, as is the annual recurrence rate [4]. It is important to note that H. pylori infection affects approximately half of the world's population, leading to a variety of stomach problems and is mostly asymptomatic [5]. H. pylori infection was associated with an increased risk of death due to gastric cancer and a much lower risk of death from stroke and lung cancer [6, 7].

The role of this microorganism in the pathogenesis of gastric ulcer (GU) and duodenal ulcer (DU) has been widely known for almost 40 years and is beyond doubt [8]. At the same time, in the publications of recent years, more and more data are devoted to the influence of this microorganism on the development of extragastric benign and malignant pathology [9, 10]. It has been established that this microorganism, through molecular mimicry, affects the absorption of nutrients and drugs taken systemically by the patient, and also causes changes in the course of many chronic diseases (diabetes mellitus, hematological pathology, diseases of the nervous, cardiovascular and respiratory systems, etc.) [11-13]. Of particular interest is the patho-

genetic link between H. pylori and diseases of the digestive system, as evidenced by numerous publications in recent years [14-18].

The aim of the study is to analyze the current state of the problem of the role of H. pylori in the pathogenesis of diseases of the digestive system.

The Stomach Cancer Pooling Project (a consortium for epidemiologic studies of stomach cancer) has published a report on the association between smoking and H. pylori seropositivity, as well as occupational risk factors, dietary patterns, and gut microbiota [15, 16]. Cases of intrafamilial bacterial infection and iatrogenic H. pylori infection during upper endoscopy have also been described [17, 18].

Gastroduodenal ulcer (GDU). Cytotoxin-associated antigen A, vacuolating cytotoxin, gene A protein, extrinsic inflammatory protein, and γ-glutamyl transpeptidase [14] are identified among the virulence factors of H. pylori in the development of gastric ulcers, and the bacterial colonization factors BabA, SabA, OipA, and HopQ in the development of gastric ulcers, effector proteins such as CagA, VacA, HtrA and outer membrane vesicles [19]. According to the study by Sharndama and Mba [20], H. pylori was found in 80% of patients with gastroesophageal reflux disease (GERD) and 90% of patients with chronic gastritis, with its presence in antrum in 100% of cases, in the body in 80%, and in the pylorus in 60% of patients. GDU manifests itself in 10% of patients infected with H. pylori and less than 1% in the uninfected group [21]. Eradication of H. pylori leads to a decrease in the frequency of peptic ulcer recurrence from 70-80% to 1-5%, and a decrease in the number of complications, especially bleeding, from 25-30% to 1-2% [22].

H. pylori produces urease, alkaline phosphatase, glucophosphatase, protease, phospholipase, hemolysin, superoxide dismutase, cytotoxic carcinogenic protein Cag A, and other substances, causing inflammatory, atrophic, and destructive changes in the mucous membrane of the gastroduodenal area [23]. The action of various virulence factors of these microorganisms leads to their active rooting in intercellular spaces and intracellular invasion, causing cell death [24]. At the same time, the infectious theory of ulcer formation does not explain the singularity of the ulcer defect, regular change of relapses and remissions, periodicity of the disease, seasonality of exacerbations, etc. [25].

Entering the gastric lumen with food, saliva, or water, H. pylori finds itself in an unfavorable environment because the hydrochloric acid of gastric juice, it is unsuitable for the bacteria's vital activity [26]. However, H. pylori produces urease, which, when combined with urea, triggers a reaction with the release of ammonia and carbon dioxide, which neutralize hydrochloric acid and create favorable conditions for the existence of the bacterium [27]. Localized stagnation around each bacterial cell and thus favorable conditions for their existence occur. Surrounded by urease and ammonia, H. pylori penetrates the layer of protective gastric mucus with its flagellated end and adheres to the gastric mucosa and endocrinocytes [28]. In addition to local alkalization, due to numerous enzymes and substances produced by bacteria, there is a local decrease in the viscosity of gastric mucus [29].

The following main pathogenetic directions of influence of Helicobacter infection on the process of ulcer formation in the duodenum are known: 1) an increase in the concentration of gastrin-releasing factor and a corresponding increase in gastrin levels; 2) a decrease in the number of D-cells in the antrum and a decrease in the concentration of somatostatin; 3) H. pylori directly causes an increase in acid production; 4) due to mucolytic action, it increases the sensitivity of the pyloroduodenal mucosa to acid; 5) provokes gastric metaplasia in the duodenum by accelerating the motility of the outlet of the stomach and the occurrence of the so-called "acid attack" due to massive discharge of gastric contents [30].

The role of H. pylori in the development of GU is more controversial, given that 60% of patients with this localization of ulcers are helicobacter-negative [29]. At the same time,

the role of concomitant helicobacteriosis in the development of GU complications is undoubted [2]. Some features of the course of peptic ulcer disease contradict the infectious theory. For example: characteristic localization of peptic ulcer along the lesser curvature of the stomach and very rarely in the area of the fundus, cardia, greater curvature; recurrence of peptic ulcer after healing in the place of its primary localization; more frequent morbidity in men (by 4-5 times), as well as the singularity of the ulcer defect [25]. Quite interesting is a clinical-experimental study in which it is proven that at the bottom of the ulcer there is always a congenital insufficiency of the development of the capillars, which leads to local ischemia. The authors refer to these disorders as "facultative" factors in the pathogenesis of ulcers [16]. It is also believed that biorhythms play a major role in the pathogenesis of ulcers [30].

H. pylori infection is one of the significant causes of persistent gastric hypersecretion resistant to antisecretory drugs. It not only enhances aggression factors but also suppresses defense factors, making the duodenal mucosa more sensitive to hydrochloric acid. H. pylori realizes its effect both through neurohumoral mechanisms and by means of dismotor disorders in the pyloroduodenal junction. On the other hand, an increase in gastric secretion, impaired acid-neutralizing function, and motility of the gastric outlet provokes the spread of the bacterium in the duodenum, creating a vicious pathogenetic circle of ulcer formation. Ulcer recurrence can occur either through recrudescence of the disease or reinfection. Recrudescence typically has a shorter time window compared to reinfection, often leading to the recurrence of H. pylori-associated diseases in the short term [23].

Influencing factors of H. pylori can be divided into two categories: 1) false-negative examination results (mainly in vivo factors); 2) small numbers of surviving or dormant H. pylori bacteria hiding in the human body (mainly in vitro factors). H. pylori itself is a major component of in vivo factors, including oral colonization, biofilm formation, and transformation into coccid forms (Fig. 1). Means and timing of re-examination, therapeutic regimen and treatment time window, as in vitro interventions are also involved in H. pylori recurrence. In vivo and in vitro factors lead to H. pylori recurrence [9].

At the same time, many factors are involved in H. pylori re-infection, such as the prevalence of H. pylori infection, living conditions, economic development, health status, etc. [23] (Fig. 2).

Gastric cancer is also closely associated with the presence of H. pylori, as evidenced by numerous studies [31-34]. According to the data of Japanese authors, gastric cancer developed (within an average follow-up period

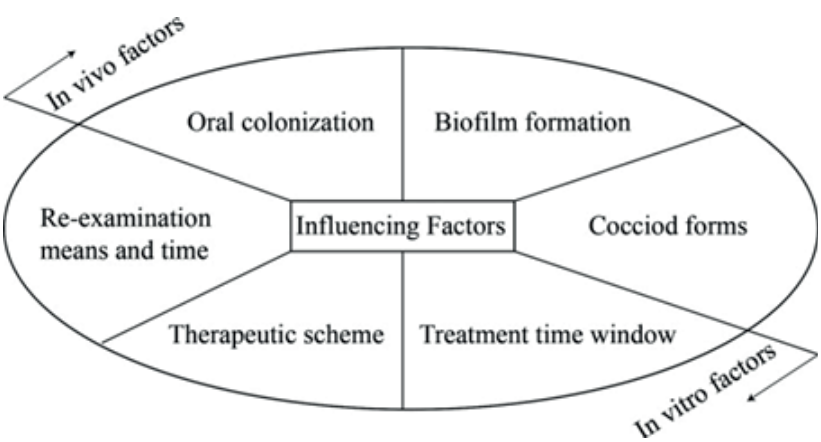

Fig. 1. Influencing factors of Helicobacter pylori recrudescence [3]

of 7.8 years) in 2.9% of patients with peptic ulcer, dyspepsia, or gastric hyperplasia who had Helicobacter infection, while none were found in uninfected patients [34]. This is due to the complex interaction between the genetics of the host, its environment and the virulence factors of the bacterial strain [35]. There are several biomarkers/characteristics of H. pylori that have been linked to cancer. Among them, the presence of certain major virulence factors, including cytotoxin-associated gene A (CagA), vacuolating cytotoxin (VacA), and extrinsic inflammatory protein A (OipA), play a significant role in provoking gastric cancer. These factors of H. pylori make it a potent carcinogen [36, 37]. Polymorphism and epigenetic changes in host gene coding (for interleukins (IL1β, IL8), transcription factors (CDX2, RUNX3), and DNA repair enzymes) and genetic variation in bacterial proteins (CagA and VacA, etc.) also increase the risk of gastric cancer [38].

Cholecystitis. H. pylori isolated from human liver tissue has ureA+, Cag(-), S2M2 Vac A genotype [39]. Antibodies to H. pylori were detected in 88.5% of patients with cholecystitis, in 84.6% of patients with gastrointestinal tract, in 73.9% of people with hypomotor dyskinesia and in 68.8% of patients with hypermotor dyskinesia [40].

However, even with pronounced destructive processes in the wall of the gallbladder, the microflora in cystic bile is detected in no more than half of the cases; this is related to the state of the patient's immune system and the bactericidal properties of bile [41]. Statistical processing of the level of Helicobacter deoxyribonucleic acid (DNA) in the tissue of the gallbladder in patients with cholecystitis showed a correlation with the female gender and increasing age of the patients. A significant association was found between the presence of Helicobacter DNA in the gallbladder epithelium and morphologically confirmed cholecystitis. The nucleotide sequence of 16S rRNA was > 99% similar to H. pylori [40].

Cholelithiasis. The mechanism of formation of pigment stones was explained by the effect of β-glucuronidase of bacteria, which leads to deconjugation of bilirubin diglucuronide, as a

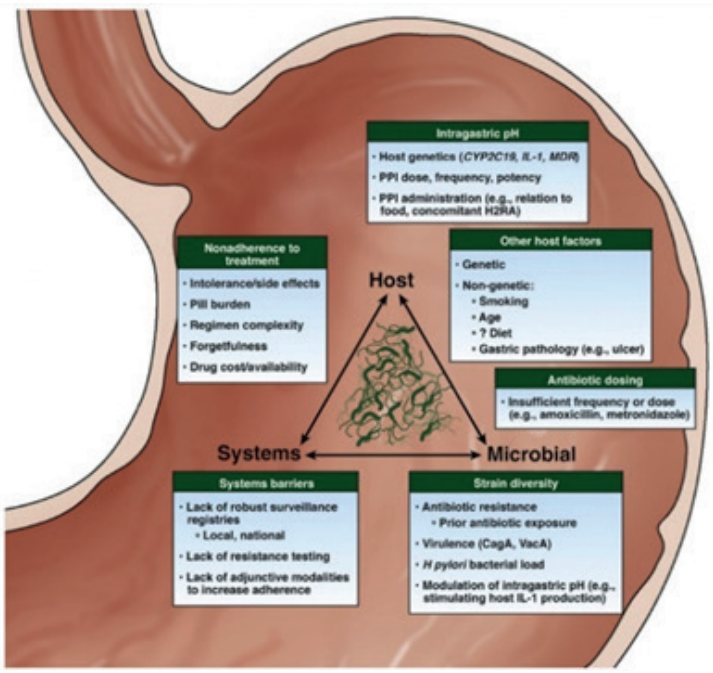

Fig. 2. Factors impacting failure to eradicate H. pylori infection. CagA cytotoxin-associated antigen A; IL, interleukin; VacA, vacuolating cytotoxin [23]

result of which insoluble unconjugated bilirubin is precipitated. The genus Helicobacter was detected in 13% of cases of hepatolithiasis and in 10% of cases of choledocholithiasis [41]. Considerably more researches are focused on the role of H. pylori in housing and communal services as a whole [39-43]. Although the organism could not be isolated in pure culture, H. pylori infection was detected by polymerase chain reaction (PCR) from gallbladder tissue and cystic bile in 31.3 and 49.9% of cases, respectively [42]. Helicobacter DNA was detected in 50% of cases of housing and communal services (H. pylori strain was identified in 91.8% of cases) [40].

At the same time, other studies have reported failures in attempts to detect Helicobacter DNA in bile or gallbladder tissue in diseases of the biliary tract [43]. However, the role of H. pylori in lithogenesis should not be completely dismissed: morphological and bacteriological studies revealed foci of gastric metaplasia in gall bladders in 45% of patients with gastrointestinal tract [41]. It has also been proven that the leading mechanism of stone formation is the potentiation of mucus (pronucleating factor) production by the gallbladder mucosa [39]. Other possible factors affecting the processes of biliary lithogenesis include various mediators of inflammation, which are secreted in response to antigenic stimulation. They affect the phase balance of bile and thereby accelerate the formation of cholesterol crystals [42]. L. Wang et al. [40] conducted a systematic review and meta-analysis of 20 studies of patients with gallstone disease, in which they provided unequivocal evidence of a link between this disease and H. pylori.

Cancer of the gallbladder and gastrointestinal tract remains a rare malignant disease of the digestive tract with a multifactorial pathophysiology [44, 45]. There is evidence that H. pylori is 3.5 times more common in patients with gallstone disease, and 9.9 times more common in biliary cancer compared to controls [16]. It is known that long-term stone-carrying is traditionally considered a risk factor for gallbladder cancer. For example, among Chilean women aged 65-70 years, in whom the prevalence of gallstone disease reaches 47%, mortality from gallbladder cancer ranks first [39]. In turn, the detection rate of gallstones in patients with gallbladder cancer reaches 80-90% [45]. Long-term stone-carrying is accompanied by impaired bile flow, bile stasis, and contamination by microorganisms, which in turn change the enterohepatic circulation of both primary and secondary bile acids, which are considered co-carcinogenic factors [46]. It has been noticed that another pathology can contribute to the development of a gallbladder tumor: non-specific ulcerative colitis, anomalies of the confluence of the duct of Wirsung with the common bile duct, and pathological reflux of pancreatic juice into the biliary tract. The probability of tumor development (up to 20-25%) increases in patients with a calcified ("porcelain") gall bladder [8].

There are also data on the detection of H. pylori in the hepatobiliary tract of patients with cholangiocarcinoma (CCA) in regions both endemic and non-endemic for Opisthorchis viverrini (OV) infection [45]. This was confirmed by experimental studies conducted by Dangtakot et al. [47]. PCR analysis of H. pylori in the stomach and bile of patients with cholestasis confirmed that the bacterium is the cause of a significant proportion of malignant diseases of the gastrointestinal tract [46]. Multilevel verification of bacterial metagenomics of ICC tissues by 16S rRNA sequencing established a link between H. pylori and ICC [48].

Liver diseases. Since an organism similar to H. pylori has been identified in samples from patients with hepatic disorders, several reports have discussed the possible role of the bacteria in liver diseases such as hepatocellular carcinoma, cirrhosis, and hepatic encephalopathy, nonalcoholic fatty liver disease, and fibrosis [49].

Nonalcoholic fatty liver disease (NAFLD) or metabolically associated steatotic liver

disease. H. pylori infection was recently identified as a pathogenetic factor in NAFLD [18]. According to Chinese researchers, H. pylori was detected in 52.36%, and the specific share of patients with NAFLD was 47.82% of cases [50]. H. pylori infection or predominance of H. pylori IgG serotype, as well as dyslipidemia and insulin resistance, could be independent predictors of the NAFLD development [51]. It was also established that a decrease in the level of adiponectin, low-density lipoprotein cholesterol and fetuin A indirectly increased insulin resistance [49, 52]. It is noted that in helicobacter-positive patients, a significant increase in body mass index, blood pressure, and triglyceride concentration is more often occur. H. pylori can cause damage to the liver with specific toxins [53], in the intestines, the bacterium increases the permeability of the mucous membrane of the small intestine, promotes the absorption of endotoxins of microorganisms, stimulating the processes of inflammation and fibrogenesis in the liver [16]. In patients with successful eradication of the bacterium, a statistically significant improvement in HOMA-IR index was noted [52, 53]. At the same time, certain clinical studies indicate the absence of a reliable connection between the development of metabolically associated steatotic liver disease and H. pylori infection [50].

Liver cirrhosis. When analyzing the etiological factors of the development of cirrhosis (alcohol, viral hepatitis B, C, D, as well as mixed genesis), it was noted that the highest level of H. pylori infection was noted in 92%, 87% and 86%, respectively, which is explained by a decrease in immunity, which develops as a result of chronic persistence of the viral component even at the stage of hepatitis [49, 54].

Endothelial dysfunction, changes in vasodilation dynamics, and neoangiogenesis are the most attractive theories regarding this issue, but the evidence comes mainly from experimental studies [3]. van Nieuwkerk et al. [54] in a case-control study found that H. pylori antibodies were present in 89% of patients with cirrhosis caused by HBV.

Research by Jeng et al. [38] showed that in patients with severe liver cirrhosis, H. pylori infection activates Kupffer cells and hydrogen peroxide to enhance TGF-β1 to trigger pro-inflammatory signaling pathways in hepatic stellate cells (HSCs) to release cytokines. Analysis of liver samples from patients with liver cirrhosis and HCV infection demonstrated that the CagA gene was more prevalent in advanced cirrhosis (28.2%) compared to early fibrosis (5.9%) [55].

Hepatocellular carcinoma (HCC) is one of the leading causes of death due to cancer in the world [56]. It has been established that Helicobacter species are cofactors that contribute to the transformation of chronic viral hepatitis into liver cirrhosis and HCC [57]. H. pylori DNA (CagA gene) was detected in liver tissue samples from HCC caused by severe forms of the hepatitis C virus (HCV) [54], but there is no connection between the presence of H. pylori and the results of quantitative PCR for HCV RNA (METAVIR system) [55]. However, other authors did not find a connection between the bacterium and HCC when examining stool samples from patients with HCC, viral genesis, by X-ray examination [58].

Pancreatic diseases. Some studies have established a possible relationship between H. pylori infection and pancreatic diseases (acute and chronic pancreatitis, autoimmune pancreatitis, diabetes and metabolic syndrome, and pancreatic cancer) [11, 16, 39, 46]. It has been proposed that H. pylori causes autoimmune pancreatitis through molecular mimicry between α-carbonic anhydrase (α-CA) and human CA type II, and between H. pylori plasminogen-binding protein and human ubiquitin protein ligase E3, which are actively expressed in pancreatic ductal and acinar cells, respectively [59].

Acute pancreatitis. In recent decades, the frequency of acute pancreatitis has steadily increased [60]. With acute pancreatitis, there

is an acute lesion of the mucous membrane of the digestive tract [61]. H. pylori in feces of the patients was detected in 84.7% of cases [62]. Two important mechanisms of the possible influence of H. pylori on the development of acute pancreatitis are distinguished: hypergastrinemia and acidification of the duodenum, which contribute to the translocation of the microorganism and its toxins into the pancreas [63].

According to Gardner [65], an increase in the number of antibodies to H. pylori in the occurrence of purulent-septic complications in acute destructive pancreatitis was noted. This fact is confirmed by other studies: positive results of a serological test for H. pylori (immunoglobulin M) after 7 days from the moment of hospitalization occur in 63.3% of patients with acute pancreatitis of moderate severity and a severe course against 15.5% of patients with a mild course of the disease. The authors established threshold levels of immunoglobulin M to H. pylori (≥1.24 IU/ml) and procalcitonin (≥0.5 mg/ml), which are associated with the risk of developing these complications [60]. However, there are publications in which this fact is denied [61].

Chronic pancreatitis. Three directions of the role of H. pylori in the development of chronic pancreatitis are known: 1) the influence on the pathogenesis of exclusively idiopathic forms, 2) the influence on the exocrine function of the pancreas, 3) feedback when chronic pancreatitis affects the physiology of the gastrointestinal tract and colonization of the pathogen [65]. Based on the examination of patients with chronic pancreatitis associated with H. pylori, the main pathogenicity factors of the bacterium (p33, p30, p26, p19, p17) were established [64]. In recent years, the role of H. pylori in the induction of autoimmune diseases has attracted much attention [66]. Via molecular mimicry, epitope spreading, bystander & polyclonal activation, dysregulation in immune response, and highly immune-dominant virulence, such as CagA, H. pylori causes tissue damage, polarity, and proliferation of the host cells leading to the modulation of host immune responses [59]. This bacterium, as part of microbiome dysbacteriosis, is also considered as a potential trigger of autoimmune inflammation of the pancreas [66].

Potential mechanisms of the influence of H. pylori on the development of autoimmune pancreatitis are shown in Fig. 3.

Pancreatic cancer. There are data indicating an increased risk of pancreatic cancer in H. pylori-positive patients due to decreased somatostatin secretion and increased secretin secretion [39]. In addition, H. pylori, as part of the microbiome dysbiosis and the so-called oncobiome, has been shown to be associated with the development of pancreatic adenocarcinoma through the stimulation of cell proliferation [66].

Antral-dominant H. pylori infection leads to increased pancreatic bicarbonate production and induces the proliferation of ductal epithelial cells, and thus may contribute to pancreatic cancer through a complex interaction with ABO genotype, dietary habits and smoking, and N-nitrosamine exposure [44]. Hirabayashi et al. [67] emphasized that H. pylori infection, especially Cag A positive strains, is a risk factor for pancreatic carcinogenesis. Some mechanisms of H. pylori that increase pancreatic cancer have been highlighted, in particular Helicobacter gastritis, which increases the concentration of gastrin and nitrosamine (N-nitroso components) [68]. H. pylori infection increases the concentration of reactive oxygen species, as well as pro-inflammatory cytokines and other mediators of inflammation. Enhanced cell proliferation and genomic DNA damage with inactivation of tumor suppressor genes can cause malignant transformation of pancreatic cells [69]. Also, after H. pylori infection, increased activity of activator protein-1, nuclear factor-kb, serum level of IL-8 and enhanced serum response element of human pancreatic cancer cells are observed. This suggests that the development of pancreatic cancer may be similar to gastric carcinogenesis. External factors that contribute to the development of pancreatic cancer, as well as gastric cancer,

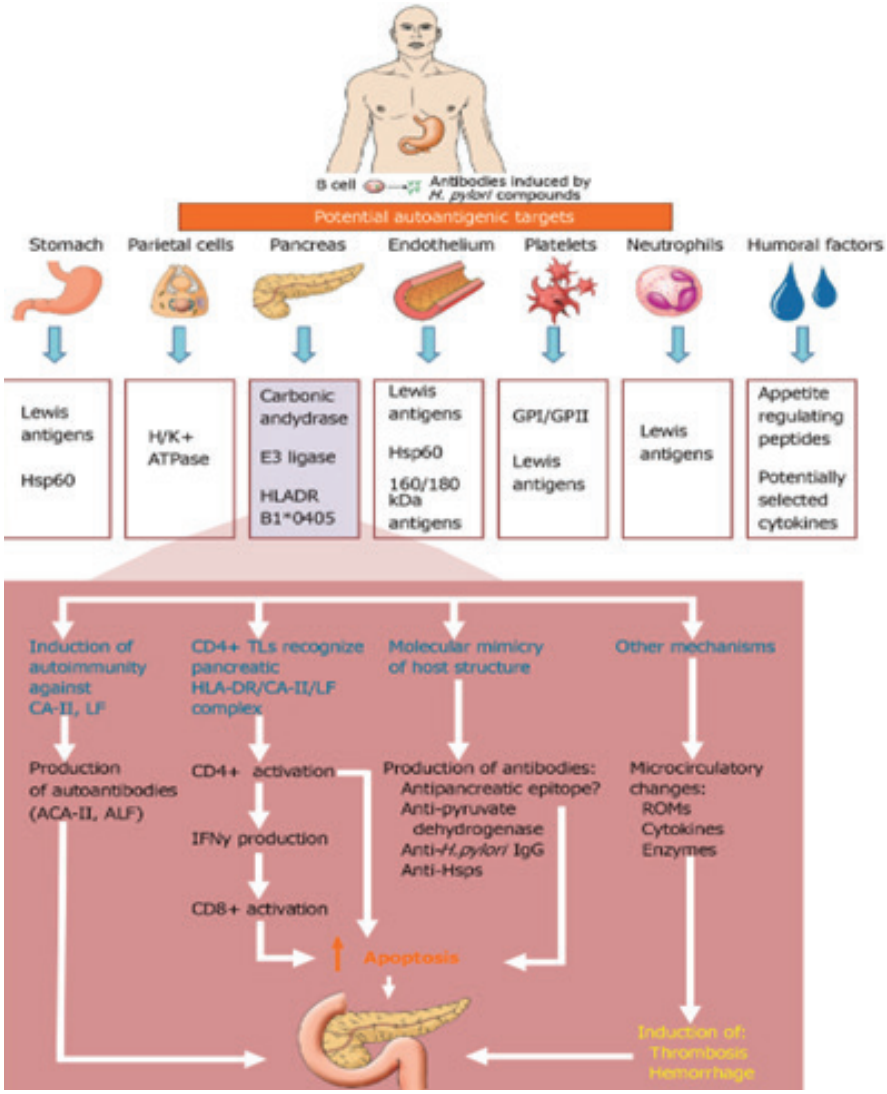

Fig. 3. Potential mechanisms by which Helicobacter pylori might contribute to autoimmune pancreatitis (Kunovsky, Dite [66]): GP: Glycoproteins; Hsp: Heat shock protein; H^+/K^+ ATPase: H^+/K^+-adenosine triphosphatase; HLA-DR: Human leukocyte class II DR antigens; CA-II: Carbonic anhydrase type II antigens; ACA-II: Anticarbonic anhydrase II antibody

include smoking, alcohol abuse, and dietary habits [70].

Based on an analysis of 20,116 subjects included in the Japan Public Health Center Prospective Study Cohort based on available data on H. pylori (anti-H. pylori) seropositivity and the presence of atrophic gastritis and their impact on the development of pancreatic cancer, concluded that no statistically significant increase or decrease in pancreatic cancer risk was observed for H. pylori and atrophic gastritis status independently or in combination [67]. This fact was confirmed by a meta-analysis of data from three cohort studies that revealed no significant association between cytotoxin-associated gene A (CagA) positive strains, CagA negative strains, cytotoxin A (VacA) positive strains, H. pylori infection and pancreatic cancer risk [68]. Permuth et al. [69] determined antibodies to 15 H. pylori proteins (seroprevalence ≥4 proteins) in the serum or blood plasma of patients with and without

pancreatic carcinoma. The seroprevalence of H. pylori proteins was 11.1%, on the basis of which it was concluded that the seroprevalence of H. pylori was not associated with the risk of developing pancreatic carcinoma.

All possible factors affecting H. pylori on the development of pancreatic cancer are shown in Fig. 4.

Factors associated with pancreatic cancer include older age, male gender, regions with high poverty, and diabetes and chronic pancreatitis [70, 71]. Gong et al. [72] demonstrated that MUC4 mucin 4 (MUC4) mRNA expression levels were associated with H. pylori infection. Xu, Zhou et al. [70] analyzed the relationship between H. pylori infection and pancreatic cancer in the PubMed, Embase, and Cochrane databases (a total of 17 studies, which included 8 case-control studies, 5 nested case-control studies, and 4 cohort studies). The results of this analysis confirmed that H. pylori infection was significantly correlated with the occurrence of pancreatic cancer, especially in economically underdeveloped regions. Li, Shu [73] investigated the relationship between H. pylori infection and pancreatic cancer based on the analysis of IgG antibodies against H. pylori, comparing the results with gastric cancer and colorectal cancer. It was found that the level of H. pylori seropositivity in pancreatic cancer is significantly higher than in colorectal cancer and is the same as in gastric cancer. Panthangi et al [74] searched major electronic databases such as PubMed, MEDLINE, Science Direct and the Cochrane Library for the association between H. pylori infection and pancreatic cancer. After a thorough review, the authors selected 15 systematic reviews, among which 6 studies (North American populations) found a significant association between the cytotoxin-associated gene A strain of H. pylori and pancreatic cancer.

The mechanisms of the bacteria's influence on the development of pancreatic cancer are described [68-74]. Bacterial infection can cause local inflammation, and with its spread through the bloodstream – systemic inflammation that induces carcinogenesis. The inflammatory response can be initiated by several types of receptors: Toll-like receptors (TLR4), which recognize the microbial ligand lipopolysaccharide, which is derived from Gram-negative bacteria, and transmit signals through them to myeloid differentiation factor 88 (MyD88) and TICAM1 (also known as

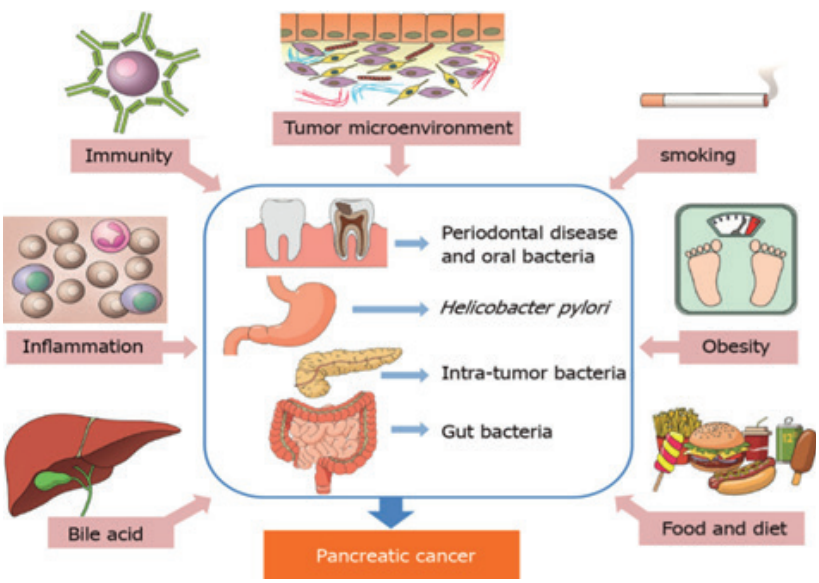

Fig. 4. Factors influencing Helicobacter pylori on the development of pancreatic cancer [66]

TRIF), which leads to the activation of nuclear factor-κB, MAPK and other signaling pathways [71]. It has been established that the bacterium can contribute to oncogenesis by suppressing immunity through innate and adaptive effects. And depletion of the intestinal microbiome by oral antibiotics caused a significant increase in antitumor interferon gamma (IFNγ) [75]. Other studies have shown that exercise has a beneficial effect on the diversity of the gut microbiota [68]. Obesity is a well-recognized risk factor for pancreatic cancer [76].

The role of H. pylori in the pathogenesis of gastroduodenal ulcer and gastric cancer is beyond doubt. However, in the literary sources of recent years, more and more information is accumulating about the connection of the bacterium with various human diseases (cardiovascular system, blood, nervous system, skin, etc.). These data are quite contradictory and controversial. Digestive system (digestive tract and digestive glands) is anatomically and functionally closely related. It is quite natural that the bacterium Helicobacter pylori, which persists in the antral part of the stomach, exerts a pathological influence on both the digestive tract and the digestive glands, causing the development of a number of diseases and their complications.

The author of this study confirm that the research and publication of the results were not associated with any conflicts regarding commercial or financial relations, relations with organizations.

І.В. Колосович

HELICOBACTER PYLORI ТА ЇЇ РОЛЬ У ПАТОГЕНЕЗІ ЗАХВОРЮВАНЬ ТРАВНОЇ СИСТЕМИ

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Helicobacter pylori є грамнегативною бактерією, досить поширеною серед населення планети. Нині найбільш глибоко вивчені патогенетичні механізми впливу бактерії на виникнення гастродуоденальної виразки та раку шлунка. Однак з'являється все більше джерел, присвячених зв'язку Helicobacter pylori з виникненням низки захворювань людини (екстрашлункових). Ці дані є досить суперечливими та контроверсійними. Враховуючи тісний анатомо-функціональний зв'язок травної системи (травний тракт та травні залози) цілком закономірно, що бактерія Helicobacter pylori, яка персистує в антральному відділі шлунка, здійснює патологічний вплив на цю систему, викликаючи розвиток низки захворювань та їх ускладнень. Метою нашого дослідження був аналіз сучасного стану проблеми ролі Helicobacter pylori в патогенезі захворювань травної системи. В цьому огляді наведено останні дані про патогенетичні механізми розвитку гастродуоденальної виразки та раку шлунка. Персистенція бактерії в панкреато-біліарну систему спричинює появу холециститу, жовчнокам'яної хвороби, у т.ч. холелітіазу, гострого та хронічного запалення підшлункової залози, неалкогольної жирової хвороби печінки та цирозу печінки. Також висвітлено різноманітні механізми канцерогенезу пухлин печінки, жовчного міхура, жовчовивідних проток та підшлункової залози, в яких безпосередню участь бере Helicobacter pylori. Подальше вивчення ролі бактерії як предиктора розвитку захворювань травної системи та їх ускладнень бачиться перспективним та актуальним.

Ключові слова: Helicobacter pylori; шлунок; печінка; підшлункова залоза; жовчний міхур; захворювання травної системи; ускладнення.

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