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THIRTY-FIVE YEARS OF THE CHORNOBYL DISASTER: RADIOLOGICAL AND MEDICAL CONSEQUENCES, STRATEGIES OF PROTECTION AND REVIVAL

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The National Report analyzed the radiological and medical consequences 35 years after the accident at the Chornobyl Nuclear Power Plant: radiation doses, the state of health of the victims and its changes in the distant period, the socio-psychological state of the residents of the territories contaminated with radionuclides, and demographic changes.

Authors of the chapters are responsible for the presentation and authenticity of the materials.

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TABLE OF CONTENTS

TERMS AND ABBREVIATIONS

ACCUP – Chornobyl accident consequences clean-up participants
ACTH – adrenocorticotropic hormone
ACUW – clean-up workers
AD – absorbed dose
AE – age at exposure
AH – arterial hypertension
AL – acute leukemia
ALL – acute lymphoblastic leukemia
AOP – antioxidant protection
ARC – areas of radiological contamination
ARS – acute radiation sickness
ARS NC – non-confirmed diagnosis of ARS
BCH – basal cell hyperplasia
BCR – B-cell receptors
BDD – birth defects development
BFM – Berlin-Frankfurt-Munster Group
BPH – benign prostatic hyperplasia
BPP – bronchopulmonary pathology
CAT – chronic autoimmune thyroiditis
CB – chronic bronchitis
CER – Clinical and Epidemiological Register
CER – Clinical and Epidemiological Register
CFS – chronic fatigue syndrome
CHD – coronary heart disease
ChNPP – Chornobyl Nuclear Power Plant
CIEC – Central Interdepartmental Expert Commission
CLL – chronic lymphocytic leukemia
CML – chronic myeloid leukemia
CMR – morphological register of thyroid cancer
COPD – chronic obstructive pulmonary disease
cRCC – conventional renal cell carcinoma
CT – chemotherapy
CTD – connective tissue dysplasia
CUW – clean-up workers
CUWs of the ChA – clean-up workers of the Chornobyl accident
CVD – cardiovascular pathology
DB – database
DEP – dyscirculatory encephalopathy
DLco – diffusion capacity of lungs
DNG – diffuse non-toxic goiter
DRF – dose reduction factor
EBC – exhaled breath condensate
EDHC – extremely dangerous and hazardous conditions
EIU – subjects exposed in utero
ENG – electronystagmography
eNOS – endothelial NO synthase
EOG – electrooculography
ERP – event related potentials
ERR/Gy – excess relative risk of leukemia per unit dose of radiation
ERV – expiratory reserve volume
EWBC – expert whole body counter
EZ – Exclusion zone
FEF_{75} – maximum volumetric rate at 75 % FVC
FEV_1– forced expiratory volume per 1 second
FVC – forced vital capacity
GSTs – glutathione-transferases
HPAS – hypothalamic-pituitary-adrenal system
HR – risk ratio
IAEA – International Atomic Energy Agency
ICRIN – International Chornobyl Research and Information Network
ICRP – International Commission on Radiological Protection
IGHV – immunoglobulin heavy chain
IPOG – State Institution «Institute of Pediatrics, Obstetrics and Gynecology of NAMS of Ukraine»

IR – ionizing radiation
ITGV – internal volume of gas in the chest
LDIR – low doses of ionizing radiation
LDRIR – low dose rate ionizing radiation
LPO – lipid peroxidation
2-MBT – 2-mercaptobenzothiazole
MDD – minimum dose detected
MHU – Ministry of Health of Ukraine
MMW – millimeter waves
MN – malignant neoplasms
MPN – myeloproliferative neoplasms
NAE – N-acyl-ethanolamines
NAFLD – non-alcoholic fatty liver disease
NCRP – National Commission on Radiological Protection (USA)
NCRU – National Cancer Registry of Ukraine
NCT – nominally clean territories
NG – nodular goiter
NPP – Nuclear Power Plant
NRBU-97 – Radiation Safety Standards of Ukraine
NRCRM – National Research Center for Radiation Medicine
NsC – nosology control
NSE – N-stearoylethanolamine
OPh – oxidative phosphorylation
OS – object of «Shelter»
PAR – population attributive risk
PFL – paradoxical fall in intelligibility
PIA – proliferative inflammatory atrophy
PIN – prostatic intraepithelial neoplasia
PTSD – post-traumatic stress disorder
PVN – paraventricular nuclei
qEEG – quantitative electroencephalogram
RADRUE – Realistic Analytical Dose Reconstruction with Uncertainty Estimation
RAW – radioactive waste
RBE – relative biological effectiveness
RCT – radioactively contaminated territories
RIBE – radiation induced bystander effect
RIRE – radiation induced rescue effect
RISBE – radiation induced secondary bystander effect
RNPP – Rivne NPP
RR – relative risk
RSPAN – Radiation sclerosing proliferative atypical nephropathy
RV – residual volume
SAH – self-assessed health
SAS sympathoadrenal system
SC – special control
SES – State Emergency Service of Ukraine
SIP – Shelter Implementation Project
SIR – standardized incidence rate
SNHL – sensorineural hearing loss
SNPs – single nucleotide polymorphisms
SRU – State Register of Ukraine of Persons Affected by the Chornobyl Catastrophe of the Ministry of Health of Ukraine
SUNPP – South Ukrainian NPP
SZ – surveillance zone
TGF-β1 – transforming growth factor
TIBE – tumor-induced bystander effects
TKI – tyrosine kinase inhibitor
TSH – thyroidstimulating hormone
TUE – transuranium elements
UACOS – Ukrainian-American Chornobyl Ocular Study
VC – vital capacity
VeD – vestibular dysfunction
WBC – whole body counters
ZGVR – Zone of granted voluntary resettlement, or 3rd zone.
ZU(O)R – Zone of unconditional (obligatory) resettlement, or 2nd zone

1. EXPOSURE DOSES

Estimation of exposure doses of participants in liquidation of consequences of the Chornobyl accident, of persons evacuated in April—May 1986 from settlements of 30-km zone, and of the population residing at radioactively contaminated territories remains an important job aimed at reduction of the influence of ionizing irradiation on health of people suffered after the Chornobyl disaster.

A structure, methodology and results of dose estimates are described in detail in previous national reports [1—4]. Hence, in this section it is summarized the most important results for the whole post-Chornobyl period concerning exposure doses of different categories of Ukrainian population, and noval data are presented obtained in this area for the last five years.

1.1. Integrated dosimetric passportization of settlements of Ukraine

The accident at Chornobyl Nuclear Power Plant (ChNPP) caused large-scale radioactive contamination of the environment. Nowadays, in 35 years after that, the contamination diminished essentially as a result of radioactive decay of the most of radionuclides of Chornobyl origin and of processes of their migration in natural environment. Exposure doses of the population at the most part of radioactively contaminated territory (RCT) already do not exceed permissible level. But at certain suffered territories, it is necessary to held the ecological and dosimetric monitoring and use countermeasures, among them restriction on consuming local milk and forest produce, etc.

Nowadays population exposure doses are formed mainly by radionuclide ^{137}Cs. At that one of the main sources of composing the dose is drinking milk of local production. Forest mushrooms and other forest produce, due to their high ability to accumulate radionuclides, also play essential role in forming exposure doses of persons who consumes this foodstuff in considerable volumes. In settlements situated at the territory of southern trace of Chornobyl radioactive fallouts, in particular in Ivankivskyi district of Kyivska oblast, radiostrontium also makes some contribution to the exposure dose. Contribution of plutonium and americium radionuclides to the exposure dose of the population is comparatively small.

It is established by the Law of Ukraine «On legal status of the areas radioactively contaminated by the Chornobyl disaster» No. 791a-XII from February 27, 1991 [5], that a territory with contamination level which can lead to exposured of population with the dose above 1 mSv per year, is reckoned radioactively contaminated after Chornobyl accident and needs actions on protection of population and restriction of additional exposure. This law establishes (Table 1.1) the following:

➢ Exclusion zone (EZ)

➢ Zone of unconditional (obligatory) resettlement (ZU(O)R), or 2nd zone;

➢ Zone of granted voluntary resettlement (ZGVR), or 3rd zone.

Estimation and analysis of exposure doses of the population residing at RCT were held practically from the first days of Chornobyl accident. Starting from 1986, in Ukraine it was held radio-ecological and dosimetric monitoring and research of space distribution of the source of exposure (radionuclide structure, power, conditions for emergency fallout), as well as of behavior of radionuclides at areas with different soil and geographic characteristics [6—10]. Regularities were investigated of forming individual and mean-group (territorial, professional, age-related) exposure doses of population in dependence on radio-ecological factors and living conditions, and also on organized coun-

Table 1.1
Description of radioactive contamination zones

Exclusion zone		ZU(O)R, or 2nd zone		ZGVR, or 3rd zone		Zone of enhanced radiation monitoring*	
number of settlements	area (km²)	number of settlements	area (km²)	number of settlements	area (km²)	number of settlements	area (km²)
76	2000	86	2200	841	23300	1290	27150

Note. *From January 1, 2015, this zone does not exist legislatively.

termeasures. Information obtained during investigations was included in databases. All this makes it possible to reproduce quite complete picture of evolution in space and time of radiation environment that was developed in Ukraine along all post-accidental period.

Reconstruction of exposure doses of the population suffered from the accident at ChNPP has started after 1991 in the frame of the program of integrated dosimetric passportization of Ukrainian settlements (Fig. 1.1). Dose calculations were based on results of annual measurements contamination by radiocesium for milk and potatoes produced in that settlements which were indicated by Ruling of Cabinet of Ministers of Ukraine N 106 [11]. Also the passportization made provision of measurement for radiocesium intake in the body of residents of suffered territories by whole body counters (WBC). Totally for the years of passportization (1991– 2013) it was made 500 thousand measurements of milk and potatoes and about 1.5 billion of WBC measurements. Nominal doses that were calculated in frame of the dosimetric passportization were aimed at grounding decisions made by the state and local authorities according to acting legislation, and therefore, the doses had quite high conservative level. They are mean-weighted by professional and aged structure of settlement residents (separately for urban and rural locality). Work made in frame of the dosimetric passportization is unprecedented both by its scale and by duration of radio-ecological and dosimetric monitoring.

From 1995 till 2008 passport (nominal) doses have been calculated annually for 2.2 thousand settlements of Ukraine. In 2011 they were estimated for 1977 settlements, in 2012 – for 186 ones, and in 2013 (the last year of official conducting of passportization) – for 354 ones. During 1991–2013 the relative number of passportized settlements, for which a passport dose did not exceed 0.5 mSv per year, increased almost twice and reached 94 % (Table 1.2).

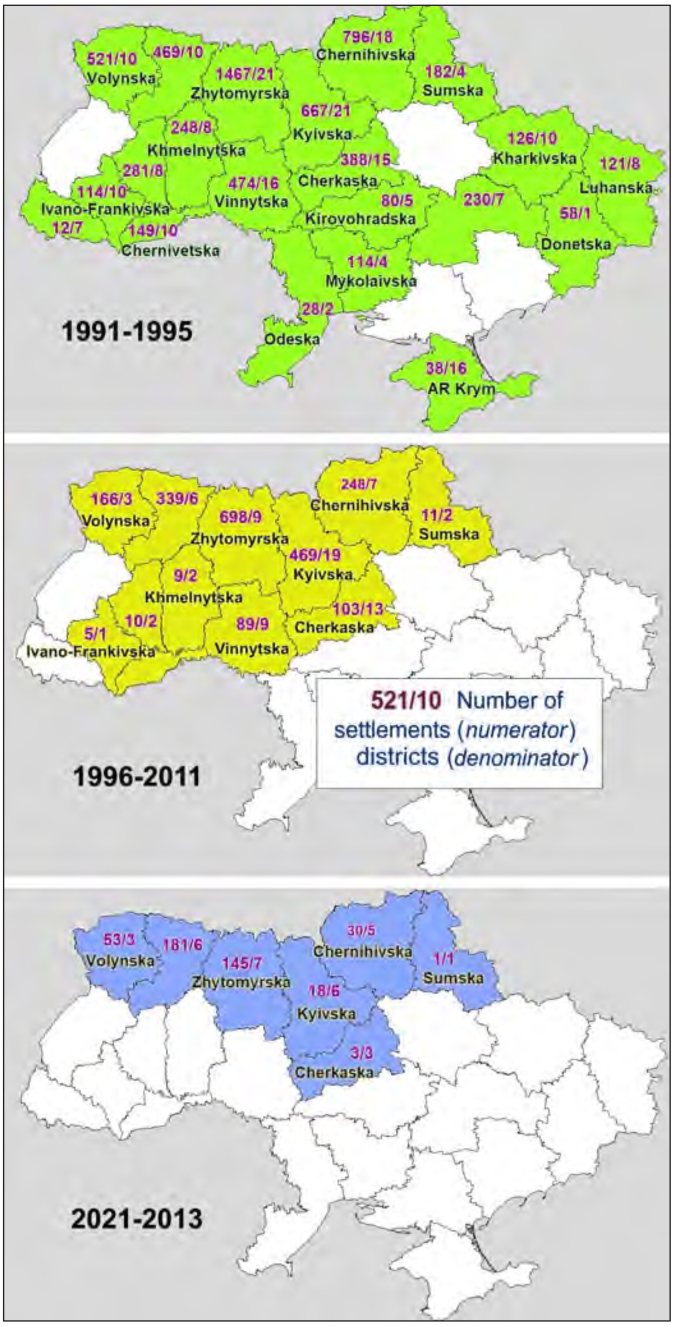

Figure 1.1. **Scales of integrated dosimetric passportization of Ukrainian settlements (1991–2013)**

Table 1.2
Change in time (1991–2013) of settlement distribution at radioactively contaminated territories of Ukraine by the value of nominal dose

Year	Number of settlements with monitoring	Relative number (%) of settlements with passport dose (mSv per year)			
		≤ 0.5	0.5–1	1–5	>5
1991	2480	51	16	31	2.7
1993	2430	52	22	25	0.78
1994	1988	48	26	25	0.35
1995	2202	52	26	22	0.09
1996	2224	59	15	25	0.27
1997	2161	63	17	20	0.42
1998	2161	62	17	20	0.32
1999	2161	64	18	18	0.42
2000	2161	66	14	20	0.28
2001	2163	67	15	18	0.23
2002	2163	68	15	17	0.14
2003	2163	71	16	13	0.09
2004	2163	72	19	9.3	–
2005	1831	78	16	5.9	–
2006	1967	82	14	3.5	0.05
2007	1596	81	15	3.6	–
2008	1925	86	12	2.2	–
2011	1977	94	5	1.3	–
2012*	186	54	32	14	–
2013*	354	58	34	8	–

Note. *Specific conditions of settlement selection for conducting monitoring in comparison with previous years.

Thus, already in 2011 practically all settlements, passportized by the value of passport dose, were situated actually out of boundary of radioactive contamination zones, indicated by the legislation of Ukraine. From other side, after 2007 there are no settlements with passport dose exceeding 5 mSv · year^{-1}, which is a limit of zone of unconditional (obligatory) resettlement. Relative number of settlements with passport dose from 1 to 5 mSv · year^{-1} for the period of 1991–2011 decreased in a quarter and in 2011 it constituted only 1.3 % (25 settlements) of all passportized settlements. Due to specific conditions for conducting passportization in 2012 and 2013, when the settlements were selected with the highest levels of contamination of milk from private households, relative part of settlements with passport dose within the interval from 1 to 5 mSv · year^{-1} achieved 14 %, though absolute number of such settlements has not practically changed compared with 2011 [6, 7, 10].

Along the whole post-accidental period, it was published sixteen Collections of integrated dosimetric passportization. The Collections accumulate results of tens and hundreds of thousand spectrometry, radiochemical and WBC measurements that were conducted in 1991–2013. These results of monitoring, together with calculated passport doses on its base, are unique information that characterizes the level and time dynamics of radiation state for each of 2161 settlements from 12 Oblasts of Ukraine. According to the last Collections (2011–2013), only in 36 settlements total passport dose exceeded 1 mSv (Table 1.3) [9, 10].

Passportization was conducted according to requirements of instructive-methodical instructions «Radiation and dosimetric passportization of the settlements of Ukrainian territory which suffered from radioactive contamination as a consequence of the Chornobyl accident, including thyroid dosimetric passportization». Instructions and practical policies: «Methods-96», approved by Ministry of Health of Ukraine in 1996 [8]. But the indicated «Methods-96» has not been renewed for long time. During the past years the situation at RCT has drastically changed, namely: it have changed demographic structure of the population, structure of production of local meal and peculiarities of consumption of that meal, proportion of ^{137}Cs and ^{90}Sr in meal, and it was obtained new data on transition coefficients «ground–vegetation» and «ground–milk».

Necessity of passportization, according to the decree of President of Ukraine [12], under new conditions dictates new approaches to passport doses estimates. Contrary to previous methodic,

Table 1.3
List of settlements of Ukraine, where passport dose in 2011–2013 exceeded 1 mSv [9, 10]

Settlements	^{137}Cs in ground,* kBq · m^{-2}	Passport dose, mSv · year^{-1}								
		2011			2012			2013		
		D^e	D^i	D^{tot}	D^e	D^i	D^{tot}	D^e	D^i	D^{tot}
Zhytomyrska Oblast. *Korostenskyi district*										
Voroneve	313	0.60	0.47	1.06	0.58	0.60	1.2	0.57	0.43	1.0
Nemyrivka	280	0.54	0.31	0.85	0.52	0.54	1.06	0.51	0.41	0.92
Zhytomyrska Oblast. *Luhynskyi district*										
Nova Rudnia	114	0.22	1.6	1.8	0.21	0.03	0.24	0.21	0.026	0.23
Zhytomyrska Oblast. *Narodytskyi district*										
Loznytsia	488	0.93	0.18	1.1	0.91	0.14	1.05	0.89	0.14	1.03
Narodychi	226	0.43	0.87	1.3	0.42	0.40	0.82	0.41	0.18	0.59
Rozsokhivske	392	0.75	0.43	1.2	0.73	0.17	0.91	0.71	0.21	0.92
Zhytomyrska Oblast. *Ovrutskyi district*										
Vystupovychi	365	0.70	0.63	1.33	0.68	0.08	0.76	0.67	0.06	0.73
Pershotravneve	144	0.27	0.19	0.47	0.27	0.84	1.1	0.26	0.23	0.49
Zhytomyrska Oblast. *Olevsk district*										
Rudnia-Ozerianska	49	0.09	1.2	1.3	0.09	0.40	0.50	0.09	0.68	0.77
Rivnenska Oblast. *Volodymyretskyi district*										
Horodets	34	0.06	0.52	0.59	0.06	1.31	1.4	0.06	0.17	0.23
Horodok	29	0.06	0.72	0.78	0.05	1.32	1.4	0.05	1.0	1.1
Rivnenska Oblast. *Dubrovytskyi district*										
Budumlia	57	0.11	1.15	1.26	0.11	1.01	1.11	0.11	1.1	1.2
V. Cheremel	93	0.18	1.09	1.27	0.17	2.17	2.35	0.17	2.2	2.3
Shakhy	64	0.12	0.45	0.57	0.12	0.52	0.64	0.12	1.2	1.3
Rivnenska Oblast. *Zarichnenskyi district*										
Bir	49	0.09	1.8	1.86	0.09	1.6	1.7	0.09	1.9	2.0
Borove	17	0.03	0.61	0.64	0.03	1.1	1.1	0.03	1.14	1.2
Kukhche	39	0.08	0.95	1.03	0.07	0.11	0.19	0.07	0.17	0.24
Lysychyn	31	0.06	1.2	1.22	0.06	1.24	1.3	0.06	1.4	1.5
Mlynok	34	0.07	0.73	0.80	0.06	0.60	0.66	0.06	1.2	1.3
Oleksandrove	31	0.06	0.80	0.86	0.06	0.94	1.0	0.06	0.82	0.88
Sernyky	52	0.10	1.4	1.5	0.10	0.93	1.03	0.1	1.3	1.4
Rivnenska Oblast. *Rokytnivskyi district*										
Berezove	39	0.07	0.69	0.77	0.07	3.8	3.9	0.07	1.0	1.1
Vezhytsia	61	0.12	2.2	2.3	0.11	2.1	2.2	0.11	2.1	2.2
Hrabun	45	0.09	2.4	2.4	0.08	2.3	2.4	0.08	1.3	1.4
Drozdyn	34	0.07	3.2	3.3	0.06	1.4	1.5	0.06	2.1	2.2
Yelne	61	0.12	1.6	1.7	0.11	2.6	2.7	0.11	1.6	1.7
Zabolottia	41	0.08	1.6	1.7	0.08	1.6	1.7	0.07	1.1	1.2
Perekhodychi	87	0.17	1.7	1.8	0.16	1.3	1.5	0.16	1.9	2.1
Poznan	23	0.04	0.5	0.54	0.04	1.1	1.2	0.04	0.44	0.48
Stare Selo	32	0.06	2.7	2.8	0.06	2.8	2.8	0.06	2.05	2.1
Khmil	19	0.04	0.76	0.8	0.04	1.8	1.9	0.04	0.75	0.79
Rivnenska Oblast. *Sarnenskyi district*										
Vyry	44	0.08	0.87	0.95	0.08	0.94	1.02	0.08	1.1	1.2
Klesiv	94	0.18	0.98	1.2	0.18	0.52	0.69	0.17	0.69	0.86
Puhach	44	0.09	1.1	1.2	0.08	1.3	1.4	0.08	1.5	1.6
Rudnia-Karpylivska	57	0.11	0.90	1.01	0.11	0.94	1.04	0.10	1.0	1.1
Chemerne	38	0.07	1.04	1.1	0.07	0.83	0.90	0.07	0.94	1.01

Notes. *Calculated for 2011 by the results of monitoring in 1992.
D^e – dose of external exposure; D^i – dose of inner exposure; D^{tot} – dose of total exposure.

calculation model of which used parameters of radio-ecological state of suffered territories of the first decade after the accident, new methodic has to take into account the radiation environment that arose at RCT last years. Decreasing of conservatism of passport doses in new methodic can be achieved based on estimates that rely directly on results of WBC measurements, which can be made among residents of a passportized settlement in the year of passportization.

1.2. Reconstruction of individualized exposure doses of subjects of State Registry of Ukraine (SRU) of persons, affected due to Chornobyl accident that reside at radioactively contaminated territories

«State Registry of Ukraine of persons, affected due to Chornobyl accident» (SRU) has been functioning since 1992. Its main task is providing information for profile scientific and medical institutions on health status of persons exposed as the result of Chornobyl disaster. Based on SRU, scientific research is performed by the following directions [4, 13]:

➢ epidemiology of malignant neoplasms;
➢ epidemiology of non-tumour diseases;
➢ epidemiological study of health state of children (evacuated or born from participants of the accident liquidation);
➢ medical and demographic consequences of the accident at Chornobyl Nuclear Power Plant (ChNPP);
➢ social and psychological problems of suffered.

SRU contains data on persons of four groups of primary registration (totally 2.5 billion persons for the end of 2020):

➤ Group 1: liquidators (~323.3 thousand persons);
➤ Group 2: evacuated (~83 thousand persons);
➤ Group 3: residents of radioactively contaminated territories (RCT) (~1.62 billion persons);
➤ Group 4: children born from parents of 1–3 groups (~445 thousand persons).

Practical absence in SRU of radiation doses (in the first place of persons residing at RCT and of children that were born from irradiated persons) till recent time has not made it possible to estimate an impact of the radiation factor on the health of the community mentioned above. Hence it is necessary to work out a system of reconstruction of exposure doses for population suffered from the accident at ChNPP, that will take account of individual information on persons registered in SRU, as well as of results from radio-ecological and dosimetric monitoring held at RCTs of Ukraine starting from 1986. The elaborated system is a set of interconnected estimation procedures of parameters that influence on the value of exposure doses for population of RCTs [14–17].

In the frame of elaboration of above mentioned system there were formulated and grounded criteria for selection of persons to subcohort from the individualization of exposure doses of SRU persons. According to the criteria, it was formed a cohort of residents of 14 northern administrative districts of Zhytomyrska, Kyivska, Rivnenska and Chernihivska Oblasts, for which the individualization of doses is possible. The cohort consists of 74 % of all the residents of that districts registered in SRU (Fig. 1.2).

Main radio-ecological parameters are determined that make influence on the value of individualized dose. Those are: the density of radioactive fallouts, radiological properties of grounds in a settlement, contents of radionuclides in meal, and levels of consumption of local products by the population.

In the first post-accidental year, the contribution of ^{137}Cs to the annual dose of external gamma irradiation of the population of RCTs was ~11 %, which is explained by main contribution of short-living isotopes ^{103}Ru, $^{132}Te+^{132}I$, ^{134}Cs, $^{95}Zr+^{95}Nb$ and others. In next years ^{137}Cs became the main dose-forming radionuclide. After 1986 the activity of ^{137}Cs in the ground decreased gradually due to radioactive decay and vertical migration to lower layers of ground cover.

«Ground-milk» transfer factors of radiocesium attained the largest values in 1987. After that, it gradually decreased. In 1995–2000 it was observed a local increasing of ^{137}Cs transition in milk, because at that period at RCTs gradual reduction of countermeasures took place, which caused jumps of radiocesium contents in milk of private households on the background of natural decreasing of ^{137}Cs radioactivity as a result of radioactive decay. Since

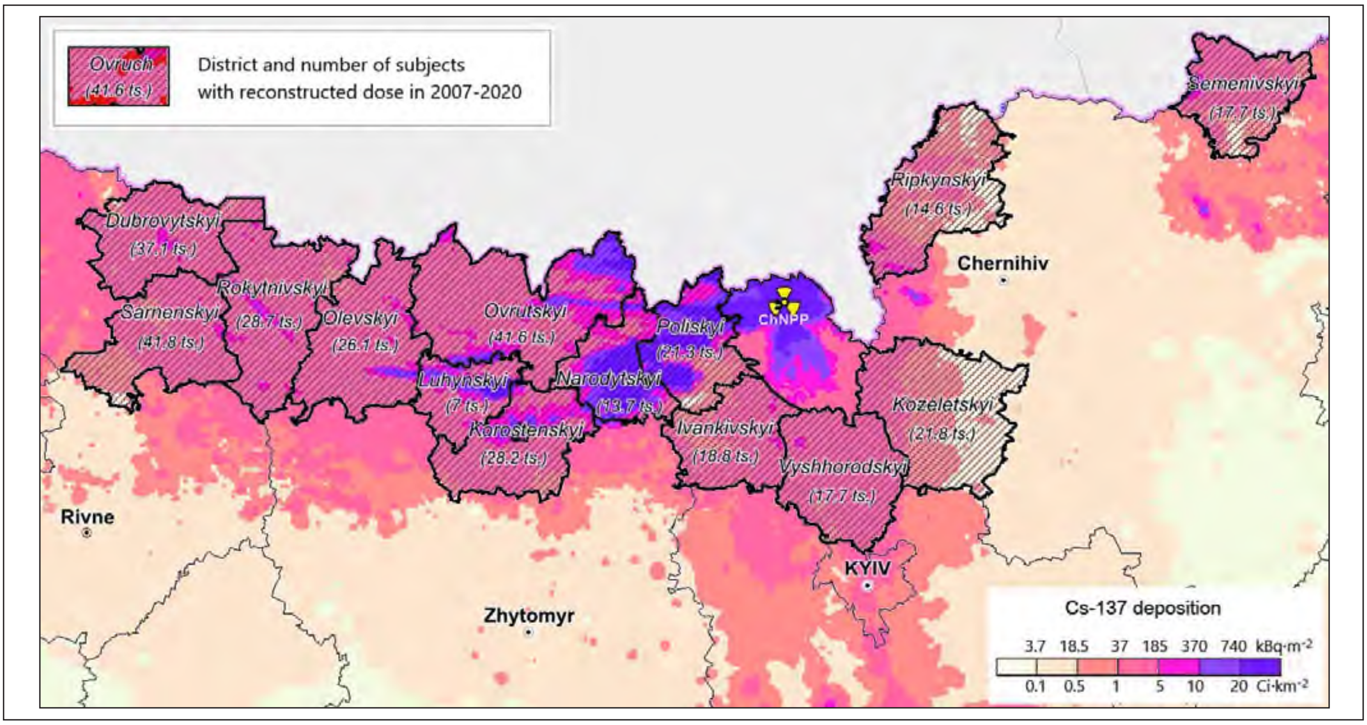

Figure 1.2. **Chart-scheme of location of 14 districts, for which it was made the individualization of exposure doses of SRU subjects**

2000 values of annual transfer factors were practically constant.

In spite of the fact that the density of ground contamination by radiocesium is the largest in Narodytskyi district of Zhytomyrska Oblast, ^{137}Cs concentration in milk of private households in this region was 2–7 times less compared with Dubrovytskyi and Rokytnivskyi districts of Rivnenska Oblast, which is related to high «ground-milk» transfer factors at turf-marsh grounds of these regions. It is an important argument in favor of using the dose criterion in zoning of RCTs.

An important part of works on individualization of exposure doses of SRU subjects became elaboration of ecological-dosimetric models of reconstruction of exposure doses for the population of RCTs. Model parameters are based first of all on generalization of results of radio-ecological (measurements of radionuclides concentration in ground and meal of local production) and dosimetric (measurement of radioiodine contents in thyroid, WBC measurement) monitoring, which were held along post-accidental period in settlements where SRU subjects reside. Taking account of the fact that frequency and size of WBC and milk monitoring differed significantly for various administrative regions and for settlements within a district, a general structure of ecological-dosimetric models is clear district-specific. Other parameters of elaborated models are related to peculiarities of population behavior and radionuclide metabolism in the body of people and agricultural animals. Individualized annual effective exposure dose of a person registered in SRU is the mean dose, which is obtained in the same settlement by representatives of the same gender-age and professional group.

Based on elaborated model, individualized exposure doses were calculated for 403 thousand persons (~16 % of all registered in SRU) that reside in 1,010 settlements of 14 the most radioactively contaminated administrative districts of Ukraine: Luhinskyi, Narodytskyi, Ovrutskyi, Korostenskyi, Olevskyi, Vyshhorodskyi, Ivankivskyi, Poliskyi, Dubrovytskyi, Rokytnivskyi, Sarnenskyi, Kozeletskyi, Ripkynskyi and Semenivskyi.

By results of calculation of individualized exposure doses of SRU persons it is determined that 70 % of SRU persons of Korostenskyi district of Zhytomyrska Oblast during 35 years after the accident (under the condition of permanent residing in the region) obtained the doses in the interval 5–20 mSv (Table 1.4). For 23 % of SRU persons of Korostenskyi district the accumulated for 35 years dose lies in the interval 20–50 mSv, and for 5.7 % of persons of this district – exceeds 50 mSv.

For 93 % of SRU persons of Narodytskyi, 73 % of Luhinskyi, ~46 % of Ovrutskyi and ~34 % of Olevskyi district, the individualized doses accumulated

Table 1.4
Distribution of SRU subjects by intervals of total effective individualized dose accumulated during 1986–2020 under the condition of permanent residing in settlements of registration

District	Interval of accumulated doses, mSv				
	≤ 5	5–10	10–20	20–50	> 50
	Relative number of persons, %				
Zhytomyrska Oblast					
Korostenskyi	1.3	28	42	23	5.6
Luhinskyi	–	0.1	27	62	11
Narodytskyi	–	0.3	7.2	34	58
Ovrutskyi	–	2.2	52	43	2.6
Olevskyi	–	5.6	61	33	0.9
Kyivska Oblast					
Vyshhorodskyi	36	27	30	6.7	0.3
Ivankivskyi	10	30	55	4.3	–
Poliskyi	20	31	27	22	–
Rivnenska Oblast					
Dubrovytskyi	–	1.8	37	58	3.2
Rokytnivskyi	–	–	16	78	6.3
Sarnenskyi	0.6	44	33	23	–
Chernihivska Oblast					
Kozeletskyi	53	34	13	–	–
Ripkynskyi	26	58	7.3	9.0	0.7
Semenivskyi	2	12	67	19	–

during the post-accidental period exceed 20 mSv. At that for 58 % of SRU persons of Narodytskyi, 73 % of Luhinskyi, ~ 46 % of Ovrutskyi and ~ 34 % of Olevskyi district, they were higher than 50 mSv. Accumulated dose lies in the interval 5–20 mSv for 7 % of SRU persons of Narodytskyi district and for 27, 54 and 66 % of Luhinskyi, Ovrutskyi and Olevskyi districts, respectively. That is dose loads obtained by SRU subjects of Korostenskyi district for 35 years after Chornobyl disaster are lower compared with other regions of Zhytomyrska Oblast. And the largest doses were obtained by SRU representatives of Narodytskyi and Luhinskyi districts.

Compared with other districts, SRU subjects of Kozeletskyi and Ripkynskyi districts obtained the lowest doses accumulated for 35 years. About 87 % of SRU persons of Kozeletskyi and 83 % of Ripkynskyi districts accumulated effective doses less than 10 mSv. Accumulated individualized doses of residents of Semenivskyi district are the highest in Chernihivska Oblast. 14 % of SRU persons of this district obtained doses less than 10 mSv, 67 % of subjects have doses in the interval 10–20 mSv, and 19 % of persons accumulated doses from 20 to 50 mSv.

Among above mentioned districts of Rivnenska Oblast the least exposure was obtained by residents of Sarnenskyi district. So, for about 77 % of them exposure dose accumulated for 35 years does not exceed 20 mSv. In Dubrovytskyi and Rokytnivskyi districts of Rivnenska Oblast practically there are no persons with the dose less than 10 mSv. Accumulated dose for majority of persons of above mentioned districts (58 % in Dubrovytskyi district and 78 % in Rokytnivskyi one) lie in the interval from 20 to 50 mSv.

Overwhelming majority of SRU persons that permanently resided in settlements of Ivankivskyi district of Kyivska Oblast (86 %) for 35 years obtained exposure dose in the interval from 5 to 20 mSv. Doses in this interval were accumulated by 57 % and 58 % of Vyshhorodskyi and Poliskyi district, respectively.

Mean exposure dose in 1986, in dependence of ecological characteristic of a district, 2–5 times exceeds the dose in 1987. For the first 5 years (1986–1990) adult SRU persons accumulate in mean ~63 % of dose obtained for the whole post-accidental period (see Table 1.5).

More than 80 % of exposure dose was accumulated by SRU subjects for the first 15 years after the accident. Total effective individualized dose accumulated in 2000–2020 does not exceed 20 % of the dose for the period 1986–2000. For the whole post-accidental period, the highest doses were obtained by SRU persons of Narodytskyi and Luhinskyi districts of Zhytomyrska Oblast, and the lowest ones –

Table 1.5
Effective individualized doses, accumulated by adult SRU persons of certain districts in different time intervals under the condition of permanent residence at settlements of registration

Oblast, district	Periods of time, *years*					
	1986–1990 («5 years»)		1986–2000 («15 years»)		1986–2020 («35 years»)	
	Accumulated dose, mSv					
	mean	95 % quantile	mean	95 % quantile	mean	95 % quantile
Zhytomyrska Oblast						
Korostenskyi	13	34	17	46	20	56
Luhinskyi	22	42	28	56	32	65
Narodytskyi	32	51	43	69	54	84
Ovrutskyi	14	26	19	35	23	44
Olevskyi	11	19	15	25	19	31
Kyivska Oblast						
Vyshhorodskyi	5.7	14	8.1	21	9.7	24
Ivankivskyi	8.6	13	11	18	13	21
Poliskyi	7.6	17	11	23	13	31
Rivnenska Oblast						
Dubrovytskyi	15	28	21	39	25	46
Rokytnivskyi	16	25	24	43	29	54
Sarnenskyi	10	25	13	33	15	39
Chernihivska Oblast						
Kozeletskyi	4.5	9.8	5.8	13	7.0	15
Ripkynskyi	5.9	21	7.6	26	9.0	30
Semenivskyi	14	23	17	28	19	31

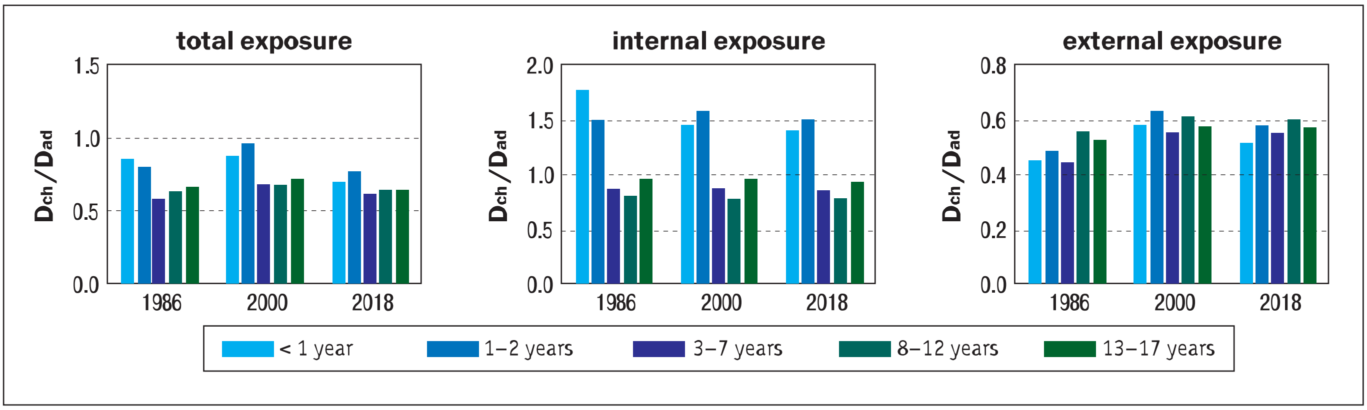

Figure 1.3. **Ratio of average annual individualized effective dose of representatives of different children's age groups to the dose of adult population**

of Kozeletskyi district of Chernihivska Oblast. Mean total effective dose accumulated by SRU subjects that were adult at the moment of accident varies from 54 mSv (Narodytskyi district) to 7.0 mSv (Kozeletskyi district).

Ratio of mean-annual effective individualized exposure doses for child's age groups (D_{ch}) to the ones for adults (D_{ad}) was evaluated for residents of the same settlement separately for internal, external and total exposure in 1986, 2000 and 2018 (see Fig. 1.3). Representatives were considered of 5 child's age groups (< 1, 1–2, 3–7, 8–12 and 13–17 years old).

Children up to 2 years were a critical age group concerning exposure doses. Their annual dose of internal exposure exceeds the one for adults in 1.5 times. The largest value of ratio D_{ch} / D_{ad} for babies in the accident year constitutes 1.8 that is explained by peculiarities of babies' nutrition; the latter consume more milk (including the one of local production) than representatives of other age groups.

Effective internal exposure doses of children from 2 to 12 years old constitute about 80 % of the dose for adult persons, exposure doses of teenagers at the age of 12–17 years practically coincide with the ones for adults. Effective external exposure doses of representatives of all children's age groups are 1.7–2.0 times lower than of adults.

Estimation system of individualized doses of SRU persons makes it possible to estimate accumulated doses for separate organs (thyroid gland, red marrow, etc.) for any persons residing at RCT of Ukraine. Thus, results obtained in current research can be used in radio-epidemiological studies on estimation of negative influence of ionizing irradiation on human health.

1.3. Long-term comprehensive monitoring of internal irradiation of the population on radioactively contaminated territories of Ukraine after the Chornobyl accident

Since 1986 specialists of the National Research Center for Radiation Medicine of National Academy of Medical Sciences of Ukraine (NRCRM) have been conducting constant mass monitoring of the internal exposure levels of the population affected by the accident on the Chornobyl Nuclear Power Plant (NPP). There were created and developed a number of new devices and methods to perform measurements of radionuclides incorporated in the human body and methods to determine the levels of population expo, both individual and averaged over the settlement (S).

A unique internal irradiation monitoring complex with a system of program, methodical and metrological support, created on the basis of the NRCRM dosimetry department, is implemented in a two-stage system of internal irradiation doses monitoring, using whole body counter (WBC) of different classes aimed at current mass screening, deeper monitoring of critical groups and solving expert and metrological tasks (Fig. 1.4).

For radiological control of patients of the Medical Center of Radiation Registry and NRCRM clinic, a stationary WBC complex is used on the basis of a double installation «Super-Jemini», WBC «Positronika» and WBC «Screenner-3M» of stationary type. For mass monitoring of the population of RCT in different years used: portable WBC type «S» (1986–2000) and mobile WBC on the basis of a powerful diesel passenger bus LAZ-42021 (1993–2002) and WBC type «Screenner-3M» (1998–2020) on the basis of a UAZ car.

In 1995–1997, in connection with the need to implement the program «General Dosimetric Certification of Settlements of Ukraine» created a single network of WBC Ukraine, which was to ensure the prompt receipt of reliable quality information on internal radiation doses to the population on RCT of Ukraine [18, 19].

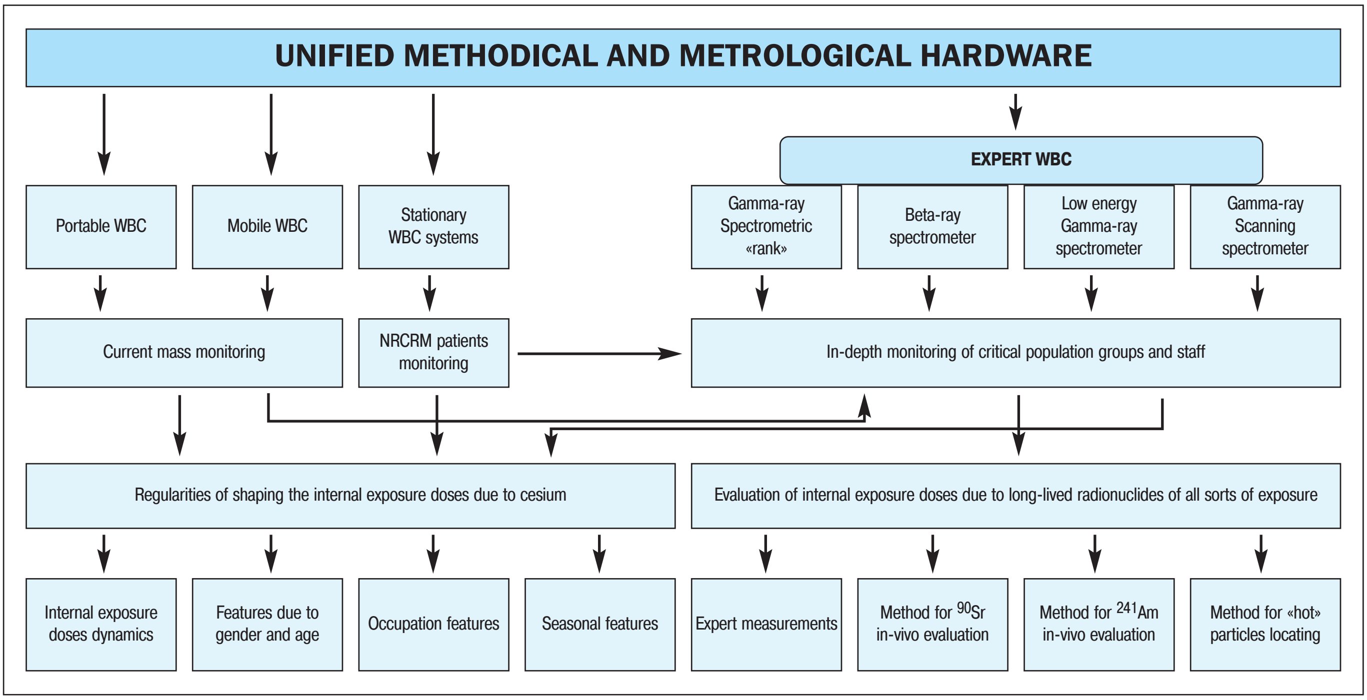

Figure 1.4. **NRCRM internal radiation dose monitoring system**

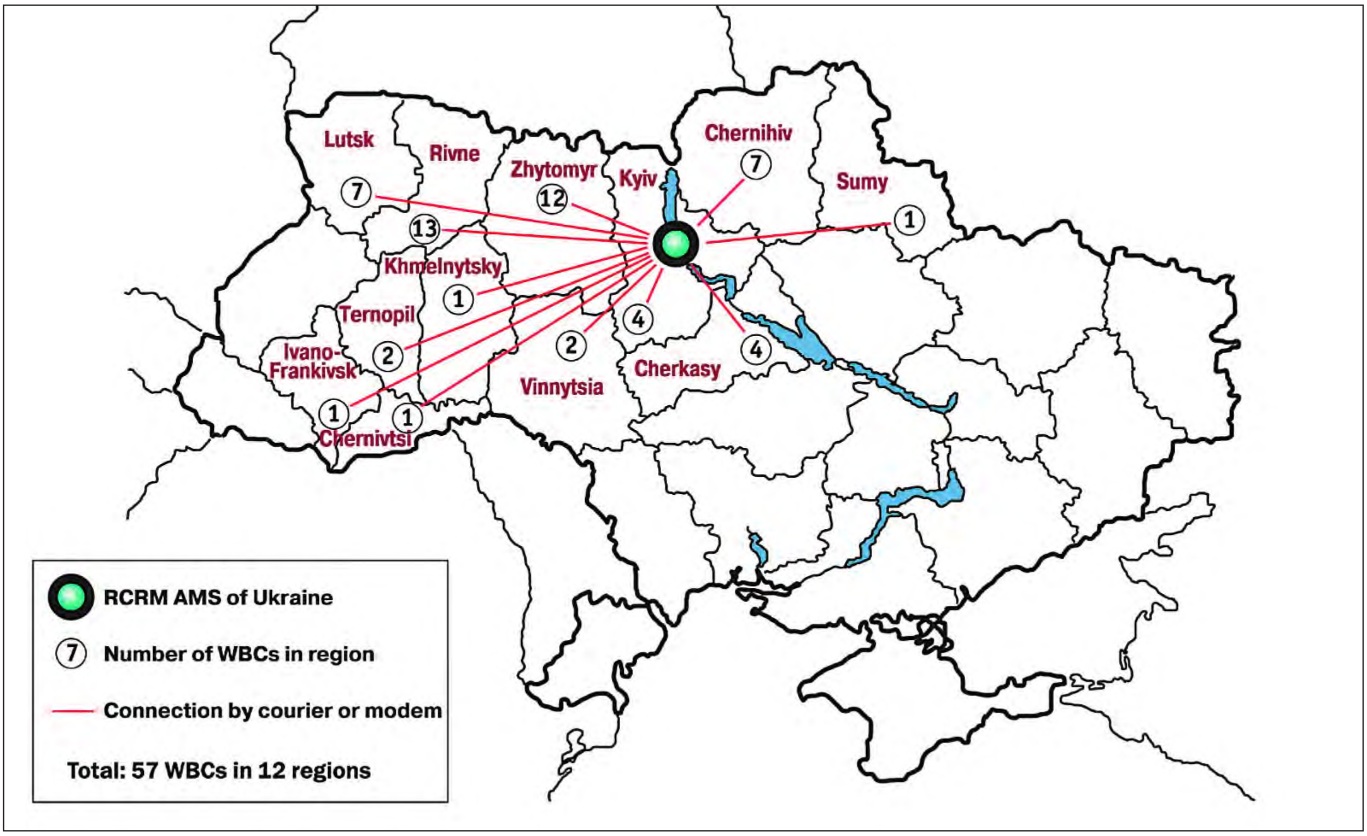

Figure 1.5. The unified WBC network in Ukraine

Medical organizations of 12 oblasts in Ukraine affected by the Chornobyl accident were provided with 57 «Skreenner-3M» WBC units, both stationary (40 units) and mobile (17 units), manufactured at the Institute of Human Ecology (Kyiv) using software and methodological and metrological software developed by NRCRM specialists who trained more than 100 operators to work on «Screenner-3M» installations, provided methodological and metrological support for these works, as well as collection, processing and verification of measurement results (Fig. 1.5).

The database (DB) of WBC-measurements of residents of Ukraine formed during the post-accident period (about 800 thousand measurements in the WBC network of Ukraine and more than 600 thousand own measurements of NRCRM) allowed to set up gender-age, seasonal, professional profiles of formation of internal radiation doses on RCT population of Ukraine and to trace dose dynamics during the post-accident period [20].

The situation in the post-accident years changed rapidly. The dynamics of internal radiation levels is extremely unstable. The values of doses in different years varied in the range of 0.01–2.0 mSv · year^{-1} with the lognormal nature of the distribution. After the decrease in 1986–1991, there was a constant (since 1992) increase in the internal radiation doses of the rural population due to the consumption of local products, as a result of the curtailment of preventive measures for radiation protection. In 1995–200, in some settlements of Rivnenska, Zhytomyrska and Kyivska Oblasts, the average levels of internal irradiation exceeded 1 mSv · year^{-1}, and individual ones reached 23 mSv · year^{-1}. In recent years, domestic exposure levels have declined and stabilized. At the same time, as durable WBC-monitoring has shown, there are a number of emergencies in Ukraine, mainly in the northern districts of Rivnenska, Zhytomyrska and Kyivska Oblasts, where internal radiation doses are very unstable and change significantly year by year and within the year, which requires control and study of the factors of such instability [18, 19].

However, since 2014, after the suspension of the State Program «General Dosimetric Certification of Settlements of Ukraine», radiological monitoring on RCT of Ukraine is practically not carried out. The only institution that studies the formation of radiation doses to the population on RCT of Ukraine and monitors the real radiation and hygiene situation is the NRCRM.

In 2016–2020, 8 expeditions were organized to conduct comprehensive radiation and hygienic monitoring in 26 settlements RCT of Rivnenska, Zhytomyrska and Kyivska Oblasts, which in recent years have recorded the highest levels of internal exposure and instability dynamics. It should be noted that expeditions carried out in the framework of research work at the NAMS of Ukraine, according to the estimate, are not funded and organized at the own expense of NRCRM specialists.

Conducted in 2016–2018 comprehensive radiation and hygienic monitoring on the RCT settlements of Rivnenska, Zhytomyrska and Kyivska Oblasts showed that the annual effective radiation doses of the population in the surveyed settlements at the current stage of the accident are formed mainly due to internal radiation doses caused by incorporation ^{137}Cs, which do not exceed 0.22 mSv · year^{-1} in Kyivska, 1.6 mSv · year^{-1} in Rivnenska, 1.2 mSv · year^{-1} in Zhytomyrska Oblasts, with the criterion of RCT 1 mSv · year^{-1} [21–25].

There were a further decrease in the average annual doses of internal radiation in the surveyed settlements: 2.6–4.1 times (0.09–0.17 mSv · year^{-1} in 2013 and 0.03–0.04 mSv · year^{-1} in 2016) in Kyivska Oblast, 1.1–1.9 times (0.10–0.13 mSv · year^{-1} in 2015 and 0.06–0.14 mSv · year^{-1} in 2018) in Zhytomyrska Oblast against the background of the lack of seasonal accumulation of radionuclides, and 1.2–1.4 times (0.21–0.33 mSv · year^{-1} in 2014 and 0.11–0.28 mSv · year^{-1} in 2017) in Rivnenska Oblast with a pronounced seasonal nature (increase in the average content of incorporated ^{137}Cs from May to October by 1.6–2.3 times). Seasonal fluctuations in the accumulation of incorporated ^{137}Cs are explained by the «harvest» of forest products in 2017 [21].

The results of the survey (were surveyed 539 people for the levels of food consumption from both private households and, separately, purchased in the retail network and local wildlife products) show that the diet of surveyed settlements residents consists mainly of products produced in private or local households. The most commonly used food products of the surveyed settlements residents all regions are dairy products and milk, potatoes and vegetables from personal or local farms, bread and bakery products purchased in the trade network. Fewer people consume wildlife products – prey, fish from local ponds, raw and canned berries, fresh and dried mushrooms, however, due to their significant contamination with ^{137}Cs, even small amounts of consumption of these products can lead to a significant radiation exposure. Analysis of the structure and dynamics of the diet of the surveyed settlements population showed a decrease in the levels of consumption of basic food products, primarily purchased through the trade network, because, according to interviewees, a decrease in purchasing power by the population in recent years [26, 27].

Annually, within the framework of radiation and hygienic monitoring, 40–80 sets samples of basic foodstuffs are collected in the farms of the inspected state of emergency, which include milk, potatoes, vegetables, and wildlife products. The analysis of the collected samples showed that the content of ^{137}Cs and ^{90}Sr in potatoes and milk of the surveyed settlements of Kyivska and Zhytomyrska Oblasts and potatoes in Rivne Oblast is lower than the permissible levels (PL) of the Hygienic Standard HS 6.6.1.1-130-2006 and the consumption of these foods cannot be significant to influence the formation of the internal radiation dose [28]. In contrast milk samples, collected from residents of Rivnenska Oblast, the content of ^{137}Cs in which has remained high in recent years. In 86 % of the samples collected in 2017 and in 76 % of the samples collected in 2020, the content of ^{137}Cs exceeds the PL of 100 Bq · l^{-1} up to 4 times. The maximum recorded values of ^{137}Cs content in the collected milk samples are 385 Bq · l^{-1} and 363 Bq · l^{-1} in 2017 and 2020, respectively.

The content of ^{90}Sr in milk samples collected in the S of Ivankivskyi district in 2019 is in the range of 2.1–9.9 Bq · l^{-1}, in 2016 – in the range of 1.3–7.4 Bq · l^{-1}, not exceeding PL HS 6.6.1.1-130-2006 20 Bq · l^{-1}, but in our opinion, given the dynamics, needs further monitoring [23].

The most contaminated with radionuclides products collected from the residents of the surveyed settlements are forest products, primarily mushrooms, especially dried, which in Ukrainian Polissya is traditionally one of the main products of the diet. The content of incorporated ^{137}Cs in fungal samples, as in previous years, significantly exceeds the permissible levels. The maximum recorded content of ^{137}Cs in samples of dried mushrooms collected in Rivnenska Oblast is 37 kBq · kg^{-1}, in Zhytomyrska Oblast – 113 kBq · kg^{-1}, in Kyivska Oblast – 223.7 kBq · kg^{-1}, which is in tens (and in Kyiv Oblast is almost 100) times higher than PL 2.5 kBq · kg^{-1}. It is clear that the use of such products, even in small quantities, will lead to the formation of significant internal radiation doses. The lack of forest products and the decrease in their share in the diets of local residents in recent years explains the decrease in the internal exposure levels of the population on the studied areas. At the same time, it is clear that in years rich in «harvest» of forest products, there is a high probability of a significant increase due to the receipt of radiocesium in the use of forest products, especially mushrooms, especially dried [21–23, 25].

Thus, the main factor in the formation of the dose of internal radiation of residents of RCT Kyivska and Zhytomyrska Oblasts at the current stage of the Chornobyl accident is the intake of ^{137}Cs in the body with forest products, primarily mushrooms, which in Polissya district traditionally occupy a significant part of the diet, milk and forest products. The current radiation and environmental situation in areas affected by the Chornobyl disaster requires continued monitoring at levels of radioactive contamination at local food from private farms and, especially, those collected in forests, and radiation doses to the population.

However, as the course on liquidation of the Chornobyl accident has shown, it is not enough to limit oneself a mass screening. The presence of nuclear-power complexes in Ukraine, the work carried out in the «Shelter», and the increase over time in the relative contribution of the internal radiation dose from radio-strontium and transuranic elements require complex, highly sensitive to all types

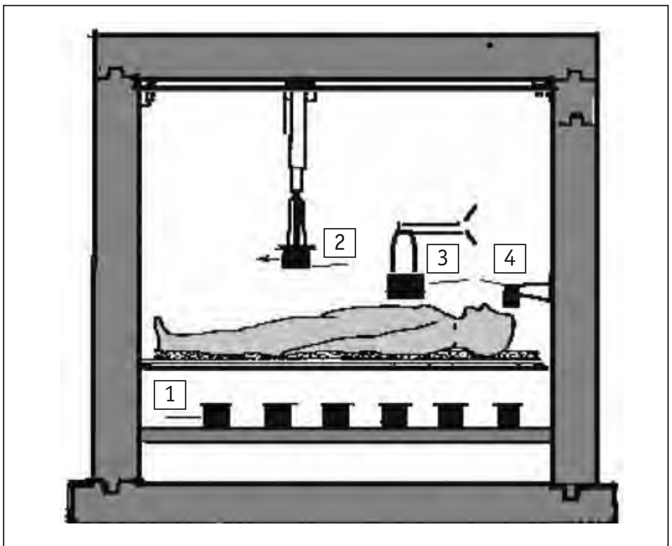

Figure 1.6. WBC detection system in a protective chamber:
1 – the «ruler» of 6 large-volume low background detection units;
2 – scanning device with detection unit;
3 – a low-energy γ-ray spectrometer;
4 – detector for β-spectroscopy.

of radiation installations. To solve expert tasks and in-depth monitoring, the NRCRM has developed and implemented an expert whole body counter (EWBC), which, unlike massive WBC-monitoring, can register alpha-, beta-, gamma-emitters in a wide range of energies. EWBC is made in the form of a low-background protective chamber, which houses a system of detectors (Fig. 1.6). The protective chamber is made of cast machined blocks at nonradioactive-pure steel 200 mm thick. It weighs up to 44 tons. Metal samples have undergone mandatory careful gamma spectrometric control. The camera provides a reduction of the radiation background in the energy range ^{137}Cs – 75.5. Integral background reduction – about 100. This allows you to achieve ultra-high sensitivity – on level 20 Bq at ^{137}Cs and 100 Bq at ^{40}K [1, 2].

The EWBC detection system includes a gamma-spectrometric «ruler» of 6 large-volume low background detection units, a low-energy gamma-ray spectrometer, consisting of two phoswich detectors for determining the transuranium elements (TUE) of the accompanying low-energy radiation. There is also a measuring channel for registering beta emitters. Above the «ruler» is a scanning system that allows you to determine the location radionuclides in the human body.

More than 10,000 expert measurements were performed at the EWBC, mostly of the staff organizations of contractors involved in the construction of the new safe confinement of the «Shelter» facility [29].

The conducted researches made it possible to identify a number of participants in the liquidation of the Chornobyl accident and NPP personnel, mainly among those performing scheduled preventive repairs in reactor modules (over 60 people) with inhalation of insoluble forms of fuel mixture in the form of «hot» particles and ^{60}Co [30].

The functioning of EWBC allowed at a qualitatively new level to solve expert missions of complex cases of a radionuclides incorporation mixture, «hot particles», to study metabolic processes, to provide metrological support of the whole complex of WBC, to provide quality control of critical groups and NPP personnel.

An example of quick response to emergencies and effective operation of a two-stage system of monitoring internal radiation doses using WBC of different classes is WBC-monitoring of personnel of the State Emergency Service of Ukraine (SES), which was involved in forest fire in the Chornobyl Exclusion Zone since April 4. until May 5, 2020:

From April 6 to May 19 on the WBC operational class «Screenner-3M» and highly sensitive EWBC measurements of the content of incorporated gamma radionuclides in rescuers of the SES after extinguishing the fire, immediately upon arrival from the exclusion zone in the NRCRM. 470 people (523 measurements) in three groups of SES personnel (SES in Kyiv, SES in Kyiv Oblast, SES in Cherkasy Oblast) were examined. The levels of radionuclide inflow into the body during firefighting in the Chornobyl Exclusion Zone were determined and the internal radiation dose due to this inflow was estimated [31, 32].

In the vast majority (95 %) of the personnel of the SES of Ukraine, examined at the WBC operational class «Screenner-3M» (more than 500 measurements), the assessment of the values of the individual effective dose of internal radiation due to ^{137}Cs in the body during firefighting, assuming that it receipts occurred during operation in the exclusion zone, did not exceed the minimum dose detected MDD (5–14 µSv). In order to clarify the results and study the distribution of radiocesium in the body of employees, a study of individual's group (10–25 % of all examined in groups) on a highly sensitive EWBC. The average value of the effective internal radiation dose in the personnel group of the SES in Kyiv, which participated in the elimination of forest fires in the exclusion zone from April 4 to May 5 (26 people) tested on EWBC, is (2.5 ± 1.1) µSv, in the personnel group of the State Emergency Service in Cherkasy Oblast, which took part in the fire on April 19–24. (9 persons) – (2.2 ± 0.6) µSv, in the personnel group of the State Emergency Service in Kyiv Oblast, which participated in the elimination of the forest fire in the exclusion zone from April 4 to May 5, 2020 (42 persons) – (4.4 ± 2.4) µSv. The maximum values are 5.1; 3.5; 11.8 µSv in the groups of Kyiv, Cherkasy and Kyiv Oblasts, respectively.

During 2016–2021, work on the support and verification of the WBC-measurement database continues. In 2016–2018, 142,695 records of the results of WBC-measurements of 1987–1993 were entered into the electronic database, which were contained on paper and were detected during the database audit in 2013–2015. The total volume of records in the database for the period 1987–1993 increased by 81.6 %. The largest number of results of WBC-measurements of 1987–1993, entered into the electronic database, concerns Zhytomyr Oblast– 100,946 records, less than Rivne Oblast– 16,255 records, Kyiv Oblast– 11,117 records and Chernihiv Oblast – 3,234 records. At present, work is underway to verify the database, restore information from paper on the results of WBC-measurements in 1986, the most valuable and important, and replenish the database [33, 35].

1.4. Doses on thyroid gland of the population of Ukraine (1986)

Radiation induced risk of thyroid cancer development among persons exposed by the radionuclide of ^{131}I in infant and adolescent age in 1986 is the main statistically significant long-term consequence of Chornobyl accident [36].

Thyroid exposure doses estimates of representatives of different gender-age groups of all the settlements of Ukraine stated for 1986 were first presented in [37]. These dose estimates presented also in national reports to 20th and 25th anniversaries of Chornobyl accident [2, 3] are based on data of about 150 thousand measurements of ^{131}I radioactivity in thyroid gland, the so-called «direct thyroid measurements» held in May-June of 1986 among the population of Ukraine [38].

But thyroid doses to population of Ukraine calculated in [37] were recently re-estimated based on renewed methodology of dose evaluation [39, 40], novel thyroid masses estimates [41], novel evaluations of ^{131}I radioactive fallouts on the ground in 1986 [42], and also on revised activity of ^{131}I radionuclide in thyroid gland [43].

Table 1.6 presents accumulated absorbed thyroid doses for different age groups, averaged by districts and weighted by the population of the regions. The table presents only that districts of Vinnytska, Zhytomyrska, Kyivska, Rivnenska, Cherkaska and Chernihivska Oblasts where the averaged thyroid exposure dose of the critical group (babies up to one year) exceeds 250 mGy.

Analysis of distribution of accumulated thyroid doses in 1986 by age groups shows that dose distributions have essential age dependence. In all the investigated districts, mean thyroid exposure dose for babies and children at age of 1–2 years is 3–4 times higher compared with the dose for adults.

Table 1.6
District-averaged population-weighted accumulated absorbed thyroid doses in 1986

#	District	Age group, years						
		< 1	1–2	3–7	8–12	13–17	≥ 18	all
		Thyroid dose, mGy						
				Vinnytska Oblast				
1	Tulchynskyi	314	271	148	101	81	77	137
2	Chechelnytskyi	253	225	124	90	74	65	117
				Zhytomyrska Oblast				
1	Yemilchynskyi	317	282	155	112	92	81	149
2	Korostenskyi	475	423	236	167	134	124	220
3	Korosten town	583	442	226	120	92	124	212
4	Luhynskyi	751	681	369	278	237	206	362
5	Malynskyi	702	598	322	217	178	169	307
6	Narodytskyi	1671	1416	777	544	461	443	715
7	Ovruchskyi	689	574	312	207	171	167	284
8	Olevskyi	347	304	172	129	103	89	167
				Kyivska Oblast				
1	Bilotserkivskyi	253	216	117	77	63	61	108
2	Bohuslavskyi	322	265	142	88	68	77	120
3	Borodianskyi	282	246	136	98	79	72	128
4	Vyshhorodskyi	322	278	153	103	86	78	146
5	Ivankivskyi	296	268	151	113	98	86	147
6	Kaharlytskyi	313	265	142	94	82	75	130
7	Makarivskyi	338	305	170	123	103	89	162
8	Poliskyi	1201	1086	610	431	352	305	569
9	Rokytnianskyi	316	281	157	111	93	82	148
10	Tarashchanskyi	281	235	127	84	70	66	115
11	Fastiv town	266	201	103	55	42	56	94
				Rivnenska Oblast				
1	Bereznivskyi	282	250	140	100	82	72	132
2	Volodymyretskyi	375	333	186	133	109	96	175
3	Dubrovytskyi	550	471	258	177	143	135	242
4	Zarichnenskyi	375	333	184	131	108	96	174
5	Varash (Kuznetsovsk) town	354	267	136	73	56	75	126
6	Rokytnivskyi	469	417	231	165	136	120	218
7	Sarnenskyi	373	315	172	115	93	90	161
				Cherkaska Oblast				
1	Zvenyhorodskyi	404	330	176	111	87	93	162
2	Kanivskyi	323	290	160	115	96	84	152
3	Kaniv town	531	403	207	108	84	113	185
4	Katerynopilskyi	291	259	144	103	84	75	136
5	Korsun-Shevchenkivskyi	253	211	113	73	58	60	105
6	Talnivskyi	278	230	124	80	63	65	115
				Chernihivska Oblast				
1	Bobrovytskyi	276	234	127	85	66	67	119
2	Horodnianskyi	268	220	117	75	62	63	115
3	Kozeletskyi	251	214	119	86	70	61	117
4	Koriukivskyi	313	257	138	86	69	72	135
5	Kulykivskyi	332	296	166	118	99	85	164
6	Nizhynskyi	252	223	125	89	72	64	119
7	Nizhyn town	303	229	118	62	48	64	105
8	Novhorod-Siverskyi	347	283	150	97	75	80	144
9	Nosivskyi	273	222	119	75	61	63	116
10	Ripkynskyi	410	384	202	149	128	116	199
11	Semenivskyi	477	384	204	131	105	110	202
12	Sosnytskyi	284	253	141	101	82	73	136
13	Chernihivskyi	659	589	341	241	202	171	325
14	Chernihiv city	333	252	130	67	53	70	109
15	Snovskyi (Shchorskyi)	260	217	117	75	61	62	114

Above mentioned groups are the most critical since thyroid mass of children up to 2 years old is by a factor of ten smaller than of adults [41]. For children aged 3–7 years, thyroid dose is approximately twice higher than for adults. Thyroid exposure doses of adolescents aged 8–12 and 13–17 years almost coincide with the doses for adults.

The highest thyroid absorbed dose was obtained in 1986 by residents of Narodytskyi, Ovrutskyi, Luhinskyi, Malynskyi districts and Korosten town of Zhytomyrska Oblast, Poliskyi district of Kyivska Oblast, Chernihivskyi district of Chernihivska Oblast, Dubrovytskyi district of Rivnenska Oblast and Kaniv town of Cherkaska Oblast. Mean dose for the critical group of these districts exceeded 500 mGy.

Figures 1.4–1.5 present maps of Ukraine of averaged by age accumulated thyroid absorbed doses for different age groups.

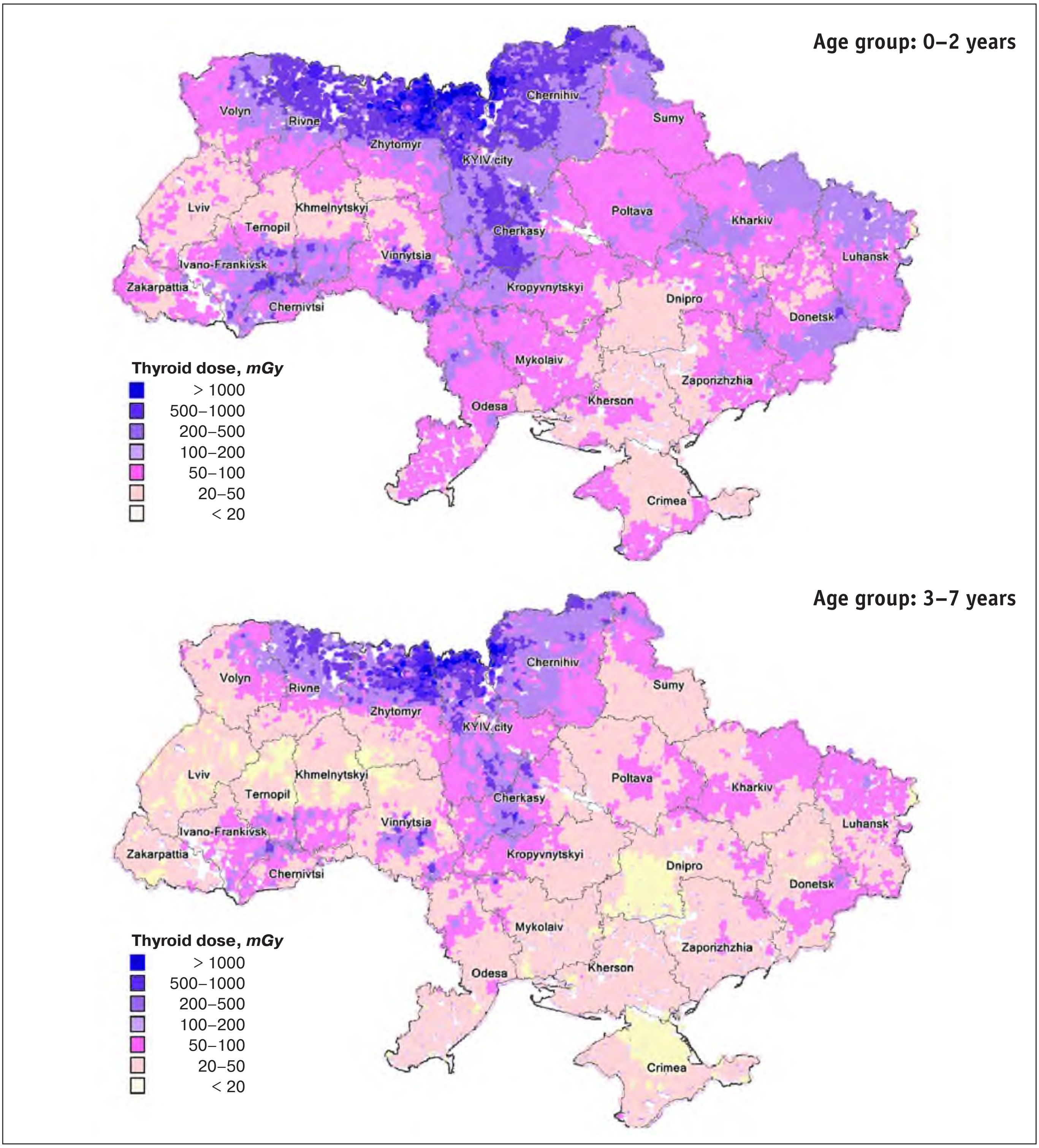

Figure 1.7. **Accumulated absorbed thyroid doses of children pre-school age that resided in Ukraine in April–July of 1986**

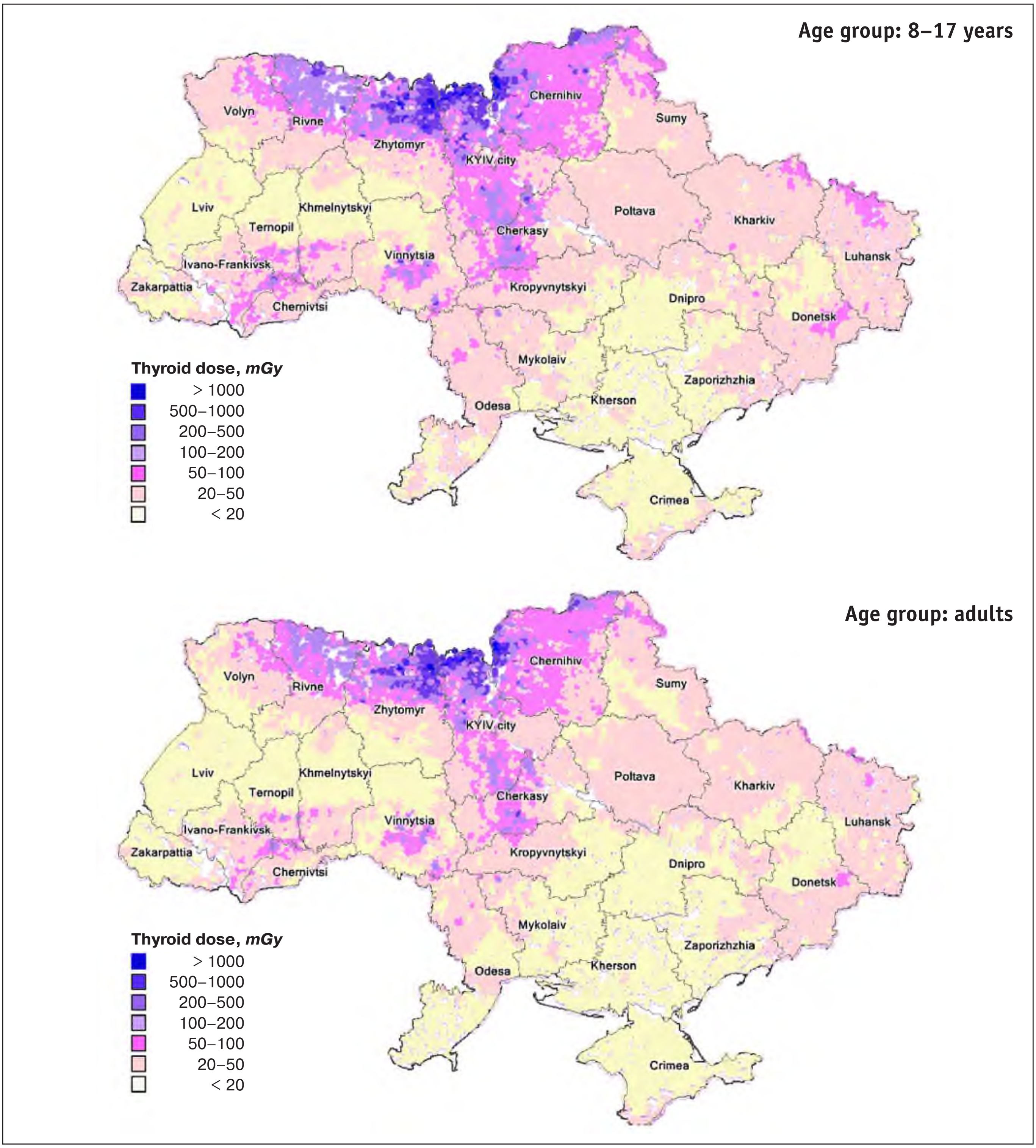

Figure 1.8. **Accumulated absorbed thyroid doses of schoolchildren and adults of Ukraine that resided in Ukraine in April–July of 1986**

1.5. Doses of clean-up workers

The total population with the official status of persons exposed to ionizing radiation after the Chornobyl accident in Ukraine was 2,025,141 in 2015 [4]. This number included 222,498 clean-up workers [4] and 90,784 evacuees and persons resettled between 1986 and 1990 from 76 settlements within the 30-km exclusion zone as well as 92 settlements in the zone of absolute (compulsory) resettlement [3].

Chornobyl clean-up workers (liquidators) are among the most numerous and most exposed cohorts affected by the Chornobyl accident. Despite the great significance of this population in medical and social aspects, as well as for studying the health effects of accidental exposure, the overall picture of liquidators' exposure remained uncertain for a long time. For instance, among the clean-up workers of 1986–1990 included into the State Registry of Ukraine of persons affected by the Chornobyl accident (SRU), only about half have individual dose records. Remained unclear both the quality of available dosimetric data and the overall success or failure of radiation protection during clean-up. Traditionally, the doses of exposure considered to be totally falsified, massive exceeding of the established dose limits were suggested. The situation with exposure of eye lens, one of the most radiosensitive organs, was also uncertain, especially with doses of beta radiation from Chornobyl mixture of radionuclides.

Therefore, over the last three decades, a large corpus of studies has been planned and largely implemented, aimed at clarifying the true radiation doses of liquidators and retrospective evaluation of the results of dosimetry monitoring during clean-up. A special role among the problems of estimation of liquidators' exposure is dedicated to dosimetric support of post-Chornobyl epidemiological studies. These studies require information on subjects' individual doses, so dosimetry requires implementation of integrated approaches.

It is generally recognized that the majority of liquidators were exposed mainly to external radiation due to radionuclides released from the reactor core during April-May 1986 and caused contamination of the premises and roofs of the Chornobyl NPP as well as adjacent territories [44–46]. Sources of external irradiation included a mixture of a wide range of beta- and gamma-emitting radionuclides. Their relative contribution has evolved over time due to differences in the half-lives of individual radionuclides in this mixture. In addition to the radioactive decay of radionuclides released from the reactor, the reduction of radiation exposure was significantly influenced by large-scale decontamination activity and the construction of the Object Shelter over the destroyed Unit 4 of the Chornobyl NPP in the fall of 1986. Therefore, the intensity (dose rate) and characteristics (energy spectrum, contribution of beta radiation) of radiation exposure of clean-up workers changed significantly over time, leading, along with extreme spatial variability of contamination, to extremely different individual doses received by liquidators working in the period from 1986 to 1990. Unfortunately, completeness and reliability of the official doses (the results of individual monitoring recorded in the State Registry of Ukraine) are insufficient, so the most reliable source of data of liquidators' exposure is retrospective dose reconstruction.

Table 1.7 shows the summary results of the external dose reconstruction for clean-up workers included into a series of the Ukrainian-American epidemiological studies.

Doses of different professional categories of liquidators vary significantly. Thus, professional atomic workers (ChNPP employees, scientists from the special expedition of the Kurchatov Institute of Atomic Energy, AC-605 workers) received the highest doses of radiation. In general, the most exposed group consists of early liquidators (participated in clean-up in April–May 1986) who had no effective system of radiation protection and radiation monitoring, and certain categories of workers who carried out work on individual tasks, mostly out of control of dosimetric monitoring services.

Evolution of average doses over the years (Table 1.7) for military liquidators – the largest category of clean-up workers – reflects adequately the change of the radiation situation in the 30-km zone and the gradual reduction of dose limits during 1987–1988. It should be noted that, on average, the radiation doses of military liquidators are significantly lower than the officially registered values and values established within public consciousness. This conclusion is in good agreement with the results of the independent analysis of official dose records and qualitative considerations regarding the features of dosimetric monitoring of military liquidators during clean-up. Another quite populous group of liquidators includes civilians who were temporarily sent on mission to the 30-km zone to perform various tasks, typically, the transportation of goods and personnel, consulting and expert assistance, participation in working meetings, specific time-limited specialized work. This group, due to its heterogeneity, shows an extremely wide range of doses, but the average and especially the median values of the dose distribution are quite low. Another feature of a large group of liquidators is that the workers had several clean-up missions, each time as part of a different category (for example, a ChNPP

Table 1.7
Individual red bone marrow external doses reconstructed by RADRUE method [45] for different categories of clean-up workers

Category	Number	Average mGy	Median mGy	Minimum mGy	Maximum mGy
Military (total)	613	90	48	0,01	1510
First year of work					
1986	331	110	64	0.13	1510
1987	149	90	54	0.01	1048
1988	75	45	20	0.22	566
1989	49	48	2	0.23	349
1990	9	29	1	0.15	120
Professional atomic workers	89	468	296	14	3285
Sent on mission	455	33	1.8	about 0	1444
Mixed*	299	228	37	0.26	3285

Note. *This category partially includes «Professional atomic workers».

employee later worked as part of the «Combinat» staff or visited the 30-km zone during short mission). As can be seen from Table 1.7, the doses of this mixed category of liquidators also vary in a wide range, and the distribution parameters are much higher than in the category of sent on mission to the 30-km zone.

It should be noted that the cohorts of subjects in both Ukrainian-American studies (leukemia and thyroid cancer) are quite representative, so exposure ranges, nature of work and distribution by professional groups (categories) of liquidators are very informative and can characterize the total population of the Ukrainian clean-up workers.

In previous years, the official dose records (SRU data) have been revised, and retrospective dose assessments of external gamma irradiation of the red bone marrow and beta irradiation of the lens of the eye have been performed. The main results of these studies were presented in the National Report 2016 [4]. In the years since its publication, the main attention has been paid to other problems of liquidator dosimetry, namely to individual dose assessment of thyroid exposure for male clean-up workers and to reconstruction of doses to the gonads of men and women, including liquidators and evacuees from Prypiat. These studies were carried out within the framework of the Ukrainian-American projects «Scientific Protocol for the study of Leukemia and Thyroid Cancer among Clean-up workers in Ukraine Following Chornobyl accident» and «Ukrainian-American trio study of parental irradiation in Chornobyl clean-up workers and evacuees and germline mutations in their offspring» (the results of the latter were not published on the date of this report, so they are not included in the current section). In addition, for the first time, the doses were estimated for female clean-up workers and evacuees, who were the subjects of the Ukrainian-German study of molecular mechanisms of breast cancer [47].

1.5.1. Thyroid doses of clean-up workers

The study of the risks of thyroid cancer in the cohort of Ukrainian liquidators is quite topical task because other epidemiological studies among the Chornobyl clean-up workers [48–50] suggest that internal irradiation of ^{131}I may have caused a radiation related risk of thyroid cancer. At the same time, there was no methodology in place for assessment of thyroid exposure due to all potential radiation components: external gamma radiation related to clean-up worker mission, internal radiation due to inhalation and oral intake of iodine, doses caused by short-lived radionuclides of iodine and tellurium. Therefore, there was a need to develop a methodology for estimating the thyroid dose of liquidators due to ^{131}I inhalation, which occurred in the early period after the Chornobyl accident [51].

Appropriate methods were developed within the Ukrainian-American study of thyroid cancer among clean-up workers (1986–2012) and the thyroid radiation doses of 607 liquidators — study subjects were reconstructed.

The development and validation of new dosimetry methods for estimating the thyroid doses of liquidators exposed to iodine radionuclides was based on the data from direct measurement of the exposure rate near the thyroid gland, performed between April 26 and May 5, 1986 for clean-up workers. These direct thyroid measurements are the best basis for estimating the doses of internal thyroid irradiation. The so-called «instrumental» doses, which are based on individual measurements, are more reliable than the so-called «environmental» doses, which are based on models that are usually used in the absence of data on the specific content of radioiodine in the thyroid gland of a subject. Data from direct measurements allowed developing a method of reconstruction of individual doses to the thyroid gland for Chornobyl liquidators and retrospectively estimate the doses for the subjects of the Ukrainian-American case-control study of thyroid cancer [52].

Study subjects were involved in various clean-up activities and were eventually exposed to different types and levels of exposure. Major categories of liquidators in this study included military (236 subjects, 38.9 % of the total); civilians who performed various short-term tasks in the 30-kilometer zone, the so-called «sent on mission» (137 subjects, 22.6 %); early liquidators (64 subjects, 10.5 %); and a mixed category, including workers who participated in clean-up several times as members of different categories (152 subjects, 25.0 %).

A special questionnaire was developed to collect information needed for the retrospective dose reconstruction, including locations, dates and working conditions of clean-up workers, as well as their place of residence during the mission. This questionnaire was a modified version of the one successfully used in the Ukrainian-American study of leukemia and related diseases [53]. Modifications included additional questions about the dates of administration of potassium iodide (KI) pills for iodine prophylaxis during clean-up mission as well as about the subject's residential history and diet during the residence in contaminated settlements, i.e., about the thyroid dose due to intake of ^{131}I, which was not directly related to clean-up mission. This questionnaire was used for individual interviews with study subjects conducted by trained personnel approximately 25–30 years after the accident. In the case of deceased or incapacitated subjects, two their proxies were interviewed: (1) the next of kin, usually, the wife who provided, in particular, epidemiological data and the names of colleagues who worked with the subject during clean-up, and (2) the subject's closest colleague who described clean-up activity of the subject. The interviewer also collected and copied all additional relevant documents from the respondent: certificates, route lists, etc.; these data could also be used in dose reconstruction.

Thyroid doses were estimated for 607 study subjects exposed due to the Chornobyl accident, including cases, i.e., liquidators who were diagnosed with thyroid cancer, and controls, i.e., liquidators who did not have the disease, but were matched to the cases by other criteria. General characteristics of thyroid exposure for different categories of liquidators-subjects of the study are given in Table 1.8. Individual thyroid doses due to external irradiation, inhalation of ^{131}I and short-lived radioactive isotopes of iodine and tellurium (^{132}I, ^{133}I, ^{135}I, ^{131m}Te and ^{132}Te) during clean-up mission, as well as oral intake of ^{131}I during residence in contaminated settlements were calculated for all study subjects. Individual doses were calculated by stochastic modeling, i.e., along with point estimates (arithmetic mean, median), individual uncertainty distributions were obtained for each subject. The average thyroid dose due to all exposure was 199 mGy (median — 47 mGy; range: 0.15 mGy — 9.0 Gy) with the following values for individual exposure pathways: external irradiation during clean-up mission — average 140 mGy (median — 20 mGy, range: 0.015 mGy — 3.6 Gy); internal due to ^{131}I inhalation — 44 mGy (median — 12 mGy; range: ~ 0 mGy — 1.7 Gy); internal due to oral ^{131}I intake during residence — 42 mGy (median — 7.3 mGy; range: 0.001 mGy — 3.4 Gy); internal due to inhalation of short-lived radionuclides of iodine and tellurium — 11 mGy (median — 1.6 mGy; range: ~ 0 mGy — 0.38 Gy). The contribution of these components of the total dose depends on subject's exposure, this information is presented in detail in Table 1.9. The internal components of the thyroid exposure to ^{131}I accounted for more than 50 % of the total thyroid dose for 45 % of subjects. Uncertainties of individual stochastic dose distributions were characterized by a mean geometric standard deviation of 2.0; 1.8; 2.0 and 2.6, respectively, for external irradiation, inhalation of ^{131}I, inhalation of short-lived radionuclides and intake during residence.

Table 1.8
Thyroid doses due to all exposure pathways by category of clean-up workers included into case-control study [52]

Category of clean-up workers	Number of subjects	Thyroid dose (mGy) due to: External irradiation		Inhalation of ^{131}I during mission		Inhalation of short-lived radionuclides during mission		Intake of ^{131}I during residence		Total	
		mean	range	mean	range	mean	range	mean	range	mean	range
Early clean-up workers	64	68	0.24–867	20	~0–194	5	~0–59	17	0.22–109	100	~0–891
Chornobyl NPP staff	1	68	–	–	–	–	–	5.9	–	74	–
Sent to assist the Chornobyl NPP staff	4	108	0.32–375	–	–	–	–	12	5.1–29	120	20–385
Staff of AC-605	6	200	3.9–788	–	–	–	–	6.7	1.7–24	206	6.7–790
Staff of Kurchatov Institute	1	1.010	–	–	–	–	–	3	–	1.010	–
Military	236	121	0.14–1.670	32	~0–277	6.5	~0–78	8.5	0.04–102	138	0.53–1.670
Sent on mission	137	24	0.01–755	2.3*	–	0.21	–	24	0.24–808	47	0.7–820
Staff of «Combinat»	6	36	0.15–187	–	–	–	–	40	8.9–122	70	0.15–196
Mixed**	152	299	0.28–3.630	57	~0–1.680	15	~0–377	122	0.001–3.430	471	1.5–9.020
Total	607	140	0.015–3.630	44	~0–1.680	11	~0–377	42	0.001–3.430	199	0.15–9.020

Notes. *In this category, only one subject was exposed due to inhalation of ^{131}I and short-lived radionuclides, so the range is not specified. **Mixed is a group of liquidators who participated in clean-up several times as members of different categories.

Table 1.9
Distribution of thyroid doses due to different exposure pathways for study subjects [52]

Interval of thyroid dose, mGy	Components of thyroid radiation dose, mGy: External irradiation		Inhalation of ^{131}I during mission		Inhalation of short-lived radionuclides during mission		Intake of ^{131}I during residence		Total	
	n	%	n	%	n	%	n	%	n	%
< 0.1	10	1.6	13	6.5	45	22.7	6	1.0	–	–
0.1–0.99	92	15.2	30	15.0	46	23.2	33	5.6	6	1.0
1.0–9.99	156	25.7	55	27.5	52	26.3	322	54.9	105	17.3
10–99.99	179	29.5	82	41.0	54	27.3	195	33.2	279	46.0
100–999.99	156	25.7	19	9.5	1	0.5	28	4.8	197	32.4
≥ 1000	14	2.3	1	0.5	–	–	3	0.5	20	3.3
Total	607	100.0	200	100.0	198	100.0	587	100.0	607	100.0

1.5.2. Doses of female clean-up workers

In contrast to the cohort of evacuees, where the population and levels of exposure were quite comparable for males and females [54], female liquidators are a very special group of clean-up workers. First, according to the SRU, only 5 % of registered liquidators are female. Similarly, women represented about 4 % (315 of 8607) of subjects of the Ukrainian-American Chornobyl Ocular Study (UACOS) [55], for which subjects were recruited randomly with regard to gender. Secondly, for qualitative reasons, one could expect that the individual radiation doses of female liquidators are much lower than the corresponding doses of male liquidators.

The immediate reason for targeted dose assessment of female clean-up workers was the study of breast cancer. In previous studies, an increase in breast cancer both among female clean-up workers [56, 57] and the female population of the most radioactively contaminated regions of Belarus and Ukraine [58] was noticed. However, the molecular mechanisms of breast cancer, which may help in distinguishing radiation induced from the spontaneous tumors, have remained unexplored. A study aimed at detecting radiation markers of breast cancer was conducted in 2008–2015 in collaboration with the Helmholtz Zentrum Munchen, Ludwig Maximilian University and NRCRM [47, 59]. In this project, breast cancer was diagnosed histologically under the age of 60 in the period from 1992 to 2014, both in women who were exposed to radiation and in non-exposed women from the control groups, matched for the place of residence, type of tumor, age at the time of diagnosis. Tumors were investigated for molecular changes with special emphasis to copy number alterations and miRNA profiles.

To search for potential subjects of the study, data on cancer patients from the National Cancer Registry of Ukraine and several clinical archives were linked with the SRU data. This linkage identified 435 patients with breast cancer among female liquidators and 14 among evacuees from the 30-km zone and the city of Prypiat. Of this total, 129 breast cancer patients met the inclusion criteria and were followed up for individual dose reconstruction of the target organ (breast). Doses [60] were calculated for 71 study subjects (58 liquidators and 13 evacuees diagnosed with breast cancer whose biomaterial was available for molecular studies and who agreed to participate in the dosimetric interview) by RADRUE [45], which was previously used for epidemiological studies and was specifically modified to estimate the radiation dose to breast. The results of dose reconstruction for 58 female liquidators (Table 1.10) showed a large variability of individual doses within the five-order range of magnitude: from 0.03 to 929 mGy, with a median as low as 5.8 mGy. As can be seen from the comparison of Table 1.7, the radiation doses of female liquidators are generally much lower than the doses of male liquidators, but in some cases can also reach substantially high values.

This study provided the first quantitative estimation of the exposure for female liquidators, who represent a limited but very important group of individuals affected by the Chornobyl accident. It should be noted that the doses of 13 women evacuated after the accident who did not take part in clean-up activities (from 4 to 45 mGy with a median of 19 mGy) are in accordance with the previous estimates for evacuees from Prypiat and the 30-km zone.

Conclusions

Summarizing the review of data on radiation doses of Chornobyl clean-up workers it is possible to make some conclusions.

1. The most exposed category are so-called early liquidators, i.e., workers who participated in the

Table 1.10
Doses (absorbed dose to breast) of the female clean-up workers – subjects of the study [60]

Year of beginning	Number of subjects	Mean mGy	Median mGy	Minimum mGy	Maximum mGy
1986	48	40	13	0.06	929
1987	7	4	3.1	0.03	14
1988	3	43	38	3.67	89
Total	58	40	5.8	0.03	929

clean-up works in April–May, 1986, under conditions of poorly explored radiation situation and lack of adequate means of dosimetric monitoring.
2. Doses of liquidators of later periods (since June 1986) are mostly in accordance with the dose limits established at that time. The radiation protection system implemented during clean-up basically fulfilled its functions and provided non-exceeding of permissible exposure.
3. The quality and completeness of dosimetric information differ significantly for different groups of liquidators, necessitating a critical approach to the use of existing dose records, retrospective assessment of individual doses and review and correction of available dosimetric data. In particular, doses of military liquidators are now endowed with significant falsification, however are biased (upwards, comparing to actual exposure) and inaccurate (have large uncertainty).
4. Studying health consequences of the Chornobyl accident among the cohort of liquidators requires extensive use of retrospective dosimetry to determine the individual doses of subjects.
5. The methods of retrospective dosimetry developed in recent years, in particular the analytical-calculation method RADRUE, allow providing the effective dosimetric support of post-Chornobyl epidemiological researches.
6. As was shown before, beta exposure made significant contribution to the eye lens doses of clean-up workers. Account of this component is inevitable for assessment of the cataract risks among clean-up workers.
7. Internal irradiation of the thyroid due to inhalation and ingestion of iodine radionuclides makes a significant contribution to the total dose of this organ for liquidators who participated in clean-up during the so-called «iodine period» of the accident.
8. The inaugural assessment of radiation doses of female clean-up workers showed on average much lower doses compared to male liquidators. At the same time, in some cases (early liquidators) the doses of female liquidators could reach significant values.

1.6. Doses of evacuees

In preceding years, stochastic modeling based on the results of direct dose rate measurements and surveys was undertaken and individual effective doses of external exposure 12,632 inhabitants of Prypiat (group A) were analyzed and summarized as well as for 14,084 inhabitants of the remaining settlements of the 30-km zone (group B). These evacuees represent 104 settlements of the 30-km zone including the cities of Prypiat and Chornobyl; 223 residents of the Belarusian part of the 30-km zone, who lived in 40 settlements were also interviewed and included in the total number of studied subjects.

In total, individual doses of external gamma radiation were calculated for 12,632 evacuees from Prypiat (group A), which is about 25 % of the evacuated population of the city. The average effective dose of this contingent, which was accumulated before the evacuation, is 10.1 mSv. Doses of 534 persons from this group exceeded 25 mSv and only 18 persons (in this group) received doses above 50 mSv. The maximum value of the effective dose was 75 mSv for the group of Prypiat town residents.

Frequency distribution of individual effective doses is shown in Fig. 1.9.

Figure 1.9 shows that the distribution of individual doses is left-asymmetric and quite broad. This distribution shape is in a good agreement with the common log-normal model of the dose distributions for the members of public. 95 % of the evacuees from Prypiat (group A) received doses below 24 mSv.

Dependences of the modes of behavior and characteristics of dose distributions from the age of persons (Table 1.11) and their professional affiliation (Table 1.12) are quite illustrative. These data except more detailed characterization of the peculiarities of exposure and explanation of dose variations, have significant prognostic value and can be used for parametrization of the public exposure models.

Calculation of doses of external exposure of persons evacuated from settlements of 30-km zone

Different model designed for the rural population was used to calculate individual doses of 14,084 people who were evacuated from the settlements of the 30-km zone. The calculation covered the peri-

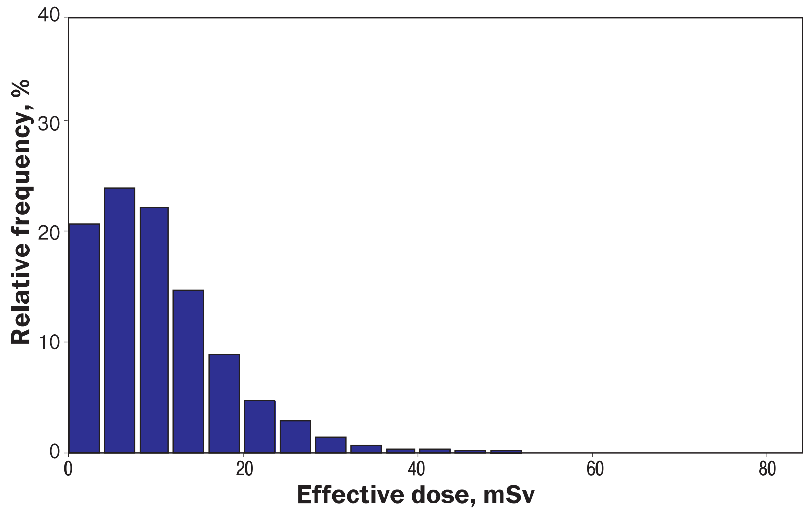

Figure 1.9. Distribution of individual doses of external radiation in 12,632 individuals who were evacuated from Prypiat. Results of deterministic calculation.

Table 1.11
Dependence of the parameters of distributions of individual doses of external exposure on the age of persons evacuated from Prypiat. Results of deterministic calculation.

Year of birth	1983–1986	1979–1982	1974–1978	1970–1973	1961–1969	1931–1968	to 1931
Age group (years)	0–3	3–7	7–12	12–16	16–25	25–55	> 55
Group size	1,597	2,104	2,133	601	1159	4456	582
Average share of outdoor time	0.14	0.17	0.18	0.21	0.25	0.25	0.21
Distribution of effective doses of external gamma irradiation (mSv)							
Arithmetic mean	8.32	9.09	9.0	10.5	10.8	11.5	10.2
Standard error of the mean	0.15	0.15	0.14	0.31	0.24	0.12	0.32
Median	7.35	7.89	7.63	9.35	9.63	10.5	8.56
Geometric mean	5.50	6.15	6.32	7.16	6.77	7.85	7.07
Geometric standard deviation (dimensionless)	3.18	3.04	2.79	3.02	3.6	3.13	2.74
75 percentile	11.2	12.2	12.2	15.1	15.3	15.6	14.2
95 percentile	20.0	21.2	21.3	24.8	25.9	25.8	23.9
Variation coefficient, %	74	75	73	72	75	70	75

Table 1.12
Dependence of the parameters of distributions of individual doses of external exposure on the professional belonging of persons evacuated from Prypiat

Professional group	Preschoolers	School students	Teachers	Medical professionals	Servicemen	Workers	Engineers	Utility workers	ChNPP employees	Housewives	Pensioners
Group size	3,494	2,945	376	202	799	2,629	670	210	452	156	375
Average share of outdoor time	0.16	0.19	0.22	0.23	0.23	0.26	0.24	0.27	0.28	0.20	0.20
Distribution of effective doses of external gamma irradiation (mSv)											
Arithmetic mean	8.81	9.4	10.2	11.5	10.9	11.5	10.8	12.6	13.0	8.94	9.51
Standard error of the mean	0.11	0.13	0.36	0.59	0.28	0.16	0.30	0.73	0.40	0.54	0.35
Median	7.72	7.99	9.66	10.8	9.6	10.5	9.66	10.8	12.4	8.54	8.11
Geometric mean	5.92	6.51	7.35	7.57	7.66	7.7	7.11	8.27	8.39	5.74	6.92
Geometric standard deviation (dimensionless)	3.11	2.88	2.72	3.16	2.86	3.21	3.46	3.09	3.84	3.25	2.53
75 percentile	11.89	12.8	13.7	16.5	14.5	15.9	14.9	16.7	18.0	12.8	13.4
95 percentile	20.64	22.6	22.4	27.4	25.1	26.2	24.7	29.7	28.2	20.1	20.4
Variation coefficient, %	74	74	68	73	72	71	72	84	66	75	70

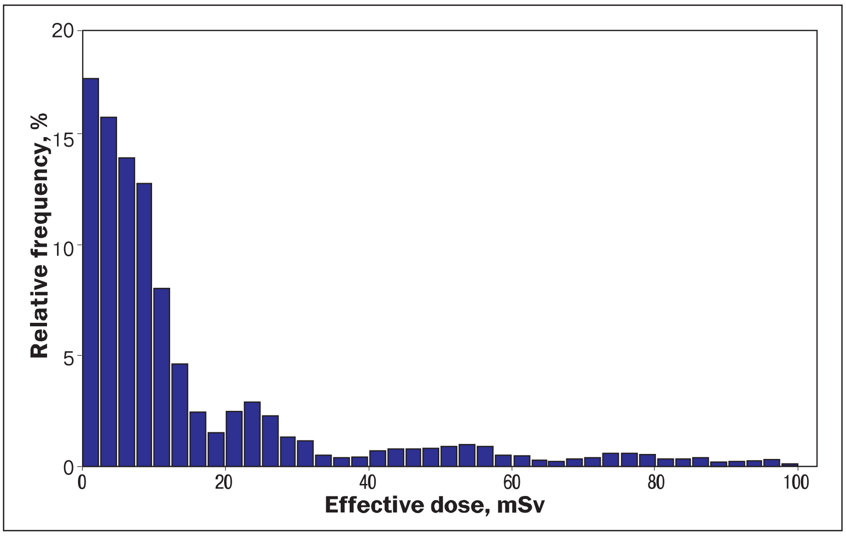

Figure 1.10. Distribution of individual doses of external exposure for 14,084 evacuees from the settlements of the 30-km zone. Results of deterministic calculation.

od from the beginning of the accident to the moment of evacuation outside the 30-km zone for each of the persons under review. 1,260 persons exceeded 50 mSv, for 120 persons the effective doses were higher than 100 mSv and only for one person with a dose of 214 mSv exposure exceeded the level of 200 mSv (Fig. 1.10).

From comparison with the average amount of time spent outdoors, which is characteristic for the urban population (21 %), it can be seen that the villagers spent much more time outdoors, which, naturally, contributed to an increased exposure. Another factor that has significant impact on the resulting dose is the duration of residents' stay in the zone of high exposure.

Location of the settlement and routes of migration prior to evacuation had the greatest impact on the doses received by evacuees from the settlements of the 30-km zone. This is caused by extreme heterogeneity of the contamination within the 30-km zone. Along with the difference in levels of relatively uniform contamination of significant territories, in the areas adjacent to the Chornobyl NPP, so-called fallout traces are noted, where contamination density is sometimes an order of magnitude greater than in the adjacent area. In order to perform more specific modeling of doses and facilitate comparison of the results, the 30-km zone was divided into five sectors (Fig. 1.11), which encompass the settlements reflected in Table 1.13.

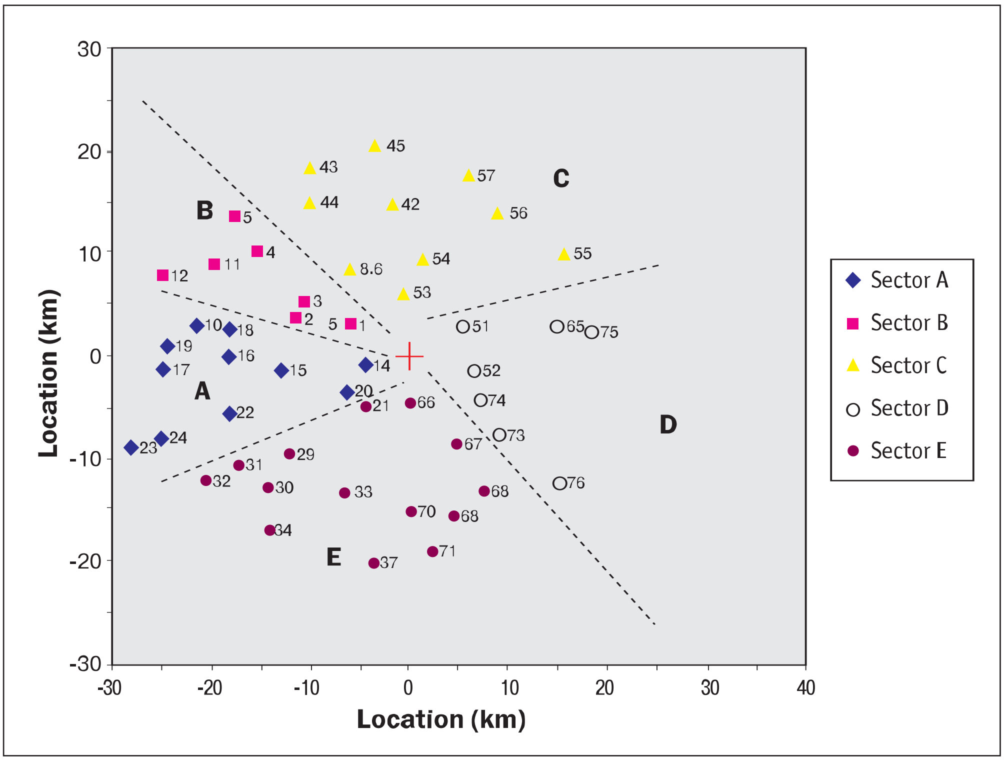

Figure 1.11. Location of settlements of 30-km zone and division into sectors (for settlement numbering and their names see the Table 1.13)

Table 1.13
Results of deterministic calculation of individual doses for the settlements of the 30-km zone. Location of settlements see Fig. 1.11.

Code	Settlement	Number of residents	Evacuation day	Share of time outdoors, %	Mean	Median	95% percentile
			Sector A				
14	Yaniv	63	3	34	22	9.5	84
20	Chystohalivka	331	7	44	61	70	98
15	Buriakivka	56	8	45	29	24	81
16	Nova Krasnytsia	89	8	48	23	23	29
18	Richytsia	382	7	50	24	26	33
17	Tovstyi Lis	408	8	51	52	60	81
19	Krasne (Tovstolis village council)	297	8	49	34	15	97
10	Rudky	43	7	32	10	12	19
22	Stara Krasnytsia	20	7	36	9.2	8.4	17
23	Vilshanka	24	10	34	10	11	13
24	Lubianka	304	10	46	12	12	16
			Sector B				
1	Novoshepelychi	815	6	37	15	13	31
2	Staroshepelychi	209	7	50	21	22	31
3	Benivka	101	8	48	18	18	26
4	Bila Soroka	7	6	41	16	-	-
5	Dovliady	10	5	36	12	10	23
12	Khatky	19	9	44	10	9	12
			Sector C				
54	Mashevo	162	8	54	75	79	96
41	Usiv	89	8	48	150	154	165
43	Molochky	2	7	34	31	-	-
55	Zalissia	2	6	36	12	-	-
56	Kriuky	14	7	44	66	-	-
57	Kulazhyn	2	8	12	28	-	-
			Sector D				
51	Zymovyshche	431	7	37	37	42	56
52	Kryva Gora	146	8	40	47	51	67
74	Starosillia	100	8	40	3	3	4
73	Koshovka	126	8	45	9	8	12
76	Paryshiv	286	8	46	4	4	5
65	Chapaivka	211	8	39	6	7	8
75	Chykalovychi	3	8	50	8	-	-
			Sector E				
66	Kopachi	432	8	40	45	53	66
67	Leliv	604	8	42	22	23	30
68	Chornobyl	4558	7	32	6	6	14
69	Zalissia	1611	8	52	7	8	10
70	Zapillia	69	9	48	6	7	8
71	Cherevach	263	9	47	5	5	8
37	Novosilky	202	9	48	6	6	8
33	Korohod	601	8	52	4	5	6
29	Stechanka	333	8	43	4	4	5
30	Roz'yizhdzhe	49	8	37	3	3	4
31	Illintsi	366	8	45	3	3	4
32	Rudnia Illinetska	15	11	36	4	4	5
34	Glynka	227	7	34	2	2	2

It was found that within one settlement the variation of individual doses is quite small. Geometric standard deviation of dose distributions within small settlements at about 1.4–2.8 reflects relative homogeneity of population from the point of view of exposure conditions, in particular their behavior. Exceptions from this rule are residents of larger settlements like Chornobyl, which include numerous groups with very different behavior patterns. In addition, migration of some residents of Chornobyl outside the city limits, as well as the independent evacuation of some of them contributed to a significant expansion of the range of doses received by the inhabitants of this settlement. Therefore, geometric standard deviation of dose distribution for evacuees from Chornobyl is very high (4.14) and is comparable to the GSD, estimated for the whole population of the 30-km zone.

In general, the uncertainty of individual dose estimates of the rural population is somewhat higher than for the case of reconstruction of doses of the urban population, but even with uncertainty at the level of 60–80 % (variation coefficient), it can be stated that such accuracy is quite adequate for the purposes of retrospective assessment of individual doses of the population evacuated as a result of the accident.

Doses received by the residents of Prypiat on the evacuation route

Obviously, since the moment of boarding buses and starting the evacuation procedure, the process of irradiation of people and the formation of their doses had not stopped. Before the final relocation to the areas not affected by the accident releases, it was still possible to cross highly contaminated areas on the evacuation route. As a result of the dedicated study, the doses received by the residents of Prypiat during the evacuation were roughly evaluated. Analysis of the survey questionnaires filled in 1988–1989 allowed identification of four main routes used by the residents of Prypiat in course of their evacuation, Description of those evacuation routes is given in Table 1.14. According to these data, the most significant route was the road to Poliske, strictly west from Prypiat. This route was used by the dominant majority of evacuees. Somewhat less significant was the route was the Kyiv direction, the path of which ran through the «red forest», Kopachi, Chornobyl, Cherevach and further to Kyiv. Two other routes were identified: by railroad towards Chernihiv and by private cars towards Belarus (road to Bila Soroka). This result is in general agreement with official data regarding evacuation of Prypiat residents.

Analysis of the radiation situation on evacuation routes showed that the entire route can be divided into two significantly different parts (phase 1): phase 1, which ran within the 5 km zone of the Chornobyl NPP, and the rest of the route (phase 2) from the boundaries of the 5 km zone to the final destination. The distinctive feature of Phase 1 is that the evacuation route crossed several extremely intense fallout traces, the scale (characteristic size) of which reached only tens or hundreds of meters. The rest of the evacuation (phase 2) took place in less contaminated areas with significantly lower dose rate variations. As a result, the assessment of doses received on specific evacuation routes was carried out separately for phase 1 and 2. In the case of Phase1, doses were manually reconstructed using radiation maps provided by Chornobyl NPP.

From the assessment of the doses received during the movement by each of the routes, it turned out that the route assumed by the preparedness plans in the direction of Poliske was in fact endowed with much higher doses than improvised Belarusian direction. The route towards Kyiv was also associated with high exposure because of passing extremely hot spot near the crossroad ChNPP-Chornobyl-Prypiat (so called «Torch» and «Red forest»). Although the rest of the route in the southern direction ran through less contaminated areas, the doses formed on the first section were quite high. The most dose intense route was the railway evacuation to Chernihiv. This route was used by about 6 % of interviewed evacuees. The trains departed from relatively contaminated Yaniv station, further, the track ran past the northern fence of the ChNPP site where the dose rate reached quite significant values. As a result, the doses received at this evacuation route turned to be the highest among all evacuation routes.

Table 1.14
Characteristics of evacuation routes from Prypiat (according to the survey)

#	Evacuation direction	Route CODE	Number of people	Percentage of total, %
1	Polissya direction	1	6831	42
2	Kyiv direction	2	4478	27
3	Chernihiv direction	3	938	6
4	Belarusian direction	4	612	4
5	No specific route specified	5	2271	14
6	To a village of the 30-km zone	6	1063	7
		Total:	16 193	100

Thus, the doses of the majority of the population of Prypiat received during the evacuation were within 11–19 mSv, which is comparable to pre-evacuation exposure of the population. It is interesting to compare these two (before and during evacuation) components of the individual doses. To do this, each of the evacuees who permanently stood within city limits before evacuation and reported his/her evacuation destination (a total of 6,908 people who were satisfied with these criteria), the individualized dose en route was assigned, Fig. 1.12 shows the distribution of partial dose contributions during evacuation. On average, 52 ± 19 % of the dose was received by the evacuators during the evacuation. In summary, adequate account of the en route evacuation dose for Prypiat residents significantly modifies the irradiation pattern for evacuees from Prypiat. As a reference, one should take Belarussian direction, which contributed only 6 % to the respective total dose.

As a result of these efforts, integral doses were evaluated separately for each of the four routes. It turned out that in terms of dose received during the evacuation, the regular evacuation route in the direction of Polissya, which was envisaged by preparedness plans, was not optimal. Evacuation in Belarussian direction resulted in an order of magnitude smaller doses than any other route. From the other hand, evacuation towards Kyiv or Chernihiv resulted in even higher doses.

Comparison of individualized dose assessments on the evacuation route with individual doses, received during occupancy in Prypiat in the period before the evacuation, showed that in a significant number of cases, the doses on the evacuation route were comparable, or even greater than those received before the evacuation.

Further research on the dosimetry of evacuees

Within the framework of the Ukrainian-American trio study of parental irradiation in Chornobyl clean-up workers and evacuees and germline mutations in their offspring (project «TRIO») doses of evacuees from Prypiat were evaluated. For this purpose, the new instrument was developed for evaluation of shielding properties of the living blocks of common designs, as well as outdoor location factors, which take into account effect of the local environment – neighboring buildings, pawed areas, lawns, etc. [61]. Based on the topographic and architectural plans rigorous modeling was performed not only for indoor locations, but also for complete environs over the whole Prypiat area. Calculations were performed using Halden Planner/HVRC VRdose® code [62], which using analytical functions is able to simulate shielding properties of buildings and other structures. Comparison with Monte Carlo calculations, which were previously used to assess location factors of certain types of houses in Prypiat [63], the new method has an advantage of quick calculation, but is somewhat inferior in terms of modeling detail (simplified method of taking into account the contribution of scattered radiation). Location factors assessed in this way were compared with the earlier values estimated by Monte Carlo method, the comparison showed a good coincidence of the results obtained by two methods.

The comprehensive reconstruction of doses of evacuators from Prypiat within the framework of the Ukrainian-American trio study of parental irradiation in Chornobyl clean-up workers and evacuees and germline mutations in their offspring (project «TRIO») also allows separate assessment of the con-

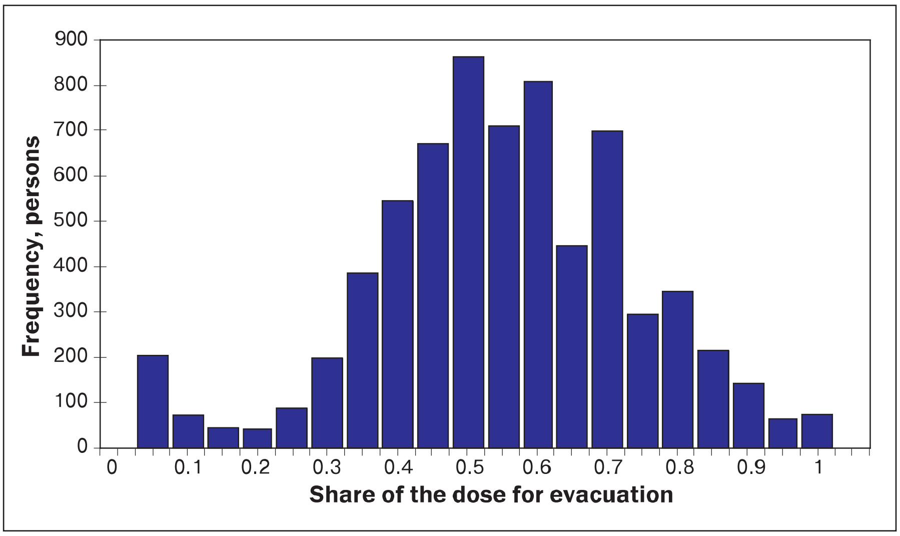

Figure 1.12. Partial contribution of the dose received during evacuation to the total dose of evacuees from Prypiat

tribution of various components to the total dose received by the evacuees: doses of external exposure during their stay in the city until the moment of evacuation, dose during evacuation and in places of intermediate evacuation (for instance Poliske which was designated an evacuation point in the preparedness plans), doses of internal exposure due to inhalation of radionuclides. In addition, it would be possible to evaluate doses of about 10 % of residents of Prypiat, who departed from the city limits before the evacuation (so-called persons with an extraordinary mode of behavior). These investigations just began promising to result in the complete picture of the doses of evacuated population and should have prognostic value for similar large radiological emergencies similar to the accidents at Chornobyl or Fukushima Dai-ichi.

2. RADIOLOGICAL EFFECTS

2.1. Acute radiation sickness as a result of the Chornobyl accident: history of exposure, time course of health in post-accident period and leading causes of death

In the first days after the accident at the Chornobyl Nuclear Power Plant (ChNPP), 499 patients with acute radiation sickness (ARS) were hospitalized. No clinical or laboratory signs confirming the diagnosis were found in most of them. In December 1986, it was officially stated that 237 patients got ARS of different severity as a result of the accident at the CNPP. Of those patients, 28 died within 11 to 96 days: 27 patients (20 patients with ARS grade 4 and 7 patients with ARS grade 3) died of extremely severe radiation-induced bone marrow failure and radiation lesions of skin, and one female patient with ARS grade 2 died of a concomitant disease with underlying recovered haematopoiesis [1]. Two more individuals died within the first day after the accident: one of them was buried under the ruins of the reactor, and the other died of fatal thermal burns in several hours after the explosion [2]. Of 237 patients with ARS, 118 were staying on treatment in Moscow Clinical Hospital No. 6 and 119 in several hospitals in Kyiv (Table 2.1).

Overdiagnosis of ARS was suggested back in 1986 [2]. An analysis of source documents was made by the Institute of Biophysics (Moscow) with the participation of experts from Research Center for Radiation Medicine (RCRM, Kyiv) under the general guidance by professor A.K. Gus'kova in the period from 1986 through 1989. Since in most patients, partial or full recovery of basic measures of haematopoiesis was observed in 3 years after the exposure, diagnoses were reviewed on a retrospective basis. Confirmation (exclusion) criteria were based on typical dynamics of hematological indices uppermost neutrophil granulocytes and thrombocytes during acute phase followed the irradiation [3, 4].

Diagnosis of ARS was cancelled in 103 patients (10 patients treated in Moscow Clinical Hospital No. 6 and 93 patients treated in Ukrainian medical centers) due to incompliance of the clinical and laboratory data with radiation bone marrow syndrome or because of lack of medical data that would make it possible to confirm the diagnosis (Table 2.1). Thus, the number of patients with ARS reduced to 134 individuals. Patients with non-confirmed diagnosis of ARS (ARS NC) definitely suffered a radiation exposure, which, however, did not result in the development of radiation-induced bone marrow syndrome.

Male patients prevailed among those exposed to radioactive irradiation: male patients comprised

Table 2.1
Distribution of the patients subject to ARS grade before the diagnosis was confirmed and after this

ARS grade	ARS was diagnosed in 1986		ARS was confirmed in 1989	
	Russia, Moscow	Ukraine, Kyiv	Russia, Moscow	Ukraine, Kyiv
ARS NC			10	93
I	31	100	23	18
II	46	13	44	6
III	21	5	21	1
IV	20	1	20	1
Total	118	119	118	119

Table 2.2
Age, gender, professional and dosimetric characteristics of the patients of ARS and ARS NC groups

Indices	ARS grade				
	ARS NC	1	2	3	4
Gender: m / f	11 / 92	3 / 38	2 / 48	0 / 22	1 / 20
Professional activity at the irradiation:					
➤ CNPP employers	29	19	21	17	13
➤ CNPP guardians	2	8	3	–	–
➤ builders	6	3	15	3	–
➤ fire-fighters	34	6	7	1	6
➤ occasionally irradiated persons	20	4	1	1	2
➤ emergency staff	12	1	3	–	–
Age at the irradiation, years	n*=103	n=41	n=50	n=22	n=21
M ± SD**	36.4±10.4	34.1±8.5	37.9±13.5	37.4±13.5	31.8±9.2
min – max	18.4–60.3	17.6–56.3	17.9–79.3	20.4–72.6	23.2–53.6
95 % CI***	34.4–38.5	31.4–36.8	34.1–41.7	31.4–43.4	27.6–36.0
Absorbed dose, Gy	n=18	n=34	n=44	n=18	n=18
M ± SD	0.4±0.3	1.0±0.6	2.4±0.9	5.1±1.5	9.9±2.2
min – max	0.1–1.0	0.1–3.3	0.5–4.9	2.9–8.2	6.4–13.7
95 % CI	0.2–0.5	0.8–1.2	2.1–2.7	4.4–5.8	8.8–11.0

Notes. *Number of patients in the sample; **mean ± standard deviation; ***confidence interval.

89.3 % of unconfirmed ARS diagnosis group, 92.7 % of ARS grade 1 group, 96.0 % of ARS grade 2 group, 100 % of ARS grade 3 group and 95.2 % of ARS grade 4 group (Table 2.2). The data of radiation anamnesis showed that among patients with confirmed ARS grade 1 to 4 there were 70 workers of the ChNPP, 11 guardians of the plant (servicemen of the internal military forces of the Ministry of Internal Affairs of the USSR) [5], 21 builders of the new power blocks 5 and 6 installations, 20 fire-fighters, 4 so-called «liquidators» (emergency staff) and 8 individuals occasionally exposed to radioactive irradiation. Occupation of 2 died patients was unknown, therefore, such patients were not included in any of the aforementioned categories of injured persons [4]. The rectified data available now in the archives of ChNPP and Chornobyl National Museum, make it possible to categorize all individuals injured during the Chornobyl disaster by their occupation as shown in Table 2.2.

The workers of the Chornobyl Nuclear Power Station formed the biggest cohort of patients with ARS of different grade – 52.2 %. The second biggest cohort (15.7 %) comprised the builders of the 5th and 6th power units, and the third biggest cohort (14.9 %) – fire fighters. Other injured included the guardians (8.2 %), occasionally exposed persons (6.0 %) and liquidators (3.0 %), i. e., those persons who were sent by their enterprises to participate in accident rescue operations in the ChNPP zone. Of 28 died persons, 20 were the workers of ChNPP, 6 – fire-fighters and 2 – occasionally exposed: just before the accident, 3 engineers of Kharkiv Turbine Works had been sent to ChNPP in order to perform testing of a turbine manufactured at the said Turbine Works. During the accident, they were staying in close vicinity to the ruined reactor. Two of them died of ARS grade 4, whereas one of them survived ARS grade 3.

Patients with ARS grade 1 to 3 and patients with unconfirmed ARS were actually of the same age group, while mean values of exposure doses differed significantly ($p < 0.001$).

Only 209 individuals were still alive by the end of 1986, including 106 ARS survivors and 103 patients with unconfirmed ARS. Of those individuals, 190 were living in the territory of Ukraine (Table 2.3), and the residual 19 persons – in other republics of the former Soviet Union.

Upon the establishment of the RCRM in Kyiv on the October 1, 1986, the 190 patients residing in Ukraine have been under regular medical supervision and treatment in the clinic of RCRM. Most Ukrainian patients and two Russian and two Belarusian patients, prior to the formation of new states out of the former Soviet republics, had been followed up in two medical centers – RCRM and the Institute of Biophysics with its clinical base at Moscow Clinical Hospital No. 6, simultaneously. Therefore, in works pub-

Table 2.3
Countries where persons with ARS and ARS NC were living since 1986

ARS grade	Russia	Ukraine	Belarus	Azerbaijan	Kazakhstan	TOTAL
ARS NC	3	99			1	103
1	3	38				41
2	5	41	2	1		49
3	3	12				15
4	1					1
Total	15	190	2	1	1	209

lished before 1991, Kyiv and Moscow study groups were almost identical. Since 1991, each patient has been examined and treated in the medical centers of his/her country.

During entire post-accidental period it was revealed the continuous growth of different organ systems diseases both in ARS survivors and ARS NC patients. Figure 2.1. demonstrates the cumulative frequency of pathological states of main five body systems in different terms after Chornobyl accident. In 25 post-accidental years the frequency of these systems different diseases approach to 100 % and reach this level for nervous and digestive system in ARS survivors. The next 10 years brought a less changes in growth of frequency rate of cardiovascular, respiratory and endocrine pathology.

Thirty patients with unconfirmed ARS and 36 ARS survivors died during the period from 1987 to 2021. Cardiovascular diseases rank first as causes of long-term mortality after exposure (Table 2.4). In the period from 1986 to 2013, sudden cardiac death was the main cause of death in 10 persons (I46.1). Either essential hypertension (I10, I11) or/and coronary heart disease (I20.1, I25.0, I25.1) were diagnosed in all such died persons. Postmortem examination of none of them showed any signs of myocardial infarction or another acute pathology that might be the cause of death. Fatal heart rhythm disorders could result in lethal outcome. Four more patients with underlying essential hypertension died of acute cerebrovascular disease (1991, 2006, 2008) (I61, I63). Chronic heart failure was the cause of death in 10 patients from 2007 to 2020 (I50.1). Two patients died due to acute myocardial infarction with acute heart failure (I21).

Oncological and oncohematological pathologies rank second among the causes of patients death. Blood diseases included three cases of myelodys-

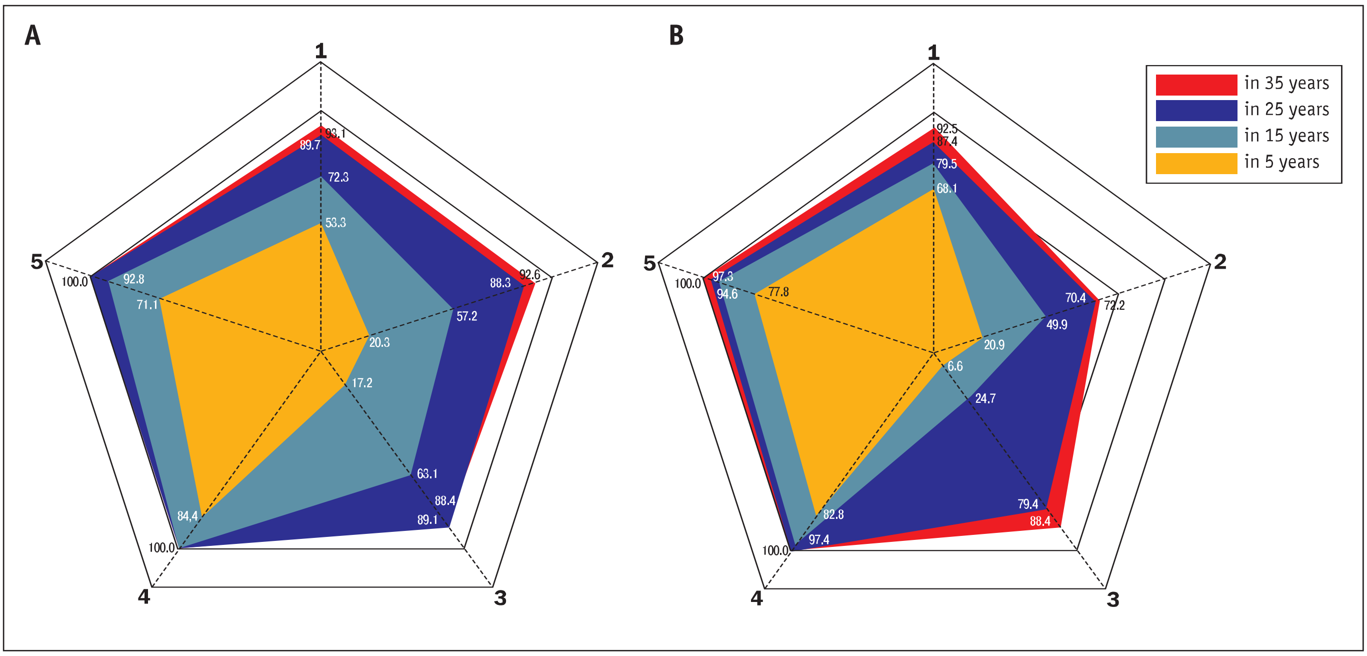

Figure 2.1. **Cumulative frequency (%) of different organ systems pathology in ARS survivors (A) and ARS NC (B) patients during post-accidental period**
1 – cardiovascular, 2 – respiratory, 3 – endocrine, 4 – nervous and 5 – digestive systems

Table 2.4
Death reasons in patients with ARS NC and ARS survivors in the post-accidental years

ARS grade	Cause of death				
	Cardiovascular diseases	Oncological and oncohematological diseases	Somatic, nervous and infectious diseases	Traumas and accidents	Total
ARS NC	12	13	3	2	30
1	5	3	1	2	11
2	6	5	4	2	17
3	3	2	2	1	8
Total	26	23	10	7	66

plastic syndrome (1993, 1998 and 2002), two cases of acute myeloid leukaemia (1998, 2019), and a case of hypoplasia of hematopoiesis (1987), chronic myeloid leukaemia (2014) and polycythemia vera (2011). Cancer of stomach and colon (three each cases) was the most frequent death reason in comparison with a cancer case of throat, urinary bladder, prostate, lung, liver, brain, maxillary sinus and mandible malignant neurinoma. One patient died due to femoral soft tissue sarcoma in 1993.

We have found no correlation between the cases of oncological or cardiac death and dose of radiation exposure or ASR grade.

Somatic and neurological diseases, and infections, including SARS-Cov-2, brought to death 10 patients. Injuries due to traffic or other accidents were lethal for seven persons.

2.2. Incidence of cancer in people affected by the Chornobyl accident

Long-term monitoring of malignant neoplasms (MN) in the groups affected by the Chornobyl disaster was initiated in the first years after this event. The work was initially started in the areas most contaminated with radionuclides. To do this, in 1987 a local database was created, which gathered personalized information (retrospectively since 1980 and current time) about all cases of MN in residents of Narodychi, Ovruch, Luhyny districts of Zhytomyr Oblasts, Borodyanka, Ivankiv, Poliske districts of Kyiv Oblast. In addition, information was collected on cases of MN in the former Chornobyl district for 1981–1985 and these data are included in the general database. Since 1989, since the establishment of the National Cancer Registry of Ukraine (NCRU), there has been a mutual exchange of information with this institution on cancer cases in the areas most contaminated with radionuclides. From 1980 to 2018, 28,166 cases with a first-time diagnosis of malignancy were registered.

The population in these areas at the time of the Chornobyl accident was 360.0 thousand people, including 74.4 thousand children aged 0–14 years. In 2018, the population of these six districts without the former Chornobyl district was 172.0 thousand persons, including 26.3 thousand children. Data from the State Registry of Victims of the Chornobyl Accident (SRU) were used to study the incidence of cancer among participants in the liquidation of the consequences of the Chornobyl accident (clean-up workers) of 1986–1987 and evacuees. There were selected and analyzed personalized data on clean-up workers 1986–1987 living in Dnipropetrovsk, Donetsk (before 2014), Kyiv, Luhansk (before 2014), Kharkiv oblasts and in Kyiv city with a total number of 77.0 thousand people in 2018 and evacuees from the exclusion zone and resettled throughout Ukraine with a total number of 66.1 thousand people in 2018. During the period 1994–2018, clean-up workers registered 13,406 new cases of MN, for 1990-2018 in the evacuees – 4,390 cases of MN [5–9].

To compare the incidence of MN by categories of victims, an indirect method of standardization was chosen, which provides for the calculation of standardized incidence ratios – SIR (%). The incidence of all forms of malignant neoplasm's was statistically significantly higher than the national average only in the clean-up workers group of 1986–1987 (Table 2.5). It should be noted that in the process of dynamic monitoring for the entire period there was a gradual decrease in indicators, so that in 2014–2018 they no exceeded national level

Таблиця 2.5
Incidence of all forms of malignant neoplasms (ICD-10: C00-C96) of the population of Ukraine affected by the Chornobyl accident (standardized incidence ratio – SIR, %)

Affected group and follow-up period	Actual number of cases	Expected number of cases	SIR, %	95 % confidence interval
Residents of areas contaminated with radionuclides (1990–2013)	16 578	20 841.3	79.5	78.3–80.8
Residents of areas contaminated with radionuclides (2014–2018)	2 970	3 343.5	88.8	85.6–92.0
Clean-up workers (1994–2013)	11 115	10 377.7	107.1	105.1–109.1
Cclean-up workers 1986–1987 (2014–2018)	2 290	2 201.5	104.0	99.8–108.3
Evacuees (1990–2013)	3 586	4 252.6	81.3	81.6–87.1
Evacuees (2014–2018)	804	695.2	115.7	107.7–123.6

(SIR = 104.0 %, 95 % CI: 99.8–108.3). Data on Ukraine for previous years [10] show that the incidence of MN is lower among residents of the most contaminated areas of Ukraine compared to residents of other territories. At the same time, over the last 5 years the incidence of evacuees has exceeded the country's population – SIR = 115.7 % (95 % CI: 107.7–123.6). This was due to an increase in the incidence of evacuated women (SIR = 121.5 %; 95 % CI: 110.8–132.1) exceeded the national level (SIR = 104.0 %; 95 % CI: 99.8–108.3).

Analyzing the reasons for the lower incidence of radiation contaminated territories residents, it should be borne in mind, that in the pre-accident period in the population of the territories adjacent to the Chornobyl NPP the incidence of malignant neoplasms was among the lowest in Ukraine.

2.2.1. Risk of malignant tumors of lymphoid, hematopoietic and related tissues (ICD-10 C.81–C.96) in the population of Ukraine affected by the Chornobyl disaster

Among some forms of malignant tumors, in the genesis of which the radiation factor can play a significant role, profound attention is drawn to tumors of lymphoid, hematopoietic and related tissues, especially leukemia, the development of which after irradiation has the shortest latency period (2–5 years), (Table 2.6).

The incidence rates of lymphoid, hematopoietic and related tissues in clean-up workers of 1986–1987 did not change significantly during the two follow-up periods – in 1994–2013 SIR = 145.1 % (95 % CI: 134.0–156.1), in 2014–2018 – SIR = 144.0 % (95 % CI: 118.8–169.3) and exceed the national level. A similar pattern is observed in the evacuees – respectively SIR = 146.1 % (95 % CI: 129.0–163.3) and SIR = 139.1 % (95 % CI: 99.4–178.9). There is some insignificant decrease in rates. Among the residents of the most contaminated with radionuclide's territories, the analyzed indicators are significantly lower – 88.3 % (95 % CI: 82.9–93.8) in 1990–2013 and

Table 2.6
Incidence of lymphoid, hematopoietic and related tissues (ICD-10 C.81-C.96) of the population of Ukraine affected by the Chornobyl accident (standardized incidence ratio – SIR, %)

Affected group and follow-up period	Actual number of cases	Expected number of cases	SIR, %	95 % confidence interval
Residents of contaminated with radionuclides territories (1990–2013)	861	975.6	88.3	82.4–94.1
Residents of contaminated with radionuclides territories (2014–2018)	150	169.0	88.8	74.6–103.0
Clean-up workers of 1986–1987 (1994–2013)	661	455.8	145.0	134.0–156.1
Clean-up workers of 1986–1987 (2014–2018)	125	86.8	144.0	118.8–169.3
Evacuated from the exclusion zone(1990–2013)	280	191.6	146.1	129.0–163.3
Evacuated from the exclusion zone(2014–2018)	47	33.8	139.1	99.4–178.9

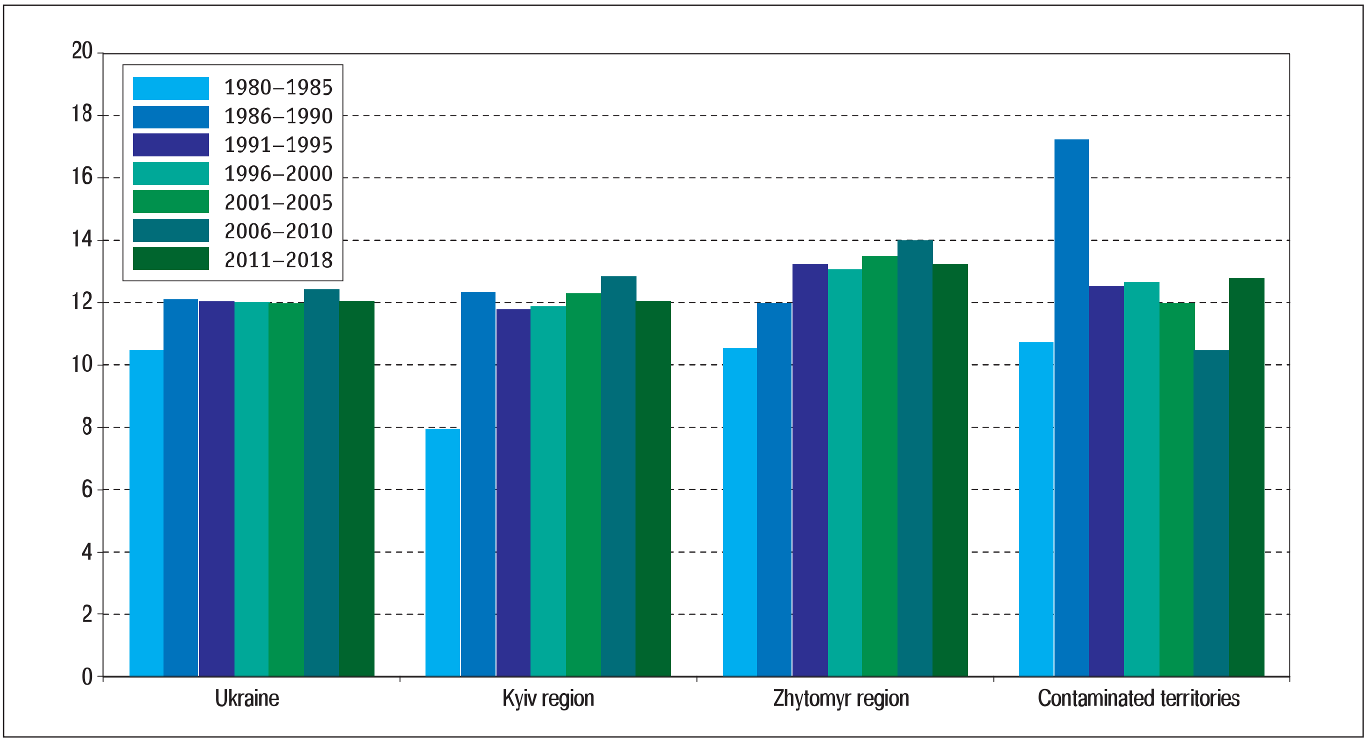

Figure 2.2. Incidence of lymphoid, hematopoietic and related tissues (ICD-10 C81-96) of the population of Ukraine, Zhytomyr, Kyiv Oblasts and 6 territories most contaminated with radionuclides in 1980–2018 (standardized by World Standard for 100,000 population)

88.8 % (74.6—103.0) in 2014—2018. It should be noted that in contrast to the population of large territorial units (Zhytomyr, Kyiv Oblasts, Ukraine as a whole) in the residents of radioactively contaminated territories in the immediate post-accident period (1986—1990) there was a significant increase in the frequency of this pathology (1.6 times). In the following years, there was a gradual decrease in their frequency to the pre-accident level (Fig. 2.2). This situation corresponds with the radiation model of leukemia development with a short latency period after exposure (2—5 years): significant increase in the incidence with its gradual decrease to baseline.

2.2.2. Leukemia

Previous experience

Leukemia is a malignant neoplasm, the significant excess of which was recorded the first among other cancers and associated with ionizing radiation of survivors after the atomic bombing of Japanese cities in 1945. The leukemia incidence is linearly dose-dependent and has the highest risk in comparison with solid cancers. The probable excess of leukemia after the Chornobyl accident was the cause of the greatest anxiety of the population and concern of the scientific community [11, 12].

The most geographical correlation studies, which were conducted in different countries, have not found convincing evidence of increased leukemia incidence despite the expected excessive occurrence of leukemia and solid cancers among the population of both adjacent and remote areas in the first years after the accident [11, 12].

Predictive estimates were largely unjustified, except for the incidence in some high-risk groups.

2.2.2.1. Leukemia in clean-up workers

Previous experience

Among those exposed to ionizing radiation due to the Chornobyl NPP accident, the highest doses were received by the accident clean-up workers. This allows determine the excessive cancer risks realization by epidemiological methods [12].

To establish the link between the leukemia incidence and the ionizing radiation effects after the Chornobyl accident, a Ukrainian-American study of the leukemia radiation risks in a cohort of Ukrainian liquidators was conducted in Ukraine.

The cohort included 110.6 thousand male clean-up workers who participated in recovery operations in the Chornobyl Exclusion Zone in 1986–1990. Epidemiological retrospective analytical case-control study was initiated in 1997 [13]. It allowed to determine the excess relative risk of leukemia per unit dose of radiation – ERR /Gy= 3.44 (95 % CI: 0.47–9.78, $p < 0{,}01$) in period 1986–2000 [13], as well as reducing the value over time to 1.26/Gy (CI: 0.03–3.58; $p = 0.041$) [4]. These results clarify the existing values of radiation risks, which are in good agreement with the known data of other studies (victims of atomic bombings, clean-up workers at the Chornobyl NPP from Russia, Belarus and the Baltic States) [11, 12].

For the first time, the radiation risks of chronic lymphocytic leukemia (CLL) and the correspondence of the values of relative risks to other forms of leukemia (non-CLL) were established, which allowed to attribute ionizing radiation to significant factors of CLL induction. The inclusion in the analysis an identified cases sample (117 of 138), allowed to determine the reliable linear nature of the dose-response as for the group of non-CLL leukemias (ERR/Gy = 2.21; 95 % CI: 0.05–7.61), and purely for CLL (ERR/Gy = 2.58; 95 % CI: 0.02–8.43). The obtained data give grounds for conclusions about the existence of radiation-induced CLL, which was not studied in most previous epidemiological studies due to the lack of excess in Japanese studies. The latter position is questionable because CLL is absent in the Japanese ethnic group. In the analysis of the attributive risk of leukemia it was found that approximately 16 % of all cases of leukemia diagnosed among clean-up workers within 20 years after the disaster were due to Chornobyl accident exposure (population attributive risk (PAR) = 16.4 % (95 % CI: 3.9–32.6) [14].

Results obtained in the last 5 years

Against the background of an increased risk of some forms of leukemia including chronic lymphocytic leukemia, possible features of the clinical course of identified cases of CLL [15] and their molecular genetic characteristics [8, 16] were studied in a cohort of 110,645 male clean-up workers. Analysis of the clinical disease course in 79 cases of CLL with a certain irradiation dose to the red bone marrow revealed a statistically significant association between younger age at the beginning of irradiation and lower survival. The latency period was not related to the red bone marrow dose or any clinical features of the disease, but was significantly shorter among smokers and older people [15].

Survival was significantly lower among those who were irradiated at a younger age ($p = 0.02$). According to the results of Cox regression analysis a statistically significant relationship was found between radiation dose and survival ($p = 0.03$) with a risk ratio (HR) of 2.38 comparing the survival of CLL cases with radiation doses higher and lower for the median value (22 mGy) [15].

Other clinical features of some leukemia forms diagnosed among liquidators were studied in separate subcohorts in special clinical trials conducted at the NRCRM.

After taking into account the radiation effect, no significant effect of other potentially negative factors influence (professional, social, alcohol consumption and smoking) on the risk of CLL was determined in the studied clean-up workers cohort. Myeloid leukemia has been shown to be at increased risk due to occupational exposure to petrol or its derivatives (OR = 2.28; 95 % CI: 1.13–6.79), regardless of the radiation dose received. The obtained values will be taken into account in further studies of risks associated with the combined action of radiation and other environmental/occupational factors for the Ukrainian population of active working age [17].

Molecular studies of the CLL gene profile in 16 clean-up workers from the cohort, in relation to 128 Ukraine and the USA patients with CLL, irradiated within the natural background, showed greater length of telomeres and mutations of the POT1 gene involved in the telomere cascade [8, 16].

A study of the risks of multiple myeloma, which is a form of malignant neoplasms of lymphoid and hematopoietic tissues from mature B-lymphocytes, was also conducted in the supplemented cohort of liquidators (150.5 thousand people) [18]. This disease has also linked to radiation exposure in a number of studies.

Taking into account the probable 10-year latency period after radiation exposure, the signs of increased incidence were determined in the period 2002–2007, i. e. 16–21 years after the accident. This trend was realized in a significant surplus during the next 5 years (2008–2013), i. e. 22–27 years after the accident, among persons over 50 years of age, with the calculated values of the standardized incidence rate (SIR) at the level of 1.86, 95 % CI: 1.27–2.44. The incidence decreases to the population levels of the relevant gender and age groups in Ukraine in subsequent years of follow-up.

Studies in recent years have shown a continuing trend towards the realization of radiation leukemia risks. It is necessary to conduct early diagnosis and treatment given the prolonged possibility of realization of the risks of radiation-induced leukemia and multiple myeloma (up to 50 years after irradiation and more). Monitoring of cases of this disease will allow to specify the amount of risks caused by irradiation in the range of low and average doses, first of all among liquidators. In addition, studies will examine the clinical features of various disease forms and possible markers of the radiation component in the pathogenesis.

2.2.2.2. Leukemia in children irradiated after the Chornobyl accident

2.2.2.2.1. Prevalence of leukemia among children – residents of areas contaminated with radionuclides after the Chornobyl accident

Quantification of health effects due to low-dose radiation exposure in childhood remains an important scientific problem. Risk for childhood leukemia after low-dose irradiation due to the Chornobyl nuclear power plant accident has been analyzed in a number of studies. Methodological differences between the studies included dose estimates, data sources and follow-up periods. An ecological study analysis of the prevalence and risks of leukemia among children – residents of Ukraine aged 1 to 19 years was performed in National research center for radiation medicine basing on the contamination status of the territory, time period, gender, and age. Three regions – Zhytomyr, Kyiv (except Kyiv city), and Chernihiv were included as areas contaminated by radioactive ^{137}Cs from 1 to 15 Ci/km^2 with annual effective doses exceeding 1.0 mSv, and Sumy region as the control (non-contaminated) area with ^{137}Cs contamination less than 1 Ci/km^2 and effective doses less than 0.5 mSv per year. The integrated database of the National Research Centre for Radiation Medicine used in the present study included 1085 childhood leukemia cases. Two aggregated periods were used for analysis: 1980–1986 (pre-accident) and 1987–2000 (post-accident). ICD-9 codes for leukemia (204–208.9) were used to perform analyses according to the extent of leukemic cells maturity (acute, chronic, and maturity unspecified leukemia), leukemic cell lineage (lymphoid, myeloid and lineage unspecified leukemia) and all leukemia cases in different age subgroups (1–4, 5–9, 10–14, and 15–19 years). Standard methods of descriptive epidemiology were used to calculate the prevalence of disease and frequency ratio in regression models. The risk assessment for leukemia revealed a number of features. A statistically significant increase in frequency ratio for acute leukemia (1.44; 95% confidence interval (CI), 1.22–1.71), myeloid leukemia (2.93; 95% CI, 1.71–5.40), cell lineage unspecified leukemia (II) (1.48; 95% CI, 1.18–1.87) and all forms of leukemia (1.59; 95% CI, 1.36–1.86) was found for the post-accident period in highly contaminated areas. The results indicate that the frequency of childhood leukemia (and of some of its types) increased in contaminated areas during the post-accident period, suggesting that radiation exposure after the Chornobyl accident might be the cause of the increase. The major limitation of the present study is the unavailability of individual doses. Due to that, all cases were dichotomized into those from highly- or less-contaminated areas, impeding risk analysis. Wide CI ranges for frequency ratios for some leukemia subtypes indicate possible changes if the control group is enlarged. That is why further analytical studies, with individual or at least group dose estimates, are needed to confirm a link between childhood leukemia and the Chornobyl accident.

2.2.2.2. Clinical and hematological features of acute leukemias in children living in radionuclide-contaminated areas of Ukraine after the Chornobyl disaster

Irradiation doses characteristic for the Chornobyl accident can be promoters of genetic and carcinogenic effects in humans and in combination with other factors contribute to the destabilization of proliferation and differentiation of hematopoietic stem cells. With prolonged exposure to negative factors, there is a possibility of developing remote stochastic effects (leukemia, lymphoma, myelodysplastic syndromes, tumors) in children living in areas contaminated with radionuclides.

From the first days of the accident to the present day, pediatricians and hematologists have been monitoring the state of hematopoiesis in children born to parents affected by the Chornobyl disaster, including those who suffered from acute radiation sickness, evacuated from Prypiat city and the 30-km zone in the first terms after the accident, and children living in radioactively contaminated areas after the Chornobyl accident [19].

The state of the hematopoietic system at different levels of the body hierarchy was studied. Clinical and epidemiological studies were conducted and the incidence of leukemia in children was analyzed. The peculiarities of hematological pathology in patients depending on radiation doses, diseases in the pedigree, data of the child's life history, influence of unfavourable factors of non-radiation nature were analyzed: content of heavy metals in the child's body (Pb, Cr, Mn, Cu, Zn, Ni, Fe in nails, hair and blood of children), the degree of integrated pollution of soil, water, air with metals – Ba, Pb, Mn, Cr, Ni, Co, V, Cu, Zn, non-radioactive Sr, and pesticides (materials of the Ministry of Environmental Protection of Ukraine).

Comprehensive assessment of the hematopoietic system of the pediatric population was performed on the basis of studying quantitative and qualitative indicators of peripheral blood and bone marrow precursor cells, biochemical parameters of blood, iron metabolism (serum iron, ferritin, transferrin, transferrin saturation coefficient, sideroblasts in bone marrow), indicators of bone tissue metabolism, bone microenvironment, starting from the stage of collagen formation. The levels of osteocalcin, calcitonin, parathyroid hormone, cortisol, pituitary thyroid-stimulating hormone in the serum of children were determined.

Criteria for the formation of high-risk groups for oncohematological pathology among the pediatric population of Ukraine and treatment and prevention measures aimed to reducing the incidence of blood diseases in children were developed and improved.

Patients with acute leukemia (AL), who were diagnosed between 1994 and 2010, were calculated doses of internal bone marrow irradiation for the entire period of their permanent residence in radioactively contaminated areas after the accident, and which were in the range from 0.09 mSv to 35.01 mSv, (average dose (5.37 ± 1.23) mSv) [20]. For other children diagnosed with AL after 2010, radiation doses were calculated according to [21], their doses ranged from 0.12 to 12.0 mSv (mean (3.66 ± 0.11) mSv). Children with connective tissue dysplasia (CTD) and the comparison group, who were residents of radioactively contaminated areas after the accident, were also monitored by the whole body counters and determined the annual dose of internal radiation, according to [22]. Irradiation doses of children with CTD ranged from (0.37 ± 0.11) mSv to (0.56 ± 0.10) mSv (mean (0.46 ± 0.07) mSv) and did not differ from the comparison group (mean (0.46 ± 0.06) mSv).

The diagnosis of AL was established on the basis of morphological features, immunophenotype of bone marrow blast cells of patients in the laboratory of the Department of Clinical Immunology of the Institute of Clinical Radiology of the NRCRM (Head of the Department Academician of NAMS of Ukraine, MD, Prof. D.A. Bazyka). Patients with acute lymphoblastic leukemia (ALL) were examined during the stages of chemotherapy (CT), which was performed according to the adapted in Ukraine protocols of the Berlin-Frankfurt-Munster Group (BFM).

The results of previous studies showed that in the first terms after the accident (45 days) in children evacuated from Prypiat city and the 30-km zone of the Chornobyl accident, quantitative changes in the hemogram were found: 63 % – neutrophilic leukocytosis with elements of eosinophilia in 21.0 %, in 1.5 % thrombocytosis was registered (platelet count above 450 G/L). Ninety percents of children showed qualitative defects in the elements of hematopoiesis: increased activity of lipid peroxidation and redox enzymes, destabilization and disruption of the integrity of erythrocyte membranes, which did not depend on their age. In subsequent periods of observation, the detected changes in blood cells were normalized and registered only in children with comorbid somatic diseases.

The influence of adverse environmental factors on the development of oncohematological diseases in children was convincingly proved on the example of Kyiv Oblast. According to the mapping of regions, the number of AL cases among children within the districts of this oblast was identified as three cluster zones, which corresponded to the nature of technogenic contamination. However, after the accident, the part of children developing oncohematological pathology at the age over 12 increased from 25 % to 34 %.

Assessment of the frequency and type of pathology in the pedigree of children with AL showed that the first place in frequency was occupied by relatives with cancer (23.3 % vs. 8.1 % in the general population). Allergic reactions, endocrine diseases occurred in relatives of patients in almost the same percentage and did not differ compared with the control group. Although children born to these parents were more likely to weigh more than 4.0 kg and show signs of constitutional lymphatism. The distribution of sick children with AL did not depend on which pregnancy of mother they were born: I, II, III or the following. Regarding the pathology in children, which was detected 3–4 years before the diagnosis of AL, they had a history of bone injuries ($p < 0.05$). The frequency of endocrine pathology and allergic reactions in the pedigree of children with AL did not differ compared with the population.

New data on the influence of pathology in the pedigree of patients on the development and prognosis of AL in children were obtained. There was a difference in the ratio of boys / girls. Thus, in the presence of cancer in close relatives of the child at diagnosis, the ratio was 1.0 : 1.0, allergic reactions – 2.0 : 1.0, endocrine pathology – 1.3 : 1.0. That is, in the presence of allergic reactions in relatives, boys were more likely to get sick than girls (rs = 0.46).

If oncological diseases were present in pedigree of children under 6 years of age, common-ALL and pre-B-ALL were more often detected. Allergic reactions and endocrine diseases in relatives of children are negative factors for the development of T-ALL and pro-B-ALL with an unfavorable course of these diseases. The best prognosis was in children with ALL up to 6 years, if the pedigree had cancer (136.4 ± 4.7) months. A worst prognosis was observed in persons older than 12 years, whose relatives had endocrine pathology and allergic reactions (56.5 ± 4.3) months. In the presence of endocrine diseases in the pedigree, children were more often diagnosed with AML (rs = 0.44).

The irradiation doses of children with AL ranged from 0.09 mSv to 35.01 mSv, children with connective tissue dysplasia and the comparison group – from 0.02 mSv to 0.56 mSv, respectively. No differences were found between the radiation doses of children and clinical-hematological parameters.

The combined effect on the child's body was found of adverse environmental factors, including ionizing radiation, diseases in the pedigree, which exacerbated the course of comorbid pathology and were promoters of malignant diseases of the blood system in children. The child's body is particularly sensitive to deleterious factors of various etiologies due to growth processes, functional instability and staged hormonal changes. The multifactorial nature of leukemogenesis requires the integration of biochemical and molecular genetic research and can be the basis for further detailed development in the field of pediatric hematology, radiobiology and ecology.

2.2.2.3. Mechanisms of radiogenic chronic lymphocytic leukemia development

Epidemiological evidences of increased risk of development under ionizing radiation (IR) and clinical features are usually taken into account to evaluate some cancer and somatic diseases as radiation-induced.

Chronic lymphocytic leukemia (CLL) of B-cell origin is one of the most common lymphoid malignancies in the Ukraine as well as in Western Europe and the USA. The question of the radiogenicity of B-CLL remains largely controversial, although a number of epidemiological studies have shown an elevated radiation-associated risk for CLL [13, 23–25]. Besides, CLL is the most common form of leukemia among clean-up workers of Chornobyl NPP accident [14, 25, 26].

The results of previous studies

1. DNA repair polymorphisms as a factor of genetic predisposition to CLL development under IR exposure. IR is a well-known risk factor for several hematological malignancies, however it's carcinogenic action are still poorly understood. They have been commonly attributed to the direct induction of mutations in oncogenes and tumor suppressor genes, or, as it was suggested, might be related to a positive selection of hematopoietic progenitor cells with certain preexisting oncogenic lesions, conferring survival advantage upon irradiation. It is known that IR as a DNA damaging agent induces a range of lesions, such as base damage, single strand breaks, double strand breaks, and DNA cross links, and therefore, nearly all DNA repair pathways might be involved in their removal. More than 130 human DNA repair genes are involved in different repair pathways. Their activity determines the accuracy and efficiency of DNA damage elimination. Mutations in DNA repair genes are rare, resulting in embryonic death or serious genetic diseases; however, single nucleotide polymorphisms (SNPs), which alter the function or efficiency of DNA repair and are associated with cancer development, have been identified [27].

We have studied the distribution of SNPs of the most well-known DNA repair genes (rs25487 of *XRCC1* gene, a component of base excision repair and the repair of single-strand breaks; rs862539 of *XRCC3* gene that participates in the homologous recombination of double-strand breaks; and rs13181 of *XPD* gene, an important component of nucleotide excision repair) in 64 CLL patients, exposed to IR due to the Chornobyl NPP accident (the main group), 114 IR non-exposed CLL patients (the group of comparison), and 103 gender- and age-matched IR-exposed controls [28]. It was found increased frequency of the low-functional rs13181 *XPD* polymorphic allele in the main group (0.47) compared to controls (0.33), OR = 1.83; 95 % CI = 1.15–2.91; ($p = 0.012$). At the same time, the frequency of *XPD* polymorphic allele in the group of comparison ($p = 0.37$) did not differ from the controls ($p = 0.402$). Furthermore, basal cell carcinoma (secondary skin cancer, the frequency of which is increased in CLL patients) was revealed mainly in the main group (78 %) and in carriers of rs13181 XPD polymorphic allele (89 %).

2. Increased risk of secondary cancer in CLL patients, clean-up workers of Chornobyl NPP accident. One feature of CLL in persons suffered due to Chornobyl NPP accident is an increased risk of secondary tumours [29, 30]. To confirm this fact, we analyzed CLL cases among residents of Kyiv for 1991–2008 according the data of Ukrainian National Cancer Registry. The cohort included 740 male CLL patients, of which 56 were clean-up workers of Chornobyl NPP accident (the data were clarified by comparing with the State Registry of persons, suffered due to Chornobyl NPP accident), and 684 were IR non-exposed. Secondary cancer was diagnosed in 74 (10 %) CLL patients: 14 (25 %) cases were revealed among clean-up workers and 60 (8.7 %) were revealed among IR non-exposed patients (OR = 2.71; 95 % CI = 1.63–4.52; $p = 0.001$). Such significant differences were primarily associated with increased frequencies of basal cell cancer and prostate cancers in group of clean-up workers [31].

The results of research of the past 5 years

1. The TP53 gene polymorphisms as risk factor of CLL development under IR exposure. Tumor suppressor *TP53* is of special interest in the study of carcinogenic effects of IR, since its product p53 protein serves as a key regulator of cellular responses to genotoxic stress (including IR action), inducing apoptosis or cell cycle arrest and DNA repair, thus restricting aberrant cell growth. Reduced activity of p53 proteins due to some SNPs of *TP53* gene leads to disruptions of these processes, genomic instability and increased radiosensitive. This is observed, in particular, in Li-Fraumeni syndrome [32, 33].

We have studied *TP53* SNPs in 236 CLL patients. The main group included 106 IR exposed CLL patients (72 clean-up workers of 1986, 16 inhabitants of radionuclide contaminated areas, and 7 evacuees) and the control group included 130 IR non-exposed CLL patients. The distribution of SNPs was compared between the main and the control groups and 503 healthy Caucasians (open data base 1000 Genomes Project; http://www.1000genomes.org/). For the first time, the distribution of 22 SNPs was analyzed in CLL patients. Some features of CLL patients regardless of IR influence and typical for IR-exposed patients only were revealed [34]. The increased frequency of T/T rs12947788 and G/G rs12951053 homozygotes ($p = 0.01$), which also associated with non-small cell lung cancer and malignant pleural mesothelioma under influence of another genotoxic agent (asbestos), was found in IR-exposed CLL patients [35]. Rare nucleotide substitution rs146340390 (c.665C>T) that significantly impaired p53 activity (24 % compared to wild type) was revealed only in the main group [36]. It was concluded that the genetic predisposition (low functional activity of DNA repair system, p53 protein) may be one of the pathogenetic factors of CLL development ander IR influence.

2. The spectrum of TP53, SF3B1, NOTCH1 mutations, and MYC oncogene amplification. Mutations of *TP53*, *SF3B1*, and *NOTCH1* genes are the most common in CLL patients and associated with aggressive course of disease [37]. Compared with 130 IR non-exposed CLL patients, in group of 106 IR-exposed due to Chornobyl NPP accident CLL patients we found: a) lower frequency of *NOTCH1* mutations (6.7 % vs 17.7 %; $p = 0.012$); b) the same frequency of *TP53* mutations among cases with mutated (11.1 %) and unmutated (11.8 %) immunoglobulin heavy chain (*IGHV*) genes; whereas in the group of comparison as well as in the others CLL cohorts *TP53* mutations were determined mainly among cases with unmutated *IGHV* genes; c) presence of *SF3B1* gene mutations in 40 % patients with *TP53* mutations, whereas *SF3B1* and *TP53* mutations were mutually exclusive in the group of comparison ($p = 0.001$) [38].

One of the mechanisms of IR influence on cells is the amplification of *MYC* oncogene. This genetic abnormality is typical feature of angiosarcomas, undifferentiated polymorphic sacromas, leiomyosarcomas that develop after irradiation [39, 40], breast cancer in women survivors of the atomic bombing of Hiroshima and Nagasaki [41]. In our study of 70 CLL patients, clean-up workers of Chornobyl NPP accident, the frequency of *MYC* amplification was 5.7 %, which does not differ from the others CLL cohorts [42].

3. The structure of B-cell receptors. Expression of functional active B-cell receptors (BCR) on leukemic cells suggests that CLL is antigen-driven disease [43]. We have previously characterized BCRs in IR-exposed CLL patients and suggested the influence of persistent viral infections for selection of malignant transformed cell [30, 44]. Thereafter we enlarged the groups of observed CLL patients (76 clean-up workers, 194 IR non-exposed patients, all men, comparable by age and place of residence), analyzed the BCR structure using modern technologies and described some BCR features in IR-exposed patients [45]. Thus, among IR-exposed CLL patients it was found decreased frequency of BCRs directed against oxidation-specific epitopes (29.4 % vs 48.6 %; $p = 0.018$), and the absence of BCR with mutated *IGHV3-23* gene involved in superantigen binding (11.1 % in the group of comparison; $p = 0.042$). It can be assumed that under IR influence the reaction on such antigens is disrupted, or these antigens are less common drivers for the selection and proliferation of malignant CLL clone.

At the same time it was revealed increased number of mutated BCRs with signs of positive antigenic selection ($\Sigma = 0.5452 \pm 0.187$) among IR-exposed CLL patients. Such BCRs reflect immune response on viral and bacterial antigens. There were no signs of antigenic selection in IR non-exposed CLL patients ($\Sigma = -0.0867 \pm 0.144$; $p = 0.013$). Thus, the differences in the *IGHV* gene usage and BCR structure indirectly indicated a change in the spectrum of antigens associated with CLL under IR exposure and are in agree with revealed immune dysfunction and increased frequency of persistent infections in irradiated persons.

2.2.2.4. The impact of BCR/ABL1-independent genetic deviation in the resistance formation to therapy with tyrosine kinase inhibitors in CML patients who were exposed to ionizing radiation following of the Chornobyl accident

Results obtained in the last 5 years

Hematopoietic cells are considered critical populations for the action of ionizing radiation, so the study of diseases of the hematopoietic system in individuals exposed to ionizing radiation is of particular interest. Data from a joint international study between the National Cancer Institute (USA) and the National Research Center for Radiation Medicine (Ukraine) showed that exposure of low-dose accident the participants suffered the Chornobyl accident is associated with a significant risk of lymphoid and non-lymphoid leukemia origin [14, 46, 47]. In addition, a number of studies have shown violations of immunogenetic parameters in the development of oncohematological diseases in individuals of this cohort and their impact on the clinical course, effectiveness of therapy and life expectancy [48].

Numerous epidemiological studies have shown an increase in dose-dependent cases of thyroid tumors due to irradiation with radioactive iodine after the Chornobyl accident with a high risk of development at a young age. The increase in morbidity and mortality from other malignant neoplasms has also been proven [49]. Despite a clear link between radiation exposure and the risk of developing tumors [50], there is currently insufficient information on molecular genetic disorders in radiation-associated leukemias.

In our previous studies, it was shown that patients exposed to ionizing radiation as a result of the Chornobyl accident did not differ in the manifestations of chronic myeloid leukemia (CML), as well as classical genetic markers in the onset of the disease compared with patients without radiation history. However, reduction of the tumor clone on tyrosine kinase inhibitor (TKI) therapy was significantly less effective in patients exposed to ionizing radiation than in patients without a history of radiation. In the group of participants in the liquidation of the Chornobyl accident, cases of primary resistance were statistically significant, and in the group of residents there was a statistically significant increase in the probability of loss of complete cytogenetic response (development of secondary resistance) to TKI therapy [51].

Decreased efficacy of tumor clone reduction on imatinib therapy in CML patients exposed to Chornobyl accident suggested the involvement of BCR/ABL1-independent mechanisms of leukemogenesis, where the initiating event may be ionizing radiation. Recent studies have shown that about one-third of patients with spontaneous CML carry not only the specific chimeric *BCR/ABL1* gene, but also mutations in other genes associated with the development of leukemia. In some cases, it has been shown that these additional molecular disorders occurred before the advent of BCR/ABL1 [52].

The study involved 22 patients exposed to ionizing radiation as a result of the Chornobyl accident. 10 patients were participants in the liquidation of the consequences of the Chornobyl accident in 1986–1988 (group 1). Group 2 consisted of 2 patients who were evacuated in 1986 and 10 residents of the enhanced radioecological control zone. The effective radiation dose in liquidators was 20–500 mSv. The calculated effective radiation dose of residents contaminated territories (due to ^{137}Cs, ^{90}Sr and $^{239-240}$Pu) was 0.5–5 mSv/year, the calculated average accumulated radiation dose «for 30 years» varied from 4.1 to 31 mSv [53].

To study the prevalence and spectrum of BCR/ABL1-independent mutations in patients with CML who were exposed to ionizing radiation as a result of the Chornobyl accident, 53 genes were sequenced by next-generation sequencing (MiniSeq) Illumina, USA) what was involved in the pathogenesis of myeloproliferative diseases. Mutations in these genes before imatinib were studied in all patients. Repeated molecular genetic testing was performed in 3–98 months in 5 patients (2 liquidators and 3 residents of contaminated territories) who were resistant to imatinib therapy. (Me = 90 months) therapy. To confirm the somatic origin of mutations in 5 patients performed a molecular genetic study of buccal epithelial cells. The comparison group consisted of 20 patients without a history of radiation who were diagnosed with CML at a hospital in the University of Jena (Germany).

As a result of target sequencing by the NGS method, mutations in the studied genes were detected in 15 of 22 (68.2 %) CML patients who were exposed to radiation as a result of the Chornobyl accident. Of these, more than one mutation was detected in 9 patients. A total of 51 mutations were detected. The most common mutations in the genes of transcription factors BCOR (6/22 patients) and BCORL1 (4/22 patients), mutations in the genes of epigenetic regulators ASXL1 (4/22 patients) and DNMT3A (4/22 patients), as well as in the gene of the cohesive complex STAG2 (4/22 patients). It is interesting to note that there was a trend to increase the frequency of mutations in liquidators (group 1) compared with the group of residents contaminated territories (group 2) (80 % vs. 54.5 %). However, the difference was not confirmed statistically ($p = 0.361$). In 4 of 5 patients, multiple mutations were detected with imatinib therapy, which Kim et al. [54], can play a key role in the development of resistance to TKI. Different patterns of mutant clones development on imatinib therapy were identified. Patient № 325 showed an increase in mutant DNMT3A clones (p.R320Q) and STAG2 (p.P442S, p.S1047F) on therapy, and new additional mutant ASXL1 clones (p.L1421I) appeared; BCOR (p.P1621R); BCORL1 (p.R1355W); JAK2 (p.L526TfsX7); KDM6A (p.P954LfsX16). Such selection of mutant clones under the pressure of TKI therapy was associated with the development of resistance and disease progression if therapy was not changed. In patient № 748, a mutation in the IKZF1 gene of A388E was detected at diagnosis, and a mutation in the CALR gene in D394H was detected after loss of CCR achieved with imatinib therapy. Probably, after suppression or irradiation of the first clone over time there was a selection of a low-level clone CALR p.D394H or mutation de novo.

Mutations detected in blood cells were not detected in buccal epithelial cells. The exception was one patient in whom a mutation in the *ASXL1* gene (p.A627GfsX8) was detected in both substrates. On the one hand, this fact may indicate that the patient has a constitutive mutation in the *ASXL1* gene that is not related to the action of radiation. A constitutive mutation in the ASXL1 gene may increase the susceptibility to leukemia and act as a driver of leukemogenesis synergistically with ionizing radiation. On the other hand, the possibility of a false-positive result of the analysis of buccal epithelial cells due to the patient's leukocytes in the biomaterial sample is not completely ruled out.

Somatic BCR/ABL1-independent mutations were detected in the vast majority (68.2 %) of patients exposed to ionizing radiation as a result of the Chornobyl accident. This was more reminiscent of the MDS or MPN phenotype and contrasted sharply with the results of a group of patients without a history of radiation, where only 4 mutations were detected in 20 patients (20.0 %) ($p = 0.004$). In the comparison group, a mutation in the CUX1 gene (p.S1134C) was detected in one patient (№ 12) and mutations in the RUNX1 gene in patients № 6, № 9 and № 10 (p.R346AfsX248; p.R107C and p.R76PfsX62, respectively). An additional mutation of the WT1 gene (p.R380QfsX5) was also identified in patient № 10. The results are consistent with other studies of BCR/ABL1-independent mutations in patients with «spontaneous» CML.

In most patients with somatic BCR/ABL1-independent mutations (10 of 12 patients), reduction of the tumor clone to a high molecular response level was not achieved throughout the follow-up period. Of these, only CCR was achieved in 4 patients. Response analysis according to ELNet 2013 criteria after 12 months of imatinib therapy revealed a trend in patients with somatic BCR/ABL1-independent mutations to increase the incidence of primary resistance (absence of CCR or BCR/ABL1 > 1 %) compared to patients without such mutations (66.7 % vs. 40.0 %, respectively). However, the statistical significance of the differences was not confirmed ($p = 0.291$). The probability of developing primary resistance increased in patients with higher mutant load and was 50.0 % in patients with one mutation, 71.4 % in patients with two or more mutations and 40.0 % in patients without somatic BCR / ABL1-independent mutations. Over the entire follow-up period, the number of patients who developed secondary resistance to TKI therapy in the form of loss of achieved CCR was also slightly higher among patients with somatic BCR/ABL1-independent mutations (50.0 % vs. 33.3 %, respectively). Progression to the acceleration phase was recorded only in the group of patients with somatic BCR/ABL1-independent mutations (2 of 12 patients). However, progression was observed only in patients with more than one somatic BCR/ABL1-independent mutation (2 of 8 patients).

The results suggest that the presence of radiation exposure in the anamnesis, even many years before the onset of CML, is an unfavorable exogenous factor that causes the development of resistance to TKI therapy. It can be assumed that ionizing radiation directly or indirectly led to mutations, including in genes associated with the development of myeloid leukemias. That is, in patients exposed to ionizing radiation, the chimeric BCR/ABL1 gene was usually not the only, and perhaps not the first, genetic disorder. The accumulation of mutations led to a more complex phenotype, which was reflected in a more aggressive course of the disease and the development of resistance to TKI therapy.

2.2.2.5. Molecular genetic features of Ph-negative myeloproliferative neoplasms in patients exposed to ionizing radiation due to Chornobyl nuclear accident

The study of the molecular genetic features of chronic Ph-negative myeloproliferative neoplasms (MPN) – polycytemia Vera, Essential Thrombocythemia and Primary Myelofibrosis demonstrated the lower rate of *JAK2* V617F and higher rate of *CALR* 1-like type mutation were among patients exposed to ionizing radiation (IR) due to the Chornobyl nuclear accident in comparison to unexposed MPN patients [55, 56]. It was found more cases negative for the usual mutations of the driver genes (*JAK2*, *MPL* and *CALR*) in the group of IR-exposed MPN patients. Additional sequence variants and genomic alterations were examined in IR-exposed and unexposed MPN by whole exome and targeted sequencing, and high-density oligo-SNP microarray platform. A wide spectrum of genomic alterations was identified in IR-exposed and unexposed MPN patients, positive for one of usual mutations of driver genes or negative for them. IR-exposed and unexposed MPN patients did not differ regarding frequencies of genomic imbalances types. Significant number of variants were detected in genes which were common for IR-exposed and unexposed MPN patients, however several alterations were identified exclusively to IR-exposed MPN patients negative for usual mutations of *JAK2*, *MPL* and *CALR* driver genes. Among these variants, *EZH2* D659G at 7q36.1 and *SUZ12* V71M at 17q11.2 with copy number losses and *ATM* S1691R at 11q22.3 with copy-neutral loss of heterozygosity that might be involved in MPN development. There were identified sequence variants which might predispose the MPN development and be related to the IR exposure. Obtained data indicate the contribution of impaired DNA transcription and epigenetic regulation to MPN development in IR-exposed subset of patients in addition to the canonical pathway. Mutations in the *DTA* gene group were detected much more often in patients with radiation history with radiation history than in patients with spontaneous disease, which indicates the peculiarities of radiation pathogenesis and possibly more frequent progression of clonal hematopoiesis of unknown potential. Mutations in the *DTA* genes were not recorded in any of the cases of spontaneous triple-negative MPNs, whereas the group of radiation-associated triple-negative MPNs was characterized by the presence of mutations *DNMT3A*, *TET2*, and *ASXL1* with high incidence and significantly higher frequency.

2.3. Thyroid cancer

Among various sites of radiation associated malignant tumors special attention is drawn to thyroid cancer. Thyroid cancer incidence reflects consequences of thyroid gland irradiation with radioactive iodine. The greatest realization of stochastic effects in this organ was noted in clean-up workers participated in recovery works in 1986–1987: in 1990–2013 SIR = 451.1 %, 95 % CI: 405.1–497.1; in 2014–2018 – SIR = 404.0 %, 95 % CI: 302.0–505.4. Quite similar are rates in evacuees – in 1990–2013 SIR = 381.3 %, 95 % CI: 336.0–426.2, in 2014–2018 – SIR = 447.8 %, 95 % CI: 352.0–543.5. The lowest level of thyroid cancer incidence was observed in residents of the small territories most highly contaminated with radionuclides – SIR = 131.3 %, 95 % CI: 119.8–142.9. This situation may be explained by the factor of migration from these territories of the population groups of highest risk of this pathology (young families with children).

The fact that thyroid cancer incidence rates are among the highest ones in Kyiv city and Kyiv Oblast (i.e., where major part of evacuees and migrants are living now) is an indirect evidence of the phenomenon mentioned in the previous paragraph. Besides it should be noted that 32 years after the accident age groups born after 1986 consist significant part of the population. In 2018 individuals aged up to 25 consisted 37.4 % of whole population of these territories. Naturally they were not subjected to thyroid exposure. That is why the risk of thyroid cancer in this age group does not differ from pre-accident level.

Table 2.7
Thyroid cancer incidence rate (ICD10 C73) of the most affected population groups of Ukraine due to the Chornobyl accident (standardized incidence ratios – SIR, %)

Group of affected population and follow-up period	Actual number of cases	Expected number of cases	SIR, %	95 % confidence interval
Residents of contaminated territories (1990–2013)	409	306.5	133.4	120.5–146.5
Residents of contaminated territories (2014–2018)	87	71.2	122.2	96.5–147.9
Clean-up workers 1986–1987 (1994–2013)	369	81.8	451.1	405.1–497.1
Clean-up workers 1986–1987 (2014–2018)	61	15.1	404.0	302.0–505.4
Evacuees from exclusion zone (1990–2013)	278	72.9	381.3	336.5–426.2
Evacuees from exclusion zone (2014–2018)	84	18.8	447.8	352.0–543.5

2.3.1. Thyroid cancer in Chornobyl accident clean-up workers

Although much is known about the radiation risk of thyroid cancer in those exposed to ionizing radiation in childhood [57, 58], negative or contradictory risk assessment results have been obtained for those irradiated in adulthood, including clean-up workers at the Chornobyl Nuclear Power Plant [59, 60].

Clean-up workers (liquidators) were exposed to both external and internal exposure to ionizing radiation in a wide range of doses. Those involved in emergency work during the first 10 days after the accident, in addition to the external radiation dose, could also receive thyroid radiation doses from inhalation of air contaminated with iodine ^{131}I and short-lived isotopes of iodine and tellurium due to long-term emissions from the destroyed reactor. They could also receive thyroid dose from food contaminated with ^{131}I while living in contaminated settlements for some time during two months after the accident [61].

The results of epidemiological studies, based on data from the National Cancer Registry and the State Registry of Victims of the Chornobyl Accident, found an increase in the incidence of thyroid cancer (in terms of the SIR) in the cohort of male liquidators (150,813 people) compared to the national level. Individual doses were not determined [62, 63]. These studies analyzed, respectively, 196 cases of thyroid cancer in Chornobyl clean-up workers that occurred during 1986–2010 with a total SIR of 3.50 (95 % CI: 3.04–4.03) [62] and 216 cases of thyroid cancer (1986–2012) with a total incidence rate – SIR 3.35 (95 % CI: 2.51–3.80) [63]. Prysyazhnyuk et al. [63] also conducted a preliminary assessment of the risk of thyroid cancer using average radiation doses. Excessive relative risk (ERR/Gy) involving alternative approaches to estimating average radiation doses, according to the authors, may be 2.38 (95 % CI: 0.60–4.15) and 2.66 (95 % CI: 0,68–4.64); as well as the attributive risk of AR/Gy – 70.4 % and 72.7 % [63]. SIR values were increased throughout the observation period, with peak values 10–18 years after the disaster (1995–2004).

To determine the radiation risk of thyroid cancer under the influence of external and internal radiation in adulthood, the National Research Center for Radiation Medicine together with the US National Cancer Institute conducted a large-scale analytical epidemiological study among Ukrainian liquidators [6, 63–65]. This study at clean-up workers at the Chornobyl NPP was based on the largest number of thyroid cancer cases with restored individual doses of this organ. The dose of external irradiation, the dose of internal irradiation of the thyroid gland from inhalation and food were determined. Each dose component was calculated using methods specifically developed by an international team of experts to study the consequences of the Chornobyl disaster [61].

In total, 149 cases of thyroid cancer were identified using the data of the National Cancer Registry and included to the analysis. 458 matched controls were selected individually for each case in the study cohort.

Individual doses of thyroid irradiation due to the action of ^{131}I due to external exposure, inhalation during work and food consumption during living in radioactively contaminated settlements were calculated for all subjects [61]. The total dose averaged 199 mGy with a range of values from 0.15 mGy to 9 Gy. The first findings of the analytical study indicate an increased risk of thyroid cancer among clean-up workers at the Chornobyl Nuclear Power Plant, although with borderline significance. The value of risk significantly depends on the morphological type of the tumour and the time of its occurrence, so that less time after irradiation and follicular tumour type are associated with a higher value of ERR/Gy [65].

The main results of this study, assessing the risks of certain forms of thyroid cancer and probably taking into account the uncertainties and limitations of the statistical model, will be published by an international team of researchers in the near future.

2.3.2. Thyroid cancer in population exposed in childhood or in utero

Although the relationship between Chornobyl radiation exposure and strong increasing of thyroid cancer incidence among irradiated children and adolescents in Belarus, Ukraine and some regions of the Russian Federation has been established in previous studies [66–68], observations and analysis of time trends of thyroid cancer among the irradiated population remains one of the priority tasks of investigation of the long-term health consequences of the Chornobyl accident [69, 70]. The main purpose of this chapter is a providing of descriptive analysis of data on the incidence of thyroid cancer in 1986–2019 in younger groups of the Ukrainian population who were exposed to radiation at early ages or born after the Chornobyl accident.

The population cancer registries [70, 71] are appropriate tools to collect information for further analysis of incidence and mortality for fixed gender and age groups and geographical regions. In Ukraine, since 1992 is established a site-specific clinical and morphological registry of thyroid cancer (CMR, State Institution «Institute of Endocrinology and Metabolism (IEM) VP Komisarenko of the National Academy of Medical Sciences (NAMS) of Ukraine») [72]. Since 1996, the National Cancer Registry of Ukraine, which accounts for all records of cancer cases of any localizations (NCRU, National Cancer Institute of the Ministry of Health of Ukraine) has started collecting data [73]. An important role is also played by the clinical registry of the State Institution «Institute of Endocrinology and Metabolism. VP Komisarenko of the National Academy of Medical Sciences of Ukraine» on the basis of the medical information system «TerDep» [74].

Current analysis of thyroid cancer incidence among younger age groups of the Ukrainian population represents methodologically a continuation of a series of previous publications [75–80]. The study subjects are divided into the following three groups by age at the time of accident and conditions of exposure:

➢ subjects exposed as children, aged 0–14 years at the time of accident (0–14 AE);

➢ subjects exposed as adolescents, aged 15–18 years at the time of accident (15–18 AE);

➢ subjects exposed prenatally (in utero), born in May–December 1986 (EIU).

The first group (0–14 AE) is the largest and includes about 11.2 million subjects; the second group (15–18 AE) is estimated at 2.2 million persons, and the size of the cohort exposed prenatally is estimated at about 0.52 million. The subjects born after the Chornobyl accident (in 1987 or later) were not irradiated by the Chornobyl exposure, and are also considered here as the population with sporadic thyroid cancer cases (not radiogenic) which can be considered as a special control group.

For the analysis by age at diagnosis, cases are subdivided into those diagnosed in children (aged 0–14 years at diagnosis), adolescents (aged 15–18 years at diagnosis), and adults (aged 19 years or more at diagnosis).

According to the level of average regional thyroid doses of children and adolescents, 27 oblasts of Ukraine was divided into two groups [81, 82]:

➢ 6 most contaminated north regions (Zhytomyr, Kyiv, Rivne, Chernihiv, Cherkasy Oblasts and Kyiv City; oblast average thyroid dose in the population of 0–18 years at the time of the accident was in a range 55–87 mGy);

➢ 21 oblasts with relatively lower levels of contamination (oblast average thyroid dose in in the population of 0–18 years estimated as 3–35 mGy).

The children and adolescents in the 6 most contaminated oblast accounted for 19–21 % of the total population of Ukraine of the corresponding age (Tables 2.8 and 2.9). It should be indicated that Zhytomyr, Kyiv, and Chernihiv Oblasts are located up to 200 km from the Chornobyl NPP, and residents of the northern districts of these oblasts received the highest thyroid radiation doses [81, 82]. In several districts of Zhytomyr and Kyiv Oblasts, the district average thyroid doses for children and adolescents exceeded 650 mGy [57].

The study period is 1986–2019, but the time trends in 2014–2019 do not include data for Donetsk, Luhansk Oblasts, the Republic of Crimea, and the city of Sevastopil. In the analysis of time trends, two-year intervals are used, and the whole observation period is divided into seven intervals: 1986–1989 – the minimum latent period [58], when only sporadic thyroid cancer cases were diagnosed and six subsequent intervals (1990–1994, 1995–1999, 2000–2004, 2005–

2009, 2010–2014, 2015–2019), when both sporadic and radiogenic thyroid carcinomas are presented among the detected cases of thyroid cancer.

Tables 2.8 and 2.9 present aggregated data on thyroid cancer cases in selected population groups, and indicate the population in groups of 6 and 21 oblasts. Table 2.8 shows the dynamics of cases over seven observation calendar periods. Table 2.9 shows the distribution of cases by age at the time of diagnosis, showing the number of thyroid cancer diagnosed in children, adolescents, and adults.

In total, the current analysis includes 16,314 cases among the irradiated population, including 12,502 cases among those exposed in childhood, 3,431 cases among exposed as adolescents, and 381 cases among persons exposed prenatally («in utero»). Among the population born since 1987, which was not exposed as a result of the Chornobyl accident, 2,920 cases of thyroid cancer have been diagnosed.

It is important to note that among the patients exposed in childhood and adolescence, more than 36 % were operated on or received radioiodine therapy and postoperative follow-up in IEM. Among patients born in 1987 and later, the corresponding indicator exceeds 42 %.

Thyroid cancer incidence trends among a population exposed as children are shown in Fig. 2.3. During the study period (1986–2019) in this group, the age varied from 0 to 14 years old in 1986 to 33–47 years old in 2019. The population size of this group was estimated as 11.1 million persons at the beginning of 1987. This group showed the

Table 2.8

Thyroid cancer cases in selected groups of Ukrainian population in 1986–2019 (by periods of diagnosis)

Groups	Groups,* mln	1986–1989	1990–1994	1995–1999	2000–2004	2005–2009	2010–2014	2015–2019	1986–2019
0–14 years at exposure	11.1	60	386	830	1 237	2 050	3 438	4 501	**12 502**
6 oblasts	2.2	15	190	382	580	823	1 326	1 822	**5 138**
21 oblasts	8.9	44	196	448	657	1 227	2 512	2 679	**7 364**
15–18 years at exposure	2.2	45	162	294	413	600	892	1 025	**3 431**
6 oblasts	0.4	9	41	91	157	226	301	374	**1 199**
21 oblasts	1.8	36	121	203	256	374	591	651	**2 232**
Subjects exposed in utero	0.5	0	4	5	27	57	113	175	**381**
6 oblasts	0.1	0	1	2	10	25	29	75	**142**
21 oblasts	0.4	0	3	3	17	32	84	100	**239**
Subjects born in 1987 and later	15.1**	0	0	13	103	289	867	1 648	**2 920**
6 oblasts	3.4**	0	0	3	31	92	302	629	**1 057**
21 oblasts	11.7**	0	0	10	72	197	565	1 019	**1 863**
Total cases		**105**	**552**	**1 142**	**1 780**	**2 996**	**5 310**	**7 349**	**19 234**

Notes. *Exposed population on January 1, 1987; **estimation of unexposed population on January 1, 2019.

Table 2.9

Thyroid cancer cases in selected groups of Ukrainian population in 1986–2019 (by age at surgery)

Groups	Population,* mln	0–14 years age at surgery	15–18 years age at surgery	19+ years age at surgery	Total
0–14 years at exposure	11.1	454	502	11 546	**12 502**
6 oblasts	2.2	276	246	4 616	**5 138**
21 oblasts	8.9	178	256	6 930	**7 364**
15–18 years at exposure	2.2	–	31	3 400	**3 431**
6 oblasts	0.4	–	5	1 194	**1 199**
21 oblasts	1.8	–	26	2 206	**2 232**
Subjects exposed in utero	0.5	13	27	341	**381**
6 oblasts	0.1	5	11	126	**142**
21 oblasts	0.4	8	16	215	**239**
Subjects born in 1987 and later	15.1**	341	511	2 068	**2 920**
6 oblasts	3.4**	120	191	746	**1 057**
21 oblasts	11.7**	221	320	1 322	**1 863**
Total cases		**808**	**1 071**	**17 355**	**19 234**

Notes. *Exposed population on January 1, 1987; **estimation of unexposed population on January 1, 2019.

maximal number of cases (12,502) with about 41% of these (5,138 cases) registered in the 6 most contaminated oblasts. A significant increase in the incidence was observed in the first post-latent period (1990–1994) and continued until the end of the study (2019). The rising trends are common to all four groups represented in Fig. 2.3 (males in six oblasts, females in six oblasts, males in 21 oblasts, females in 21 oblasts), although the growth rate and incidences are different for each group. For the low dose oblasts, the increasing incidence is largely determined by the attained age; in the highdose oblasts, there is an additional contribution of radiogenic component as well as the factor of screening intensity. The maximal incidence is expectedly observed in females from 6 contaminated areas (about 28 cases per 100,000 person-years). Incidence rates in the most contaminated areas are significantly higher than those in low-contaminated regions, although their ratio tends to be lower.

Incidence rates in individuals exposed as adolescents are presented in Fig. 2.4. The population size of this group is estimated at 2.2 million. In 2019, the age of this group reached 48–52 years old. The cumulative number of cases is 3,431, of which 1,199 (35 %) were diagnosed in 6 oblasts with maximal thyroid doses. The main trends of incidence for males and females, in general, are similar to those exposed during childhood. The incidence in females from the 6 most contaminated oblasts reached 26 cases per 100,000 person-years at the end of the observation period.

Importantly, the interpretation of the number of cases and incidence in the groups defined by age at diagnosis (at surgery) should take into account that the composition of such groups changes from year to year as the cohorts become older. Both the size of the population and the proportion of exposed and unexposed subjects in the group are changing.

Figure 2.5 shows the incidence trends for the childhood population (0–14 years at the time of surgery). The incidence in this group was approximately 0.1 cases per 100,000 children in the latent period (1986–1989), and then showed a sharp increase in the early post-latent period (1990–1992). After 1998, the increased incidence of women and men from 6 oblasts began to decline with the transition of the population, the most exposed group (0–4 years at the time of the accident), to older age groups. Since 2001, this age group does not include irradiated persons (including prenatally irradiated persons). In the following

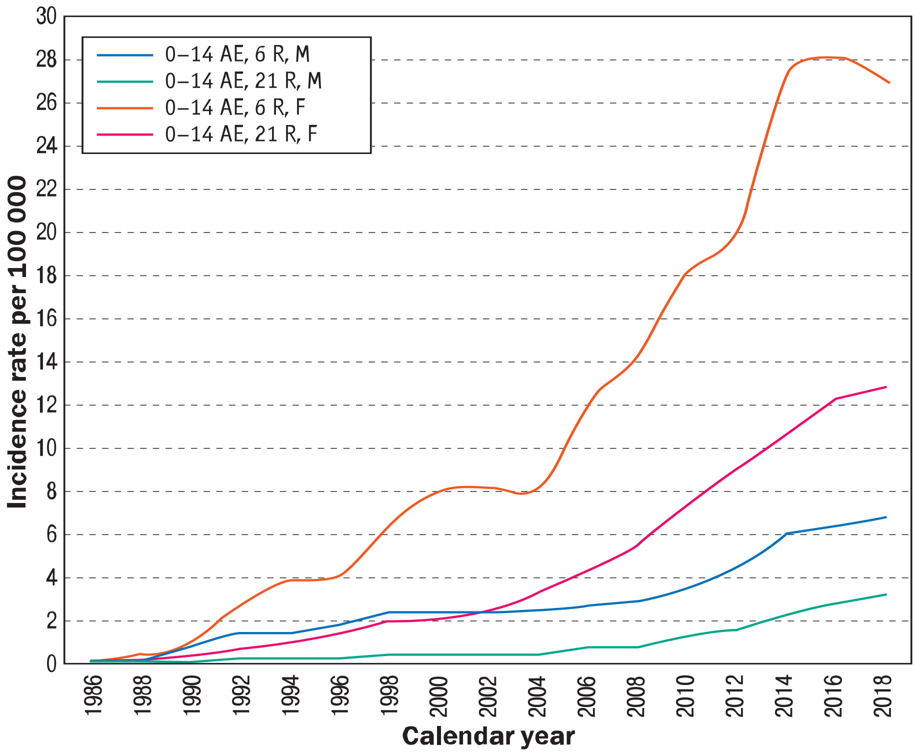

Figure 2.3. Time trends of thyroid cancer incidence in 6 and 21 oblasts of Ukraine for cohort aged 0–14 years at exposure

AE – age at exposure; 6R – 6 northern oblasts; 21R – other 21 oblasts; F – female; M – male

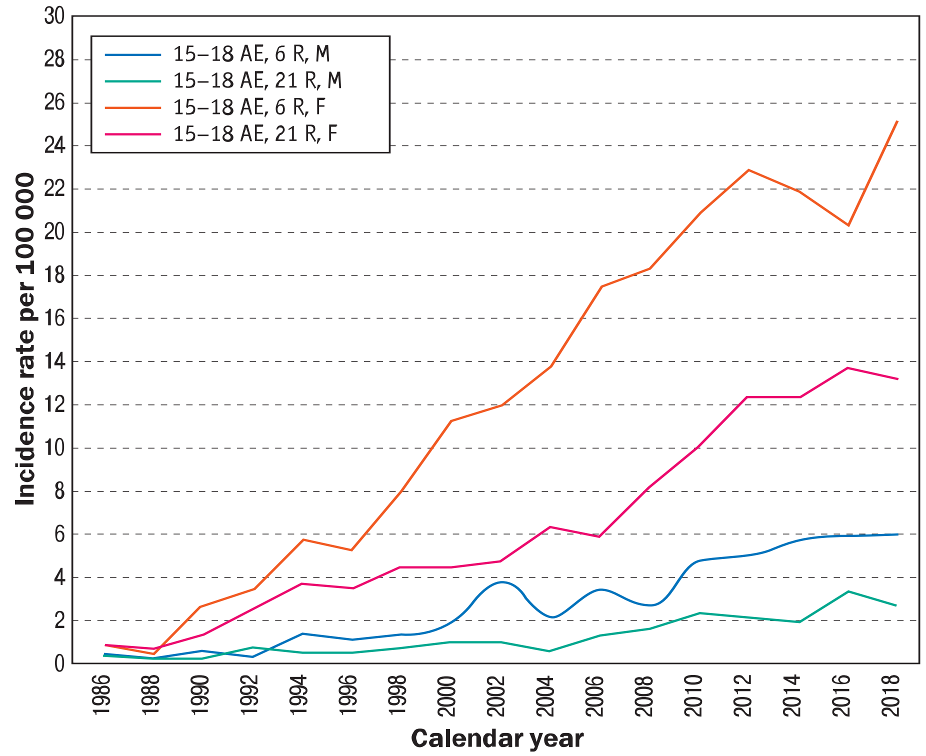

Figure 2.4. **Time trends of thyroid cancer incidence in 6 and 21 oblasts of Ukraine for cohort aged 15–18 years at exposure**

AE – age at exposure; 6R – 6 northern oblasts; 21R – other 21 oblasts; F –female; M – male

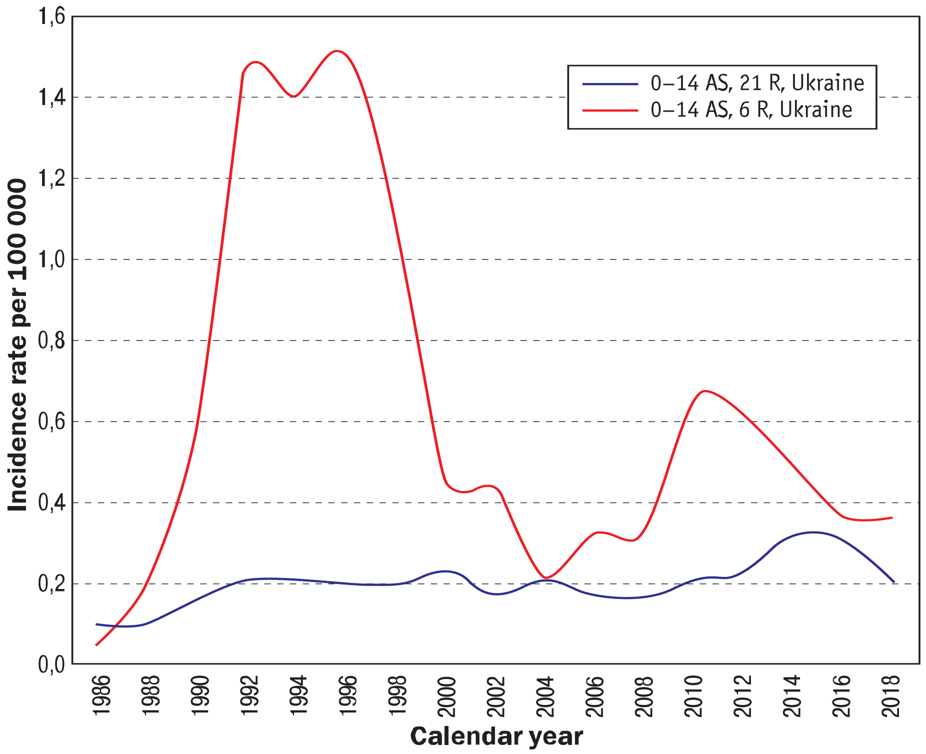

Figure 2.5. **Time trends of thyroid cancer incidence in 6 and 21 oblasts of Ukraine for cohort aged 0–14 years at surgery**

AS – age at surgery; 6R – 6 northern oblasts; 21R – other 21 oblasts; F –female; M – male

years, the incidence of the population of 6 contaminated oblasts is slightly higher than in less contaminated oblasts, which may be explained not only by the presence of the radiation component but also indicate increased screening in the northern oblasts.

In the age group of 15—18 years at the time of diagnosis, the increase in the incidence of thyroid cancer in 6 oblasts with high thyroid doses was smoother than in the group of children. The incidence reached its maximum for women and men in 1998—2002. The irradiated population has not been represented in this group since 2006, after which the incidence in 6 and 21 oblasts showed close values for both men and women.

Among the adult population aged 19 years and older at the time of surgery, the incidence trends differed markedly from the younger groups (Fig. 2.6). This group has no upper age limit, its size, average age, and age structure changes each year. The incidence in each of the four population groups shows a growing trend. Maximum incidence rates are observed in women from 6 contaminated oblasts, followed by incidence rates for women from 21 oblasts, followed by men from 6 oblasts, and minimum incidence in men from 21 oblasts. It should be noted that in the cohort of «adults», irradiated and non-irradiated persons have been «mixed» since 2006.

Analysis of histological features of post-Chornobyl thyroid carcinomas [83—85] shows the dominance of papillary carcinomas among all types of thyroid carcinomas. The papillary carcinomas present more than 90 % for all age-, gender groups during all observed time intervals. Exactly papillary thyroid carcinomas are usually interpreted as radiation-induced tumors [58, 86].

Age and gender dependence of incidence rates is important for the interpretation of observed incidence time trends and prognosis of future indicators. Age and gender-specific incidence rates of thyroid cancer for the general population of Ukraine in 2006, 2010, and 2012 are pointed out in Fig. 2.7. In general, the dependence of incidence on age remains fairly stable during the observation period. The incidence of thyroid cancer for both genders shows minimal values in early childhood (0—9 years), rapid growth between the ages of 10 and 50—55 years with different speed and amplitude for men and women. The maximum incidence reaches at the age of 55—65 years. In age groups older than 70 years there is a decrease of thyroid cancer incidence.

Time trends of age-standardized incidence rate (Ukrainian standard) of thyroid cancer whole population of Ukraine (Fig. 2.8) show a monotonous increase. During the observation period (1999—2019), the incidence rate doubled for females and for males. At the end of the observation period, the incidence of thyroid cancer in

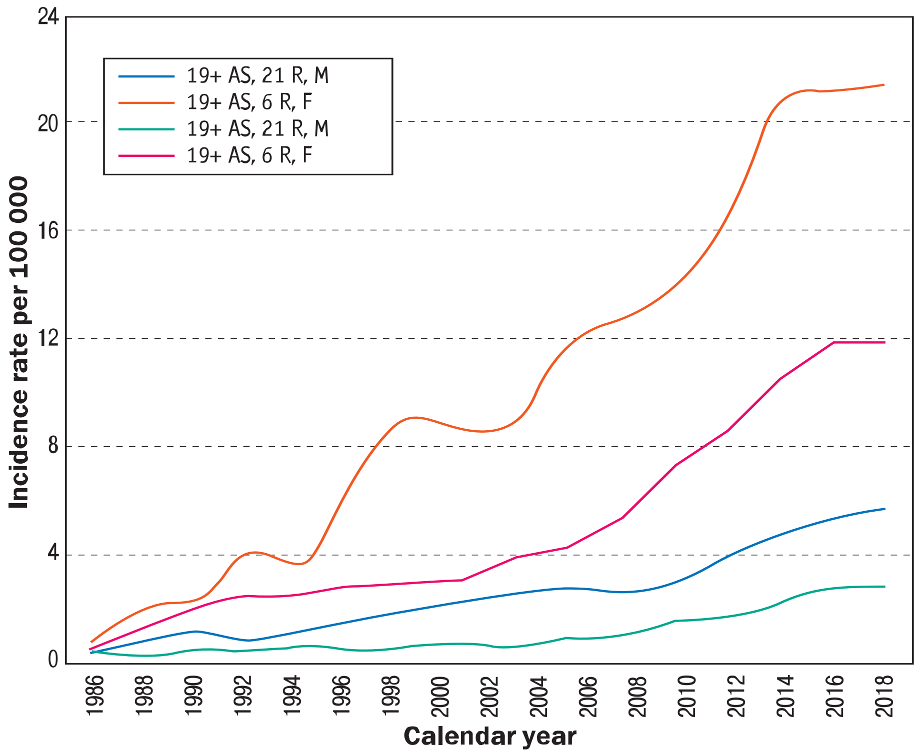

Figure 2.6. **Time trends of thyroid cancer incidence among adults aged 19–46 years at surgery**
AS – age at surgery; 6R – 6 northern oblasts of Ukraine; 21R – rest 21 oblasts of Ukraine; F – female; M – male

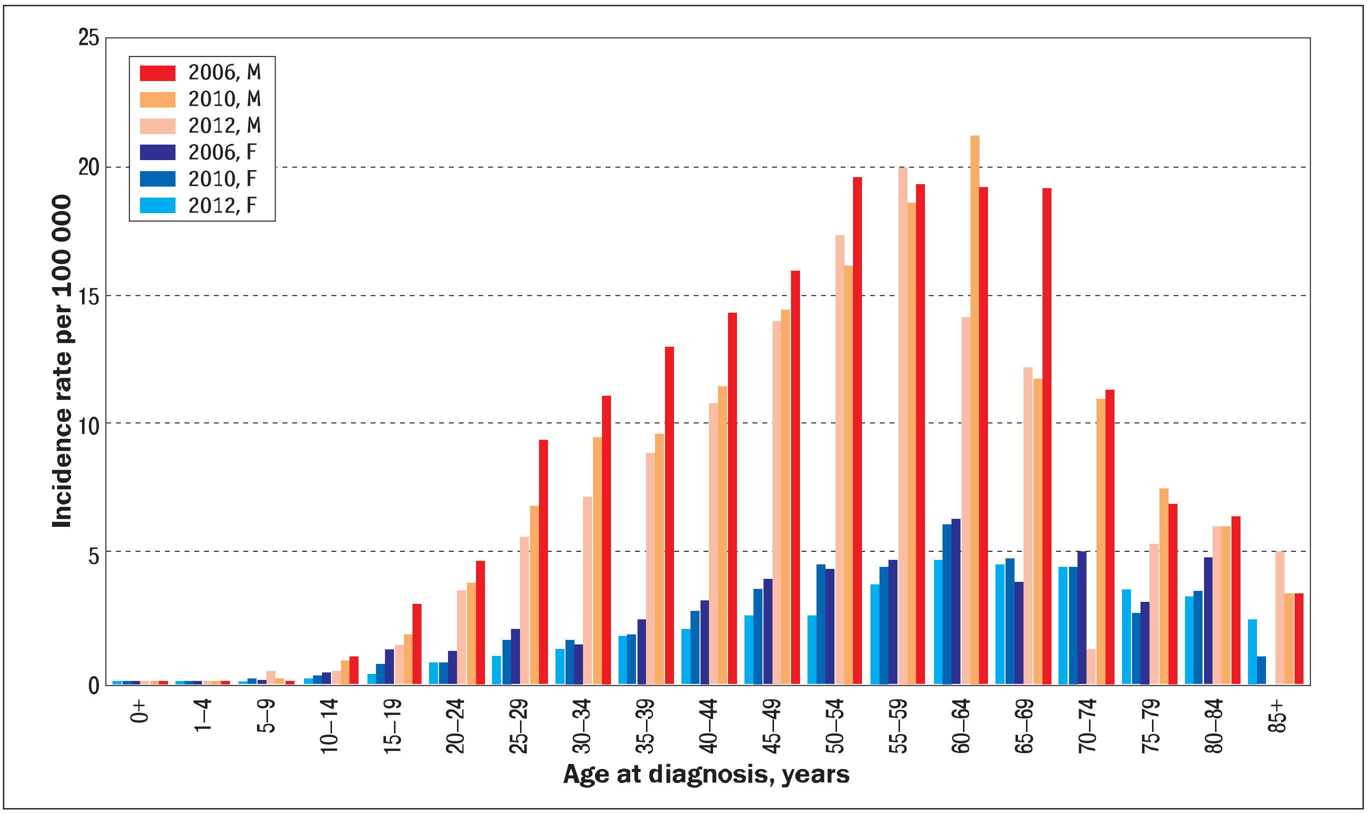

Figure 2.7. **Age and gender specific incidence rates of thyroid cancer in general population of Ukraine in 2006, 2010 and 2012 according to NCRU data [73]**
F – female; M – male

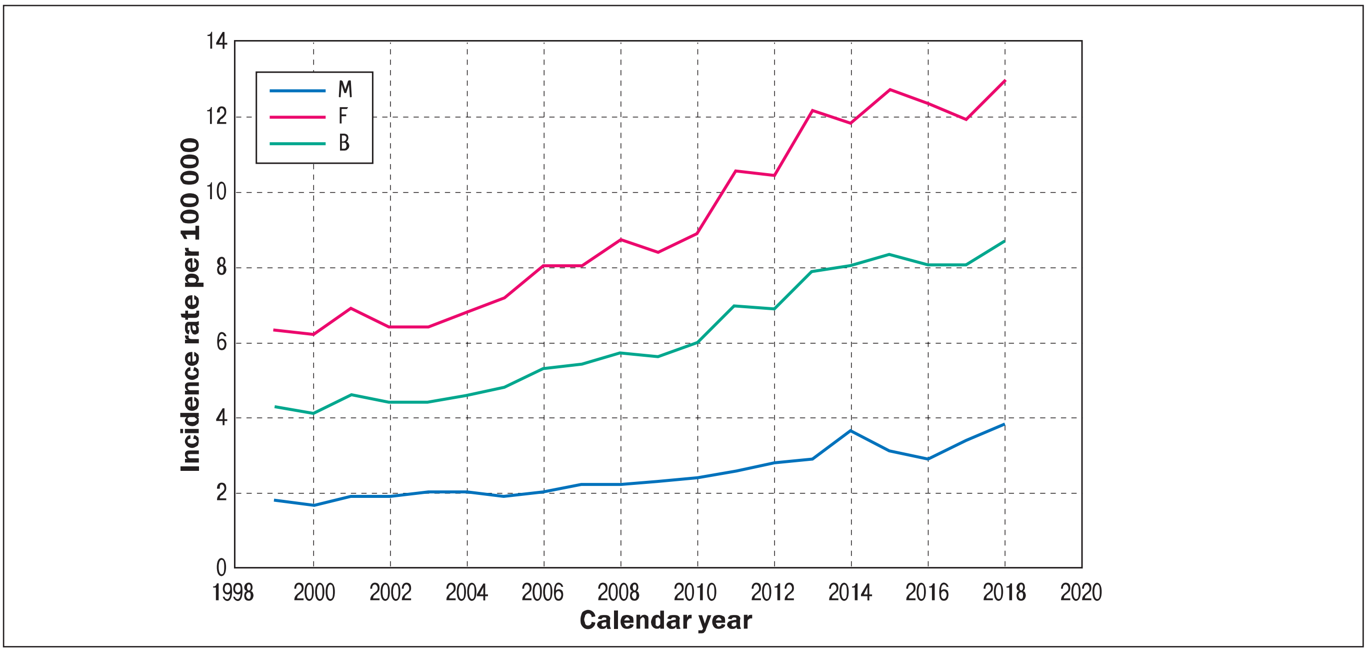

Figure 2.8. **Time trends of age-standardized incidence rate (Ukrainian standard) of thyroid cancer according to NCRU data [73]**
F – female; M – male; B – both

Ukraine is slightly outweighing the mid-European indicators, but a factor 1.5–2 lower than that for the countries, which demonstrate the maximum indicators of thyroid cancer incidence (Italy, France, Croatia) [62].

In summary, this chapter demonstrates that among the exposed population of children and adolescents (aged 0–18 years at the time of the accident), there has been a significant increase in thyroid cancer incidence after the minimal period of latency. This tendency persists for the period of 29 years (1990–2019). At the same time, the incidence rate in the 6 most contaminated oblasts exceeded that in 21 low contaminated oblasts for all post-latent study periods.

By age at diagnosis, peak incidences in childhood and adolescent groups were observed in 1995–1997 and 2000–2002, respectively. Since 2002 there are no exposed subjects (including the «in utero» cohort) in the childhood group and since 2006 in the adolescent group. Thus, in these age categories, all childhood and adolescent cases of radiogenic thyroid cancer have been realized. In the corresponding groups of unexposed subjects aged 0–14 and 15–18 years at the time of diagnosis, thyroid cancer incidence is comparable to the average rate in European countries [62].

Incidence of sporadic thyroid cancer markedly increases from the age of 25–30 years old, such trend extended up to the age of 60–65. It may, therefore, be expected that the proportion of radiogenic cancers in Ukraine will decline, even in the regions with relatively high levels of radiation exposure. Thyroid cancer radiation risk studies as for LSS cohort [58, 87], as well as Chornobyl cohorts [88–90], indicate monotonic decreasing of excess relative risk (ERR/Gy) with time since exposure. At the same time, a statistically significant contribution of radiation-induced thyroid cancers developing after acute external irradiation can be observed even 50–60 years after exposure [87]. These facts justify the importance of future monitoring and analysis of the incidence of thyroid cancer in the population groups exposed as a result of the Chornobyl accident.

2.3.3. Dependence of radiogenic thyroid cancer risks on hereditary factors

The incidence of thyroid cancer reflects the effects of post-Chornobyl radiation due to radioactive iodine. Determination of the DNA repair genes *XRCC1 and XPD polymorphism in persons with thyroid cancer*, who were exposed to ionizing radiation, was done to disclosure the mechanisms of the oncological pathology occurrence in persons with impact of ionizing radiation in history, and the introduction of measures to prevent it. In the group of evacuees and residents from areas contaminated with radionuclides the increased level of chromosomal aberrations was registered and the association of *XPD* Lys751Gln and *XRCC1* Arg399Gln genes polymorphisms with an increased level of spontaneous chromosomal aberrations in the culture of peripheral blood lymphocytes was revealed. The frequency of homozygous carriers of minor alleles of *XPD* and *XRCC1* genes in patients with thyroid cancer with a history of radiation exposure was significantly higher than in patients with spontaneous thyroid cancer. The carriage of homozygous minor allele of DNA repair genes *XRCC1* Gln399Gln and *XPD* Gln751Gln is a risk factor for thyroid cancer under the influence of ionizing radiation and may be the basis for forming a group of increased risk of predisposition to develop radiation-associated cancer pathology of the thyroid gland.

2.4. Breast cancer

Previous experience

The female breast is considered one of the most radiosensitive organs. The risk of breast cancer in women exposed to the factors of the Chornobyl accident, especially at a young age, remains a serious public health problem in most affected countries even 30 years or more after the accident.

Excessive radiation-induced cases of breast cancer have been found in women irradiated by the atomic bombing of Hiroshima and Nagasaki [95]. The highest incidence of cancers was in those who received radiation at the age of 10–19 years. The attributive radiation risk of breast cancer, according to observations and calculations performed on the Japanese cohort (LSS[1]), which affected by a nuclear bomb, was 27 %.

Even 35 years after the Chornobyl accident, the connection between the effects of ionizing radiation and the incidence of breast cancer as a result of this event remains uncertain because the study of the incidence of this pathology was conducted mainly in the framework of descriptive epidemiological studies.

A geographical correlation study conducted by an international team examined the potential connection between radiation exposure and breast cancer incidence in Belarus and Ukraine [96]. An analysis

[1]LSS – the Life Span Study, a cohort study of atomic bomb survivors (Japan).

of pooled Belarusian and Ukrainian data for 1999–2001 showed a significantly increased relative risk (RR) of breast cancer in residents of areas with an average cumulative dose of 40 mSv or more. In particular, this risk was observed in a subcohort of women who were younger than 45 at the time of the accident.

Results obtained in the last 5 years

In contrast, the results of a recent study in Ukraine and Belarus [97] covering the period 1986–2016 did not show an increased radiation risk of breast cancer in women under 45 at the time of the accident compared to women over 45. In the study, indicators standardized by time, age and the effect of urbanization, do not indicate an increase in incidence depending on the average cumulative dose per breast.

Thus, the relationship between breast cancer and low doses of ionizing radiation due to the Chornobyl accident has long been unclear, mainly due to the lack of analytical studies that would include the reconstruction of individual doses to breast cancer. It should also be borne in mind that many factors of a non-radiation nature play an important role in the genesis of this pathology.

Among different groups of the population affected by the Chornobyl accident (female clean-up workers, evacuated women from the exclusion zone, residents of the most contaminated areas), only female liquidators of 1986–1987 showed a significant increase in the incidence of breast cancer, which exceeds national indicators 1.5–1.6 times (Table 2.6). Significant excess of this pathology in female clean-up workers 1986–1987 participation, calculated in the indicators of the standardized incidence ratio (SIR) in 1990–2013 was 157.8 %, 95 % CI: 140.9–174.7, in 2014–2018. – 149.0 %, 95 % CI: 111.9–186.1).

The incidence of breast cancer in residents of radioactively contaminated areas and evacuated women did not exceed national rates throughout the observation period. Due to the fact that the latent period of development of radiation-induced breast cancer is quite long, it is necessary to continue monitoring this pathology at the long-term stage of monitoring.

It becomes clear that the factors that played a decisive role in forming the incidence rate before the Chornobyl accident continue to significantly influence the frequency of this pathology throughout the observation period.

There is also a need for more informative analytical studies (cohort, case-control), which will allow to objectively assess the radiation risks of breast cancer at low doses of radiation associated with the Chornobyl accident.

Thus, summarizing the results of the analysis of the incidence of various groups of affected by the Chornobyl accident over more than 30 years of observation using descriptive and analytical epidemiology, we can conclude that among most forms of malignant tumors, thyroid cancer and leukemia have the greatest grounds to be classified as diseases associated with exposure to ionizing radiation caused by the Chornobyl accident.

Because certain types of solid tumors after radiation exposure have different latency periods (10 to 30 years), there is a need for further monitoring of cancer with special attention to such pathologies as cancer of the esophagus, stomach, lungs, colon, breast, ovary, kidney, bladder, multiple myeloma.

Table 2.10

Incidence of breast cancer (ICD-10: C50) of the female population of Ukraine affected by the Chornobyl accident (standardized incidence ratio – SIR, %)

Category of affected and observation period	Actual number of cases	Expected number of cases	SIR, %	95 % confidence interval
Inhabitants of radionuclide-contaminated areas (1990–2013)	1286	2088.8	61.6	58.2–64.9
Inhabitants of radionuclide-contaminated areas (2014–2018)	310	349.5	88.7	78.8–98.6
Participants in the liquidation of the consequences of the Chornobyl accident 1986–1987 (1994–2013)	336	212.9	157.8	140.9–174.7
Participants in the liquidation of the consequences of the Chornobyl accident 1986–1987 (2014–2018)	62	41.6	149.0	111.9–186.1
Evacuated from the exclusion zone (1990–2013)	345	433.4	79.6	71.2–88.0
Evacuated from the exclusion zone (2014–2018)	108	102.5	105.4	85.5–125.3

2.5. Effect of long-term low levels of ionizing radiation on the urogenital organs (kidneys, urinary bladder, prostate, testis)

State Institution «Institute of Urology of the National Academy of Medical Sciences of Ukraine» is the leading scientific center for the study of tumors of the urogenital organs, in which for many years experience has been accumulated in the study of modern methods of clinical and histological diagnosis, improvement of classifications, prevention and treatment of bladder cancer, tumors of the kidney, prostate, as well as the study of features morphogenesis of precancer and a number of background conditions for the development of tumors of the urogenital organs.

After the Chornobyl accident, the prevalence and incidence of kidney cancer, bladder cancer, prostate cancer and testicular cancer in Ukraine are growing significantly every year, as evidenced by comparative epidemiological studies [98].

During the last 35 years, unique molecular genetic studies of clinical surgical and biopsy material of patients living in radio-contaminated regions of Ukraine have been conducted in the laboratory of pathology of the Institute of Urology of the National Academy of Medical Sciences of Ukraine (Head – Academician of the National Academy of Medical Sciences of Ukraine, Corresponding Member of the National Academy of Sciences of Ukraine, Professor, MD Alina M. Romanenko). The researches allowed for the first time to gain completely new insights into the molecular basis of the pathogenesis of kidney, bladder, prostate and testicular diseases, in particular – to describe a previously unknown form of chronic radiation nephropathy, to investigate early molecular changes in conventional renal cell cancer and the urinary bladder cancer in conditions of long-term chronic exposure to low doses of ionizing radiation (IR), as well as for the first time to describe and investigate the pathogenesis of so-called Chornobyl cystitis and the pathogenesis of benign prostatic hyperplasia and male infertility in Ukraine [99].

Effect of long-term low levels of ionizing radiation on renal cell carcinoma and peritumoral renal tissue

During the last 35 years, the Institute of Urology of the National Academy of Medical Sciences of Ukraine has conducted epidemiological, histological, immunohistochemical and molecular genetic studies of various forms of conventional renal cell carcinoma (cRCC), oncocytoma, peritumoral renal tissue in patients living in radio-contaminated regions of Ukraine with different doses of IR. Immunohistochemical and molecular genetic studies of renal cell carcinoma were conducted jointly with the Department of Pathology of the Medical School of the University of Valencia, Spain (Head – Professor Antonio Llombart-Bosh) on the basis of many years of scientific cooperation between SI «Institute of Urology of the National Academy of Medical Sciences of Ukraine» and the Department of Pathology of the Medical School of the University of Valencia, Spain [100–114].

The results of comprehensive histological studies, as well as molecular genetic analysis indicate that patients with cRCC, who live for a long time on radio-contaminated with radionuclides ^{137}Cs due to the Chornobyl accident, areas of Ukraine and Kyiv, there is a set of prognostic unfavorable trends and signs, which allowed us to draw the following conclusions:

1. The obtained data show a high level of expression of p53, p14ARF, p21WAF1/CIP1, Ki-67, mdm2, cyclin D1, cyclin G, ubiquitin genes in the group of Ukrainian patients with cRCC in comparison with similar cRCCs of the Spanish group. Damage to the regulation of the cell cycle of irradiated cells accelerates their promotion processes, increasing the possibility of genetic mutations. In this case, p14ARF primarily responds to continuous stimuli of low doses of ionizing radiation, leading to loss of control over the main points of the cell cycle with subsequent general deregulation of the mitotic cycle, which leads to tumor progression. Thus, our studies have shown that the expression of proteins p53, p14ARF, p21WAF1/CIP1, Ki-67, mdm2, cyclin D1, cyclin G, ubiquitin, in cRCC cells of Ukrainian patients living in radio-contaminated regions, associated with the processes of increasing tumor progression due to constant and long-term exposure to low doses of ionizing radiation.
2. Increased proliferative activity and aggressiveness of tumors, accompanied by hyperexpression of K-ras, C-erbb-2, and PCNA oncoproteins in cRCCs, in combination with the detection of signs

of chronic radiation nephropathy in peritumoral renal tissue correlates with the radiation exposure in patients with cRCC, living in radio-contaminated regions, and confirms the promoter effect of long-term low doses of ionizing radiation IR on the processes of carcinogenesis in the kidney. It should be noted that prognostically unfavorable K-ras and C-erbb-2 positive cases in cRCCs are known to be associated with a high probability of metastasis.

3. A new histological form of nephropathy has been identified as «Radiation sclerosing proliferative atypical nephropathy» (RSPAN), which develops in combination with areas of tubuloepithelial nuclear atypia and cancer in situ in peritumoral renal tissue in patients living in radio-contaminated regions (is confirmed by the «Certificate of state registration of copyright» №4914, 2001).

4. It is proved that constant prolonged oxidative stress induced by long-term action of low doses of IR on cRCCs in patients living in radio-contaminated regions can play an important and leading role in the development of tumor progression due to destruction of intracellular transduction signaling systems accompanied by inactivation passage.

5. Hypermethylation promoter of the p14ARF gene in peritumoral renal tissue is due to the occurrence of regulatory disorders in the G1-S phase of the cell cycle, which contributes to the development of precancerous changes in the kidney and the progression of cRCC.

6. Chronic, but regular and permanent activation of the INK4A/ARF locus on chromosome 9p21, which is a target for oxidative stress, in turn causes activation of the p38MARK signaling cascade and causes damage and loss of cell checkpoint functions with subsequent violation of control over the processes of mitotic cell division, which ultimately leads to its malignant transformation.

7. Molecular promoters and inhibitors of apoptosis are the target of low doses of IR in the long-term and chronic effects of IR in renal cell carcinogenesis.

Thus, the unfavorable trend of increasing the incidence of cRCCs in radio-contaminated regions with changes in the biology of tumors in patients with cRCC revealed convincingly testifies to the ecological pathomorphosis of cRCC in Ukraine after the Chornobyl accident. The results indicate the need for priority use in this category of patients with new generation anticancer target drugs.

Effect of low levels of ionizing radiation on the urinary bladder urothelium

From 1993 to the present, the Institute of Urology of the National Academy of Medical Sciences of Ukraine conducts constant monitoring of patients with chronic cystitis with benign prostatic hyperplasia (BPH), who underwent coded multiple biopsy of the mucosa of the urinary bladder wall – from neck, orifice of both ureters and dome.

The first histological and immunohistochemical studies in1993–1994 were performed at the Institute of Urology of the National Academy of Medical Sciences of Ukraine together with the Department of Pathology (Head Professor Christer Bush) of Uppsala Medical University (Sweden), and in 1995–1996 – together with Department of Pathology (Head Professor Gregor Mikutz) of the Medical University of Innsbruck (Austria).

From 1996 to 2005, histological, immunohistochemical, and molecular genetic studies of multiple bladder biopsies in men with benign prostatic hyperplasia and in women with chronic cystitis were conducted in conjunction with the Department of Pathology (Head Professor Shoji Fukushima) Medical Osaka University (Japan). Many years of international research of the effects of low doses of ionizing radiation on the urothelium of the urinary bladder leads to the following conclusions:

1. Long-term exposure to low doses of ionizing radiation on the urothelium of the bladder leads to the development of the chronic proliferative atypical cystitis with large areas of sclerosis and increased angiogenesis in lamina propria, as well as multiple areas of dysplasia and cancer in situ, which was called «Chornobyl» cystitis.

2. In the pathogenesis of «Chornobyl» cystitis at the first stage, there is an increase in the expression of p53, cyclin D1, PCNA, mdm2 and p21WAF1/cip1, which is accompanied by activation of the p38MAPK signaling cascade, accumulation of polypeptides (subunits), transcription nuclear factor NF-κB, as well as the emergence of specific mutations in the p53 gene with a predominance of G:C on A:T in CpG dinucleotides in codon 245 exons 4–7 in 53 % of patients with «Chornobyl» cystitis.

3. Hyperexpression of 8-OHdG, iNOS and COX2 in the urothelium of the urinary bladder in patients with «Chornobyl» cystitis confirms the importance of oxidative stress in its pathogenesis.

4. The connection between oxidative stress induced by long-term exposure of low doses of IR to the urothelium of the urinary bladder, and pronounced activation of reparative processes in DNA, as an early response in the form of an adaptive attempt to restore cellular homeostasis. However, repair of damaged DNA (both pathways – excisional nucleotide repair and excisional repair of bases), especially in areas of dysplasia and urothelial cancer in situ, has proved ineffective and incapable, and should therefore be assessed as a process, that promotes carcinogenesis.

5. Cytokines of cell membranes, in particular transforming growth factor (TGF-β1), as well as intercellular compounds in the urothelium of the urinary bladder, which are responsible for paracrine/autocrine signaling (via β-catenin/E-cadherin complexes) are an early target at permanent long-term exposure to low doses of IR.

6. Hyperexpression of growth factor receptors (FGFR3, EGFRI and EGFR2neu), as well as the paradoxical accumulation of ubiquitin- and SUMO-dependent proteins of intracellular proteolysis confirm the molecular damage in the regulatory system of auto- and paracrine intracellular proteolysis of proteins followed by aberrant regulation of the cell cycle, which in turn can lead to forced cell transformation, promotion and tumor progression of the of the urinary bladder urothelium [115–131].

The effect of long-term low levels of ionizing radiation on the prostate

From 1993 to the present, the Institute of Urology of the National Academy of Medical Sciences of Ukraine has been constantly monitoring patients with benign prostatic hyperplasia (BPH), who undergo coded multiple biopsy during transvesical adenomectomy. Long-term studies have been conducted to assess the development of radiation-dependent lesions in patients with BPH, living in radio-contaminated areas with radionuclides ^{137}Cs in Ukraine.

In particular, statistical analysis of morphological changes in prostate tissue showed an increase of almost 2 times, compared with the control group from clean regions (15.55 ± 3.63 %), the incidence of prostatic intraepithelial neoplasia (PIN) in groups of patients living in radio-contaminated with radionuclides ^{137}Cs areas of Ukraine and in Kyiv (35.53 ± 4.79 % and 29.78 ± 4.57 %, respectively) [132–138].

Immunohistochemical determination of PCNA protein expression and histochemical determination of AgNOR proteins revealed a significant increase of the proliferative activity of the prostate epithelium in groups of patients with benign prostatic hyperplasia living in radio-contaminated areas of Ukraine and in Kyiv city, ($p < 0.001$). The highest indicators of PCNA expression index and the number of granules of AgNOR proteins were found in areas of PIN in patients living in radio-contaminated areas of Ukraine, where they were 12.02 ± 1.62 % and 6.92 ± 1.43 %, respectively.

Histochemical determination of epithelial cell apoptosis showed a significant increase, compared with the control group, apoptosis index in groups of patients living in radio-contaminated areas of Ukraine and in Kyiv (0.05 ± 0.03 %, 2.64 ± 0.05 % and 3.96 ± 1.32 %, respectively, $p < 0.001$). The highest apoptosis index was observed in the areas of PIN in the group of patients-residents of radio-contaminated areas of Ukraine (10.21 ± 4.44 %), which can be regarded as a protective reaction of the human body in response to chronic exposure of low doses of ionizing radiation.

Later, comprehensive studies of the effects of low levels of ionizing radiation on the prostate were conducted jointly by the Institute of Urology of the National Academy of Medical Sciences of Ukraine and the Department of Laboratory Medicine, Tumor Biology MAS University Hospital, Lund University, Malmo, Sweden [139–142].

In particular, BPH samples obtained by adenomectomy were studied in 30 patients from the so-called clean areas without radio-contamination (control group 1) and 90 patients from ^{137}Cs -contaminated areas of Ukraine (group 2). These BPH samples were examined histological and immunohistochemical methods. Proteins γ-H2AX, iNOS, Ki-67, p53, p63, p27Kip1 and Bcl-2 were studied by IHC in BPH samples in all patients.

We have described chronic proliferative atypical prostatitis, accompanied by large areas of sclerosis of stromal connective tissue with increased angiogenesis, which is often observed in cases of BPH group 2. Interestingly, these lesions were associated with a sharp increase in proliferative inflammatory atrophy (PIA) basal cell hyperplasia (BCH) with cellular atypia, as well as with areas of PIN.

Significant differences between groups 1 and 2 of BPH cases were found in elevated levels of immunohistochemical expression of γ-H2AX, iNOS, Ki-67, p53 and Bcl-2 proteins, especially in PIA and BCH areas with cellular atypia in group 2, which may be important early molecular markers of radio-induced prostate carcinogenesis. An increase ^{137}Cs in the urine was also found in group 2 of patients with BPH.

Our studies also demonstrate changes in cell cycle regulation, in particular, apoptotic regulatory molecules due to overexpression of γ-H2AX and iNOS in PIA and BCH zones with cellular atypia may also be important early molecular markers in the pathogenesis of radio-induced carcinogenesis.

The obtained data confirm the relationship between long-term exposure of low doses of ^{137}Cs in patients with BPH, residents of radioactively contaminated areas of Ukraine, and the development of chronic proliferative atypical prostatitis – preneoplastic condition in humans.

Effect of long-term low levels of ionizing radiation on testicular tissue

The medical consequences of the Chornobyl accident have been the subject of much research and today there is no doubt about the significant carcinogenic effects of low doses of ionizing radiation. Therefore, the growing incidence of germ cell tumors in Ukraine, especially in the last decade, confirms the relevance of comprehensive research to establish the cause and effect of this situation. Currently, germ cell tumors in Ukraine occur in 3–4 cases per 100 thousand male population and are the fourth leading cause of death from cancer among young men [98, 143].

Among the etiological factors in testicular carcinogenesis, the association of germ cell tumors with male infertility, which is confirmed in many studies by N.E. Skakkebek et al. [144–147]. It should be emphasized that in Ukraine there are very high prevalence and incidence of male infertility [98].

In recent years, the Institute of Urology of the National Academy of Medical Sciences of Ukraine has conducted comprehensive studies [148–166], which clearly demonstrated the existing causal links between spermatogenesis disorders and ionizing radiation and testicular carcinogenesis in Ukraine.

Thus, as a result of studies of testicular tissue in infertile men and peritumoral tissue and germ cell tumors, molecular epigenetic mechanisms underlying disorders of spermatogenesis have been identified – activation of ubiquitination and sumoylation processes in testicular cells, Claudin 11, violation of the regulatory effect of TGF-beta.

It has been established, that the influence of small doses of ionizing radiation, as an etiological factor, leads to natural changes in the structural components of the testis, as well as molecular changes, including epigenetic, which must be characterized as ecological pathomorphosis of male infertility, causing spermatogenesis.

In addition, we proved the participation of ubiquitin-proteolysis system in the initiation of carcinogenesis in the testis. In particular, in the peritumoral testicular tissue in the spermatogenic epithelium there are intensive processes of ubiquitination, which correlate with certain patterns of expression of Ubiquitin in male infertility at a general higher immunohistochemical factor – 3.5–4 times, compared with 2.5–3 times, compared to observations from ^{137}Cs-contaminated regions.

Based on the obtained results, we developed and presented a scheme of pathogenetic mechanisms of spermatogenesis disorders, ecological pathomorphosis of male infertility and initiation of carcinogenesis in the testis under the influence of ionizing radiation (Fig. 2.9) [165, 166].

Thus, disruption of ubiquitin-proteasomal proteolysis, disruption at the molecular level of components of the blood-testis barrier, disruption of the regulatory effect of TGF-β on the cell cycle play a crucial role in the pathogenesis of male infertility and initiation of testicular carcinogenesis.

Exposure of low doses of ionizing radiation, as an additional etiological factor, leads to changes in the structural components of the testis, as well as molecular, including epigenetic changes, which can be described as ecological pathomorphosis, leading to impaired spermatogenesis and increased risk of malignancy.

In summary, we can state, that patients with blocked spermatogenesis, in which atypical germ cell neoplasia in situ (GCNIS) are detected in the testicular tissue, are at increased risk of testicular carcinogenesis. The presence of additional etiological factors, such as chronic low doses of ionizing radiation, may be a factor in the initiation and progression of testicular carcinogenesis in patients with impaired spermatogenesis living in radio-contaminated areas of Ukraine [166].

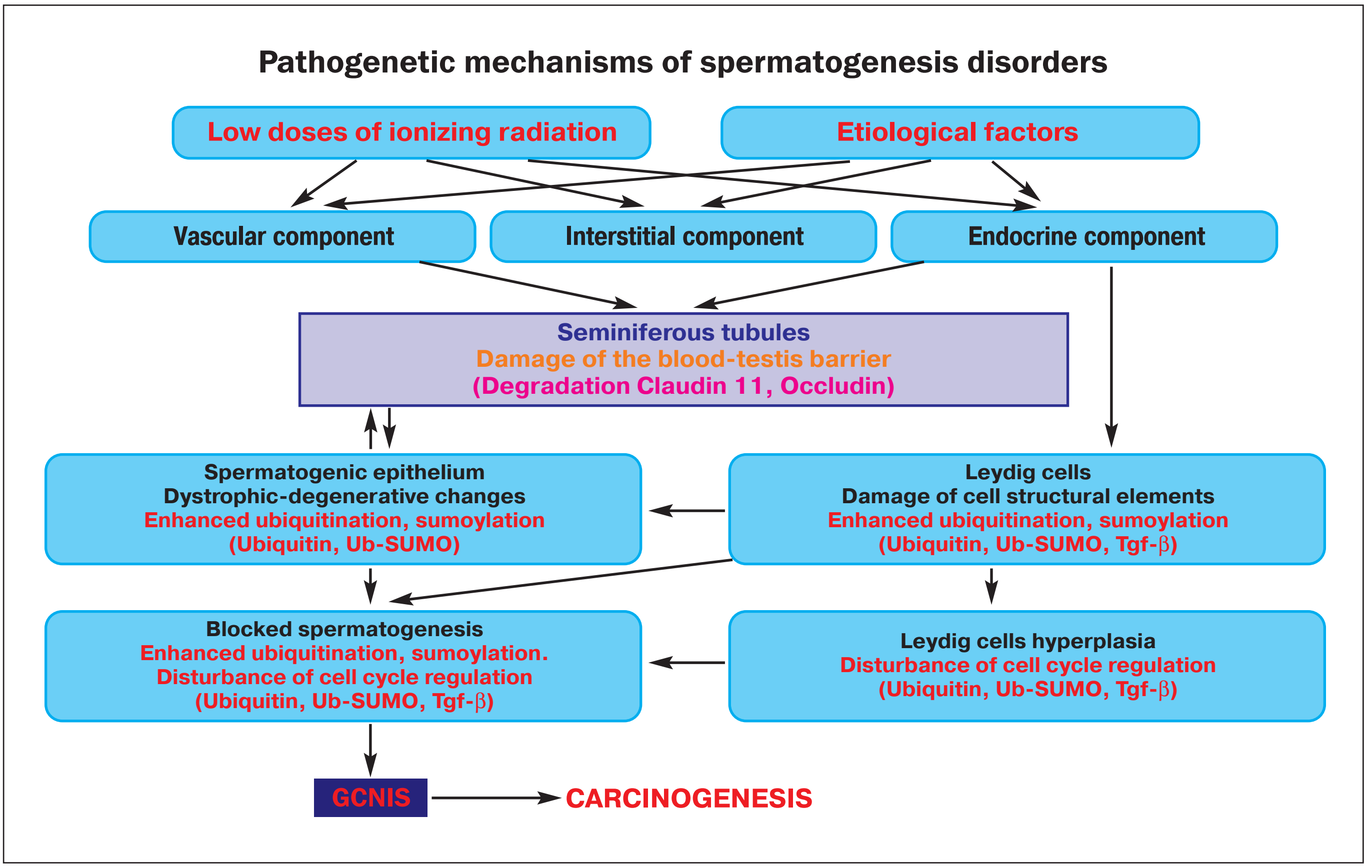

Figure 2.9. Scheme of pathogenetic mechanisms of spermatogenesis disorders, ecological pathomorphosis of male infertility and initiation of carcinogenesis in the testis under the influence of ionizing radiation [166]

During the last 35 years, the Institute of Urology of the National Academy of Medical Sciences of Ukraine has studied and developed the molecular genetic basis of the pathogenesis and ecological pathomorphosis of urological diseases in people living in radioactively contaminated regions of Ukraine. In particular, radiation carcinogenesis in the kidneys, bladder, prostate and testis was studied – and for the first time, the molecular genetic mechanisms of radiation nephropathy, kidney cancer, Chornobyl cystitis, benign prostatic hyperplasia with sites of PIN, male infertility with GCNIS, which formed the basis of the proposed criteria for early diagnosis, individual prediction of the clinical course of the disease and recommended for implemented in the development of new optimal schemes and algorithms for prevention and treatment of these diseases.

The results of the researches were presented in many international scientific forums, presented in a series of more than 100 scientific articles, which were published mainly in leading American, European and Japanese journals, as well as in five monographs, methodical recommendations, 4 information letters, 8 patents of Ukraine for inventions are issued.

2.6. Radiation damages of the eye

2.6.1. Radiation cataracts and radiation retinopathies

Radiation cataracts

Previous experience

Recognized effect of radiation exposure is radiation (irradiation) cataract. It has a specific clinical picture that allows to clearly distinguish it from other types of cataracts [167–169]. In the prevalence structure of all cataracts its proportion is insignificant, but specific radiation damage localization near the optical axis of the eye makes the radiation cataract clinically significant, its development can cause rapid loss of vision [168].

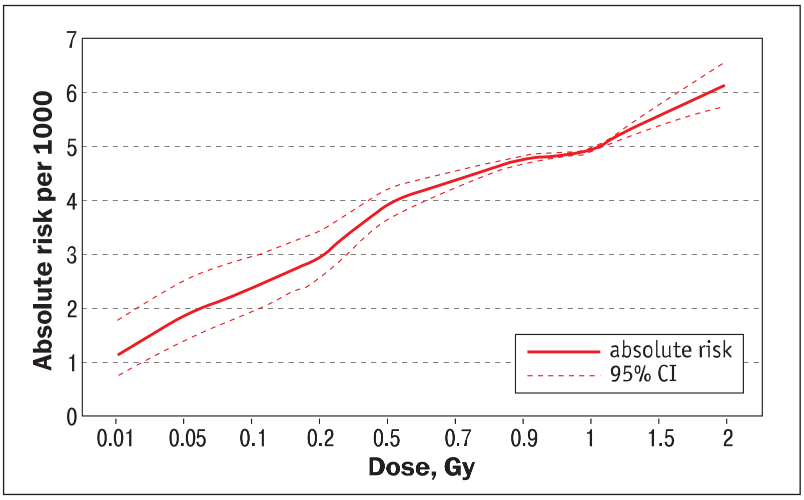

Figure 2.10. **The absolute risk of radiation cataract (per 1000 of exposed people) depending on the dose [170]**

Correlative analysis showed that there is a weak inverse link between radiation doses and duration of the latent period (r = 0.27). At doses up to 100 mGy latent period lasted (9.5 ± 0.19) years, 500 mGy or more — (8.8 ± 0.66) years, 1 Gy or more — (8.0 ± 1.0) years. The highest incidence of radiation cataract was registered 8–9 years after exposure.

The risk of radiation cataract depends on the radiation-absorbed dose. It is proved that a typical clinical picture of radiation cataract can occur at doses much lower than 0.25 Gy. In a separate study of 2,094 patients with documented dose rates [170] radiation cataract was diagnosed in 61 individuals (2.91 %) — the results of initial and repeated examinations; range of doses in patients with radiation cataract ranged from 20 mGy to 2 Gy.

The graph (Fig. 2.10) shows a dose dependence of the disease. The increase of calculated risk is proportional to the increase in the dose absorbed, the curve has a break point at the dose of 50 mGy, then with the increase in a dose risk increases faster; another break — in the area of doses around 1 Gy.

Additive-relative risk of radiation cataract was 3.451 (1.347; 5.555) per 1 Gy. The data received show that the threshold dose for radiation cataract incidence is whether too low, or there is no threshold at all, that is favor the view that radiation cataract is as a stochastic effect of radiation exposure [168, 170].

In 2014 IAEA set a new dose limit for the lens of the eye for occupational exposure— 20 mSv per year [171, 172]. In previous ICRP and NCRP believed that the minimum dose required to obtain the cataract is 2 Gy in one exposure and 5 Gy for fractionated or long exposures, and the old dose limit of IAEA was 150 mSv per year [173, 174]. ICRP in Publications 118 recognized the extreme sensitivity of the lens to acute, fractional, prolonged and chronic exposure [175, 176].

Radiation retinopathies. Among the various changes in the eye fundus in persons who worked in the first days of the Chornobyl accident in the most radioactively contaminated zones, we identified 2 forms of retynopathy caused by the action of ionizing radiation (IR), with enough clinical picture. One of them was named by us «syndrome of chestnut», another – «syndrome of diffraction grate» [167, 168]. In the remote period, remote manifestations of these rare syndromes were observed [167, 168].

Results obtained over the past 5 years

Conducted in 2020 of clinical signs of specific radiation cataracts in victims of the Chornobyl catastrophe analysis [177] showed that 226 cases of specific radiation cataracts (a small part of all cataracts) after the Chornobyl accident.

The first clinical sign of radiation cataract is the appearance of a small haze under a back capsule of a lens, polychromatic variability. At the periphery of the lens may appear point opacities.

With reliable sign of radiation cataract is the appearance of cluster of vacuoles, point opacities between posterior capsule and cortex of the lens. Over time, with the progression of cataract, these clusters merge in small opacity near the posterior pole, which gradually increases in size, becomes thicker and becomes denser [177].

First, the cataract is a cellulose, sharply separated from the environment, round or irregular form of opacity, which is somewhat reminiscent of porous mountain rock. In form, it is a meniscus, at first it may be deep-bumped, then flat-bumped, then double-convex.

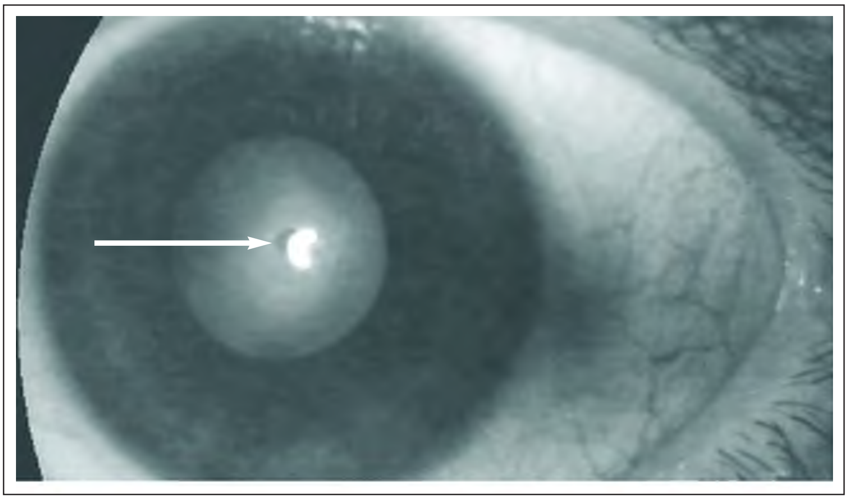

Figure 2.11. **First stage of radiation cataract in red reflex background photo [177]**

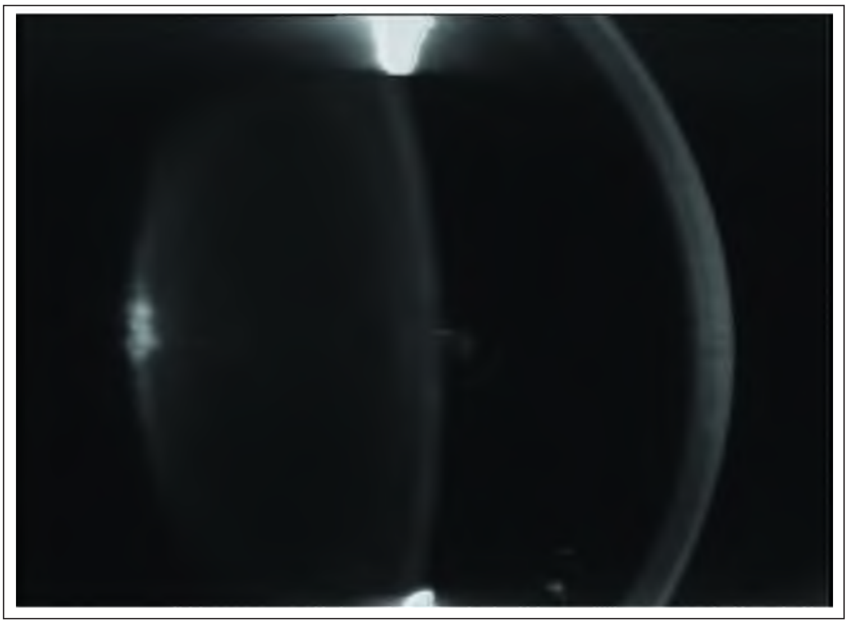

Figure 2.12. **First stage of radiation cataract in in Scheimpflug image [177]**

In Fig. 2.10 the stage I of radiation cataract (by classification [169]) in red reflex background photo presented, in Fig 2.11 the stage I of radiation cataract in Scheimpflug image presented.

Gradually there is an increase in the density and volume of opacity. In some cases, it begins to resemble a torus, while others acquire a stellar form (Fig. 2.12).

Around it there appears a border with a cluster of point opacities and vacuoles that form rays or bands directed toward the equator, and may subsequently cover the entire back surface of the lens [177].

Later, may appear a central opacity under an anterior capsule, consisting of a cluster of point opacities and vacuoles, and never reaches intensity such as opacity at the posterior pole (Fig. 2.13).

Often, especially in young people, most of the damaged fibers move from the equator to the poles of the lens, the posterior subcapsular opacity stabilizes and is gradually pushed by new crystalline fibers deep into the lens, into the bark. In this state, turbidity can remain during the next life; complete clouding of the cover develops mainly due to age or complicated cataracts [177].

It should be remembered about the possibility of simultaneous development of various types of acquired cataracts, the development of radiation cataracts or radiation and age cataracts simultaneously on the background of congenital cataract. Thus, at the same time, 2 or 3 diagnosis of cataracts of different etiology can be established when one eye is examined [177].

We have demonstrated previously that, the mode value for the latency period for the identified post-Chornobyl cases of radiation cataract was 8–9 years, however, new cases of cataracts continued to be detected. In 2020, the case of radiation cataracts was described in detail, the appearance of which was documented 29 years after the influ-

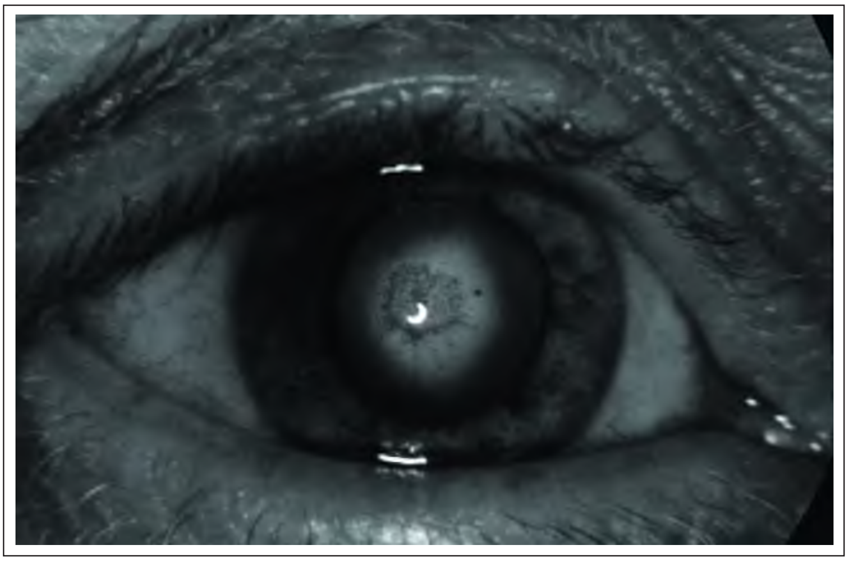

Figure 2.13. **The second stage of radiation cataracts, against the background of a red reflex [177]**

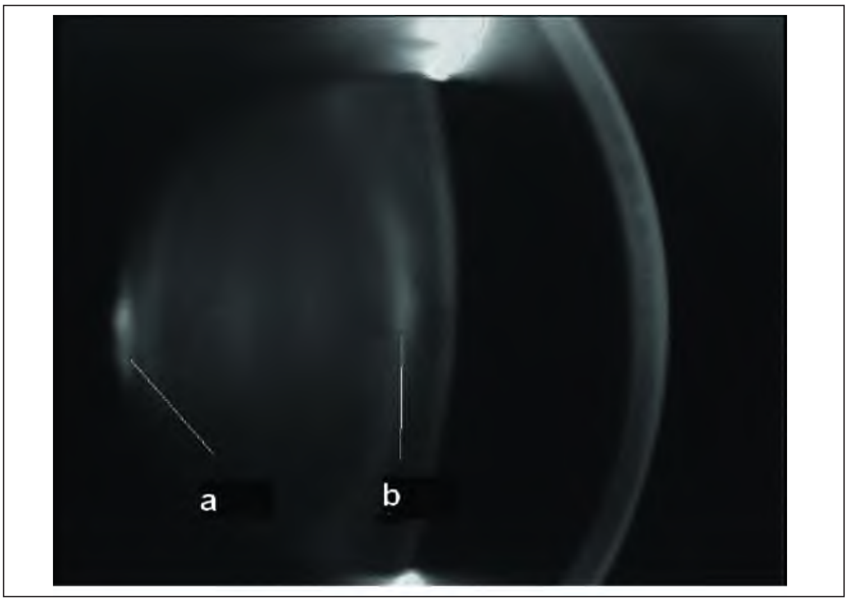

Figure 2.14. **Posterior (a) and anterior (b) opacities, radiation cataract in Scheimpflug image [177]**

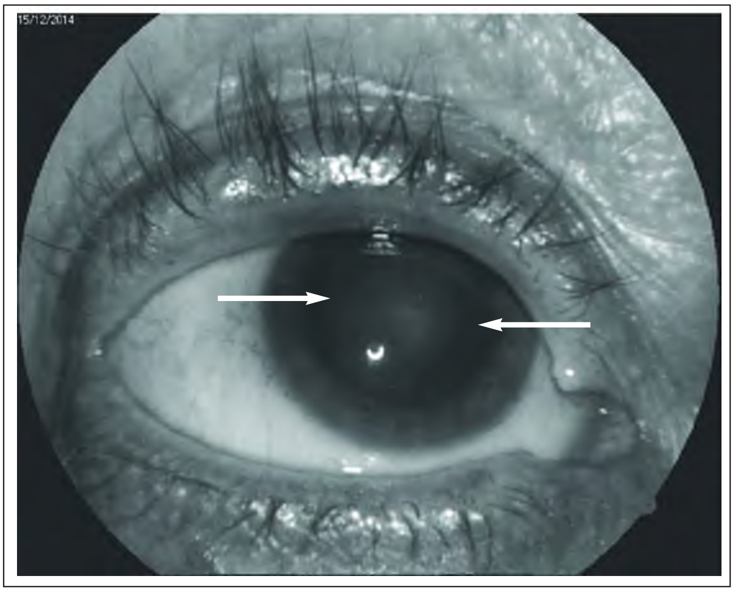

Figure 2.15. **Peripheral cortical opacity and no central subcapsular opacification in the patient S., right eye on the red reflex photograph taken with a fundus camera during the examination on 15.12.2014. Clouding of the lens on the periphery, there are no central subcapsular clouds.**

ence of IR [178]. In Fig. 2.14 and 2.15, respectively, photos of the patient's S. cover are shown 28 years 8 months and 29 years 5 months after radiation exposure. Thus, it has been proven that radiation cataracts can occur 29 years after radiation exposure.

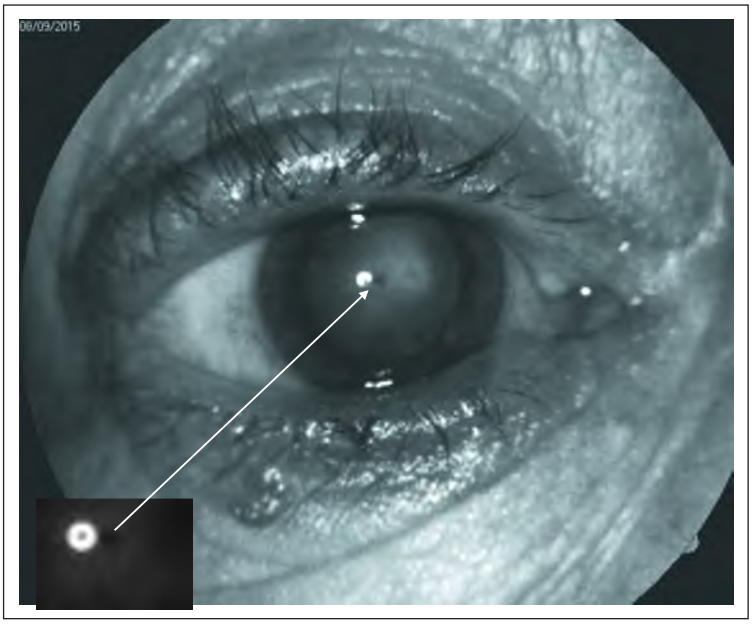

Figure 2.16. **A posterior, central subcapsular opacification in the patient S. right eye on the red reflex photograph taken with a fundus camera during the examination on 08.09.2015. The appearance of the posterior central subcapsular clouding.**

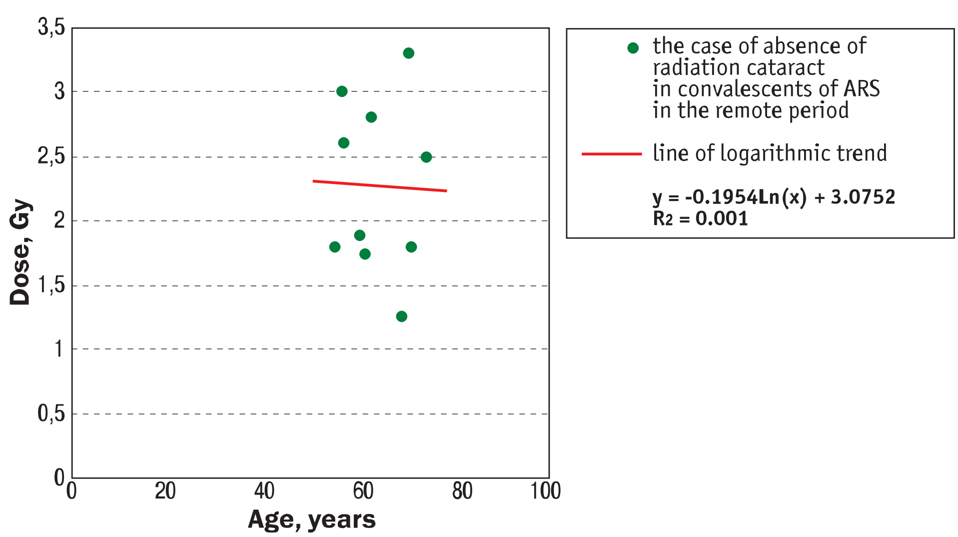

Figure 2.17. **Distribution of cases of absence of radiation cataracts depending on radiation dose and age at the time of examination of reconvalescents of acute radiation sickness [179]**

Data of ophthalmological observation of 53 reconvalescents of acute radiation sickness (period of observation from 01.12.2010 to 31.03.2019) showed that radiation cataracts, with its characteristic clinical picture were detected in 32 people; involutional cataracts were observed in 42 people, in 33 of them – the first stage of cataracts, in 9 – the second stage [179]. Thus, the majority of reconvalescents of ARS had combined lens changes – a combination of involutional and radiation cataracts. At the same time, 14 people had not manifestations of radiation cataract, and 4 people had not clear manifestations of involutional cataract. The average dose of irradiation in this subgroup was (2.27 ± 0.22) Gy (the doses are known for 10 people ranged from 1.25 to 3.3 Gy). The distribution of cases of absence of radiation cataract, depending on the dose of irradiation is in Fig. 2.16.

Based on the notions of the non-stochastic nature of radiation cataract, it should be expected that it is available to all persons with a dose load, which far exceeds the values that they consider threshold today [175, 176]. Therefore, the absence of it's signs in the remote period in the reconvalescents of acute radiation disease may indicate that this well-known radiation-induced effect is stochastic [179].

Thus, over the past 5 years, new data on the clinical features of radiation cataracts have been obtained. Consequently, the latent period of radiation cataract can exceed 29 years. Analysis of the clinical features of lens pathology in reconvalescents of acute radiation disease provided new evidence in favor of the previously proposed assumption [168, 170] regarding the stochastic nature of radiation cataracts.

2.6.2. Ophthalmic radiogenic effects, that have deterministic features

Previous experience

A dose dependent disorders of permanent retinal potential generation in irradiated persons. The pigment epithelium of the retina, the photoreceptors and choroid take part in forming a permanent potential of the eye. Retinal permanent potential generation disorders presented in radiation-exposed persons with the dose loading over 200 mGy [168].

A dose dependent decrease in accommodation capacity. Evidence of a dose-dependent effect of decreasing the capacity for accommodation has been observed. At radiation doses of 150 mGy this effect is already registered. It is shown that the loss of accommodative ability is described by both linear and logarithmic models and is 0.78 D/Gy. This is direct evidence of radiation aging as decreasing the capacity for accommodation is the main and objective signs of aging [180].

Preclinical specific changes in the eye in children living in radiation-contaminated areas. Two parallel studies — «Pittsburgh Project» (US–Ukraine), and the study conducted by NRCRM in Ivankiv district of Kyiv Oblast detected specific soft cataract in children living in the contaminated areas [181, 182]. Its prevalence depends on the contamination of the area with Cs-137 (χ^2= 5.27, $p < 0.05$). In the late period in areas with higher levels of radiation contamination a further increase in the prevalence of these changes was observed [182].

Eye pathology in persons affected by radiation exposure

It is proved that the prevalence of *involutional cataracts* in Chornobyl clean-up workers is significantly higher than the control levels; there is a clearly observed shift to early incidence of this medical condition towards younger age groups. So, for example, the relative risk for clean-up workers under 40 compared with the corresponding age group of the control was 15.89 (CI: 2.22–110.82); for the age group of 40–49 year olds — RR = 8.7 (CI: 4.02–18.85); for 50–59 year olds — RR = 3.86 (CI: 2.17–6.88). The prevalence of this type of cataract was determined by the age of the examined people, period of time under risk and a dose. The relative risk depending on the dose and the time period of 5 years under risk is presented in Fig. 2.17.

Violation of microcirculation in the conjunctiva is one of the earliest effects of radiation exposure, later a significant increase in the prevalence of *retinal angiopathy* is observed, as well as increased prevalence of angiosclerosis. For the first time it has been proved that the development of retinal angiopathy is dose dependent; the relative risk of retinal angiopathy in the exposed with a dose of 0.3–0.7 Gy compared with those irradiated with a dose of 0.3 Gy was 1.65 (1.02–2.67), χ^2 = 4.15; p = 0.041 [168, 183].

The most typical kind of retinal pathology in the exposed individuals proved to be *central chorioreti-*

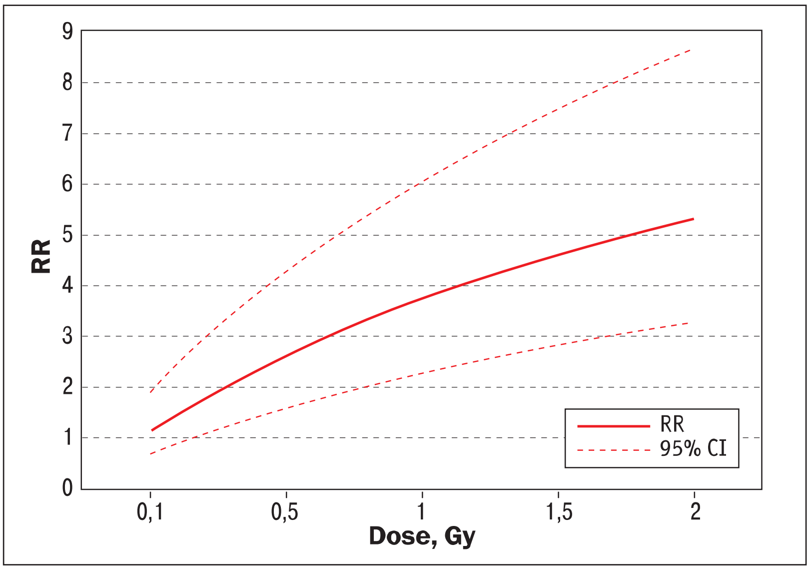

Figure 2.18. **The relative risk of involution cataract depending on the dose and the 5-year time period under risk [168]**

nal degeneration (*macular degeneration*), its prevalence in Chornobyl clean-up workers was 224.83 ± 5.8 per 1000 persons, that far outweighs the control figures (55.56 ± 13.5 per 1000 persons). Macular degeneration absolute accumulated risks were mostly influenced by the age of the patients, time at risk and a dose.

The greatest is an influence of such factors, as an age (relative risk – 1.727 (1.498–1.727) per 1 year, an excess of relative risk – 1.076 (1.056–1.095) per 1 year), a time of stay under a risk and a dose (relative risk 6.453 (3.115–13.37), an excess of relative risk – 1.253 (1.137–1.37) per 1 $\sqrt{}$ (d × t), where d is a dose of whole-body irradiation, Gy, t is a time of a stay under a risk, years. It should be noted that the effects of dose and age are added up [168].

Eye status in persons those irradiated *in utero* as the result the Chornobyl disaster

Relative risk of the ophthalmic pathology occurrence for those exposed *in utero* in relation to the comparison group was 1.66 (1.47–1.88). There was observed significantly higher incidence of congenital cataracts (RR = 6.22 (1.34–28.96)) in those exposed *in utero* whose mothers received a total effective dose of 75 mSv or higher, compared with those whose mothers' dose was less than 75 mSv [184].

Results obtained over the past 5 years

Central chorioretinal degeneration (macular degeneration). The results of examination (at the age of 14–30 years) of 84 individuals exposed in utero as a result of the Chornobyl disaster, shoved, that in the under 30 age group of the antenatally exposed there already appear macular degenerations whose clinical picture resembles age-related macular degeneration, but develop extremely early. The prevalence of macular degeneration (95.23 ± 32.03 per 1000) is reliably higher for exposed *in utero* at the age of 14–30 years ($\chi^2 = 7.827$, $p = 0.0026$) compared with non-irradiated control at the same age (17.86 ± 10.31 per 1000) [185].

The results of the optical coherence tomography (OCT) of the reconvalescent ARS showed that the thickness of retina in the foveolar and a paramacular area in persons suffered an ARS, is probably higher than in control. These changes observed in all reconvalescence of ARS – both in persons with manifestations of macular dystrophy, and in those who have not been detected by its clinical manifestations. For the first time, the presence of a correlation (r = 0.51) between thickness of retina in the macular zone and irradiation dose [186] was detected. The results open an opportunity to find ways to correct the changes in the macular zone in radiation-expandable persons.

In recent years studies aimed at finding ways to treat and prevent macular degeneration in irradiated persons. The results of prolonged 12–24-month monitoring showed the effectiveness of the combination of lutein complex and antioxidants to treat the initial stage of macular degeneration in persons, working in conditions of the ionizing radiation influence in small doses [187].

Eye vessels pathology. The research of the state of microcirculation in the conjunctiva revealed the presence of significant irregularities in exposure persons already in the early period after irradiation. Degree and frequency of microvessels pathology is dependence of the dose accumulation. In the remote period changes of hemomicrocirculation, the share of vascular and perivascular changes, dose dependences for microcirculation changes are remained [188].

The results of prolonged observation of two cohorts ChNPP clean-up workers showed that the pathology of the retina vessels – the most common pathology of the eye in persons, who have undergone radiation exposure, can be expected in 4–5 years after exposure. The main factors of risk of its development in the cohorts of ChNPP clean-up workers are the age and dose of external exposure. The relative risk of angiopathy (due to the model) to the dose of irradiation, is 1.29, a relative interval – (1.07–1.56). It is shown that the main factors that determine the risk of angiopathy of the retina are age and time of risk, the contribution of radiation dose is less [189].

The primary incidence of retinal angiopathy has reached the first maximum 9 years after radiation exposure, repeated rise was observed 13 years after irradiation [189].

The results state of the retina vessels analysis in 1 948 evacuated from the city of Pripiat at the age below 20 year and 583 irradiated *in utero* as a result of the Chornobyl disaster showed that the emergence of remote radiation effects depends on the age in which a person has exposed to irradiation. Thus, the consequences for irradiated *in utero* will be worse than for irradiated ages 4–7 [190].

Glaucoma. According to the reports that appeared in recent years, open-angle glaucoma increased may be the most distantly of the effects of ionizing radiation on the eye [191]. Japanese authors recently informed about the presence of relationship between the higher prevalence of normal-tension glaucoma and radiation dose in Japanese atomic bomb survivors irradiated at doses 0–4 Gy, with estimated OR at 1 Gy of 1.31 (1.11–1.53], although the specific causal mechanism remains unclear [192]. Hereinafter, in 1,640 Japanese atomic bomb survivors 196 cases of glaucoma (12 %) were revealed [193].

Study of blood flow state in the ciliary body and the state of anterior chamber angle of the eye in radiation-exposing persons allowed a statistically significant reduction of blood flow in the ciliary body. Increased risk of involutionary changes in the anterior chamber angle of the eye observed in cohort of ChNPP clean-up workers, RR = 3.5 (1.27–9.5). Similar changes are characterized by residents of radioactive contaminated territories. Radiation-induced reduction of blood flow in the ciliary body can significantly reduce the production of intraocular fluid, which over a period of time compensates for the reduction of outflow due to changes in the angle of the anterior chamber. Presence of these changes can explain the features of the pathogenesis of glaucoma in irradiated persons – late manifestation and, at the same time, severe course [194].

2.7. Dynamics of sensorineural hearing loss and postural balance of vestibular dysfunction during rehabilitation and corrective measures in clean-up workers of the accident at Chornobyl nuclear power plant: results of 35-year monitoring

Introduction

The study of the effect of ionizing radiation (IR) on sensory systems, in particular on the vestibular and acoustic systems due to accident at the Chornobyl Nuclear Power Plant, continues to be one of the current issues at the national and global levels both at the present and in the future [195–197].

Promising tasks at present are the study of somato-sensory information, the important components of which are vestibular, visual, acoustic and other sensory systems for investigating the motor functions and postural balance and other sensory sensations [198–202]. Their study is of great importance for determining the professional suitability, working capacity and viability of individuals, including clean-up workers of the Chornobyl accident (CUWs of the ChA).

It is known that the functional states of the vestibular and acoustic systems are one of the reliable criteria for assessing human health.

According to the data of some authors [198, 203] the vestibular and acoustic systems are anatomically, physiologically and functionally closely related not only to each other but also to the departments of the central nervous system, such as cerebral circulation system and other body systems, which makes them highly sensitive to changes in internal and external environments. Therefore, the study of these systems caused by IR as a result of the Chornobyl accident, in addition to scientific, is important in practical radiation medicine [204].

For 35 post-accident years we examined 8957 males' CUWs of ChA, who were sent with individual IR doses for clinical examination and assessment of the functional state of the vestibular and acoustic systems from SI «National Research Center for Radiation Medicine of NAMS of Ukraine» at our Institute. They were included in the clinical and epidemiological registry of the abovementioned center, agreeing on the necessary diagnostic, treatment, rehabilitation and corrective measures.

Studying disorders of these systems [199, 205] in the dynamics of all post-accident years was carried out on the basis of long-term monitoring of objective indicators of clinical and electrophysiological examinations, and epidemiological studies in practically healthy, workable people before accident who were affected by IR and became CUWs of the ChA.

Among them were CUWs of the ChA after acute radiation sickness, after exposure to IR in small doses (0.20–0.50 Gy) with a relatively short duration of IR, namely in the first two months of work after the accident, as well as the same small doses IR during long-term work by the shift method (6–8 years) in the exclusion zone.

Both external control of 102 drivers and 50 practically healthy persons without IR in the anamnesis, and internal control (420 drivers' clean-up workers of the ChA) of the same age, whose IR dose was less than 5.0 cGy) were used.

Processing of tne results was carried out with the assistance of software packages SYSTAT, EPICURE and EGRET.

The results of previous 30-year examinations

New solutions to the scientific problem during long-term monitoring in the dynamics of post-accident years (1986–2016), consisting in increasing the efficiency of diagnostic, therapeutic, preventive and expert measures in vestibular dysfunction (VeD) and sensorineural hearing loss (SNHL) on the basis of determination in the ChA CUWs of clinical and electrophysiological disturbances, mainly in the central departments of vestibular and acoustic systems with various doses and duration of action of IR.

The regularities of formation, progression, increase of VeD and SNHL in comorbid diseases with complex and severe syndromes, which lead to reduction of life expectancy, were studied [206].

In particular, these comorbid diseases, based on epidemiological studies and long-term monitoring, are complicated, as we have studied, by premature age-related hearing loss (presbyacuzis praecox), premature sclerotic changes in the retinal vessels, and premature atherosclerosis of the aorta, which can be considered as a symptomocomplex of premature aging of the body in CUWs of the ChA [205].

Peculiarities of the clinical course of VeD and SNHL of different manifestations in ChA CUWs, who were exposed to IR at different doses during different time intervals, were studied.

It has been shown for the first time that the frequency and degree of disorders increase with increasing exposure to the dose of IR. These phenomena are described by a mathematical model that takes into account the dose, time at risk, age of the patient and concomitant pathology.

The occurrence of deterministic radiation effects at doses greater than 0.20 Gy, at which they cause the persistent clinical and electrophysiological changes in the functional state of the vestibular and acoustic systems, was determined.

The commonality of mechanisms and sequence of VeD and SNHL development in CUWs of the ChA, is studied on the basis of long-term monitoring in the dynamics of post-accident years. VeD is manifested clinically and electrophysiologically earlier and more often than SNHL.

For the first time it was established that the progression of VeD in CUWs of the ChA in the dynamics of post-accident years is manifested by an increase in spontaneous symptoms (changes in postural balance, manifestation of spontaneous nystagmus) and the state of transformation of experimental nystagmus from clonic to tonic-clonic, later to tonic, indicating an increase in disorders in the brainstem structures of the vestibular system, the deepening of cerebral phenomena, hypertension syndrome in the development of cerebrovascular pathology.

For the first time, clinical and electrophysiological characteristics were studied and diagnostic criteria for assessing VeD in the development of three stages of dyscirculatory encephalopathy (DEP), as well as features of the clinical course of VeD in vaso-insular, sympatho-adrenal and mixed crises of vascular disorders were added.

It was first investigated that the parameters of nystagmus (spontaneous and experimental), namely: a decrease in the nystagmus amplitude, the average angular velocity of its slow phase are affected by changes in the form of a decrease in the values of the generation of the constant eye potential, which are a specific direct effect of IR, arising in the dynamics of post-accident years in CUWs of the ChNPP, indicating the interaction of inhibitory processes in visual and vestibular disorders were added.

It was first clarified on the basis of clinical and electrophysiological examinations, in particular, in electrooculography (EOG) and electronystagmography (ENG), as well as in a case-control epidemiological study, that in CUWs of the ChA there is a direct relationship between the degree of visual acuity and the degree of VeD manifestation ($r = 0.458$).

For the first time, the role of changes in the microcirculatory bed and changes in blood circulation in the main vessels of the head and neck in the development of VeD and SNHL in CUWs of the ChA depending on the dose and duration of IR.

Substantiated and expanded tactics for treatment of VeD with antihomotoxic drugs, as well as hirudotherapy [207, 208], which were effective for improving and stabilizing the progressive forms of VeD and SNHL, for prevention of thrombosis in hypertension and cerebrovascular diseases, for health improvement and strengthening the body in

CUWs of the ChA, increasing their social activity and quality of life.

The purpose of surveys over the past five years: is to study the dynamics of the postural balance of vestibular dysfunction and sensorineural hearing loss in rehabilitation and corrective measures in CUWs of the ChA in the distant post-accident years 2016–2020.

113 CUWs of the ChA were selected from archival materials, who worked in shifts in the Chornobyl Exclusion Zone for 6–8 years from the end of 1986 to 1992 or 1994, in whom, according to physical dosimetry, individual small doses of IR amounted to 0.20–0.50 Gy.

Patients selected for work in the exclusion zone were aged 30–34 years. At the medical examination, they were practically healthy. Using a complex of modern standard audiometric, vestibulometric and electrophysiological methods that can be reproduced, the auditory and vestibular functions within the physiological norm were recorded in them. In 2016–2020, the selected CUWs of the ChA were aged 65–69 years.

The control group for these examinations consisted of 20 people from other regions of Ukraine of the same age 65–69 years who did not undergo IR.

Thresholds of perception of tonal sounds on air and bone conductivities in the frequency range between 0.250 and 8.0 kHz were determined. The thresholds of 100 % intelligibility of peech tests [209, 210] and the phenomenon of paradoxical fall in their intelligibility (PFI) at the maximum intensity of the audiometer (120 dB) in percent (%) were recorded during speech audiometry. The presence of the Tullio phenomenon was determined (with increasing intensity of sounds and speech tests, dizziness and objective manifestation of this sensory reaction – spontaneous nystagmus appear during the examination). These tests were performed by audiometers MA-31 (Germany) and «Uteri» (Denmark).

Vestibulometry is based on V.G. Bazarov's scheme [203] with registration of postural balance (static equilibrium – by the methods of kephalography and kinetic equilibrium using walking and writing Fukuda tests) [211, 212].

Electronystagmography (ENG) of spontaneous, positional nystagmus and experimental nystagmus reaction caused by classical functional stimulations (caloric and rotational) was performed with the computer neurocomplex of SPE «DX – system» (Ukraine) taking into account vestibulo-sensory and vestibulo-vegetative pathological reflexes by L. Khilov [213].

The nature of vestibular dysfunction was determined by I.B. Soldatov et al. [214], and the degree of its manifestation – according to V.G. Bazarov [203].

For kinesiorehabilitation, the method of G.S. Fedorova, which is adapted for VeD disorders of central and mixed types was used. It does not require special equipment, it can be performed both in medical and at home conditions and in health improving institutions. When analyzing the effectiveness of kinesiorehabilitation, a complex of vestibulometric changes was taken into account, both vestibulo-somatic, vestibulo-sensory, and vestibulo-vegetative pathological reactions [109, 215].

When analyzing audiometric examinations in the dynamics of post-accident years, the attention to the age-related changes in SNHL was paid in CUWs of the ChA. There are two forms of such SNHL. The first was age (presbyacuzis) [216], the second was premature age (presbyacuzis praecox) [210, 217].

Researchers [210, 216, 218] have studied and created patterns that can be used to determine age and premature age-related hearing loss by age categories, starting from 40 years through each lived decades. They are included in the international qualification of diseases of the 10th revision (ICD-10), which belong to the rubric H.91 [219]. *These disorders are not specific to the people affected by IR.*

Based on epidemiological studies, we have reliably established that a second form of SNHL – premature age (presbyacuzis praecox), which progressed in the dynamics of different post-accident years according to characteristic parameters in the range of changes in age categories was recorded in most CUWs of the ChA.

In the individuals of control group, the thresholds of sounds according to tonal audiometry indicated the bilateral symmetrical auditory changes by type of age SNHL (presbyacuzis), the symmetrical bilateral, without the phenomena of delayed increase in 100 % intelligibility of speech tests and paradoxical fall in its intelligibility at the maximum intensity of the audiometer with the absence of the Tullio phenomenon.

However, the age form of presbyacuzis is not registered in CUWs of the ChA in any case in different older age categories.

In the last five years, bilateral, almost symmetrical SNHL by presbyacuzis praecox type was recorded with audiometry in 90 people (76.0 %) from 113 CUWs of the ChA. It is characteristic of premature hearing changes in the age group conditionally divided according to the state of intelligibility of speech tests into the 1st and the 2nd main groups.

The first main group includes 34 people out of 90 patients (38.0 %), in whom the results of speech tests showed delayed intelligibility of speech tests, which reached 100 % at the level of 90–110 dB, without signs of a paradoxical fall in intelligibility of speech at a maximum audiometer intensity of 120 dB, without the Tullio phenomenon. The dose of IR was in the range of 0.20–0.25 Gy.

Group 2, the main group, consisted of 56 people out of 90 patients (62 %), in whom delayed intelligibility of speech tests was revealed in presbyacuzis praecox, which did not reach 100 % intelligibility and was with signs of its paradoxical fall, as well as the presence of positive phenomenon Tullio with the maximum intensity of the audiometer.

The 3rd main group includes the remaining 23 people from 113 CUWs of the ChA (24 %), in whom SNHL of III and IV degrees was noted by audiometry, which refer to socially inadequate hearing disorders, which are included in ICD-10 by rubric H.90 [219].

The phenomena of delayed intelligibility of speech tests, which did not reach 100 % intelligibility and were with the phenomena of a paradoxical fall in their intelligibility at the limit of audiometer intensity (120 dB), with positive Tullio phenomenon were revealed in them.

It is worth paying attention to the fact that in CUWs of the ChA in the 1st and the 2nd groups with presbyacuzis praecox the phenomena of slow increase of legibility of speech tests in comparison with average values of tonal thresholds at frequencies of 500–4000 Hz which are included in the conversational range of normal hearing persons are noted. These phenomena are especially manifested in CUWs of the ChA with SNHL of a socially inadequate degree.

They indicate an increase in inhibitory processes in the cortical parts of the auditory system, where the spoken language (ie indicate the progression of cognitive impairments) is analysed.

The manifestations of a paradoxical fall in the intelligibility of speech tests and spoken language with increasing their volume and the presence of the Tullio phenomenon indicate a disorder of the interaction between the processes of excitation and inhibition in the cortical parts of the speaker system, resulting in auditory discomfort.

For the first time we studied that auditory discomfort contributes to postural balance disorders and the manifestation of pathological somato-sensory disorders in the form of dizziness and spontaneous nystagmus in the presence of the Tulio phenomenon, pathological vestibulo-vegetative reflexes: nausea, vascular reactions with increased or decreased blood pressure, increased sweating of the skin and tinnitus. These disorders significantly limit the communicative contacts, reduce social activity and promote solitude.

The results of audiometric examinations revealed increasing manifestations of auditory discomfort in CUWs in the 2nd group with hearing loss by type of presbyacuzis praecox and in the 3rd group with socially inadequate hearing of III and IV degrees.

It should be emphasized that they received a dose of 0.26–0.50 Gy with prolonged irradiation in comparison with the 1st group, in which the dose of IR was 0.20–0.25 Gy.

It has been studied that the use of digital hearing aids in binaural pair improves the speech intelligibility by balancing the sensory processes of excitation and inhibition in the auditory cortical structures of the brain.

In addition, the phenomena of the paradoxical fall in speech intelligibility are reduced and the Tullio phenomenon are reduced or disappeared. This makes it possible to use the hearing aids to expand the range of volume of sounds and speech, which activates communicative contacts in CUWs.

The results of examinations of thresholds of tonal and speech hearing on the audiometric form of persons of the control group with presbyacuzis and two groups (the 1st and the 2nd groups with presbyacuzis praecox in CUWs of the ChA are given. It should be emphasized that they received a dose of 0.26–0.50 Gy with prolonged irradiation in comparison with the 1st group, in which the dose of IR was 0.20–0.25 Gy.

In Fig. 2.18 the results of examinations of thresholds of tonal and speech hearing on the audiometric form of persons of the control group with presbyacuzis and two groups (the 1st and the 2nd groups) with presbyacuzis praecox in CUWs of the ChA, tonal audiometry in CUWs of 66-year-old patient

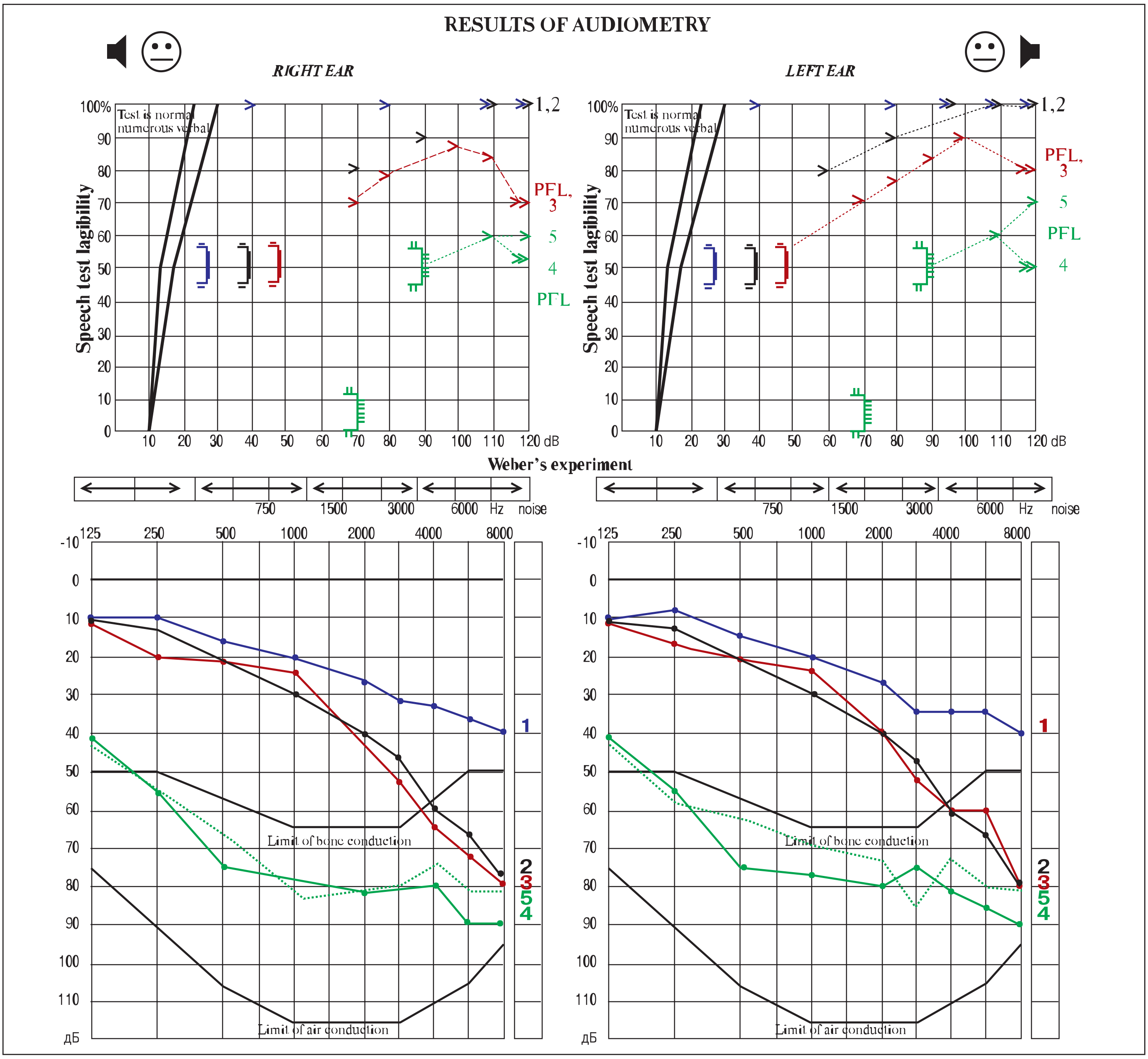

Figure 2.19. **Results of tonal and speech audiometry in persons of the control group with presbyacuzis, CUW of the 1st and 2nd groups with presbyacuzis praecox, as well as CUW of the 3rd group, patient Sh., 66 years old with socially inadequate hearing IV degree**

Symbols for audiometric examination, shown in Fig. 2.19:

1 – the 1 blue line shows the parameters, developed by the patterns, of tonal hearing loss in the age category of 60–69 years according to the presbyacuzis type in the patients of control group. Tonal thresholds are consistent with the thresholds of 100 % intelligibility of speech tests, without the phenomena of their slowing down, as well as without the phenomena of PFL, without the Tullio phenomenon;

2 – the 2 black line shows the tonal thresholds that correspond to the parameters of premature SNHL (presbyacuzis praecox) in the age category of 60–69 years. They were recorded in CUWs of the 1st group, in which the slow intelligibility of speech tests with the achievement of 100 % of its intelligibility, without the phenomena of paradoxical fall in intelligibility and without the Tullio phenomenon at the maximum intensity of the audiometer was noted;

3 – the 3 red line shows the tonal thresholds corresponding to hearing loss by presbyacuzis praecox type of the above mentioned age, which were defined in CUWs of the 2nd group with slow intelligibility of speech tests, without 100 % intelligibility of speech, with the phenomena of paradoxical fall in its intelligibility and with the presence of a positive Tullio phenomenon at the maximum intensity of the audiometer;

4 – the 4 solid green line shows the thresholds of tonal audiometry in CUWs of 66-year-old patient (Sh) who received a dose of IR 0.39 Gy, with socially inadequate IV degree of SNHL before wearing binaural hearing aids and up to 6 months of kinesiorehabilitation;

5 – the 5 dotted green line shows audiometry data of the same patient (Sh.), 66 years old men after the above-mentioned corrective and kinesiorehabilitation;

> – thresholds of legibility of language test are marked by the same color which denotes the results of tonal audiometry of the presented groups;

>> – the phenomenon of a paradoxical drop in the intelligibility of speech tests a the intensity limit of the audiometer 120 dB which are dtnoted by the same color of tonal test of prenented groups, with the presence of Tullio phenomenon.

Table 2.11
Quantitative indicators of postural balance in vestibular dysfunction before and after kinesiorehabilitation in the CUWs of 3 groups and control group

Group	Static equilibrium		Kinetic equilibrium			
	Index of kephalography, deviation in absolute units		Coordinating writer Fukuda test, degrees		Coordinating stepping Fukuda test, degrees	
	before	after	before	after	before	after
1	4.7 ±0.2	4.0±0.1*	13.5±0.1	8.5±0.1*	75.5±1.1	68. 9±1.0*
2	5.6±0.2	4.9 ±0.2*	18. 5±0.1	11.5±0.1*	82.5±1.1	76.5±1.1*
3	5.9±0.1	5.1 ±0.2*	26.6±0.1	20.6 ±0.1*	95. 5±1.2	83.5 ±1.2*
K	3.6±0.2	2.9±0.2*	11.3±0.1	7.9±0.1*	50.5±1.2	41.7±1.3*

Note. *The difference between the indicators before and after 6 months of kinesiorehabilitation with physical exercise is significant at $p < 0.05$.

(Sh.) who received a dose of IR 0.39 Gy, with socially inadequate IV degree of SNHL before wearing binaural hearing aids and up to 6 months of kinesiorehabilitationVestibulometric examinations in 2016–2020 revealed bilateral, almost symmetrical VeD with dissociated manifestations of vestibulo-somatic, vestibulo-sensory and vestibulo-vegetative pathological reactions of central and mixed type of the II and the III degrees of manifestation in all the CUWs but in persons of the control group of the same age category – within the first degree.

The increase of spontaneous symptoms (postural balance disorders, the appearance of spontaneous nystagmus), as well as the increase of qualitative and quantitative changes in the experimental nystagmus response under functional loads have been studied in the dynamics of long-term monitoring in the CUWs.

In addition, it was found that spontaneous nystagmus and vertigo as somato-sensory pathological reactions disrupt vision fixation, as well as accuracy and fine sensitivity when performing certain tasks. These disorders reduce the professional suitability and working capacity [220].

It was first determinet that pathological somatosensore ant pathoiogical vestibulo- vegetative reactions of vestibular dysfunction are promising in the study of complex mechanisms of movement, their effect on the progression of diseases of organs ant systems, as well as tne need for further development of objective methods for their examinations.

It was noted for the first time that pathological vestibulosomatic reactions play an important role in studying disorders of balance and orientation of patients in space. Our examinations indicate that the vestibule-sensory responses are of great importance for understanding the complex mechanisms of human movement, taking into account their interaction *with other sensory systems of the body with the participation of cognitive treatments in CNS*.

The average statistical indicators of postural balance of VeD before and after 6 months of kinesiorehabilitation in the CUWs of 3 groups of age category 60–69 years in comparison with the indicators of persons of the control group of similar age category in the last five years are given in Table 2.11.

It should be emphasized that an increase in pathological vestibulo-vegetative reflexes (nausea, instability of vascular tone, dysrhythmia), which contribute to the progression of cardiovascular, neuropsychiatric and digestive diseases were identified in the CUWs.

The obtained results are promising for the search for further objective methods of vestibular dysfunction examinations, and also require further analysis of the accumulated factual material.

Conclusions

In was found that premature age-related hearing loss by the type presbyacuzis praecox, which corresponds to certain age categories, as well as the type of socially inadequate hearing disorders continues to be dominated in all examined clean-up workers in the remote post-accidental years.

The dependence of auditory discomfort in the clean-up workers of the Chornobyl accident, who had significantly more manifestations during the long-term exposure to ionizing radiation at a dose of 0,26–0,50 Gy than those in whom the dose of ionizing radiation was 0,20–0,25 Gy, was studied.

It has been studied that hearing correction with special digital hearing aids reduces hearing discomfort, improves the communication contacts in clean-up structures of the brain.

The last five years of the post-accidental period show progressive changes in postural balance and a significant improvement in its indices in our patients during kinesiorehabilitation with physical exercises.

It was first determined that pathological vestibulo-somatic, pathological vestibulo-sensory and pathological vestibulo-vegetative reactions of vestibular dysfunction are promising in the study of complex mechanisms of movement, their effect on the progression of diseases of organs and systems, as well as the need for further development of objective methods for their examinations.

2.8. Radiation-induced targeted and non-targeted cytogenetic effects in human somatic cells in different terms following Chornobyl disaster

Because one of the main biological targets for ionizing radiation (IR) is the genome of somatic and germ cells, exactly the degree of its damage in different terms following irradiation is the criterion of the adverse effects of radiation exposure on human. Therefore one from priority scientific directions in radiation genetics is the study of features of radiation-induced injuries in human genome – both direct (targeted) in the irradiated cells and indirect (untargeted) in the unexposed cells.

The main method for detection and evaluation of radiation-induced targeted and un-targeted genetic effects according to IAEA and WHO recommendations (1986, 2001, 2011) remains cytogenetic (determination the frequency of chromosome aberrations in human peripheral blood lymphocytes) which until today is considered as official method for emergency and retrospective biological indications and biological dosimetry of radiation human exposure.

In order to increase the preparedness of the world biodosimetric community for large-scale radiation accidents and nuclear terrorism, in 2005 an international network «BioDoseNet» was established under the auspices of the WHO, in which the NRCRM cytogenetic laboratory was incorporated. In this laboratory from September 1986 to nowadays the targeted and untargeted cytogenetic effects of IR in different terms after the Chornobyl disaster were studied.

Research of the *first twenty years* were mainly aimed at establishing the fact of radiation exposure and verification of radiation doses based on the detection of classical targeted cytogenetic effects by the frequency of unstable (dicentrics) and stable (translocatios) chromosome type aberrations, which are specific markers of human radiation exposure. Aberrations of chromatid type were considered as indicators of radiation-induced chromosome instability.

The selective cytogenetic monitoring systematically was conducted among the critical groups of high priority (around 3500 people) exposed in Ukraine to Chornobyl disaster factors of varying intensity – liquidators with different radiation doses including patients recovered from acute radiation sickness; Chornobyl nuclear power plant and Shelter's staff; evacuees; children and adults from areas contaminated by radionuclides; self-settlers from 30-km alienation zone; some professional groups (foresters, tractor drivers), lived and worked in areas of heavy radioactive contamination. In the last decade cytogenetic examination of persons who had occupational contact with ionizing radiation while participated in conversion of the «Shelter» into ecologically safe system was carried out.

Chromosome aberrations were identified using conventional analysis of uniformly stained (as a rule) and differentially GTG stained (selectively) metaphase chromosomes; in some cases (participating in the Ukrainian-American project «Leukemia») used FISH-WCP technique.

The summarized results of these researches allowed the detection of patterns concerning targeted cytogenetic effects in persons of the Chornobyl contingent.

Established, that in all observed groups for about two decades remained the increased level of cytogenetic radiation markers. Mean-group frequencies of targeted radiogenic cytogenetic effects differed depending on the nature, intensity, duration of radiation exposure, time that passed after irradiation, but significantly varying individual cytogenetic parameters under identical radiation exposure depend on age and individual radiosensitivity. The frequency of unstable chromosome aberrations (dicentrics) gradually reduced over time (but with preservation of its residual quantity that exceeded spontaneous level for about 20 years), while stable radiogenic markers (translocations) remained almost at the same level after acute radiation exposure and accumulated under chronic irradiation. Cytogenetic effect does not always positively correlated with official doses of radiation, which could be associated both with the individual peculiarities of the elimination unstable and some part of stable chromosome aberrations as well as with incorrectness of official doses, which was confirmed by us using method FISH – WCP. In all exposed groups the increase of individual and mean-group frequencies of chromatid type aberrations was observed that could be as the result of radiation-induced chromosome instability and, therefore, increased sensitivity of cells to exposure of other mutagenic factors as well as the manifestation of the universal phenomenon «bystander response» – radiation induced bystander effect (RIBE).

The obtained results testified the destabilization of human genome induced by Chornobyl disaster factors. With the passage of time dynamics of radiation-induced somatic chromosome mutagenesis was characterized by gradual change in the frequency and spectra of chromosome abnormalities which allowed to suggest the contribution of not only targeted but also untargeted effects to development of chromosome instability in victims of Chornobyl disaster.

Therefore in the remote terms following Chornobyl disaster arose the need to conduct fundamental investigations for assessment the radiogenic damage of human genome – identifying not only residual mutagenic effects of ionizing radiation in directly exposed targeted cells, but also untargeted effects.

Untargeted effects include various forms of radiation-induced genome instability (delayed, hidden, transmissible) – a phenomenon in which the irradiated cells accumulate over time multiple changes which promote the transition of stable genome of normal cells into unstable genome typical in particular for malignant cells; and also bystander effect – secondary changes in the genome of non-irradiated cells. Suggest that in delayed terms after human radiation exposure exactly these long-term effects can play a leading role in the realization as stochastic (especially cancer) as well as some forms of unstochastic (multifactorial) diseases, that caused priority of research in this area.

In cytogenetic laboratory purposeful research of radiation-induced untargeted cytogenetic effects was conducted *since 2005*.

Developed and used own, adapted and implemented known experimental models for studying the individual radiosensitivity; various forms of radiation-induced chromosomal instability; radiation-induced (RIBE) and tumor-induced (TIBE) bystander effects.

Shown the possibility of expression and persistence of delayed and transmissible chromosomal instability in the offspring of irradiated parents, which confirmed the high sensitivity of the child's body to the mutagenic effect of ionizing radiation. Found not only persistence but also increase of chromosome sensitivity in successive generations of human somatic cells to testing mutagenic exposure in vitro that leading to higher increase the percentage of hypersensitive persons with hidden chromosomal instability. Proved the existence of the association between radiation-modified increase in genetically determined individual sensitivity to the testing mutagenic (chemical and radiation) exposure in vitro and the realization of oncological pathology (on the example of lung cancer) in hypersensitive individuals. Established cytogenetic patterns of induction and persistence of chromosomal instability as a result of RIBE development and the possibility of its modifying by antioxidant vitamin complex (water-soluble form of vitamin A, E and C). Shown synergism between two manifestations of the «bystander response» phenomenon – the presence of TIBE led to the increase in the manifestation of RIBE, which may contribute to the realization of secondary malignancies in cancer patients, complicating the prognosis for health and subsequent survival of such patients. Registered so-called radiation induced rescue effect (RIRE) – the impact of non-irradiated cells on irradiated ones during their long-term co-cultivation, in the realization of which malignant cells are affected by feedback signals from normal cells, that may increase the activation of repair systems in them, thereby reducing the effectiveness of chemical or radiation oncotherapy. Established significant interindividual variability regarding the degree of chromosome damages in each studied untargeted cytogenetic effects and lack of positive correlation between background and induced frequencies of chromosomal aberrations. Found significant differences between the chromosome aberrations spectra when compared targeted and untargeted cytogenetic effects, that confirm the correctness of using for retrospective biodosimetry the human radiation exposure only classical cytogenetic markers of chromosome type. Chromatid-type aberrations are markers of chromosomal instability, which is characteristic for the development of RIBE.

Considering the potential possibility for radiological emergency situations and the threat of nuclear terrorism, the radioprotective properties of astaxanthin (carotenoid from xanthophylls' group) are investigated in cytogenetic laboratory *sinse 2015*.

In the *in vitro* experiments the peculiarities of the modifying effect of astaxanthin on radiation-induced chromosomal injuries depending on the stage of the cell cycle were revealed – the significant weakening of the mutagenic effect of ionizing radiation when exposed to G_0 stage and no radioprotective effect in cells exposed on S and G_2 stages of cell cycle.

However, astaxanthin did not affect the cytogenetic manifestations of RIBE and TIBE, which requires further study. Since 2021 the cytogenetic study of the radiation induced secondary bystander effect (RISBE) and the radiation induced rescue effect (RIRE) was also planned.

Thus, the data obtained indicate an increase in the intensity of somatic chromosome mutagenesis in human not only in the nearest but in the delayed terms (35 years) following the Chornobyl disaster as a result of radiation induced both targeted and untargeted cytogenetic effects, which can be considered as one of the risk factors for the realization of pathology with the genetic component (in particular, malignant transformation of cells) and confirm the need to continue as applied as fundamental cytogenetic studies.

2.9. Effects in immune system

2.9.1. State of the cellular immunity of patients affected by the Chornobyl accident

The results of long-term research studies confirm the role of the immune system in the realization of the long-term effects of the Chornobyl accident on the health of the population, especially Chornobyl clean-up workers. Long-term changes in immunological reactivity in the affected contingents of persons can both aggravate the course of existing diseases and contribute to the induction of new ones. In the remote period after radiation exposure (30–35 years), Chornobyl clean-up workers show changes in the cellular and humoral immunity, this leads to a violation of the anti-infectious immune response, immune surveillance, and support for chronic inflammation.

For 30 years after the Chornobyl accident, Chornobyl clean-up workers and residents from radioactively contaminated areas observed an combined imbalance in the functional state of the immune system, which was determined by changes in membrane structures, cell subset disorganization; disrupted proliferation, functional activity of T-lymphocytes. The revealed changes in the immune system indicate the need to develop new approaches to determining the manifestations of immunological deficiency. To date, studies of immunological reactivity in Chornobyl clean-up workers have acquired a new direction – molecular genetic, but, the study of the features of the functioning of immune system at the cellular level continues and remains important for identifying typical disorders in immune system, which will contribute to improving the results of treatment, primary and secondary prevention.

According to the results of the study of the subset of peripheral blood leukocyte subsets in Chornobyl clean-up workers 33 years after radiation exposure, no significant differences were found in the mean counts of $CD45^{+}14^{-}$ lymphocytes and $CD45^{+}14^{-}$ granulocytes in comparison with the parameters of non-irradiated persons (further – control group). Along with this, it was revealed that the decrease the population of peripheral blood monocytes in Chornobyl clean-up workers has a unidirectional tendency, depending on the radiation dose. In a period of reconstitution of immune system (from 2 to 10 years) monocyte counts were increased and regards as a compensatory protective reaction. So, with an increase in the radiation dose, the count of $CD45^{+}14^{+}$ monocytes decreases. According to the group mean values, the content of $CD45^{+}14^{+}$ monocytes was the lowest in Chornobyl clean-up workers with a radiation dose of $D \geq 500$ mSv, as shown in Fig. 2.20.

However, significant correlations were not found between the radiation dose and the level of monocytes. A dose-dependent decrease in the monocyte population in Chornobyl clean-up workers was also observed 17 years after radiation exposure [221], confirmation of this fact 30 years after irradiation is evidence of the long-term effects of ionizing radiation in immune system and the likelihood of developing neoplastic diseases of the hematopoietic systems in the remote period after radiation exposure.

An analysis of cytometric data on the subset of peripheral blood lymphocytes of Chornobyl clean-up workers showed that in the remote period after radiation exposure (33 years later) the mean counts of T- and B-lymphocytes is within the age norms. Also, in Chornobyl clean-up workers, there was no significant difference in the group mean values of parameters of the main subsets of peripheral blood lymphocytes in comparison with the results of the control group. A correlation analysis showed the presence of a significant positive linear relationship between the relative $CD3^{+}19^{-}$ T-lymphocyte counts and radiation dose ($r = 0.26$; $p < 0.05$) (Fig. 2.21).

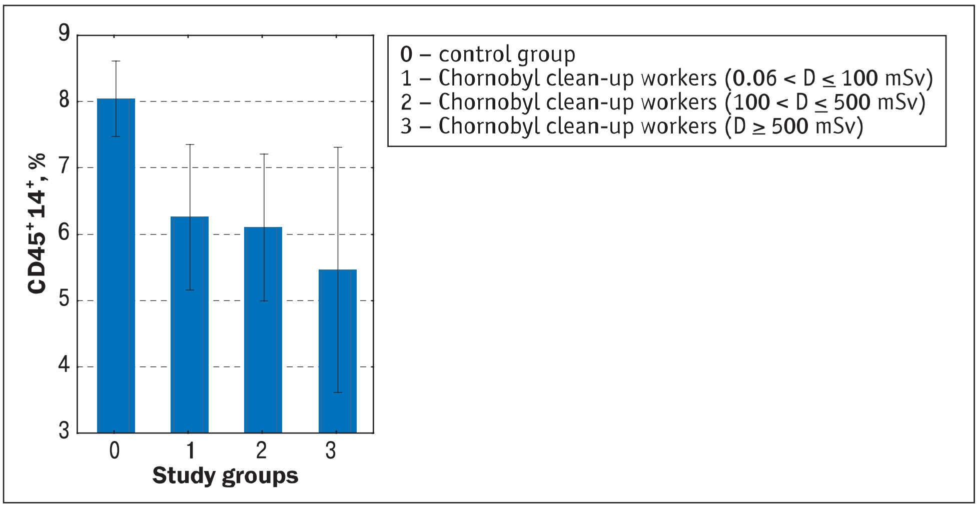

Figure 2.20. The relative $CD45^{+}14^{+}$ monocyte counts in the peripheral blood of persons in the study groups

Table 2.12 presents data on the content and ratio of regulatory subsets of peripheral blood T-lymphocytes – T-helpers/inducers and cytotoxic T-cells in Chornobyl clean-up workers in the remote period after radiation exposure. Despite the fact that a group means values of the relative T-helpers and cytotoxic T-lymphocytes counts are within the normal range, an imbalance of immunoregulatory subsets was determined in persons exposed to ionizing radiation. Against the background of a statistically significant decrease in the count of $CD4^{+}8^{-}$ T-helpers, an increase in the level of $CD8^{+}4^{-}$ cytotoxic T-lymphocytes was determined. Such changes in the subset of helpers/cytotoxic T-lymphocytes lead to a decrease ($p < 0.001$) of the $CD4^{+}/CD8^{+}$ immunoregulatory coefficient to 1.24 in comparison with the parameter of the control group, which was 1.79. The ratio of regulatory populations of T-lymphocytes $CD4^{+}/CD8^{+}$, according to the group mean values of the sample, is at the lower limit of the norm. The revealed violations in the immune system indicate the presence of immunosuppression in Chornobyl clean-up workers in the remote period after radiation exposure (Table 2.12).

In order to establish the contribution of the radiation factor to the formation of immunological deficiency in the remote period after radiation exposure at Chornobyl clean-up workers, an additional detailed analysis of the subset organization of T-lymphocytes, depending on the radiation dose, was performed. A characteristic change in the regulation of the immune response in Chornobyl clean-up workers is the redistribution of subsets of T-helpers and cytotoxic T-lymphocytes. According to the data of the mean values in Chornobyl clean-up workers, a decrease in the content of $CD4^{+}8^{-}$ T-helpers is observe in all exposed subgroups. A statistically significant result in comparison with the control group ($p < 0.001$) was determined in subgroups with a radiation dose ($0.06 < D \leq 100$ mSv) and ($100 < D \leq 500$ mSv). An

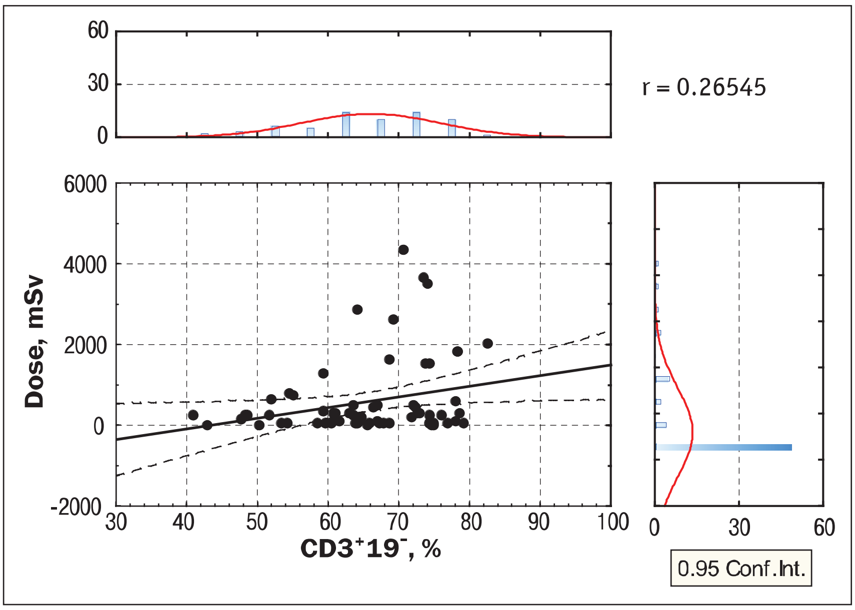

Figure 2.21. Correlation between the relative $CD3^{+}19^{-}$ T-lymphocyte counts and radiation dose in a group of Chornobyl clean-up workers in the remote period after radiation exposure

Table 2.12
The mean counts of subsets of T-lymphocytes in peripheral blood of Chornobyl clean-up workers in the remote period after radiation exposure, (M ± SD), (%)

Group	N	Parameters			
		$CD4^{+}8^{-}$	$CD8^{+}4^{-}$	$CD4^{+}/CD8^{+}$	$CD4^{+}8^{+}$
Control	31	40.75 ± 8.39	23.90 ± 5.38	1.79 ± 0.57	1.34 ± 1.42
Chornobyl clean-up workers	104	33.22 ± 9.95*↓	30.27 ± 9.05*↑	1.24 ± 0.65*↓	1.40 ± 1.35

Note. *$p < 0.001$ vs the control group.

Таблиця 2.13
The relative level of subsets of T-lymphocytes in peripheral blood of Chornobyl clean-up workers in the remote period after radiation exposure, depending on the radiation dose, (M ± SD), (%)

Parameters	Group			
	Control (n = 31)	Chornobyl clean-up workers		
		$0.06 < D \leq 100$ mSv (n = 27)	$100 < D \leq 500$ mSv (n = 24)	$D \geq 500$ mSv (n = 16)
$CD4^{+}8^{-}$ T-lymphocytes	40.75 ± 8.39	32.50 ± 9.26*↓	32.66 ± 10.08*↓	36.45± 10.67
$CD8^{+}4^{-}$ T-lymphocytes	23.90 ± 5.83	30.25 ± 7.96*↑	26.49± 7.23	28.44 ± 9.82
$CD4^{+}/CD8^{+}$ ratio	1.79 ± 0.57	1.16 ± 0.48*↓	1.36 ± 0.65*↓	1.54 ± 0.96
$CD4^{+}8^{+}$ T-lymphocytes	1.34 ± 1.42	1.30 ± 1.00	1.77 ± 1.81	1.79 ± 0.57

Note. *$p < 0.001$ vs the control group.

increase in the relative of $CD8^{+}4^{-}$ cytotoxic T-lymphocytes counts was noted in all subgroups of Chornobyl clean-up workers, a statistically significant difference was determined only in the subgroup with a low dose of radiation ($0.06 < D \leq 100$ mSv). The results are presented in Table 2.12.

A similar tendency of changes was established in the group mean values of the $CD4^{+}/CD8^{+}$ ratio. A decrease of this parameter in relation to the control group was recorded in the subgroups of Chornobyl clean-up workers with a radiation dose of $D \leq 500$ mSv, and in the subgroup $0.06 < D \leq 100$ mSv, this parameter is at the lower limit of the norm (Table 2.12).

The analysis of correlations confirms the obtained result and the fact of a decrease in the $CD4^{+}/CD8^{+}$ ratio in the exposed. A linear dependence of the radiation dose and the redistribution of immunoregulatory subsets has been established. The absolute value of the correlation coefficient $r = 0.25$; $p < 0.05$ (Fig. 2.22).

The presence of an imbalance in the immunoregulatory subsets of lymphocytes was established in a significant number of Chornobyl clean-up workers in the remote period after radiation exposure. In total, among the examined, 66.0 % of persons with an altered $CD4^{+}/CD8^{+}$ ratio were identified. A decrease in the immunoregulatory coefficient (< 1.2)

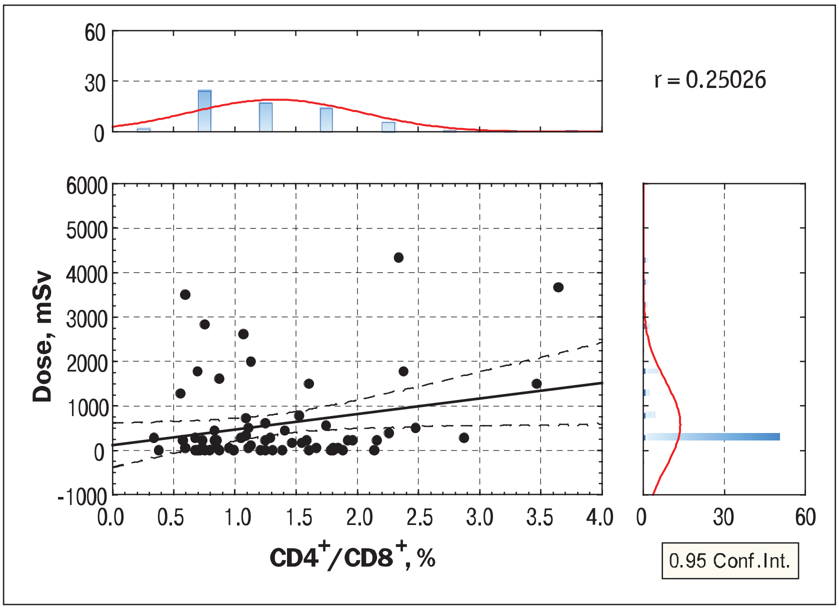

Figure 2.22. Correlation of the immunoregulatory coefficient $CD4^{+}/CD8^{+}$ and radiation dose of Chornobyl clean-up workers in the remote period after radiation exposure

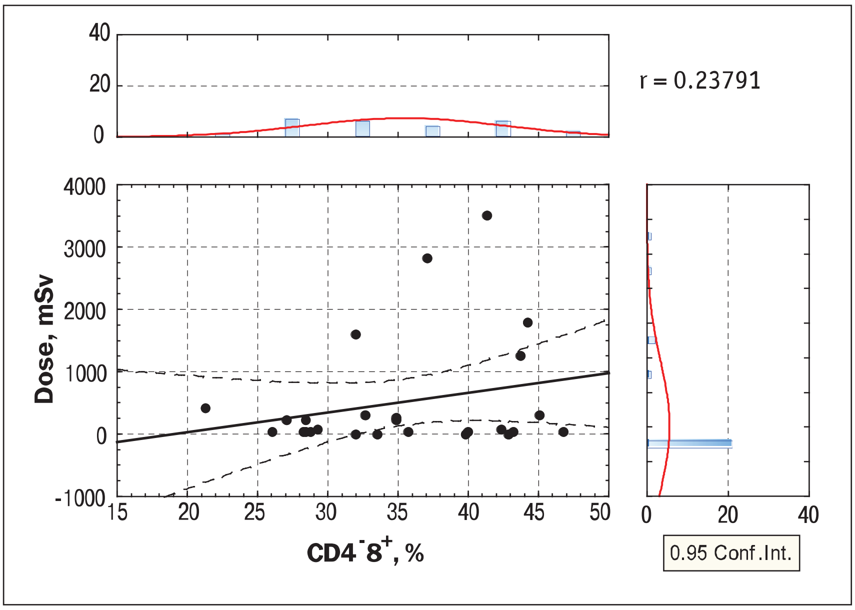

Figure 2.23. **Correlation of the relative level of $CD4^-CD8^+$ T-lymphocytes and radiation dose in Chornobyl clean-up workers, with an immunodeficiency in the remote period after radiation exposure**

was recorded in 56.3 % of persons, of whom the value of the coefficient (≤ 1) was 44.6 % of those with existing immunodeficiency states; ultra-high levels (≥ 2.5) of this parameter were determined in 9.7 % of Chornobyl clean-up workers.

Frequency analysis showed that the immunodeficiency state, a decrease in the $CD4^+/CD8^+$ ratio (≤ 1) prevailed in Chornobyl clean-up workers, exposed in low doses – up to 100 mSv. Thus, in the subgroup with a radiation dose of $0.06 < D \leq 100$ mSv, a decrease of this parameter was determined in 54 %; in the subgroup with a radiation dose of $100 < D \leq 500$ mSv in 27 % and in the subgroup of Chornobyl clean-up workers, exposed in doses of more than 500 mSv – in 19 % of the persons. A decrease in the $CD4^+/CD8^+$ ratio is combined with an increase in the relative content of $CD8^+4^-$ T-lymphocytes in Chornobyl clean-up workers, which have an immunodeficiency state in the remote period after irradiation. In this category of persons, a positive correlation between the radiation dose and the subset of cytotoxic T-lymphocytes ($r = 0.23$; $p < 0.05$) was determined (Fig. 2.23).

The significance of the increase in the level of $CD4^+8^+$ T-lymphocytes in peripheral blood remains unclear, it is thought that $CD4^+8^+$ T-lymphocytes are involved in adaptive immune reactions, including in response to various infectious agents. It is also known that $CD4^+8^+$ T cells inhibit *in vitro* the maturation of dendritic cells and the proliferation of $CD4^+$ T-helpers [222]. The $CD4^+8^+$ T-lymphocytes are detected up to 3 % in peripheral blood of almost healthy people [223]. Their number increases with age [224].

Today, there is only a tendency to an increase in this population in the peripheral blood of Chornobyl clean-up workers, especially in the subgroup with a radiation dose $D > 500$ mSv (Table 2.13). Along with this, a positive correlation was found between the relative level of $CD4^+8^+$ T-lymphocytes and the spontaneous expression of Cyclin D1 in peripheral blood lymphocytes in Chornobyl clean-up workers (Fig. 2.24).

The decrease of expression of activation antigens persists in Chornobyl clean-up workers in the remote period after radiation exposure. The mean values of the activated $CD4^+$ T-helpers with the expression of the receptor to IL-2 in Chornobyl clean-up workers significantly differ ($p < 0.001$) from those in the control group. These data are confirmed by analyzing the count of activated T-lymphocytes depending on the radiation dose. A significant result of a decrease in the relative level of $CD4^+25^+$ T-lymphocytes is observed in all subgroups of Chornobyl clean-up workers, however, the lowest level ($p < 0.001$) of activated T-helpers was identified in the subgroup of Chornobyl clean-up workers, exposed at low doses ($0.06 < D \leq 100$ mSv). At the same time, against the background of a decrease $CD4^+25^+$ T-helpers, a decrease in the percentage of activated $CD4^-25^+$ cytotoxic T-lymphocytes and $HLA\text{-}DR^+$ B-lymphocytes was determined in the subgroup of Chornobyl clean-up workers, exposed at doses ≥ 500 mSv. This may be due to a deficiency in the synthesis of IL-2, impaired reception and cell interaction, and indicate a decrease in the functional properties of T- and B-lymphocytes. Table 2.14–2.15 shows the results of

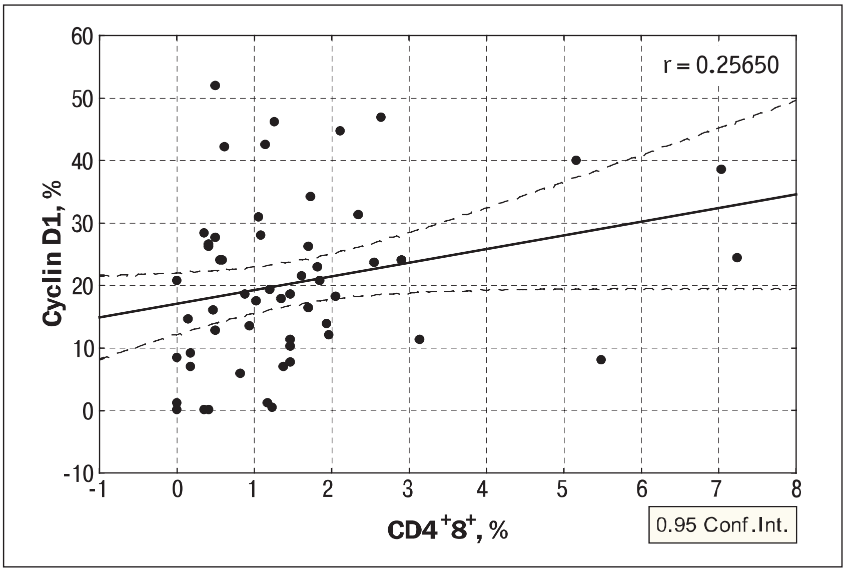

Figure 2.24. **Correlation between the $CD4^{+}8^{+}$ T-lymphocyte counts and the expression of Cyclin D1 in the lymphocytes of the peripheral blood of Chornobyl clean-up workers in the remote period after radiation exposure**

studies of the content of activated peripheral blood lymphocytes of Chornobyl clean-up workers in the remote period after radiation exposure (33 years later) and depending on the radiation dose.

Thus, the violations of the immune status are persist in Chornobyl clean-up workers in the remote period after radiation exposure (30–33 years after the accident) in a wide range of doses of 0.06–4310 mSv. The subset of peripheral blood leukocytes is characterized by a stable level of $CD45^{+}14^{-}$ lymphocytes and granulocytes with a decrease in the relative count of $CD45^{+}14^{+}$ monocytes. An imbalance of immunoregulatory subsets of T-lymphocytes, signs of immunosuppression with a decrease in the $CD4^{+}/CD8^{+}$ ratio, which is combined with a dose-dependent ($r = 0.23$; $p < 0.05$) increase in the relative level of cytotoxic T-lymphocytes, were revealed. Immunodeficiency state, according to the $CD4^{+}/CD8^{+}$ ratio (< 1.2), was found in 56.3 % of the Chornobyl clean-up workers, mainly in the subgroup with a low radiation dose of $0.06 < D \leq 100$ mSv. There was a tendency to an increase $CD4^{+}8^{+}$ T-lymphocytes, especially in the subgroup with a radiation dose $D > 500$ mSv and a positive correlation dependence ($r = 0.23$; $p < 0.05$) between the count of $CD4^{+}8^{+}$ T-lymphocytes and expression of Cyclin D1 in peripheral blood lymphocytes of Chornobyl clean-up workers, which probably contributes to the

Table 2.14

The relative level of activated T- and B-lymphocytes in peripheral blood of Chornobyl clean-up workers in the remote period after radiation exposure, (M ± SD), (%)

Group	N	Parameters			
		$CD3^{+}HLA\text{-}DR^{+}$	$CD4^{+}25^{+}$	$CD4^{-}25^{+}$	$CD3^{-}HLA\text{-}DR^{+}$
Control	31	5.65 ± 2.89	2.86 ± 2.40	1.18 ± 0.92	13.80 ± 11.70
Chornobyl clean-up workers	104	5.99 ± 3.57	1.12 ± 1.71**↓	0.87 ± 1.38	10.31 ± 5.26*↓

Notes. *$p < 0.01$; **$p < 0.001$ vs the control group.

Table 2.15

The relative level of activated T- and B-lymphocytes in peripheral blood of Chornobyl clean-up workers in the remote period after radiation exposure, depending on the radiation dose, (M ± SD), (%)

Parameters	Group			
	Control (n = 31)	Chornobyl clean-up workers		
		$0.06 < D \leq 100$ mSv (n = 27)	$100 < D \leq 500$ mSv (n = 24)	$D \geq 500$ mSv (n = 16)
$CD3^{+}HLA\text{-}DR^{+}$	5.65 ± 2.89	5.84 ± 3.38	5.78 ± 3.91	5.92± 2.44
$CD4^{+}25^{+}$	2.86 ± 2.40	0.64 ± 0.62**↓	0.86± 2.22*↓	0.94 ± 0.64*↓
$CD4^{-}25^{+}$	1.18 ± 0.92	0.61 ± 0.63	1.26 ± 2.23	0.22 ± 0.009*↓
$CD3^{-}HLA\text{-}DR^{+}$	13.80 ± 11.70	10.20 ± 6.18	10.20 ± 4.78	10.96 ± 5.40

Notes. *$p < 0.05$; **$p < 0.001$ vs the control group.

inhibition of the proliferation of $CD4^+$ T-helpers and the formation of immunological deficiency.

Characteristic changes in the immune system of persons exposed at doses D > 500 mSv are the presence of an imbalance in TCR^+ subsets of immunocompetent cells and decrease in the relative levels of activated T- and B-lymphocytes. Changes in the T-cell mediated immunity depend on the radiation dose.

The results of the study supplement the available data on violations in the immune system of Chornobyl clean-up workers, exposed to radiation in the dose range from 0.06 to 4310 mSv, which allows to trace the dynamics of immunological changes and the recovery rate of the immune system. The detected immunological changes in Chornobyl clean-up workers are the rationale for dynamic monitoring of this category of persons for diagnosis of immunodeficiency conditions including cancer and lymphoproliferative diseases. The obtained data should be taken into account when assessing the individual sensitivity of people to radiation exposure, taking into account their age. Monitoring is in need of the state of the immune system of Chornobyl clean-up workers in the remote period after radiation exposure to develop new and improve existing approaches to prevention, treatment and monitoring of diseases in this cohort of persons.

2.9.2. Implementation of new biological markers in diagnostics of effects of ionizing radiation in human immune system

Ionizing radiation exposure could induce substantial effects to human health. The negative experience gained after accidents in Chornobyl and Fukushima clearly demonstrates a critical need to search for sensitive biological markers for retrospective individual doses estimates that could be extremely important not only for determining treatment pathways, but for prognosis of the remote stochastic effects such as genomic instability or cancer [225].

Several technologies of biological dosimetry are used now: chromosome dicentrics assay is regarded as a «golden standard» for dose estimates; micronuclei cytokine block; multicolor fluorescence hybridization *in situ* analysis of chromosome translocations [226, 227]; analysis of a phosphorylated form of histone H2AX expression and gene expression profiles. Determination of dicentric chromosomes and complex chromosomal abnormalities is difficult, time consuming; some of the methods are currently under development, which delays their use in emergency radiation situations. There is an urgent need to develop markers suitable for biological dosimetry in the early period after a low dose exposure and in the remote period after irradiation.

Gene expression as a biological marker of the long-term effects of ionizing radiation

The effects of ionizing radiation lead to the activation of signal transduction pathways and associated changes in gene expression. The study of changes in gene expression at the early period after radiation exposure is one of the ways to provide a faster estimate of individual doses, which is based on the determination of changes at the level of RNA transcripts [228, 229]. Some studies suggest the development of gene expression profiles in peripheral blood lymphocytes as an alternative approach in radiation biodosimetry [230, 231], which can easily provide identification of promising molecular biomarkers [232, 233]. Recent studies have shown that the gene signature induced by ionizing radiation is specific, long-lasting and accurate in dosimetric estimate in both mice and humans [234, 235]. Most of these studies used peripheral blood cells (peripheral blood mononuclear cells, whole blood, cultured lymphocytes) using polymerase chain reaction (PCR). Thus, gene expression is sensitive to the effects of ionizing radiation. Today, there is a sufficient data to recommend the analysis of gene expression profiles in peripheral blood lymphocytes in order to search for biomarkers of the long-term effects of ionizing radiation.

Genes-markers of long-term effects of radiation

Over the past 10 years, the laboratory of immunocytology of the NRCRM has studied the expression of genes that are involved in the regulation of DNA repair processes, cell cycle, apoptosis, cell aging and immune response: *TP53, TP53I3, FASLG, BAX, BIRC5, NFKB1, NFKB2, TERF1, TERF2, TERT, DDB2, BRCA1, TGFBR1, CDKN1B, CDKN2A, CCND1, CDKN1A, MKNK2, MADD, MAPK14, CSF2, VEGFA, CLSTN2, GSTM1, IFNG, IL1B, MCF2L, SERPINB9, STAT3*. Exposed group con-

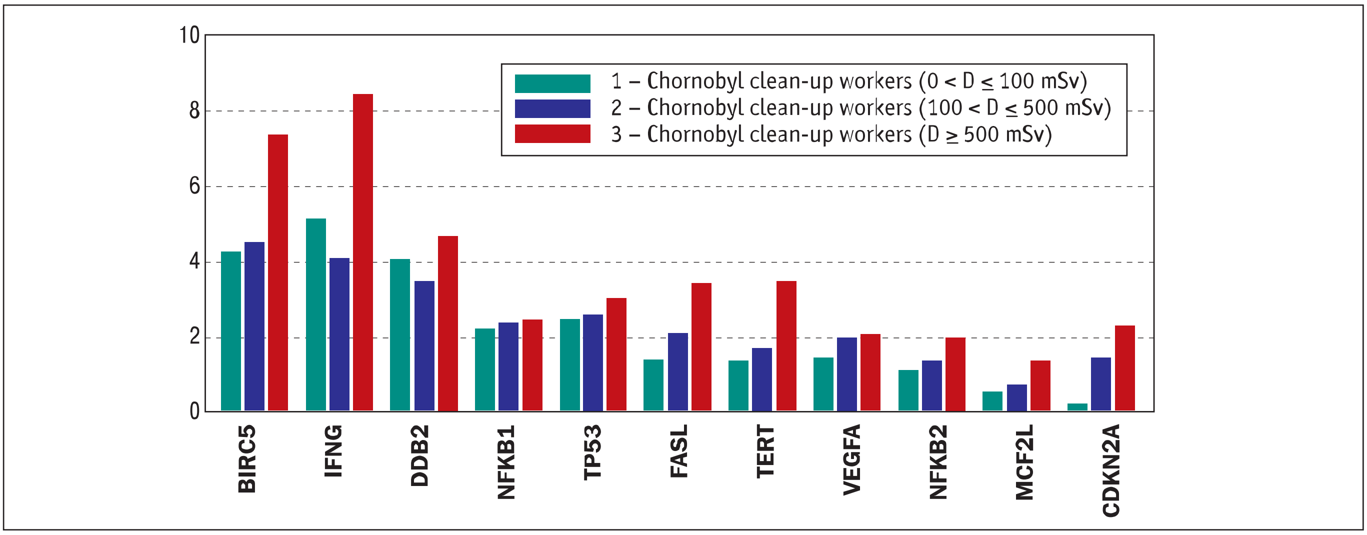

Figure 2.25. **Overexpression of candidate genes associated with the effects of ionizing radiation**

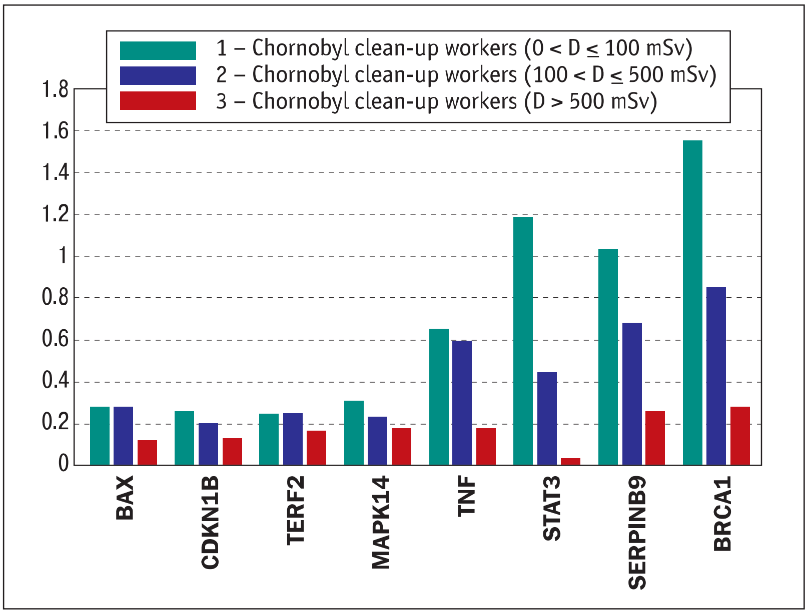

Figure 2.26. **Decreased expression of candidate genes associated with the effects of ionizing radiation**

sisted from Chornobyl clean-up workers. To determine the effects of radiation, the exposed group was divided according to radiation doses: up to 100 mSv (I subgroup); 100–500 mSv (II subgroup) and over 500 mSv (III subgroup).

To determine the effects of ionizing radiation , it is recommended to study the expression of *TP53, FASLG, BIRC5, NFKB1, NFKB2, TERT, DDB2, CDKN2A, VEGFA, IFNG, MCF2L*, genes, demonstrating a dose-dependent overexpression (Fig. 2.25), and *BAX, TERF2, BRCA1, MAPK14, STAT3, TNF, SERPINB9* genes, the expression level of which in the remote period after radiation exposure is decreased with an increase of radiation dose (Fig. 2.26).

The basis for the development of immunological deficiency and an increased risk of cell transformation in the remote period after radiation exposure are dose-related disorders of gene regulation of the main homeostatic mechanisms of the cell. There were established an imbalance in the expression of pro- and anti-apoptotic genes (*TP53, TP53I3, FASLG, BAX, BIRC5*) and incompleteness of the apoptosis process in the dose range over 500 mSv; cell senescence and TERT associated risk of transformation of immunocompetent cells through TP53-mediated regulation; violations of cyclin-kinase regulation of the cell cycle, differentiation and signal transduction (*CCND1, CDKN1A, CDKN2A, CDKN1B, TGFBR1, MAPK14*) [236].

Table 2.16 presents generalized results of studies that demonstrate changes in gene expression, which was found in peripheral blood leukocytes of Chornobyl clean-up workers in the remote period after radiation exposure (30 years ago) in different dose range.

Table 2.16
Changes in gene expression in Chornobyl clean-up workers in the remote period after radiation exposure (30 years ago) in different dose range

Dose range, mSv	Increased gene expression	Decreased gene expression	Significantly altered gene expression ($p < 0.05$)
≤ 100	*TP53, TP53I3, DDB2, NFKB1*	*MADD, FASL, MKNK2, TER1, TERF2, BRCA1, MAPK14, GFBR1, CCND1, DKN1A, CDKN1B*	*MKNK2, TERF1, TERF2, DDB2, TGFBR1, CCND1, CDKN1A, CDKN1B*
100–500	*TP53, TP53I3, FASLG, TERT, DDB2, NFKB1, VEGFA, MCF2L*	*MADD, MKNK2, TERF1, TERF2, BRCA1, NFKB2, MAPK14, GFBR, CCND1, DKN1A, CDKN1B, IL1B, STAT3*	*TERF1, TERF2, BRCA1, FKB1, NFKB2, MAPK14, TGFBR1, DKN1A, CDKN1B*
> 500	*TP53, TP53I3, BIRC5, BAX, BIRC5, FASLG, TERT, DDB2, CSF2, VEGFA, MCF2L, IFNG*	*BAX, MADD, MKNK2, TERF1, TERF2, BRCA1, MAPK14, GFBR1, CCND1, DKN1A, CDKN1B, DKN2A, IL1B, CLSTN2, STAT3*	*TP53, BAX, BERC5, FASL, MADD, TERF2, TERT, BRCA1, DDB2, NFKB1, MAPK14, GFBR1, CDKN1B, DKN2A, MCF2L, IFNG, IL1B, CLSTN2, STAT3*

Genes-markers of professional radiological exposure
The introduction of innovative technologies leads to an increase in dose loads during professional and medical exposure. It is important to determine biological markers that increase the efficiency of diagnostics of radiation effects and professional selection. The professional groups requiring such an approach, first of all, include the staff of the 30-kilometer zone, in particular, the Chornobyl Nuclear Power Plant industrial site. Research carried out by the NRCRM contributes to consensus on the genetic mechanisms of response to radiation exposure within professional limits, including the incorporation of transuranic elements.

Changes in the human genome due to the action of low-dose ionizing radiation could alter signal transduction, apoptosis, proliferative activity, and the intensity of cell senescence. The direction of changes in gene expression is different; there is a certain threshold of changes in expression. The general picture of changes in professional radiation exposure up to 35 mSv – inhibition of gene expression, while at an integrated radiation dose over 35 mSv, most of the studied genes are overexpressed [237].

BAX, BIRC5, CDKN1B, CSF, DDB2, NFKB2, TERF1 and *TERF2* genes are overexpressed at doses up to 35 mSv and show increased expression at doses above 35 mSv. The expression of genes *BRCA1, CCND1, CDKN1A, CDKN2A* and *VEGFA* is also reduced at radiation doses higher than 35 mSv (Table 2.13). One of the key markers is a decrease in *BRCA1* gene expression after irradiation at doses up to 35 mSv. This gene and the protein of the same name are involved in DNA repair, regulation of the cell cycle, and maintenance of genetic stability [238]. Changes in *BRCA1* on the background of decreased expression of the *CDKN1A* indicate a decrease in genetic control, dysregulation of DNA repair, and activation of proliferative activity.

An overexpression was demonstrated of genes involved in the regulation of apoptosis and stress response – *TP53, MAPK14*, as well as the gene-regulator of the immune response *NFKB1* after radiation exposure at doses up to 35 mSv (Table 2.17). Changes in *NFKB* gene expression have been described in autoimmune diseases, cancer transformation, and persistent viral infections. Overexpression of the *DDB2* gene can also be associated with the activation of adaptive processes. One of the effects of radiation is changes in the expression of genes that regulate telomere length, telomere-telomerase complex and cell senescence – *TERF1, TERF2, TERT* (Table 2.17). The expression of these genes was suppressed at doses up to 35 mSv, while overexpression of the *TERT* gene was found at a dose above 35 mSv, the activity of which contributes to the uncontrolled elongation of telomeric sequences characteristic of malignant transformed cells. The *TP53* gene was overexpressed at different dose ranges (Table 2.17).

Correlations between RQ of gene expression and professional radiation dose for *BAX, CCND1, CDKN1B, CDKN2A, DDB2, MKNK2, TERF2, TP53, FASLG* genes were established in a group of Chornobyl Shelter staff; for genes *MKNK2, CDKN1B, NFKB1, CSF2, FASLG, TERF2* at a radiation dose < 35 mSv; for genes *BRCA1, CCND1, CDKN1A* – at a radiation dose > 35 mSv [237].

Thus, at professional exposure in doses exceeding 35 mSv, markers are defined of a changed gene regulation of cell senescence of immune cells: a tendency to decrease the relative quantity of *TERF1* and *TERF2* expression associated with upregulation

Table 2.17
Changes in gene expression during professional exposure

Dose range, mSv	Increased gene expression	Decreased gene expression	Significantly altered gene expression ($p < 0.05$)
2.16–84.16	*TP53, CDKN1B, CSF2, DDB2, MAPK14, MKNK2, NFKB1, NFKB2*	*BAX, BIRC5, BRCA1, CCND1, CDKN1A, CDKN2A, FASLG, MADD, TERF1, TERF2, TERT, TGFBR1, TP53I3, VEGFA*	*BRCA1, CCND1, CDKN1A, CDKN2A, VEGFA, FASLG*
< 35	*TP53, MAPK14, NFKB1*	*BAX, BIRC5, CSF2, DDB2, BAX, BIRC5, BRCA1, CCND1, CDKN1A, CDKN2A, CDKN1B, MADD, NFKB2, TERF1, TERF2, TERT, TGFBR1, TP53I3, VEGFA*	*BRCA1, CCND1, CDKN1A, CDKN2A, VEGFA*
> 35	*TP53, TP53I3, BAX, BIRC5, CDKN1B, CSF, DDB2, MAPK14, MKNK2, NFKB1, NFKB2, TERT*	*CCND1, CDKN2A, FASLG, MADD, TGFBR1, VEGFA, TERF1, TERF2*	*TP53, DDB2*

of *TERT* gene; at professional exposure in doses up to 35 mSv, marker processes are changes in the gene regulation of adaptive and reparative processes: inactivation of *BRCA1*-mediated DNA repair and regulation of cell cycle pathways, overexpression of *DDB2* gene; a decreased expression of the *TGFBR1* gene regulator of signal transduction, an imbalance in the control system of the main checkpoints of the cell cycle (decreased expression of the *CCND1, CDKN1A, CDKN1A, CDKN2A*); tension in the antitumor surveillance system: overexpression of the *TP53* gene.

The results indicate that impaired expression of genes that regulate signal transduction, proliferative activity, cell senescence and apoptosis can be used as biological markers of the effects of professional radiation exposure.

Proteomic biomarkers of ionizing radiation

The identification of radiation-associated protein biomarkers is a difficult task due to the time and dose variability of their expression levels. Numerous proteomic studies of disorders of protein levels after exposure to high doses of ionizing radiation in various biological fluids, in particular, in urine, blood serum, etc., dedicated to the identification of biological markers of exposure and sensitivity to radiation and can be used in radiation emergencies [239–241]. To investigate the mechanisms underlying individual sensitivity, S. Skiold et al. (2015) compared protein profiles in peripheral blood leukocytes irradiated ex vivo with 0.1 and 150 mGy in persons with different radiosensitivity. Proteomic analysis showed a unique «protein signature» in different examined groups. This suggested that the response to oxidative stress, coagulation and the acute phase of the response are markers in determining radiosensitivity [242]. Despite the fact that studies devoted the effects of low doses of ionizing radiation on the protein balance remain few, such data show that the effects of high doses of radiation lead to detected changes in biological fluids, which may be marker when exposed to low doses. The following questions remain unresolved: whether protein imbalances are radiation-associated, unique, and not due to the general physiological state, in particular inflammation; whether the marker is protein balance when exposed to low doses of ionizing radiation.

A study was perforemed in the laboratory of immunocytology of the NRCRM of the intracellular expression of Cyclin D1, a protein-regulator of the cell cycle and proliferation, and gamma-H2AX histone a marker of double DNA breaks.

Expression of cytoplasmic protein Cyclin D1 in peripheral blood lymphocytes as a marker of early and late effects of radiation

Cyclin D1 protein is a product of *CCND1* gene and is part of the molecular complex Cyclin D1–CDK4 that phosphorylates Rb and specifically regulates cell cycle during G_1/S–phase transition. Acute irradiation at high doses > 10 Gy reduces *CCND1* expression and triggers the proteosomal ubiquitin-dependent degradation mechanism of Cyclin D1 to provide the blocking of the cell cycle in the G_1/S-phase [243]. Low doses of ionizing radiation (100–250 mGy) induce an increase in Cyclin D1 expression, which promotes cell proliferation [244]. Excessive levels of Cyclin D1 primarily at the G_1/S-checkpoint and in the S-phase, due to chronic exposure at low doses (500 mGy), induce the formation of DSBs [245]. Cyclin D1 is considered as a biomarker for assessing the effects of long-term exposure to low doses of radiation [246], cell senescence [247] and risks of oncogenesis [248].

A dose-dependent overexpression of the cytoplasmic protein Cyclin D1 was determined in peripheral blood lymphocytes; the highest mean values of the relative level of Cyclin D1 were recorded at doses exceeding 35 mSv in the early period after professional exposure to low doses of radiation. The strength of the «dose-effect» correlation increases at doses above 35 mSv ($r = 0.69$; $p < 0.05$), while in the range up to 35 mSv, the correlation between the radiation dose and Cyclin D1 expression was not found.

The study of *CCND1* gene expression and the spontaneous level of Cyclin D1 in the peripheral blood lymphocytes of Chornobyl clean-up workers showed a decrease in *CCND1* expression and an increase the level of Cyclin D1 in the remote period after exposure. The maximum increase in the spontaneous expression of Cyclin D1 was found at a dose of ≥ 500 mSv (Fig. 2.27), which was accompanied by a violation of Cyclin D1-dependent regulation of the cell cycle of peripheral blood lymphocytes after mitogen activation (Fig. 2.28). The decrease PHA-induced expression of Cyclin D1 in lymphocytes reflects the narrowing of the ability to respond to additional stimulation.

The increase in the level of Cyclin D1 in the remote period after exposure is probably due to the inactivation of the mechanisms of its degradation. At ultrahigh levels of spontaneous expression of Cyclin D1 in peripheral blood lymphocytes, patients are included in the risk groups for the development of long-term effects of radiation.

The combination of increased spontaneous expression of Cyclin D1 in peripheral blood lymphocytes of Chornobyl clean-up workers with a decrease in response after PHA stimulation reflects changes in the regulation of lymphocyte proliferation and cell cycle, possibly to provide a block of the cell cycle at the G_1/S checkpoint, initiation of senescence and apoptosis of defective cells in G_1/S phase of the cell cycle and persistence of DSBs in the remote period after radiation exposure as a manifestation of genome instability.

Cyclin D1 can be a biological marker for assessing both medical effects associated with ionizing radiation, and an additional indicator of biodosimetry during professional or accidental exposure.

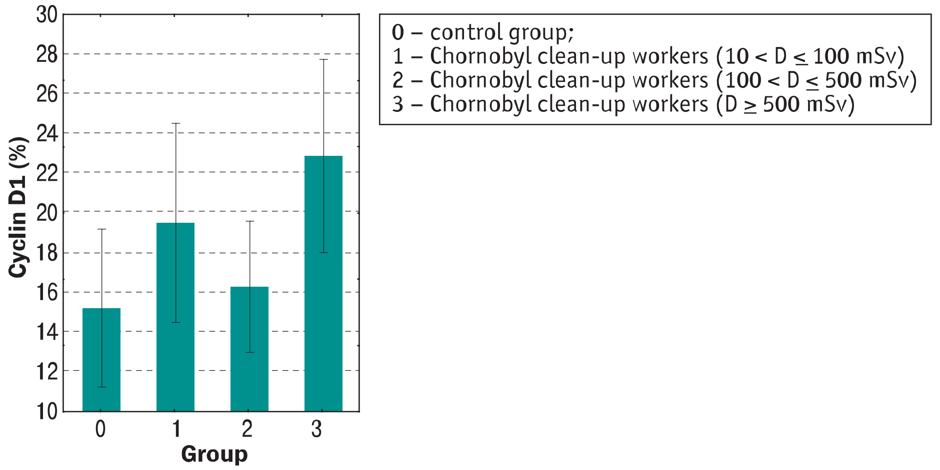

Figure 2.27. **Relative level of spontaneous Cyclin D1 expression in peripheral blood lymphocytes of persons from the study groups**

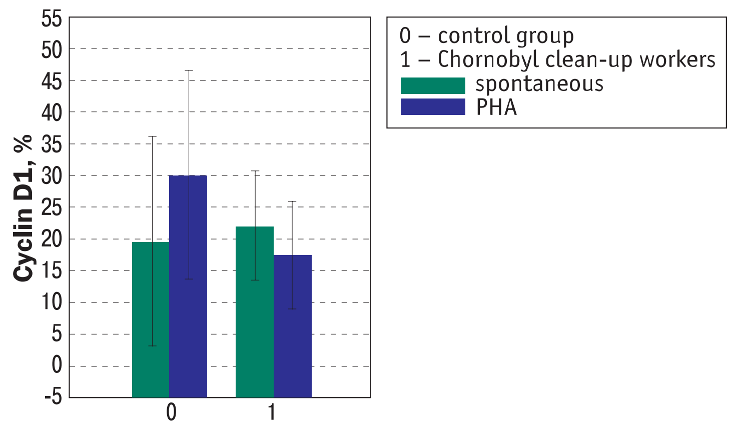

Figure 2.28. **Relative level of spontaneous and mitogen-induced Cyclin D1 expression in peripheral blood lymphocytes of persons from the study groups**

Phosphorylated form of histone H2AX is a biological marker of radiation exposure

Histone H2AX is a variant of histone H2A, which is phosphorylated by serine 139 due to the presence of DSBs, the emergence of which is caused by the action of negative factors, including ionizing radiation [249]. The phosphorylated form of H2AX (γ-H2AX) accumulates in regions of chromosomes with double breaks and is considered as an additional marker of chromosomal abnormalities [250]. Despite the rapid kinetics of the formation of γ-H2AX loci and their disappearance within 6–8 hours, γ-H2AX is considered a reliable marker of DSBs, with high sensitivity to ionizing radiation [251, 252]. Analysis of the intracellular expression of γ-H2AX may be more useful as a biological indicator of radiation exposure than a biodosimeter.

A research is been performed during last 10 years in the laboratory of immunocytology of the NRCRM on the intracellular expression of histone γ-H2AX in peripheral blood lymphocytes of Chornobyl clean-up workers by flow cytometry, and the substantial changes in expression of the phosphorylated form of histone H2AX have been determined in clean-up workers exposed in a dose range of 500–1000 mSv (Fig. 2.29).

Thus, there is a tendency to an increase the expression of the phosphorylated form of histone γ-H2AX in peripheral blood lymphocytes of Chornobyl clean-up workers, exposed to 500–1000 mSv, may reflect the inefficiency of the repair mechanisms and the presence of secondary genome instability in the remote period after radiation exposure.

Telomere length as a biomarker of radiation exposure

Telomere length varies on an individual level and decreases with age. Cells with short or damaged telomeric sequences are characterized by increased genetic instability, which may play a role in carcinogenesis. Many studies have demonstrated a strong correlation between telomere length and radiosensitivity both *in vitro* and *in vivo* [253]. Therefore, the determination of telomere length and telomere dysfunction is important in predicting individual radiosensitivity and long-term risks of the development of pathological conditions that may arise as a result of ionizing radiation [254, 255].

The main methods for determining telomere length are real-time PCR and fluorescence *in situ* hybridization-flow cytometry (flow-FISH). The sensitivity of the methods differs insignificantly, while the flow-FISH method allows combining the investigation of telomere length with subset and cell cycle analysis, that gives advantage in the diagnosis of the effects of radiation.

Long-term studies of the relative telomere length in peripheral blood leukocytes of Chornobyl clean-up workers by the flow-FISH, carried out at the NRCRM, confirmed the assumption of relationship between changes in telomere length and radiation dose in the remote period after radiation exposure (Table 2.18).

The radiation-induced shortening in leukocyte telomere length was determined in the acute radiation syndrome survivors, exposed to doses of more than 500 mSv, and, to a lesser extent, in other groups of exposed. Telomere shortening of chromosome regions may be a signal that triggers cell senescence. The presence of replicative aging leads to a decrease in the efficiency of the system that detects DNA damage and is involved in the repair of genomic DNA. Such errors in DNA repair system in the remote period after radiation exposure can lead to clinical pathology, such as malignant transformation, and serve as a sign of genomic instability. The study was conducted of the expression of genes that regu-

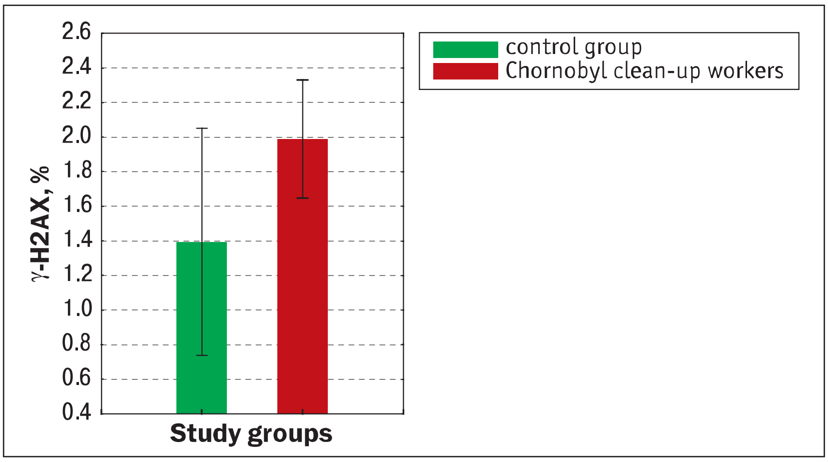

Figure 2.29. **Relative level of expression of histone γ-H2AX in peripheral blood lymphocytes of persons from the study groups**

Таблиця 2.18
The relative telomere length in peripheral blood leukocytes of Chornobyl clean-up workers, depending on the radiation dose, (M ± SD, in conventional units)

Parameter	Group		
	Control (n = 21)	Chornobyl clean-up workers	
		0.64 < D ≤ 500 mSv (n = 39)	D ≥ 500 mSv (n = 12)
RTL	17.22 ± 1.70	15.57 ± 3.63	15.47 ± 2.02*

Note. *p ≤ 0,01 vs the control group.

late the length of the telomere-telomerase complex *TERT*, *TERF1* and *TERF2* in the peripheral blood leukocytes of Chornobyl clean-up workers [237].

The factors that modulate the dose-effect dependence include a presence of somatic and psychosomatic pathology, upregulation of *TERT* gene; that encodes telomerase reverse transcriptase. Radiation-induced inhibition of the expression of T-loop inhibitors *TERF1* and *TERF2* genes, that is detected in the remote period after radiation exposure, can initiate the activation of the mechanisms of early replicative aging of leukocytes, and under conditions of overexpression of the *TERT*, it can be a factor of cell transformation.

Thus, the introduction of modern molecular technologies allows us to propose the latest biological markers of radiation dose, the introduction of which will increase the efficiency of biological dosimetry and identification of radiation effects in the range of low doses and dose rates, including during irradiation within professional limits. Based on the results of the NRCRM research and international experience, recommendations have been developed for the introduction of functional biological markers – gene expression, telomere length, as well as the content of intracellular proteins that are involved in the epigenetic regulation of nuclear processes – transcription, replication and repair [237]:

➤ The biological markers of doses up to 100 mSv are changes in the gene expression of *MKNK2, TERF1, TERF2, DDB2, TGFBR1, CCND1, CDKN1A, CDKN1B* and the relative length of telomeres; in the dose range from 100 to 500 mSv are gene expression of *TERF1, TERF2, BRCA1, NFKB1, NFKB2, MAPK14, TGFBR1, CDKN1A, CDKN1B*, relative telomere length and spontaneous expression of Cyclin D1 protein; at doses over 500 mSv are gene expression of *TP53, BAX, BIRC5, FASL, MADD, TERF2, TERT, BRCA1, DDB2, NFKB1, MAPK14, TGFBR1, CDKN1B, CDKN2A, MCF2L, IFNG, IL1B, CLSTN2, STAT3*, relative telomere lengths and expression of histone γ-H2AX in the remote period after radiation exposure.

➤ It is recommended to use biological markers – expression of genes *BRCA1, CCND1, CDKN1A, CDKN2A, VEGFA*, relative telomere length, spontaneous expression of Cyclin D1 protein and histone gamma-H2AX after professional radiation exposure at doses not exceeding the established limits. It is recommended to use biological markers – expression of *TP53, DDB2* genes, relative telomere length, and spontaneous expression of Cyclin D1 protein and histone γ-H2AX after professional radiation exposure at doses of more than 35 mSv.

➤ The recommended biological markers are a supplement to the existing cytogenetic methods of dose assessment in the early period after exposure and an alternative to them in chronic exposure within professional limits, or in the remote period after radiation exposure, when most of the existing cytogenetic methods are insufficient.

2.9.3. Radiation-induced changes in gene expression associated with non-tumor effects of remote period after radiation exposure in Chornobyl clean-up workers

The problem of the effects of low doses radiation on human health after the Chornobyl accident isn't resolved, as there is no certainty about the effect of low doses radiation on the risk of developing non-cancer diseases, in particular, bronchopulmonary (BPP) and cardiovascular pathology (CVD), which, along with cancer, occupy the first place in the structure of mortality of exposed population. More evidence is needed to conclude whether radiation exposure is a factor that increases the incidence of non-cancer diseases and mortality. Gene expression is a sensitive indicator of both somatic disorders in the human body and radiation exposure, and the implementation of modern genomic technologies may shed light on the relationship between radiation dose, genetic changes and the occurrence of non-cancerous pathologies.

During the last decade, the laboratory of immunocytology of the NRCRM has been conducting molecular genetic studies of radiation-associated disorders of gene expression in Chornobyl clean-up workers and obtained intermediate results and a number of conclusions.

Gene expression in peripheral blood leukocytes of Chornobyl clean-up workers with bronchopulmonary pathology

The analysis of gene expression in peripheral blood leukocytes of Chornobyl clean-up workers with the main diseases of the respiratory system (chronic bronchitis, CB; chronic obstructive pulmonary disease, COPD) showed an overexpression of genes *BCL2, CSF2, CLSTN2, ILB, TNF, CDKN2A* in groups of patients with chronic bronchitis and elevated mean values of RQ in the group of workers with *COPD*. The overexpression of *TP53* and *GSTM1* genes was detected only in a group of Chornobyl clean-up workers with chronic bronchitis. A decrease in group mean values of RQ of the *SERPINB9, MCF2L* was found in the group of patients with chronic bronchitis with the lowest mean figures in the group of patients with COPD [256].

The association of «gene–disease» was determined on statistical models stratified separately for each disease and gene. Logistic regression was used to calculate odds ratio (OR). To identify the features of gene regulation in certain types of somatic pathology, radar diagrams were constructed, which are an attempt to identify and compare the main signaling pathways in which overexpressed genes are involved. Each axis of the diagrams is a representation of the percentage of pathway activation frequencies that are derived from enhanced and overexpressed genes.

Assessing the ratio of chances between gene expression and the development of respiratory pathology in Chornobyl clean-up workers revealed a close associative relationship between the development of CB/COPD and changes in gene expression (OR > 1) *CLSTN2, GSTM1, SERPINB9, TERF2, TERT, TNF, TP53, VEGFA*. The radar diagrams (Fig. 2.30, 2.31) show the received data on the percentage of frequencies of activation genetic pathways, which are obtained from enhanced and overexpressed genes in Chornobyl clean-up workers with pulmonary pathology. The activation of genes that regulate the immune response was confirmed in both CB and COPD; activation of genes that regulate angiogenesis and cell differentiation in COPD, activation of genes that regulate cell adhesion in CB and COPD, as well as genes that regulate telomere length and cell aging in COPD, in the group of Chornobyl clean-up workers [256].

Changes in gene expression in peripheral blood leukocytes of Chornobyl clean-up workers with cardiovascular diseases

It was studied of the changes in gene expression in peripheral blood leukocytes of the Chornobyl clean-up workers with CVD, namely CHD (coronary heart disease) and AH (arterial hypertension). An

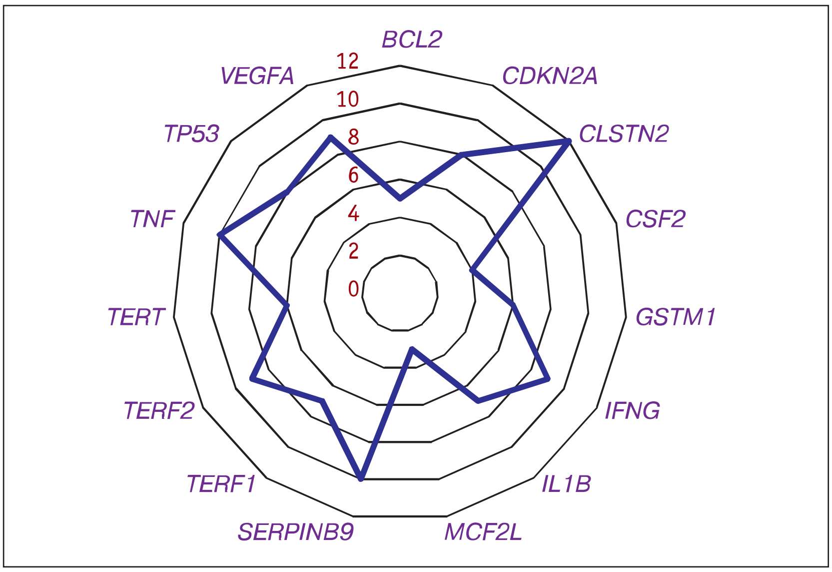

Figure 2.30. Enhanced and overexpression of genes in peripheral blood leukocytes of Chornobyl clean-up workers with CB

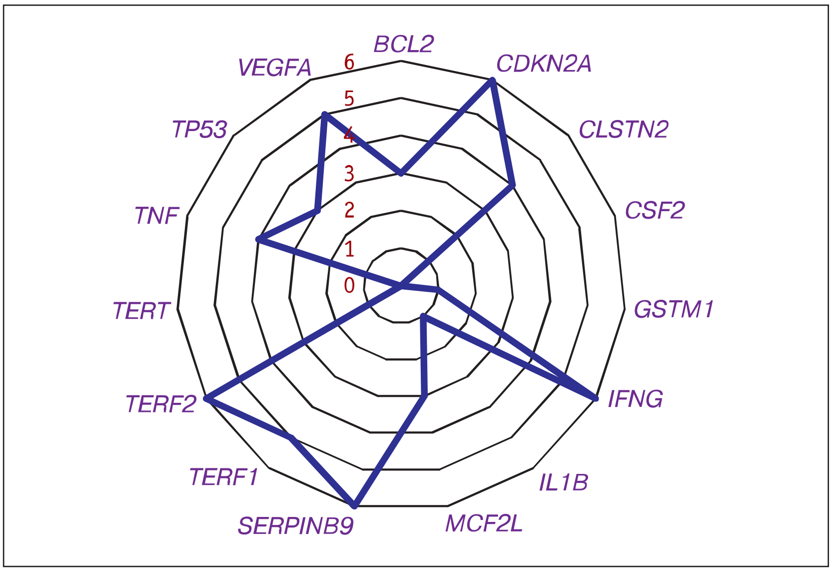

Figure 2.31. **Enhanced and overexpression of genes in peripheral blood leukocytes of Chornobyl clean-up workers with COPD**

increase of mean group index of RQ of *CSF2* was found in the group of persons with AH and CHD; *GSTM1* gene expression did not change compared with control in persons with AH, but was significantly increased in the group of persons with CHD and a combination of these pathological conditions. Glutathione appears to have marked antioxidant activities and therefore may prevent CVD. H. Shimizu et al. [257] have been shown that low levels of plasma glutathione are closely associated with CVD and its clinical types. In studies [256], the association between the AH and changes in the expression of the gene encoding the cytoplasmic glutathione-S-transferase *GSTM1* and the genes that regulate the inflammatory response *IFNG, CSF2, TNF* is clearly defined. The OR for these genes were high. The connection with similar significance was found for the *VEGFA* gene that could be explained, given its role in the processes of angiogenesis. OR for *VEGFA* was more than 1 in both CHD and AH. The mean group index of RQ of *VEGFA* in Chornobyl clean-up workers with CHD group significantly increased compared to the control [256].

Close associative relationship between the development of AH and expression of genes-regulators of the telomero-telomerase complex *TERF1* and *TERT* was found in main group, which is probably related to the age characteristics of this group. The results of the study of the expression of genes that regulate the immune response were ambiguous: overexpression of *IFNG* gene was detected in a group of patients with CHD, which was not observed in the case of another gene that regulates proinflammatory processes – *IL1B*. However, there is a tendency to increase the average RQ of *SERPINB9* gene in groups of patients with CHD, AH and in the group with a combined effect of the two pathologies. Changes in the expression of *TP53* gene in the AH group were statistically significant. The role of gene-oncosuppressor *TP53* was noted in the detection of activation of signaling pathways of gene regulation of the development of CVD in the remote period after radiation exposure. Radar diagrams show the activation of *TP53, IFNG, IL1B, CLSTN2, CDKN2A, TERF1* genes in peripheral blood leukocytes of Chornobyl clean-up workers with AH (Fig. 2.32) and *IL1B, CLSTN2, TNF, BCL2* genes in peripheral blood leukocytes of Chornobyl clean-up workers with CHD (Fig. 2.33).

To determine changes in gene expression, which associated with the studied types of somatic diseases in the remote period after radiation exposure, it is recommended to include to the examination complex the investigation of genes regulating the immune response, in particular inflammatory reactions *CSF2, IFNG, ILB, TNF*; expression of genes that regulate cell proliferation, senescence and apoptosis *TP53, BCL2, MCF2L, CDKN2A, SERPINB9, TERF1, TERF2, TERT*; genes that regulate cell adhesion and angiogenesis *CLSTN2* and *VEGF* (Table 2.19).

A state of health of Chornobyl clean-up workers was characterized by the presence of two or more somatic diseases. Various approaches, including genetic, are used to search for the causes of the combined pathology. In recent years, research has emerged sets of genes that are associated with comorbid pathology [258]. Based on the hypothesis of a genetic link between diseases, it is possible not only to identify new genetic variants, but also to

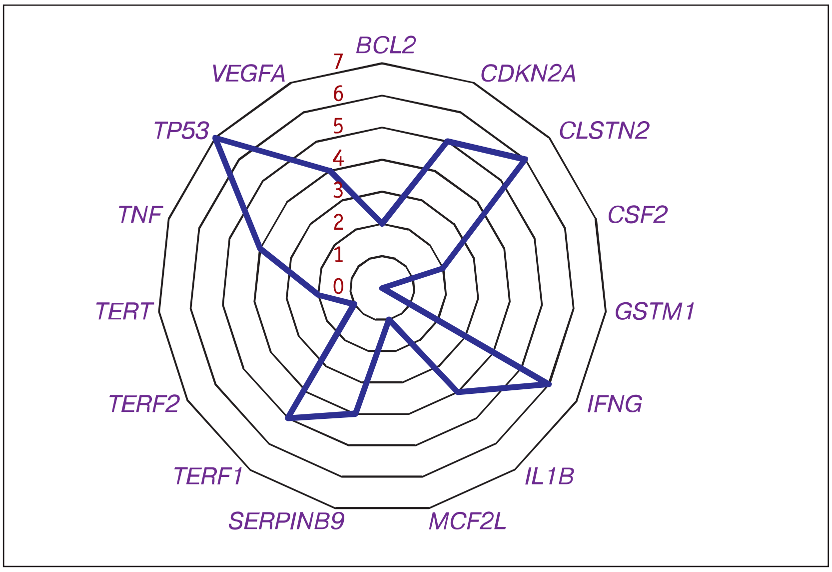

Figure 2.32. **Enhanced and overexpression of genes in peripheral blood leukocytes of Chornobyl clean-up workers with AH**

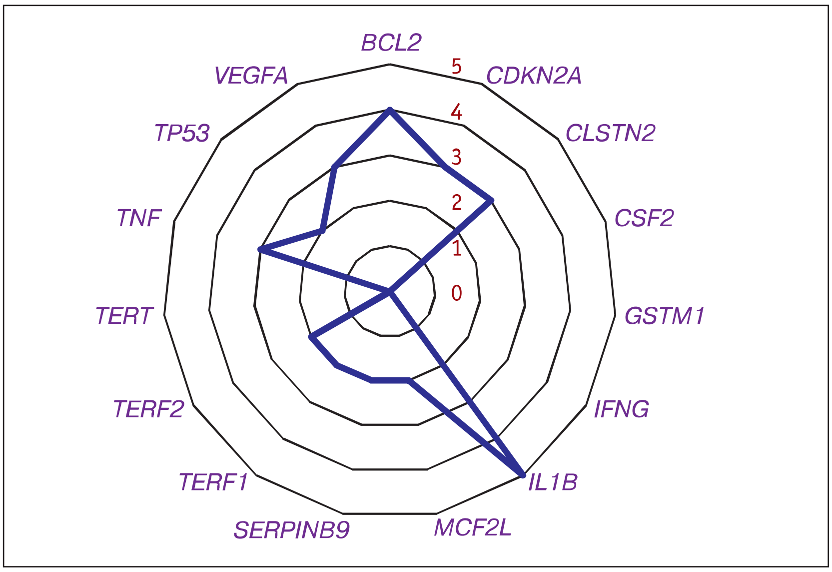

Figure 2.33. **Enhanced and overexpression of genes in peripheral blood leukocytes of Chornobyl clean-up workers with CHD**

Table 2.19
Changes in gene expression, which associated with non-cancer effects of Chornobyl clean-up workers in the remote period after radiation exposure

Nosological form of somatic pathology	Changes in gene expression
BPP	*CLSTN2, GSTM1, SERPINB9, TERF1, TERF2, TERT, TNF, TP53, VEGFA*
CVD	*CDKN2A, CLSTN2, CSF2, GSTM1, IFNG, TERF1, TERT, TNF, VEGFA*

identify new loci of susceptibility for each of the comorbid conditions. The main result of the study of comorbidity for pathologies of different physiological systems is the commonality of genetic factors in the development of combined pathology. The significance of individual disorders in common genes is also confirmed by the example of the development of pathologies that are rarely combined, suggesting that the same biological mechanisms may affect the development of different diseases in various ways.

Confirmation of this hypothesis to a certain extent were the results carried out in the laboratory of immunocytology of the NRCRM, which demonstrate changes in gene regulation of the main pathological mechanisms of CVD and BPP in Chornobyl clean-up workers in 30–33 years after radiation exposure, associated with changes in the expression of genes that regulate the immune response, proliferation, adhesion and angiogenesis, cell senescence and death. Such changes are characterized by the commonality of genetic reactions with a shift (activation) towards those signaling pathways that are physiologically or genetically determined, protective or associated with the development of other pathologies.

Increased expression of genes, that are associated with apoptosis and kinase activity (*BCL2, CLSTN2, CDKN2*), immune inflammation (*CSF2, IL1B, TNF*) was found in peripheral blood leukocytes of Chornobyl clean-up workers with BPP; expression of the *TP53* gene and the *GSTM1* gene, which associated with the glutathione system was significantly elevated in the group of workers with CB, whereas in patients with more severe stage of COPD, no increase was detected; the expression of *SERPINB9* and *MCF2L* genes was reduced, which indicates the depletion of protective reserves.

As a result of the study of specific gene mechanisms and gene markers that are involved in the pathogenetic pathways of development of certain CVD clinical types in Chornobyl clean-up workers, the following results were obtained: increased *GSTM1* gene expression (glutathione system) and no changes in angiogenesis-related *VEGF* gene expression were found in patients with CHD; increased expression of *TP53, VEGFA* and *IFNG* genes was detected in patients with AH. The combination of CHD and AH showed an increase in the expression of the *CSF2* gene, *TERF1* and *TERF2* genes, which are involved in the regulation of telomere length. Thus, CHD has been shown to involve the oxidative homeostasis system, whereas AH is associated with the expression of angiogenesis and immune inflammation genes.

The obtained results of studies of changes in gene expression in Chornobyl clean-up workers create the basis for the formation of molecular genetic criteria for assessing radiobiological manifestations in the pathogenesis of somatic pathology in the remote period after radiation exposure due to the Chornobyl accident.

3. NON-NEOPLASTIC EFFECTS IN THE LATE PERIOD

3.1. Non-neoplastic effects in the late period of ChNPP accident

3.1.1. Non-neoplastic effects in the Chornobyl accident consequences clean-up participants of 1986–1987 period

Introduction

Consequences of the Chornobyl catastrophe for the health of population of Ukraine remain a far underestimated and undefined problem. The multidirectional radiation-environmental, radiation-hygienic, epidemiological, clinical, experimental, and radiobiological studies are required for the reasonable solution of this issue. Other health risk factors not directly related to the Chornobyl accident should be taken into account here, namely social, economic, psychological, cultural and ethnic, etc., the impact of which on health deterioration in affected population may significantly outweigh just the impact of Chornobyl accident [1–7].

However, during 30 years after the Chornobyl catastrophe a lot of scientific data on post-accident health disorders in the affected population were accumulated, justifying a need to increase the effectiveness of medical and social protection. Such problems include prevention of the somatic non-neoplastic diseases.

According to results of epidemiological studies carried out at the State Institution «National Research Center for Radiation Medicine of National Academy of Medical Sciences of Ukraine» (NRCRM) it was established that already in 2012 the share of patients with general somatic diseases among the Chornobyl accident consequences clean-up participants (ACCUP) of 1986–1987 period was 95 %, while among evacuees from the ChNPP 30-kilometer zone aged 18–60 years being 87.9 %.

In the long-term and late periods upon accident (1998–2012) a high levels of disability and mortality rates from non-neoplastic diseases were established in population aged 18–60 at the time of the Chornobyl accident, specifically in the accident consequences liquidation participants (1986–1987 period), evacuees, and residents of radiologically contaminated territories (RCT) [8–10].

By 2030, given current rate of mortality from non-neoplastic diseases in affected population, the persons whose age at the time of Chornobyl accident was 30 years or more will be almost excluded from the medical observation contingents.

General characterization of the studied contingents

A large number of population of Ukraine was affected by the Chornobyl accident consequences. The 365,780 persons from population of Ukraine were involved in the clean-up of accident consequences in the period from 1986 to 1990. Of them 196,423 persons participated in recovery operations in 1986–1987, and 91.6 thousand children and adults were evacuated from the ChNPP 30-kilometer zone.

According to the Resolution of the Cabinet of Ministers of Ukraine dated 23.07.1993 #106 and the Decree of the Cabinet of Ministers of Ukraine #37-r dated 27.01.1995 the 69 districts and 3 urban-type settlements, 2,207 settlements (without exclusion zone) located in 12 oblasts of Ukraine were referred to RCT with spotted soil contamination density of 1 Ci · km^{-2} or more.

Total population of the RCT in Ukraine was 2,986,750 people, including 579,807 children under the age of 15 at the time of accident. Of this number the 23,137 persons including 3,552 children under the age of 15 lived in 92 settlements of zone II, 821,785 people in zone III (835 settlements, 168,529 children under the age of 15), and 2,141,828 people in zone IV (290 settlements, 407,626 children under the age of 15).

Three study cohorts were formed on the basis of medical information system «The State Registry of Ukraine of Persons Affected by the Chornobyl Catastrophe of the Ministry of Health of Ukraine» (SRU) for the epidemiological research and assessments of post-accident health disorders in survivors due to non-neoplastic morbidity, disability and mortality.

The Chornobyl NPP ACCUP of 1986-1987 period (males, n = 68,145) were included in cohort I; evacuees from the exclusion zone (both genders, n = 42,982) in cohort II, residents of RCT (both genders, n = 98,902) in cohort III. All cohorts included only persons whose age at the date of Chornobyl accident was 18–60 years.

Numerical distribution of the cohort I by age groups and whole-body external radiation dose is given in Table 3.1.

Numerical composition of the cohort II by age groups is presented in Table 3.2.

Unfortunately, the data on radiation doses in evacuees from the Chornobyl NPP 30-km zone contained in the SRU are very limited. In this regard, the values of whole-body external radiation

Table 3.1
Quantitative distribution of male ACCUP of 1986–1987 period cohort with established average doses of whole-body external exposure and age at the date of Chornobyl accident (X ± m)

Parameter	Whole-body external radiation dose, Gy				
	0–0.049	0.05–0.09	0.1–0.199	0.2–0.249	0.25–0.7
ACCUP of 1986–1987 period aged 18–39 at the time of exposure					
Average age, years	28.8 ± 5.4	30.2 ± 5.1	28.7 ± 5.2	28.8 ± 5.1	28.8 ± 5.2
Average dose, Gy	0.023 ± 0.015	0.084 ± 0.013	0.15± 0.033	0.221 ± 0.015	0.259 ± 0.036
Persons in total	6 214	17 777	14 690	14 618	6 462
ACCUP of 1986–1987 period aged 40–60 at the time of exposure					
Average age, years	45.4 ± 5.0	42.6 ± 3.6	44.4 ± 4.6	43.5 ± 3.8	44.2 ± 4.2
Average dose, Gy	0.022 ± 0.015	0.082 ± 0.014	0.149 ± 0.031	0.221± 0.015	0.281 ± 0.084
Persons in total	922	1 686	1 390	1 080	706

Table 3.2
Quantitative distribution of evacuees from 30-kilometer zone cohort by age at the date of Chornobyl accident and by gender (persons)

Gender	Age at the time of accident, years		
	18–39	40–60	18–60
Male	11 540	6 593	18 133
Female	15 836	9 013	24 849
In total	27 376	15 606	42 982

Table 3.3
Characteristics of dose subgroups in percent from population of Prypiat city and other settlements of the 30-kilometer zone (external exposure) [11]

Dose subgroup, cGy	Prypiat city (49 360 persons)	Number of people	30-kilometer zone (40 239 persons)	Number of people
0–5	98.58	48 669	86.17	34 686
> 5	1.28	642	10.50	4 225
> 10	0.14	69	3.20	1 288
> 25	–	–	0.10	40
> 50	–	–	0.03	12

Table 3.4
Frequency distribution of thyroid radiation doses in the surveyed evacuees from the 30-kilometer zone in different age subgroups [11]

Age group, years	Median distribution, cGy	Maximum dose, cGy	% doses over 200 cGy
< 1	247.70	447.2	57
1–3	167.60	499.7	42.60
4–7	79.80	497.8	19.90
8–11	26.12	166.1	5.41
12–15	17.22	124.1	2.37
16–18	14.80	57.0	2.07
> 18	24.66	80.0	3.62

Table 3.5
Numerical composition of RCT residents by age groups, gender and values of accumulated total effective dose of ionizing radiation for the post-accident period (abs. number of persons)

Dose interval, mSv	Females			Males			Total		
	18–39	18–60	40–60	18–39	18–60	40–60	18–39	18–60	40–60
0–5	2 511	5 865	3 354	2 082	3 947	1 865	4 593	9 812	5 219
5–10	2 147	4 878	2 731	1 830	3 374	1 544	3 977	8 252	4 275
10–20	7 661	13 797	6 136	6 231	10 317	4 086	13 892	24 114	10 222
20–30	3 646	7 384	3 738	3 883	6 310	2 427	7 529	13 694	6 165
30–40	1 541	3 200	1 659	1 450	2 520	1 070	2 991	5 720	2 729
40 and over	963	1 978	1 015	867	1 609	742	1 830	3 587	1 757

Table 3.6
Numerical composition of RCT residents by age groups, gender and internal radiation doses on thyroid by iodine isotopes (abs. number of persons)

Dose interval, mGy	Females		Males		Total	
	18–39	40–60	18–39	40–60	18–39	40–60
0–20	261	548	62	74	323	622
20–50	6 567	5 770	4 213	3 122	10 780	8 892
50–100	4 883	5162	3 902	3 111	8 785	8 273
100–200	6 275	6 120	4 791	3 023	11 066	9 143
200–500	471	1 008	3 311	2 305	3 782	3 313
500 and over	12	25	64	99	76	124

doses and doses of internal irradiation on thyroid gland by iodine isotopes are represented here (Tables 3.3, 3.4), been also stated in a scientific publication [9].

The RCT population has been exposed and continues to be exposed to long-term chronic ionizing irradiation in small and low doses, formed mainly due to external and internal irradiation from ^{134}Cs, ^{137}Cs, incorporated by inhalation and orally.

Values of radiation doses accumulated during the exposure period were used in studies of health effects of chronic long-term ionizing irradiation.

Distribution of numerical composition of the RCT inhabitants (cohort II) by age groups, gender and the values of accumulated total effective doses of ionizing radiation for the post-accident period is given in Table 3.5.

RCT inhabitants, along with exposure to the long half-life radionuclides, had received internal irradiation of thyroid, mainly by the ^{131}I (in late April and May 1986). Distribution of numerical composition of the cohort III by age groups, gender and internal radiation doses on thyroid by iodine isotopes is given in Table 3.6.

Incidence

According to the results of conducted research it was established that health state of the Chornobyl NPP ACCUP of 1986–1987 period had significantly deteriorated due to non-neoplastic diseases. The share of healthy and nominally healthy people decreased from 68 % in 1988 to 5.5 % in 2012, while the share of people with chronic diseases increased from 32.4 % to 94.5 % (Fig. 3.1).

Figure 3.2 shows a dynamic pattern of non-neoplastic disease incidence in ACCUP of 1986–1987 period depending on the age at the time of accident by 5-year observation periods. Increased non-neoplastic disease incidence was established in the first 6 years since accident and in the period from 1998 to 2007, i. e. 12–21 years upon accident. In the period of 2008–2016, i. e. 22–30 years upon, there was a gradual decrease in the overall incidence of non-neoplastic diseases.

Proceeding from data presented in Fig. 3.2 the levels of non-neoplastic disease incidence in all observation periods were highest in the subcohort of persons whose age at the time of accident was 40–60 years, which was undoubtedly associated with the «Age» factor impact.

Three main periods can be fully determined, namely «early» (first 6 post-accident years), «long-term» (12–21 years), and «late» (22–30 years) over time in reference to the peculiarities of incidence rate for the specific classes, groups and forms of non-neoplastic diseases.

An increased level of mental and behavioral disorders (Fig. 3.3), nervous disorders (Fig. 3.4) and dis-

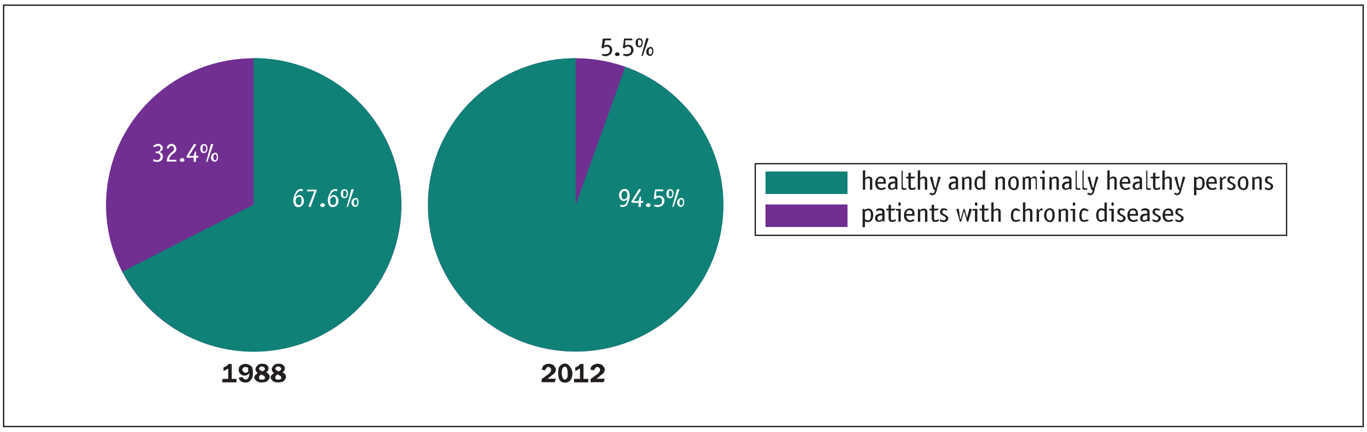

Figure 3.1. Distribution of Chornobyl ACCUP of 1986–1987 period cohort by health state indices in 1988 and 2012 (according to the SRU data)

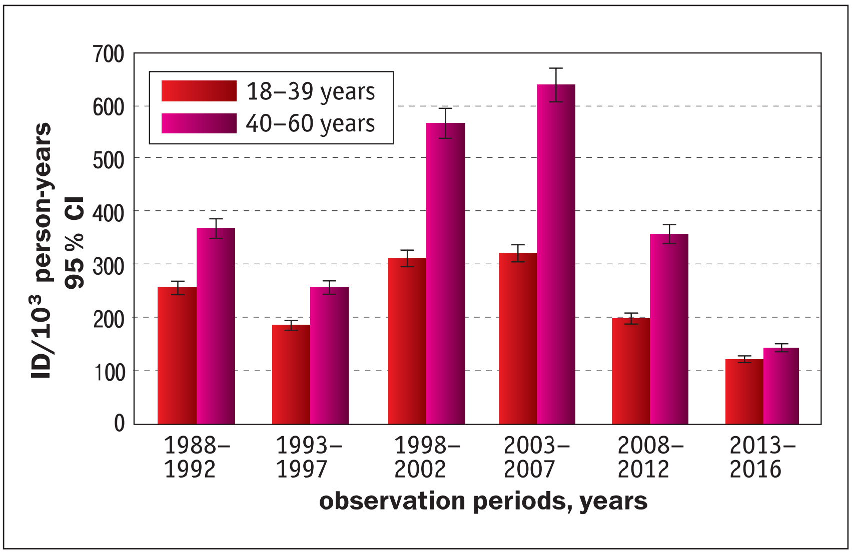

Figure 3.2. Dynamic pattern of general level of non-neoplastic disease incidence (codes 240.0–739.9 by ICD–9, E00.0–N99.9 by ICD–10) in ACCUP of 1986–1987 period by for 5-year observation periods, depending on the age at the time of accident

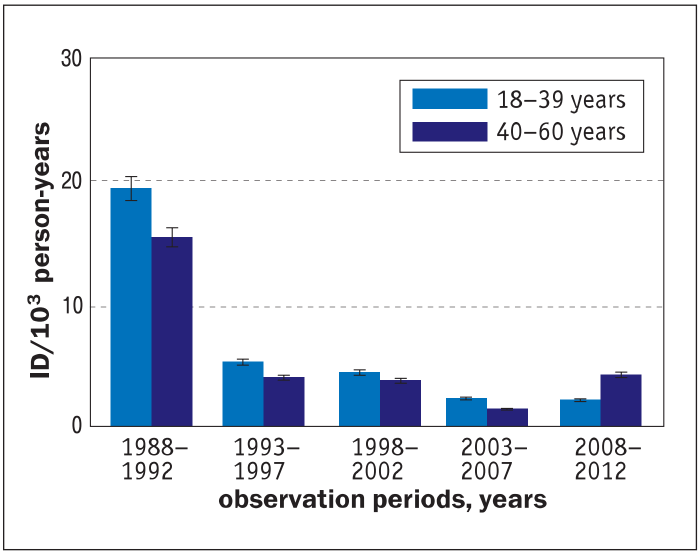

Figure 3.3. Dynamic pattern of incidence of mental and behavioral disorders (codes 290–319 by ICD–9, F00–F99 by ICD–10) in ACCUP of 1986–1987 period depending on the age at the time of accident

orders the autonomic nervous system (Fig. 3.5) was attributable for the «early» period there.

The «long-term» period (12–21 years from the date of accident) was characterized by an increase in the incidence of chronic forms of non-neoplastic diseases.

The «late» period (22–30 years from the date of accident) featured a gradual decrease in the level of non-neoplastic disease incidence. These features are demonstrated on an example of dynamic pattern of the incidence rate of circulatory, respiratory, digestion, and endocrine system diseases in Fig. 3.6–3.9.

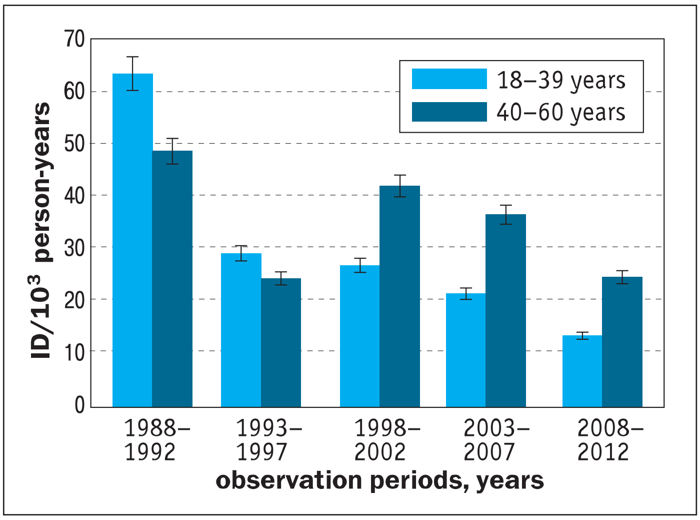

Figure 3.4. Dynamic pattern of incidence of nervous system diseases (codes 320.0–359.9 by ICD–9, G00–G99 by ICD–10) in ACCUP of 1986–1987 period depending on the age at the time of accident

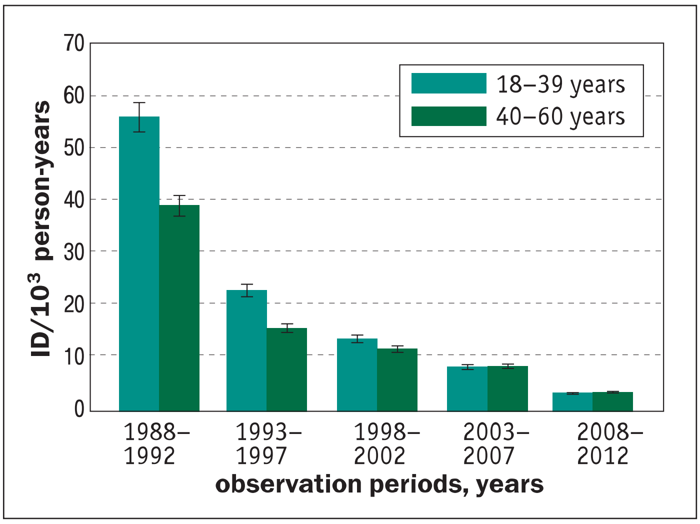

Figure 3.5. Dynamic pattern of incidence of autonomic nervous system disorders in ACCUP of 1986–1987 period depending on the age at the time of accident

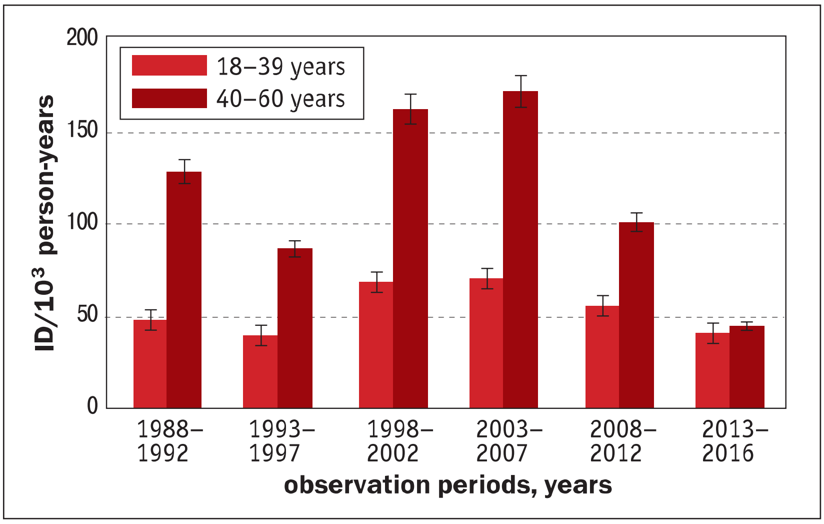

Figure 3.6. Dynamic pattern of incidence of circulatory system diseases (codes 390.0–459.9 ICD–9, I00–I99 ICD-10) in ACCUP of 1986–1987 period depending on the age at the time of accident

Structure of non-neoplastic disease incidence in the «early» and «late» periods in the ACCUP of 1986–1987 term of recovery operations is presented in Table 3.7.

Currently the scope of diseases of circulatory system, digestive organs, muscular and genitourinary systems, and respiratory organs is the main share in the structure of non-neoplastic disease incidence in persons aged 18–39 years at the date of accident. In persons aged 40–60 years the main share is represented by the diseases of digestive, circulatory, muscular system, respiratory organs and genitourinary system.

These data are essential for planning and implementing of preventive measures.

The non-neoplastic effects of ionizing irradiation are one of the important issues in contemporary

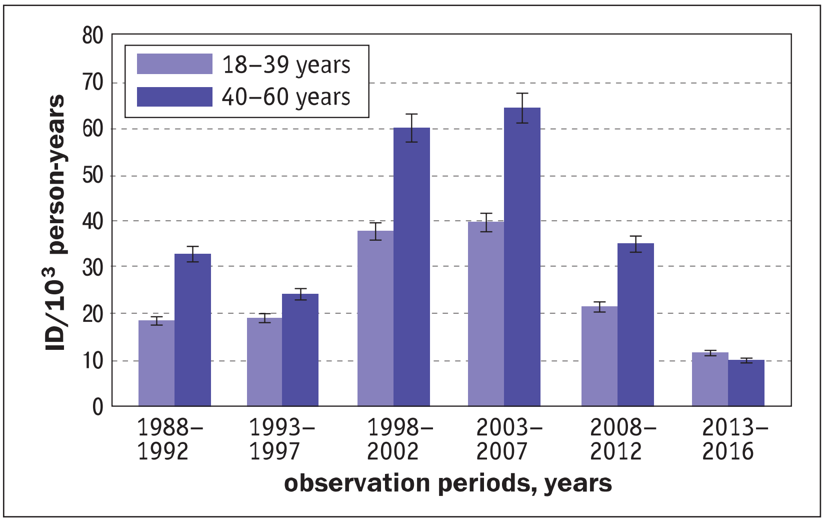

Figure 3.7. **Dynamic pattern of incidence of respiratory diseases (codes 460.0–519.9 ICD–9, J00–J99 ICD–10) in ACCUP of 1986–1987 period depending on the age at the time of accident**

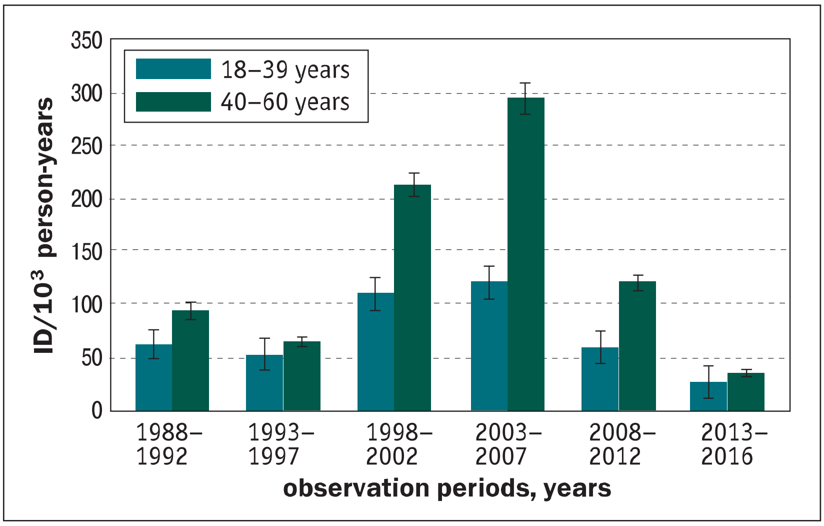

Figure 3.8. **Dynamic pattern of incidence of digestive system diseases (codes 520.0–579.9 ICD–9, K00–K93 ICD–10) in ACCUP of 1986–1987 period depending on the age at the time of accident**

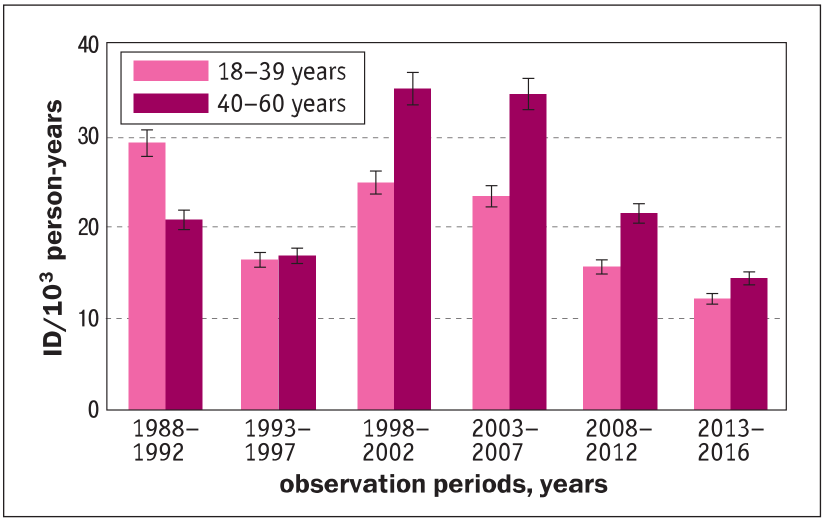

Figure 3.9. **Dynamic pattern of incidence of endocrine system diseases,eating and metabolic disorders (codes 240–269 ICD–9, E00–E90 ICD–10) in ACCUP of 1986–1987 period depending on the age at the time of accident**

radiobiology and radiation medicine. Particular attention in this regard is paid to the effects of low radiation doses [10–11].

Bases on analytical approach a connection between the development of major non-neoplastic diseases in the post-accident period in ACCUP of 1986–1987 term of recovery operations was established with the external whole-body γ-irradiation (Table 3.8).

Reliable values of relative risk (RR) at the 95 % CI in ACCUP aged 18–39 years at the date of the accident were obtained under the exposure doses in a range of 0.05–0.7 Gy in the development of diseases of circulatory system, respiratory organs, nervous system, and digestive organs – in a range of 0.25–0.7 Gy.

In ACCUP whose age at the date of the accident was 40–60 years the stable reliable values of RR at the

Table 3.7

Structure of the non-neoplastic disease incidence during the observation periods of 1988–1992 and 2013–2016 in ACCUP of 1986–1987 period taking into account the age at the date of accident (in per cent)

Non-neoplastic diseases	Code by MKX-10	Periods of observation, years			
		1988–1992		2013–2016	
		age at the date of accident, years			
		18–39	40–60	18–39	40–60
Circulatory system diseases	I00.0–I99.9	17.8	32.1	33.0	31.0
Respiratory diseases	J00.0–J99.9	6.9	8.3	9.0	7.0
Digestive system diseases	K00.0–K93.9	23.2	23.8	22.0	25.0
Mental and behavioral disorders	F00.0–F99.9	7.2	3.9	1.0	1.0
Nervous system diseases	G00.0–G99.9	23.4	12.2	4.0	4.0
Endocrine diseases, eating and metabolic disorders	E00.0–E90.9	16.8	5.2	10.0	10.0
Muscular system and connective tissue diseases	M00.0 –M99.9	8.8	12.3	11.0	12.0
Genitourinary system diseases	N00.0–N99.9	1.9	2.2	10.0	10.0

Table 3.8

Risks of development of certain classes of non-neoplastic diseases in ACCUP of 1986–1987 period (1988–2012 term of survey) depending on whole-body external irradiation dose and age at the time of exposure (RR values with 90 % CI presented in italic type)

Dose, Gy	Age of ACCUP at the time of exposure			
	up to 40 years		40–60 years	
	RR (95 % CI)	ERR/Gy^{-1}	RR (95 % CI)	ERR/Gy^{-1}
Circulatory system diseases (I00.0–I99.9 ICD–10)				
0.05–0.099	1.35 (1.32; 1.37)	4.17 (4.13; 4.2)	1 (0.91; 1.1)	
0.1–0.199	1.19 (1.11; 1.27)	1.27 (1.25; 1.28)	1.12 (1.1; 1.18)	0.8 (0.75; 0.85)
0.2–0.249	1.18 (1.16; 1.2)	0.8 (0.74; 0.83)	1.07 (0.96; 1.2)	
0.25–0.7	1.37 (1.14; 1.34)	1.41 (1.39; 1.46)	1.15 (1.02; 1.3)	0.53 (0.47; 0.59)
Respiratory system diseases (J00–J99.9 ICD–10)				
0.05–0.099	1.16 (1.15; 1.17)	1.95 (1.8; 2.1)	1.03 (1.02; 1.04)	0.35 (0.34; 0.36)
0.1–0.199	1.07 (0.9; 1.17)		0.97 (0.96; 0.99)	
0.2–0.249	1.1 (1.0; 1.2)	0.47 (0.4; 0.54)	0.89 (0.88; 0.9)	
0.25–0.7	1.29 (1.25; 1.33)	1.1 (0.9; 1.3)	0.93 (0.92; 0.95)	
Digestive system diseases (K00–K93.9 ICD–10)				
0.05–0.099	1.05 (1.04; 1.03)	0.58 (0.56; 0.6)	0.92 (0.91; 0.93)	
0.1–0.199	1.01 (0.96; 1.06)		0.97 (0.96; 0.98)	
0.2–0.249	1.09 (0.99; 1.19)		0.91 (0.89; 0.92)	
0.25–0.7	1.33 (1.28; 1.38)	1.26 (1.23; 1.29)	1.25 (1.23; 1.28)	0.9 (0.89; 0.92)
Nervous system diseases (G00.0–G99.9 ICD–10)				
0.05–0.099	1.12 (1.05; 1.19)	1.42 (1.2; 1.44)	1.04 (1.02; 1.05)	0.43 (0.42; 0.44)
0.1–0.199	1.16 (1.1; 1.22)	1.07 (1.03; 1.11)	*1.01 (1.0; 1.02)*	
0.2–0.249	1.12 (1.1; 1.14)	0.55 (0.52; 0.58)	*1.08 (1.06; 1.09)*	
0.25–0.7	1.19 (1.15; 1.23)	0.73 (0.7; 0.76)	*1.08 (1.06; 1.1)*	0.27 (0.25; 0.29)

95 % CI were obtained mainly in the development of diseases of circulatory system at a dose of 0.1 Gy or more, diseases of respiratory, nervous system and digestive organs in a range of 0.25–0.7 Gy (0.33 Gy average dose), diseases of nervous system in a dose range of 0.05–0.099 Gy (0.022 Gy average dose). There was an uncertainty in the RR assessments for non-neoplastic diseases in other dosage intervals in older age group of ACCUP, which may be due to insufficient power of epidemiological study. However, one can assume from data presented in Table 3.8 that the radiosensitivity to ionizing radiation of specific organs and systems in human decreases with age.

Taking into account the leading role of circulatory system in health deterioration of population involved in the consequences of the Chornobyl catastrophe, the Table 3.9 shows more detailed results of the assessment of effects of ionizing radiation consequently to accident on the development of certain groups and forms of circulatory system diseases in the Chornobyl NPP ACCUP of 1986–1987 period given the age on the date of accident.

The reliable RR values in the Chornobyl NPP ACCUP aged 18–39 years at the date of accident were established foremost for the development of

Table 3.9

Risks of development of circulatory system diseases in ACCUP of 1986–1987 period depending on whole body external irradiation dose and age at the time of accident for the 25-year post-accident period (RR values with 90 % CI presented in italic type)

Dose, Gy	Age of ACCUP at the time of exposure			
	up to 40 years		40–60 years	
	RR (95 % CI)	ERR/Gy^{-1}	RR (95 % CI)	ERR/Gy^{-1}
Circulatory system diseases (I00.0–I99.9 ICD–10)				
0.05–0.099	1.35 (1.32; 1.37)	4.17 (4.13; 4.2)	1 (0.91; 1.1)	
0.1–0.199	1.19 (1.11; 1.27)	1.27 (1.25; 1.28)	1.12 (1.1; 1.18)	0.8 (0.75; 0.85)
0.2–0.249	1.18 (1.16; 1.2)	0.8 (0.74; 0.83)	*1.07 (0.96; 1.2)*	
0.25–0.7	1.37 (1.14; 1.34)	1.41 (1.39; 1.46)	1.15 (1.02; 1.3)	0.53 (0.47; 0.59)
Coronary heart disease (I20.0–I25.0 ICD–10)				
0.05–0.099	1.38 (1.33; 1.42)	4.52 (4.49; 4.55)	0.87 (0.75; 1.0)	
0.1–0.199	1.18 (1.02; 1.36)	1.2 (1.18; 1.22)	0.99 (0.92; 1.1)	
0.2–0.249	1.27 (1.23; 1.32)	1.22 (1.2; 1.24)	0.95 (0.8; 1.13)	
0.25–0.7	1.32 (1.27; 1.37)	1.24 (1.2; 1.26)	0.96 (0.8; 1.16)	
Cerebrovascular diseases (I60.0–I69.8 ICD–10)				
0.05–0.099	1.27 (1.22; 1.33)	3.2 (3.18; 3.24)	0.92 (0.76;1.1)	
0.1–0.199	*1.01 (0.83; 1.22)*		*1.06 (0.95; 1.2)*	
0.2–0.249	1.07 (1.02; 1.12)	0.32 (0.3; 0.33)	*1.07 (0.86; 1.3)*	
0.25–0.7	1.51 (1.44; 1.59)	1.97 (1.93; 2)	*1.18 (0.9; 1.48)*	
Diseases of arteries, arterioles and capillaries (I70.0–I79.8 ICD–10)				
0.05–0.099	1.48 (1.38; 1.59)	5.71 (5.68; 5 75)	0.97 (0.7; 1.32)	
0.1–0.199	*1.22 (0.9; 1.65)*		*1.1 (0.9; 1.32)*	
0.2–0.249	1.14 (1.07; 1.23)	0.63 (0.62; 0.64)	0.92 (0.6; 1.32)	
0.25–0.7	1.65 (1.52; 1.78)	2.51 (2.47; 2.54)	1.44 (1.01; 2.06)	1.56 (1.47; 1.65)
Diseases of veins and lymph vessels (I80.0–I89.9 ICD–10)				
0.05–0.099	1.39 (1.32; 1.46)	4.6 (4.61; 4.67)	*1.24 (0.93; 1.64)*	
0.1–0.199	*1.2 (0.97; 1.49)*		*1.3 (0.9; 1.72)*	
0.2–0.249	1.18 (1.12; 1.24)	0.8 (0.79; 0.83)	*1.25 (0.9; 1.72)*	
0.25–0.7	1.4 (1.32; 1.48)	1.54 (1.51; 1.57)	1.45 (1.03; 2.02)	1.6 (1.5; 1.69)

coronary heart disease, cerebrovascular diseases, artery and vein diseases at external γ-irradiation whole-body doses of 0.05 Gy or more.

In persons of the older age group of ACCUP the reliable values of RR were established for the development of diseases of veins, lymphatic vessels, arteries, arterioles, and capillaries in a dose range of 0.25–0.7 Gy.

Disability

The epidemiological studies have shown that the long-term period from the date of Chornobyl accident was characterized by a gradual increase in disability level from non-neoplastic diseases in the ACCUP of 1986–1987 period (Fig. 3.10).

The increase in disability occurred in 1993 and reached maximum values between 2008 and 2016.

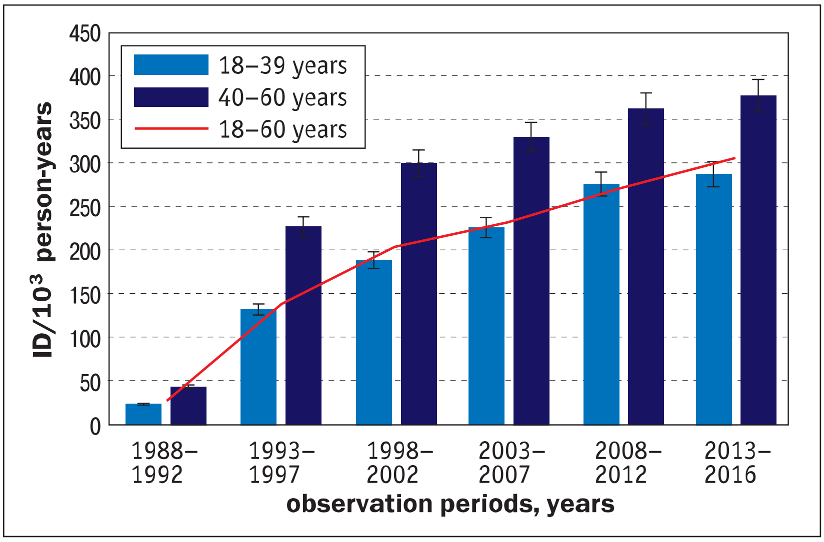

Figure 3.10. Dynamic pattern of general level of disability from non-neoplastic diseases in Chornobyl NPP ACCUP of 1986–1987 period depending on age at the time of Chornobyl accident and time after accident

Table 3.10
Structure of disability from non-neoplastic diseases in ACCUP of 1986–1987 period depending on age at the time of accident in the late period of survey (2013–2016)

Classes of diseases	ICD–10 code	Age at the time of accident (years)	
		18–39	40–60
Circulatory system diseases	I00.0–I99.9	65	75
Respiratory diseases	J00.0–J99.9	2	3
Digestive system diseases	K00.0–K93.9	7	5
Mental and behavioral disorders	F00.0–F99.9	2	1
Nervous system diseases	G00.0–G99.9	18	11
Endocrine diseases, eating and metabolic disorders	E00.0–E90.9	4	3
Muscular system and connective tissue diseases	M00.0 –M99.9	1	1
Genitourinary system diseases	N00.0–N99.9	1	1

In all periods of observation the highest rates of disability were established in persons aged 40–60 years at the date of accident. This should be explained firstly by the «Age» factor influence.

Nowadays the main shares in the structure of disability causes in ACCUP (Table 3.10) are diseases of circulatory and nervous system, digestive organs, and endocrine system mainly due to non-neoplastic thyroid diseases.

The presented data on disability in the studied contingent are important for the organization and providing of medical and recreational assistance to survivors in the long-term period of Chornobyl accident.

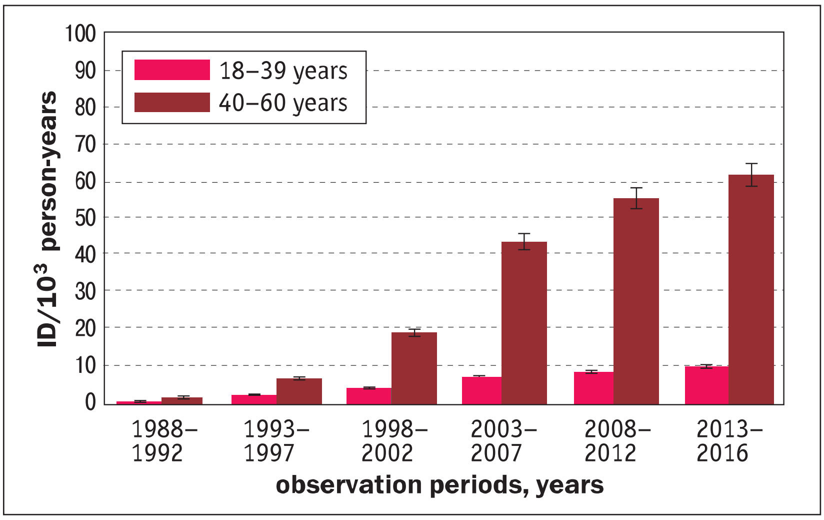

Figure 3.11. Dynamic pattern of mortality rate from non-neoplastic diseases in Chornobyl NPP ACCUP of 1986–1987 period given the age at the time of Chornobyl accident

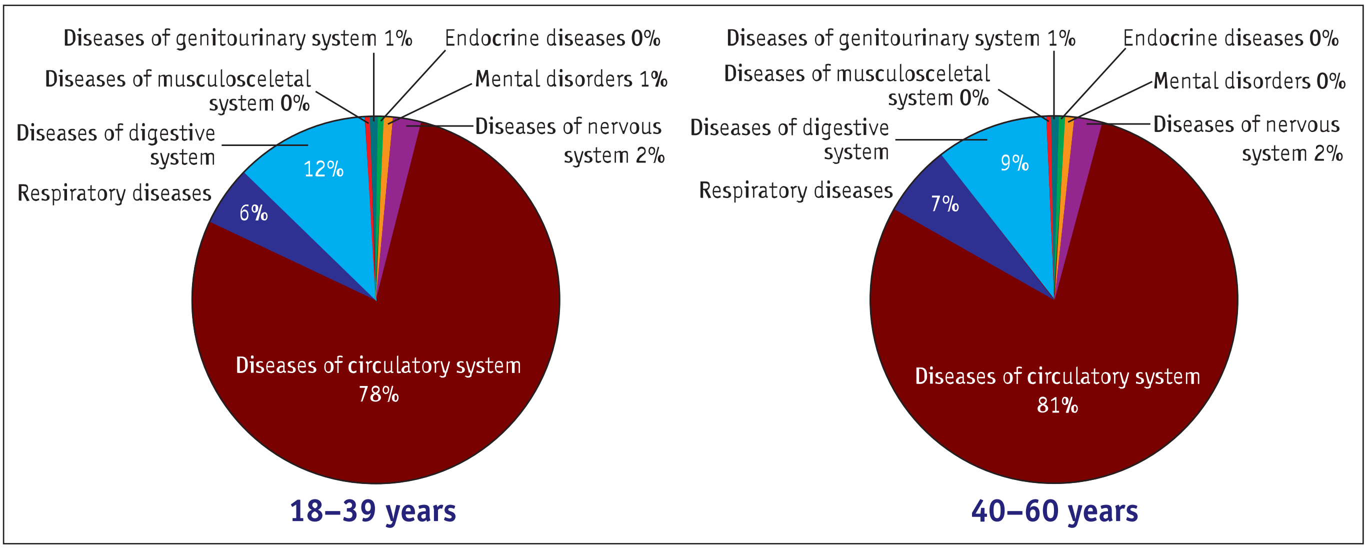

Figure 3.12. Structure of mortality from non-neoplastic diseases in Chornobyl ACCUP of 1986–1987 period depending on the age at the time of Chornobyl accident in the late period of survey (2013–2016)

Mortality

The post-accident period was characterized by a gradual increase of mortality rate from non-neoplastic diseases in the ACCUP of 1986–1987 period (Fig. 3.11).

Mortality rates increased during the study period among individuals in both younger and older age groups with a peak in the late post-accident period (2013–2016). The highest mortality rate was established in persons aged 40–60 years at the date of accident. During this time period the age of these persons was from 67 to 90. Obviously the high mortality rate from non-neoplastic diseases in this age group of ACCUP was as in the case of disability due to the «Age» factor influence.

However, according to data in Fig. 3.11 the high mortality rates in ACCUP of the older age group were noted in previous periods (2003–2007 and 2008–2012) too, which was considered as a manifestation of the accelerated health loss effect due to the factors of Chornobyl catastrophe (stress, ionizing irradiation) in particular. Continuation of research in this field is advisable.

Circulatory system diseases make up the main share in the structure of mortality in both younger and older age groups of Chornobyl accident consequences clean-up participants of 1986–1987 term of work (Fig. 3.12) in the late observation period. Diseases of digestive and respiratory systems make up a significant proportion too.

3.1.2. Non-neoplastic effects in adult evacuees

The results of long-term epidemiological studies of the medical consequences of the Chornobyl disaster, which covered the period from 1988 to 2016, show that the health of the population evacuated from the Chornobyl Exclusion Zone at the age of 18–60 deteriorated in the post-accident period.

Morbidity

During the observation period 1988–2016, 178,622 cases of non-neoplastic diseases were registered among the adult evacuated population (Table 3.11).

As evidenced by the data in Table 3.11 the largest number of cases falls on the classes: diseases of the circulatory system, digestive and respiratory organs, diseases of the endocrine and nervous systems.

The general level of non-neoplastic morbidity of the evacuated population for the entire observation period (1988–2016) depending on age and gender is shown in Fig. 3.13.

The highest incidence rate was found in persons aged 40–60 years of the male gender on the date of the accident. In women, a high level of non-neoplastic morbidity was determined in both age groups.

Among the factors influencing the non-neoplastic morbidity of evacuees, age at the date of the accident is significant (Fig. 3.14–3.16).

The dynamics of the overall level of non-neoplastic morbidity is wavy. First: a high incidence rate, regardless of age and gender, occurs in the first 7 years after the accident. In the periods 1998–2007, the incidence increased, reaching the highest levels.

From 2008 to 2016, there has been a decrease in morbidity regardless of age and gender. Secondly, in persons aged 18–39 years on the date of the acci-

Table 3.11
The total number of cases of non-neoplastic diseases in the adult evacuated population for the period 1988–2016

Class, group of the disease, clinical entity	Code ICD–10	Adult evacuated population		
		18–39 років	40–60 років	18–60 років
		number of cases	number of cases	number of cases
Непухлинні хвороби		113 609	65 013	178 622
Хвороби ендокринної системи	E00–E90.9	7 121	3 075	10 196
Розлади психіки	F00–F99.9	1 882	931	2 813
Хвороби нервової системи	G00–G99.9	11 125	4 579	15 704
Хвороби ока	H00–H59.9	6 535	5 184	11 719
Хвороби системи кровообігу	I00–I99.9	17 221	19 584	36 805
Хвороби органів дихання	J00–J99.9	15 335	5 867	21 202
Хвороби органів травлення	K00–K93.9	33 641	14 924	48 565
Хвороби кістково-м’язової системи	M00–M99.9	13 536	7 753	21 289
Хвороби сечостатевої системи	N00–N99.9	7 213	3 116	10 329

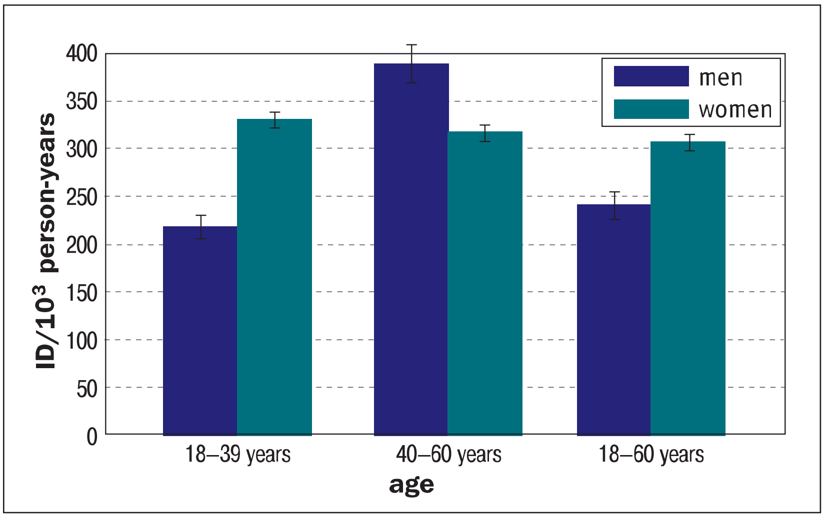

Figure 3.13. **Overall level of non-neoplastic morbidity of the evacuated population for the entire observation period (1988–2016) depending on age and gender**

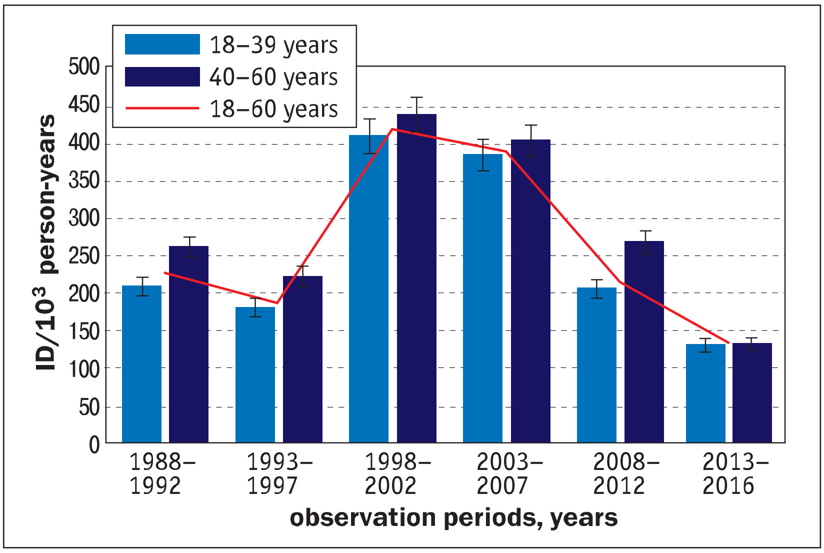

Figure 3.14. **Post-accident dynamics of the general level of non-neoplastic morbidity population evacuated from the 30-km zone of the Chornobyl NPP, according to observation periods depending on age at the date of the accident**

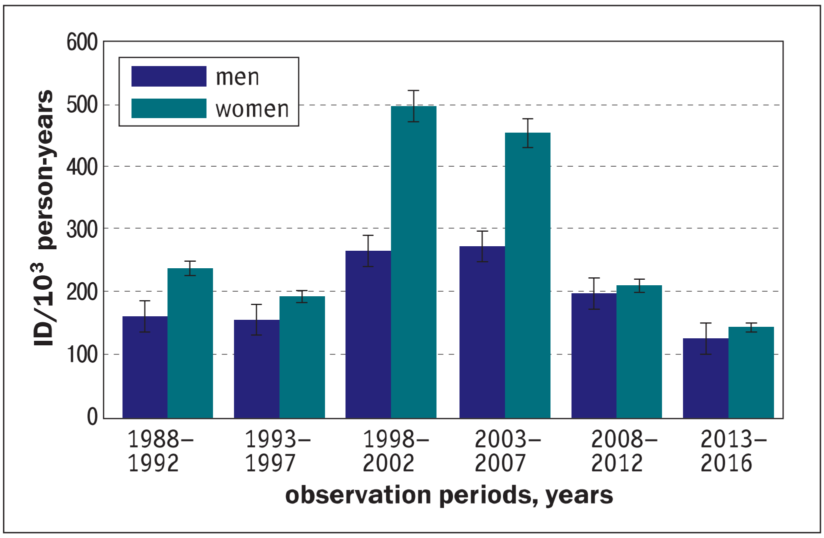

Figure 3.15. **Dynamics of the overall level of non-neoplastic morbidity by observation periods in evacuees aged 18–39 years depending on gender**

dent, the highest levels of non-neoplastic morbidity in all observation periods are observed in women.

The development of certain classes of non-neoplastic diseases, including diseases of the digestive, respiratory, circulatory, musculoskeletal and genitourinary systems, is delayed. The increase in the incidence of these diseases occurs mainly in 1998–2007.

Thus, in the dynamics of the level of morbidity by individual classes, groups and forms of non-neoplastic diseases in the evacuated population aged 18–60 years on the date of the accident can be identified three main periods: «early» (first 7 post-accident years); «Remote» (12–21 years); «Late» (22–30 years).

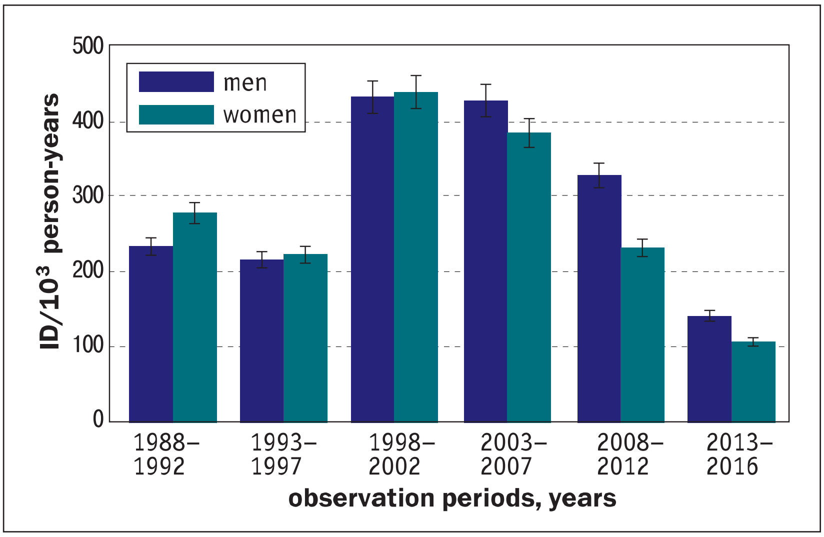

Figure 3.16. **Dynamics of the overall level of non-neoplastic morbidity by observation periods in evacuees aged 40–60 years depending on gender**

For the «early» period is characterized by an increased level of mental disorders and behavioral disorders (Fig. 3.17), especially vegetative-vascular dystonia, disorders of the nervous system, especially autonomic (Fig. 3.18), diseases of the endocrine system (Fig. 3.19), hypertension.

The structure of endocrine diseases, eating disorders and metabolic disorders is dominated by thy-

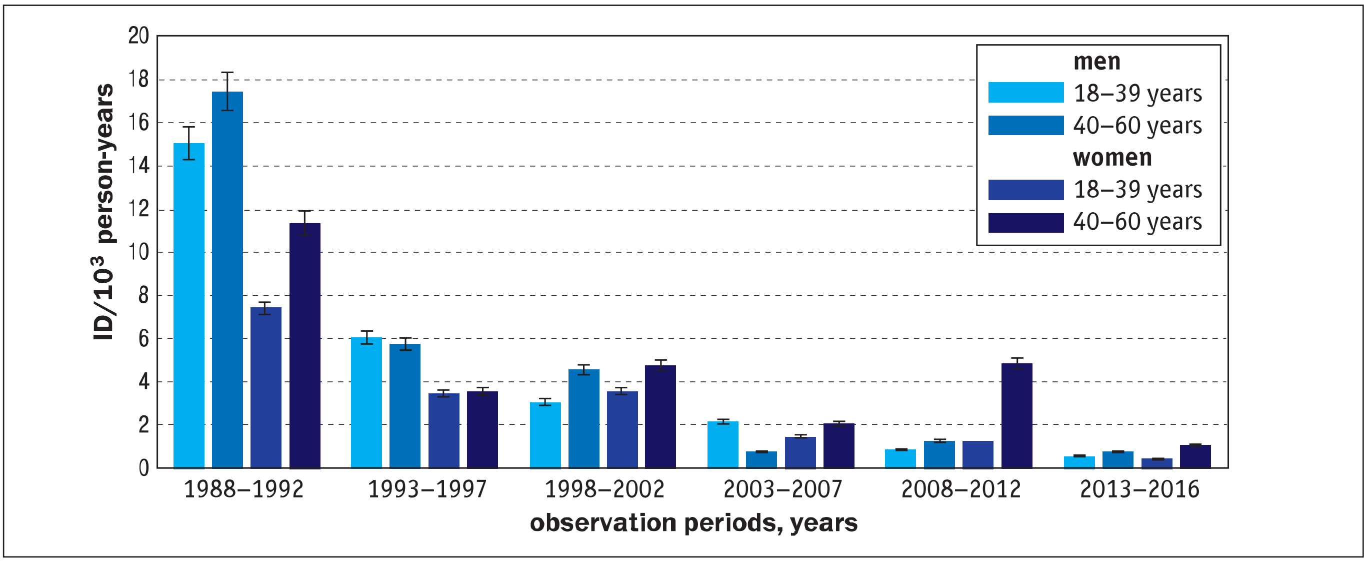

Figure 3.17. **Dynamics of the incidence of mental disorders and behavioral disorders (code 290–319 for ICD–9, F00–F99 for ICD–10) in evacuees depending on age and gender on the date of the accident**

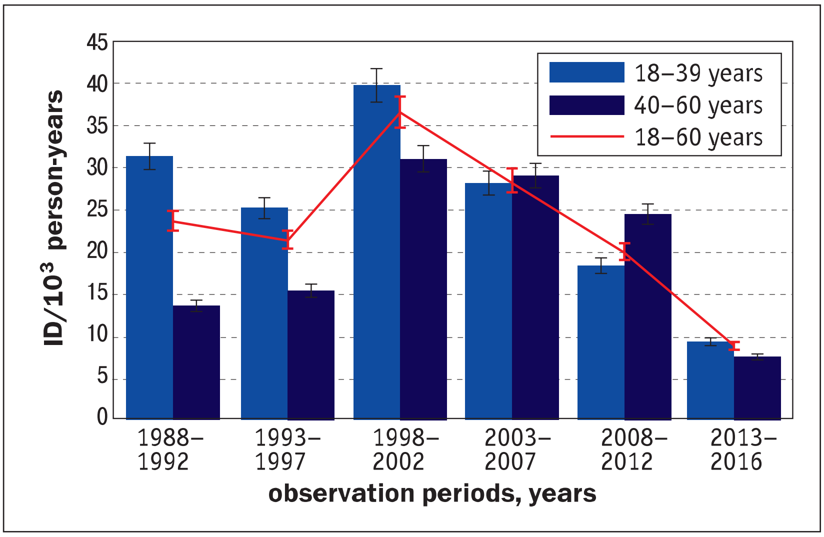

Figure 3.18. **Dynamics of the level of diseases of the nervous system in evacuees depending on age at the date of the accident**

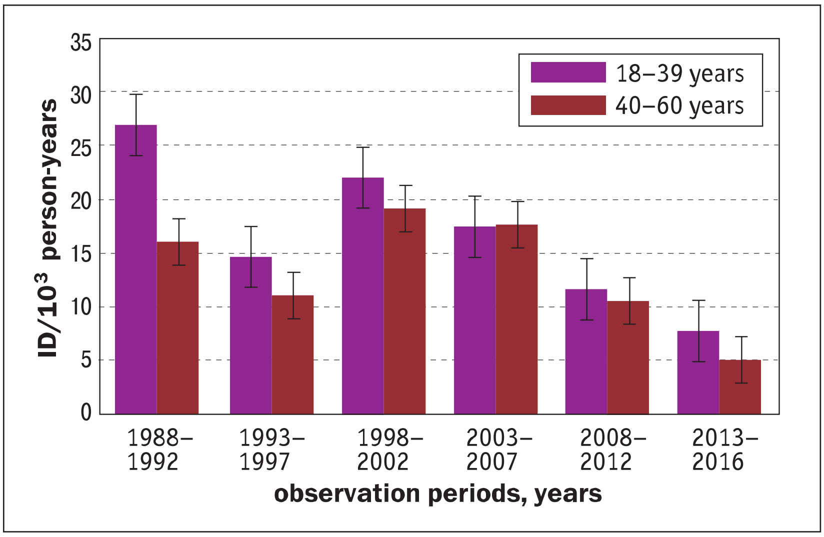

Figure 3.19. Dynamics of the incidence of endocrine diseases, eating disordersand metabolic disorders of evacuees depending on age at the date of the accident

roid disease, and among the nosological groups — thyroid disease associated with iodine deficiency with a maximum level in the early period, non-toxic nodular goiter in the distant period and chronic thyroiditis in the thyroid gland.

The «remote» period (12—21 years from the date of the accident) is characterized by an increase in the level of chronic forms of non-neoplastic diseases. The highest incidence rates for all classes of diseases were registered in this period (Fig. 3.20—3.24).

At a later stage of the study (22—30 years after the accident) changes in the dynamics of the disease did not differ depending on age: in all cases there was a

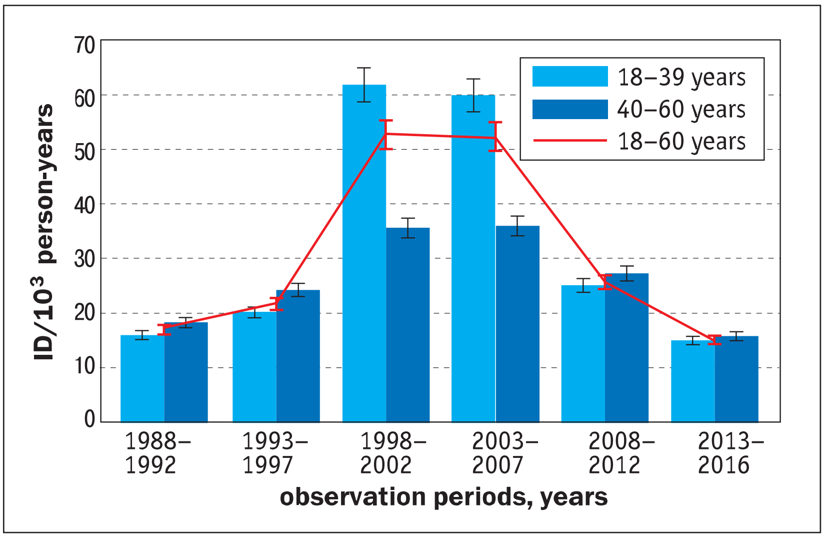

Figure 3.20. Dynamics of the incidence of respiratory diseases evacuated depending on age at the date of the accident

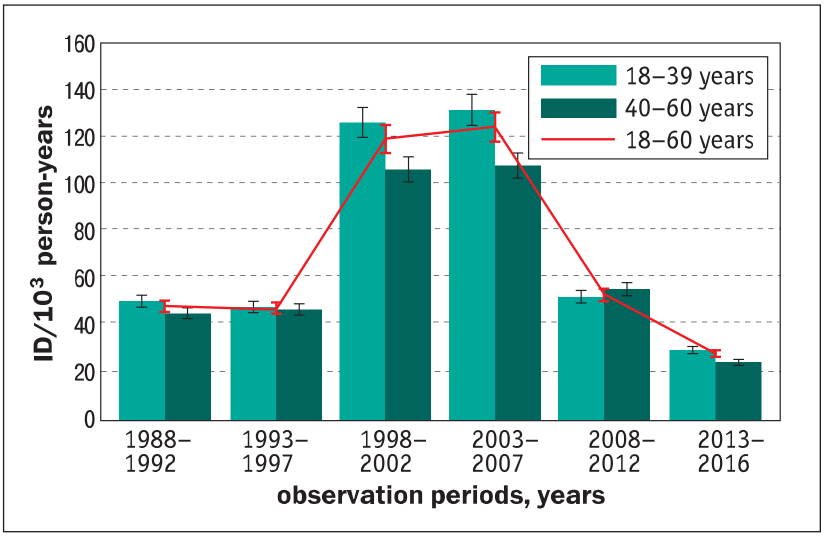

Figure 3.21. Dynamics of the incidence of diseases of the digestive system in evacuees depending on age at the date of the accident

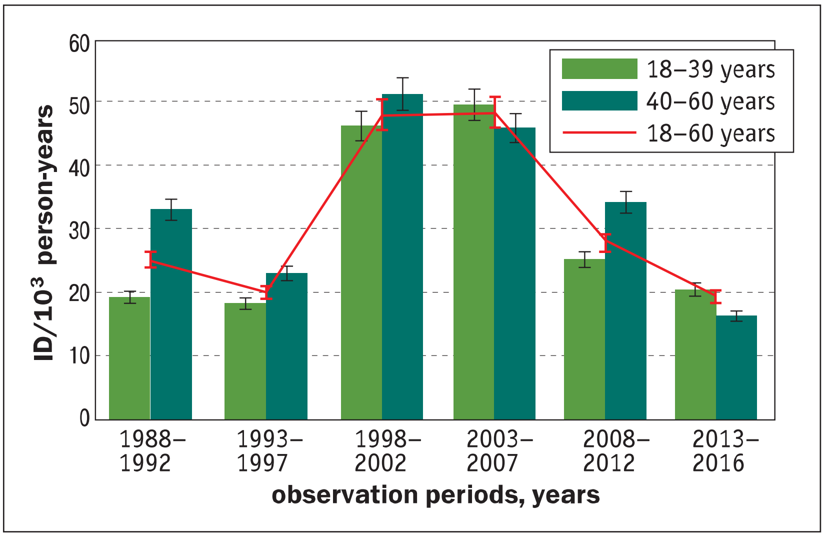

Figure 3.22. **Dynamics of the incidence of diseases of the musculoskeletal system in evacuees depending on age at the date of the accident**

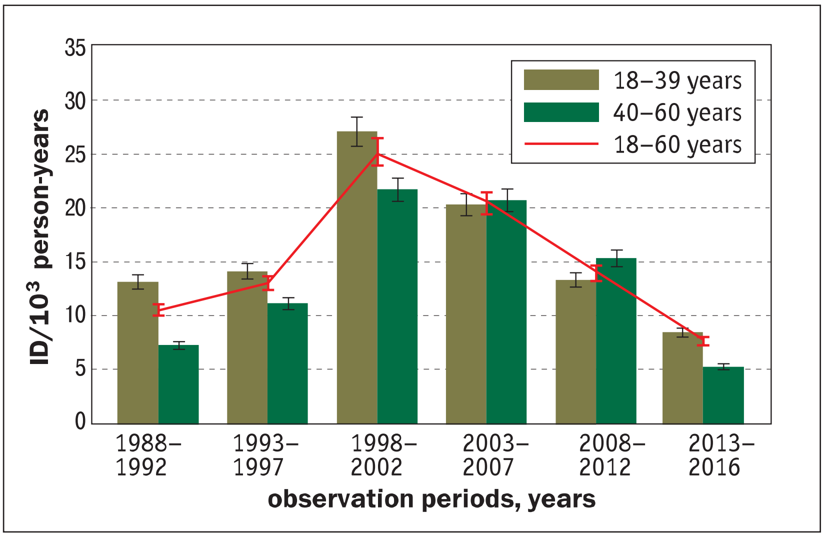

Figure 3.23. **Dynamics of the incidence of diseases of the genitourinary system in evacuees depending on age at the date of the accident**

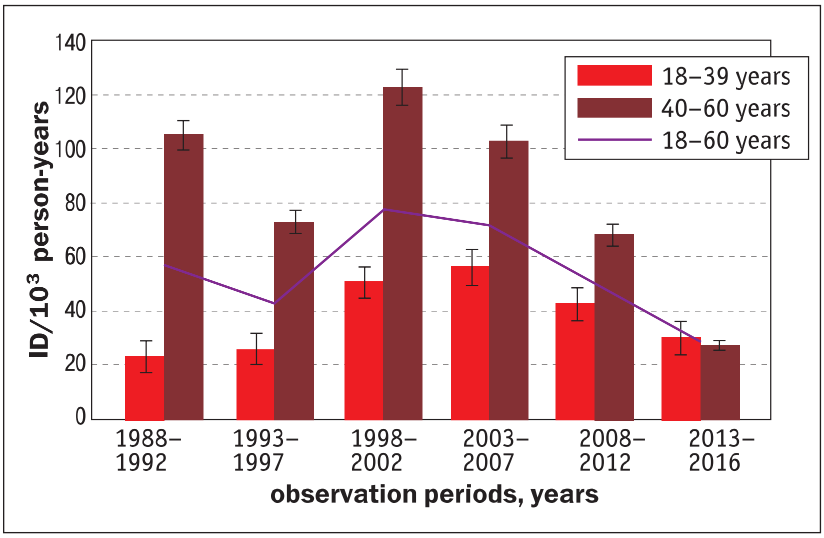

Figure 3.24. **Dynamics of the incidence of diseases of the circulatory system in evacuees depending on age at the date of the accident**

significant reduction in the incidence. It can be assumed that this is a consequence of the stress suffered by the evacuees, especially in the first years after the accident.

Analyzing the structure of non-neoplastic morbidity in certain age groups in the last observation period 2013–2016 (Fig. 3.25), the following should be noted.

Regardless of age, the first rank in the structure is occupied by diseases of the circulatory system. Higher percentage of evacuees aged 18–39 was the following classes of diseases: diseases of the digestive

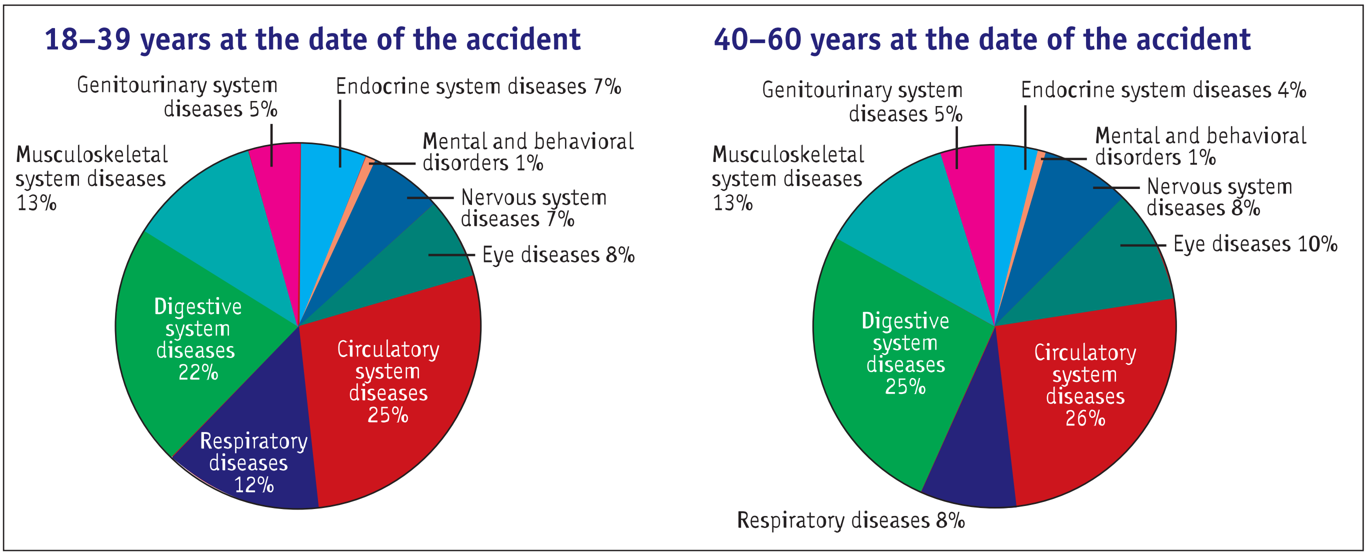

Figure 3.25. **The structure of non-neoplastic morbidity of the population evacuated from the 30-km zone of the ChNPP in the «late» observation period depending on age at the date of the accident**

and respiratory organs, diseases of the musculoskeletal system, endocrine diseases, diseases of the genitourinary system, mental disorders. In the age group of 40—60 years, the ranks of morbidity are occupied by diseases of the digestive and musculoskeletal systems, eye and respiratory diseases. It

Table 3.12
Relative risks of development of the main diseases of the IC for separate periods of observation in the cohort of the evacuated population depending on the age on the date of the accident and the dose of thyroid irradiation. Control – dose group ≤ 0.3 Gy

Observation periods, years	Dose of thyroid irradiation, Gy					
	> 0.3–0.75		> 0.75–2.0		> 2.0	
	RR (95 % CI)	ERR (95 % CI)	RR (95 % CI)	ERR (95 % CI)	RR (95 % CI)	ERR (95 % CI)
			18–39 years			
1988–1992	1.88 1.09–4.47	1.80 1.08–4.30	2.15 1.23–4.99	0.81 0.35–1.86	1.75 1.02–5.35	0.18 0.06–0.54
1993–1997	1.08 0.71–1.88	0.16 0.09–0.28	0.30 0.14–0.64		0.26 0.08–0.85	
1998–2002	1.78* 1.12–2.81	1.59* 1.01–2.53	0.55 0.32–0.97		0.61 0.29–1.30	
2003–2007	2.09* 1.14–3.84	2.25* 1.22–4.13	1.00 0.58–2.08		2.26* 1.00–5.12	0.29 0.13–0.67
2008–2012	1.84* 1.06–3.20	1.73* 1.07–3.00	0.74 0.37–1.49		1.21 0.90–2.89	1.49* 1.02–4.17
2013–2016	3.59* 1.37–9.38	5.33* 2.04–13.92	1.46* 1.01–4.21	0.33 0.11–0.93	2.71* 1.36–8.53	0.40 0.13–1.27
			40–60 years			
1988–1992	0.62 0.34–1.15		0.62 0.38–1.0		1.46 1.02–2.38	0.11 0.07–0.18
1993–1997	1.23* 1.00–2.24	0.42 0.23–0.76	0.75 0.42–1.31		0.41 0.19–0.92	
1998–2002	1.30* 1.02–2.30	0.54 0.31–0.96	0.40 0.21–0.74		0.20 0.08–0.52	
2003–2007	0.56 0.19–1.68		0.13 0.01–1.24		0.59 0.16–2.17	
2008–2012	0.20 0.05– 0.80		0.18 0.04–0.72		0.15 0.02–1.28	
2013–2016	0.17 0.03–0.93		0.18 0.04–0.82		0.16 0.02–1.34	

Note. *p < 0.05

should be assumed that the differences in morbidity rates are in some way related to the peculiarities of the medical effects of factors such as «psychosocial stress». In the early post-accident period, there is a «screening effect», especially in the elderly (> 40 years).

These data are consistent with data from studies conducted in the Russian Federation, which determined that the first place in the structure of the incidence of evacuees are diseases of the IC (21.3 %), the second – diseases of the digestive system (15.6 %), the third – bone diseases, muscular system (14.4 %), fourth place – the respiratory system (11.7 %).

Based on the analytical analysis, the connection between the development of the main non-neoplastic diseases in the evacuees in the post-accident period and the effect of thyroid irradiation and external ionizing γ-irradiation of the whole body was established. These data are important for the planning and implementation of preventive measures.

As a result of the literature review, it was found that the radiation situation at the time of the Chornobyl accident was determined mainly by iodine radionuclides, mainly ^{131}I, in particular, in the evacuated population. Therefore, it was essential to analyze the relationship between the development of major diseases of the IC in the adult evacuated population, in the remote period of the accident, depending on the dose of thyroid irradiation with iodine isotopes.

Studies of the risks of developing diseases of the IC have identified certain differences in the indicators depending on the age of the evacuees on the date of the accident (Table 3.12).

Table 3.13

Relative risks of non-neoplastic diseases by individual groups depending on the age of those evacuated on the date of the accident in 1993–2007, 1993–2012, 1988–2016

Class, group of the disease	Age on the date of the accident	Dose of thyroid irradiation, Gy					
		0.31–0.75		0.76–2.0		over 2.0	
		RR (95 % CI)	ERR (95 % CI)	RR (95 % CI)	ERR (95 % CI)	RR (95 % CI)	ERR (95 % CI)
1993–2007							
Diseases of the endocrine system	18–39	0.96 0.61–1.51		0.48 0.28–0.81		0.51 0.24–1.09	
	40–60	0.97 0.40–2.34		0.74 0.33–1.68		0.70 0.26–1.88	
Diseases of the nervous system	18–39	1.28 0.75–2.18	0.59 0.34–0.99	0.89 0.51–1.55		0.49 0.19–1.29	
	40–60	0.55 0.24–1.29		0.35 0.16–0.79		0.48 0.19–.22	
Diseases of the circulatory system	18–39	1.64* 1.21–2.22	1.32 0.98–1.79	0.57 0.39–0.83		0.75 0.46–1.23	
	40–60	1.26 0.87–1.84	0.48 0.33–0.69	0.57 0.38–0.84		0.37 0.21–0.64	
1993–2012							
Diseases of the endocrine system	18–39	1.05 0.70–1.59	0.11 0.71–1.07	0.51 0.31–0.83		0.58 0.29–1.16	
	40–60	0.93 0.42–2.04		0.67 0.32–1.42		0.57 0.22–1.48	
1988–2016							
Diseases of the endocrine system	18–39	1.32 0.92–1.89	0.65 0.45–0.94	0.75 0.50–1.13		0.65 0.35–1.19	
	40–60	0.81 0.45–1.47		0.46 0.26–.85		0.47 0.23–0.98	
Diseases of the nervous system	18–39	1.35 0.89–2.05	0.73 0.48–1.10	1.04 0.67–1.60	0.03 0.02–.04	0.87 0.46–1.63	
	40–60	0.63 0.30–1.31		0.34 0.16–0.70		0.67 0.32–1.42	
Diseases of the circulatory system	18–39	1.85* 1.45–2.35	1.74 1.37–2.22	0.77 0.58–1.03		1.02 0.70–1.47	0.04 0.03–0.06
	40–60	0.86 0.64–1.16		0.52 0.39–0.70		0.61 0.44–0.86	

Note. *p < 0.05

At the age of 18–39 years on the date of the accident, statistically significant RR was registered in the first and third periods in all dose intervals. In the second period, significant relative risks were obtained in dose groups > 0.3–0.75 Gy and > 2.0 Gy.

When analyzing the risk of developing of the circulatory system diseases in the cohort of evacuees aged 40–60 years on the date of the accident, significant relative risks in the first period with a thyroid radiation dose > 2.0 Gy. In the second period, relative risks were registered at an irradiation dose > 0.3–0.75 Gy. In the third period, in contrast to persons aged 18–39 years at the date of the accident, no relative risks were obtained.

The relative risks of non-neoplastic diseases for certain groups of non-neoplastic diseases depending on the age of those evacuated at the time of the accident in 1993–2007, 1993–2012 and 1988–2016 are given in Table. 3.13.

According to the data obtained, the maximum established values of relative risks for most groups of non-neoplastic diseases are registered at a dose of 0.31–0.75 Gy in both age categories, except for diseases of the nervous system in the evacuated population aged 40–60 years (1988–2016), when the highest levels of RR with a thyroid radiation dose > 2.0 Gy. A statistically significant risk was found only for IC diseases in the evacuated population aged 18–39 years at the time of the accident. The risks of developing diseases of the nervous and endocrine systems in smaller doses are insignificant. A more in-depth analysis and assessment of the impact of internal irradiation of the thyroid gland ^{131}I on the development of non-neoplastic diseases in the adult evacuated population was carried out on the example of diseases of the circulatory system, based on the fact that in the structure of non-neoplastic diseases they rank firest. Relative risks and excesses of relative risks of development of

Table 3.14

Relative risks and excesses of relative risks of development of the main diseases of the circulatory system in the adult evacuated population depending on the age and radiation dose of the thyroid gland for the observation period 1988–2016. Control – dose group ≤ 0.3 Gy

Diseases of the circulatory system	Code ICD–10	Dose of thyroid irradiation, Gy					
		> 0.3–0.75		> 0.75–2.0		> 2.0	
		RR (95 % CI)	ERR/Gy (95 % CI)	RR (95 % CI)	ERR/Гр (95 % CI)	RR (95 % CI)	ERR/Gy (95 % CI)
18–39 years							
Diseases of the circulatory system:	I 00–I 99.9	1.88* 1.09–4.47	1.80 1.08–4.30	2.15 1.23–4.99	0.81 0.35-1.86	1.75* 1.02–5.35	0.18 0.06–0.54
➢ hypertension	I 10.0–I 15.9	1.06 0.89–1.62	0.13 0.08–0.19	0.59 0.36–0.96		0.81 0.43–1.50	
➢ ischemic heart diseases	I 20–I 25.9	1.93* 1.17–3.19	1.92* 1.16–3.17	0.62 0.33–1.18		0.88 0.40–1.98	
➢ cerebrovascular diseases	I 60–I 69.9	3.01* 1.80–5.06	4.15* 2.47–6.96	0.80 0.42–1.54		0.67 0.25–1.79	
➢ diseases of arteries, arterioles and capillaries	I 70.0–1 79.8	5.93* 2.71–11.22	10.14* 1.22–24.18	1.79 1.07–4.73	0.55 0.50–1.06	1.39* 1.06–4.03	0.42 0.30–1.01
➢ diseases of veins, lymphatic vessels and lymph nodes	I 80–I 89.9	1.81* 1.07–4.90	1.67* 1.02–4.51	1.04 0.85–3.11	0.03 0.01–0.09	4.66* 1.72–12.59	0.86 0.32–2.33
40–60 years							
Diseases of the circulatory system:	I 00–I 99.9	0.62 0.34–1.15		0.62 0.38–1.0		1.46* 1.02–2.38	0.11 0.07–0.18
➢ hypertension	I 10.0–I 15.9	0.49 0.26–0.93		0.35 0.19–0.62		0.29 0.13–0.64	
➢ ischemic heart diseases	I 20–I 25.9	1.14 0.90–1.87	0.26 0.18–0.43	0.79 0.50–1.26		0.70 0.40–1.24	
➢ cerebrovascular diseases	I 60–I 69.9	1.18 0.92–2.27	0.33 0.18–0.64	0.49 0.25–0.98		0.60 0.27–1.33	
➢ diseases of arteries, arterioles and capillaries	I 70.0–I 79.8	0.11 0.01–0.90		0.06 0.02–0.48		0.39 0.10–1.49	
➢ diseases of veins, lymphatic vessels and lymph nodes	I 80–I 89.9	0.93 0.28–3.04		0.58 0.18–1.82		1.79 0.91–5.26	

Note. *$p < 0.05$.

Table 3.15
Relative risks of development of separate groups of diseases of the circulatory system in the evacuated population, depending on the doses of external irradiation of the whole body and age on the date of the accident. Control – dose group < 0.05 Gy

Diseases of the circulatory system	Doses of external irradiation of the whole body, Gy								
	0.05–0.099			0.10–0.325			0.05–0.325		
	RR	CI–	CI+	RR	CI–	CI+	RR	CI–	CI+
Adult evacuated population 18–39 years of age									
Diseases of the circulatory system:	1.08*	1.01	1.16	0.89	0.79	1.01	1.05	0.98	1.12
➢ hypertension	1.19*	1.01	1.41	0.86	0.63	1.17	1.14	0.97	1.33
➢ ischemic heart diseases	1.47*	1.00	2.15	1.58	0.88	2.85	1.49	1.03	2.15
➢ cerebrovascular diseases	1.09	0.93	1.27	0.99	0.76	1.30	1.07	0.92	1.24
➢ diseases of arteries, arterioles and capillaries	1.13	0.86	1.48	0.66	0.38	1.16	1.04	0.80	1.36
Adult evacuated population 40–60 years of age									
Diseases of the circulatory system:	0.98	0.80	1.21	0.98	0.74	1.31	0.98	0.81	1.20
➢ hypertension	1.13	0.63	2.04	0.97	0.41	2.26	1.10	0.62	1.95
➢ ischemic heart diseases	1.24	0.61	2.49	1.76	0.75	4.15	1.35	0.69	2.64
➢ cerebrovascular diseases	1.13	0.78	1.63	1.18	0.72	1.94	1.14	0.80	1.63
➢ diseases of arteries, arterioles and capillaries	1.04	0.58	1.85	1.03	0.46	2.30	1.04	0.59	1.81

the main diseases of the circulatory system at the evacuated population are presented in Table 3.14.

Significant relative risk values and relative risk excesses in evacuees aged 18–39 years have been established in the development of coronary heart disease, cerebrovascular disease, arterial, arteriole and capillary disease, and venous, lymphatic, and lymph node disease with a dose of internal radiation in the range > 0.3–0.75 Gy.

Significant dose-dependent effect in the age group of evacuees 40–60 years was found with a thyroid radiation dose > 2.0 Gy only for the class of diseases of the circulatory system and the group – diseases of veins, lymph vessels and lymph nodes.

Relative risks of development of separate groups of IC diseases in the evacuated population. depending on the doses of external radiation of the whole body and age are given in Table. 3.15.

Evacuees aged 18–39 years at the time of the accident had significant relative risks of developing hypertensive disease – 1.19 (1.01–1.41) and coronary heart disease – 1.47 (1.00–2.15) with an external radiation dose of 0.05–0.099 Gy, for other species and nosological forms – unreliable. In the dose range of 0.05–0.099, the relative risks of coronary heart disease are 1.47 (1.0–2.15) higher than for hypertensive disease – 1.19 (1.01–1.41), and in the dose range 0.10–0.245 Gy higher RR for coronary heart disease, cerebrovascular diseases, diseases of arteries, arterioles and capillaries.

The study revealed a clear pattern, which was that in the dose range of 0.05–0.099 RR development of diseases of the IC for all nosological forms, except for CVD, in persons aged 18–39 years at the time of the accident is higher than in the age group 40–60 years. The opposite picture was detected with dose intervals of 0.10–0.245 Gy.

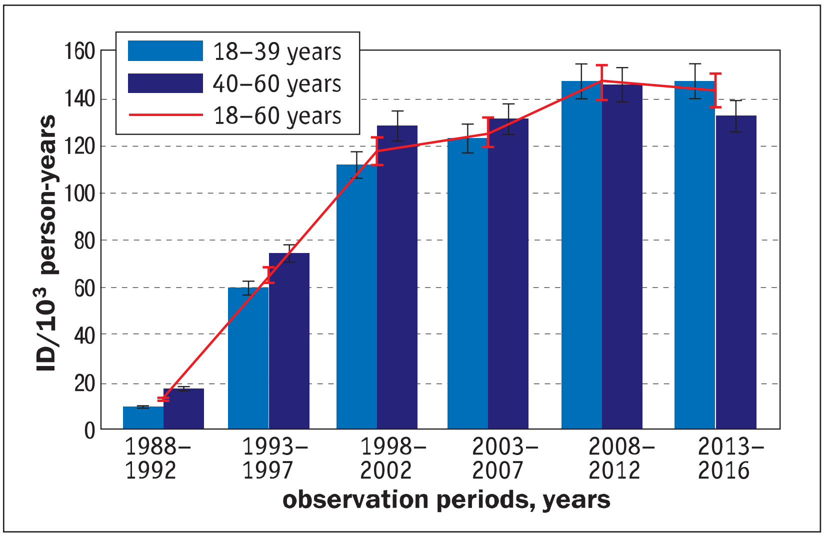

Figure 3.26. **Post-accident dynamics of the level of disability from non-neoplastic diseases in the evacuated population depending on age at the time of the accident**

Disability

In the post-accident period, there is an increase in the level of disability of the evacuated population (Fig. 3.26). The increase in the level of disability practically began in 1993 and reached its maximum values in the period from 2008 to 2016. During this period, the same trends of increasing disability was in the two groups (18–39 and 40–60 years).

The total number of recognized disabled among the adult evacuated population for the period 1988–2016 is presented in Table 3.16.

Analysis of the structure of disability due to non-neoplastic diseases depending on the age of the evacuees at the time of the accident by disease classes for the entire observation period (1988–2016) showed that the first place regardless of age is occupied by diseases of the circulatory system, the second place – diseases of the nervous system and digestive organs (Fig. 3.27).

Mortality

The results of the epidemiological study of mortality from non-neoplastic diseases of the adult evacuated population (Fig. 3.28) show that in the post-accident period mortality from non-neoplastic diseases increased significantly, reaching peak values in the long term, after which there is a gradual decrease, but mortality rates in the last period (2013–2016) exceed the indicators of the early period (1988–1992) at the age of 18–39 by 5.9 times, and at the age of 40–60 by 2.8 times. Mortality at the age of 40–60 years exceeds the mortality rate at the age of 18–39 years during all observation periods. It is obvious that the high mortality rate of this age group from non-neoplastic diseases is due to the influence of the «age» factor.

The total number of deaths from non-neoplastic diseases among the adult evacuated popula-

Table 3.16
The total number of disabled people among the adult evacuated population, depending on age at the time of the accident for the period 1988–2016

Class, group of the disease	Code ICD–10	Adult evacuated population	
		18–39 years	40–60 years
Non-tumor diseases		42,862	21,178
Diseases of the endocrine system	E00–E90.9	3,037	1,435
Mental and behavioral disorders	F00–F99.9	786	166
Diseases of the nervous system	G00–G99.9	10,541	1,843
Diseases of the eyes	H00–H59.9	316	174
Diseases of the circulatory system	I00–I99.9	20,749	14,361
Respiratory diseases	J00–J99.9	1,217	816
Diseases of the digestive system	K00–K93.9	4,371	1,496
Diseases of the musculoskeletal system	M00–M99.9	1,228	623
Diseases of the genitourinary system	N00–N99.9	617	284

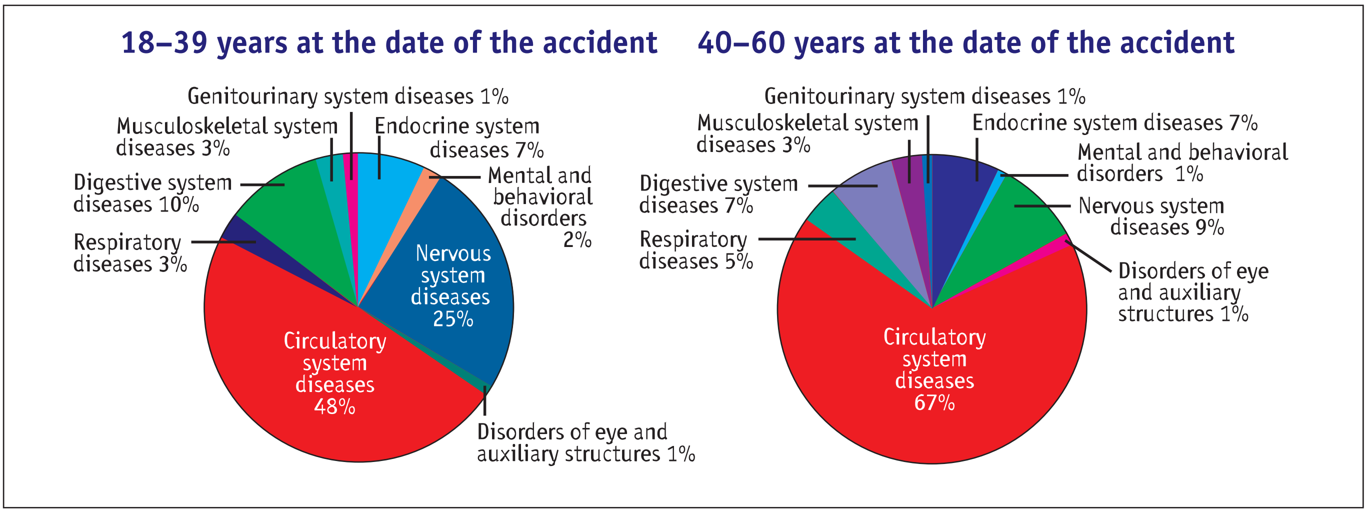

Figure 3.27. **Structure of disability from non-neoplastic diseases of the population evacuated from the 30-km zone of the Chornobyl NPP by disease classes for the observation period (1988–2016) depending on age at the date of the accident**

tion for the period 1988—2016 is presented in Table 3.17.

In all periods of observation, mortality in men is higher than in women (Fig. 3.29, 3.30) and only in the last period at the age of 40—60 years the picture changes to the opposite.

In the structure of causes of death from non-neoplastic diseases, the main share falls on diseases of the circulatory system, both younger and older age groups of the adult evacuated population (Fig. 3.31). Digestive and respiratory diseases occupy a significant share.

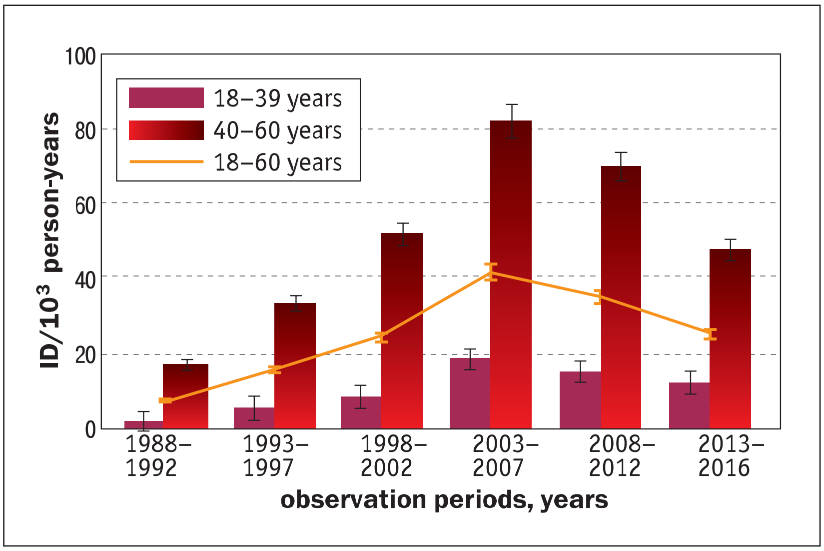

Figure 3.28. Post-accident dynamics of the overall mortality rate from non-neoplastic diseases of the evacuated population depending on age at the date of the accident

Table 3.17
The total number of deaths from non-neoplastic diseases for the entire period 1988–2016, depending on age at the date of the accident

Class, group of the disease	Code ICD–10	Adult evacuated population		
		18–39 years	40–60 years	18–60 years
Non-tumor diseases		1,721	4,744	6,465
Diseases of the endocrine system	E00–E90.9	18	29	47
Mental and behavioral disorders	F00–F99.9	11	6	17
Diseases of the nervous system	G00–G99.9	75	35	107
Diseases of the eyes	H00–H59.9	4	10	14
Diseases of the circulatory system	I00–I99.9	1,293	4,375	5,668
Respiratory diseases	J00–J99.9	100	124	224
Diseases of the digestive system	K00–K93.9	199	136	335
Diseases of the musculoskeletal system	M00–M99.9	6	9	15
Diseases of the genitourinary system	N00–N99.9	18	20	38

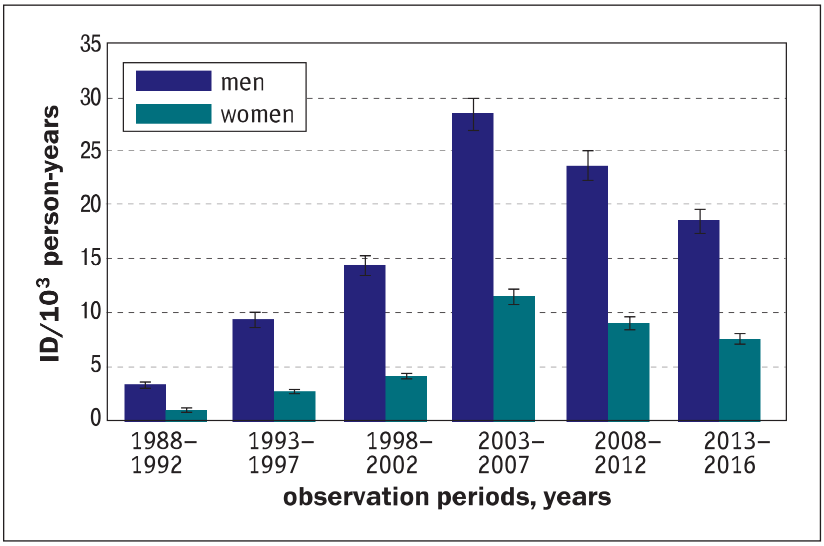

Figure 3.29. Post-accident dynamics of mortality from non-neoplastic diseases of the evacuated population aged 18–39 years on the date of the accident, depending on gender

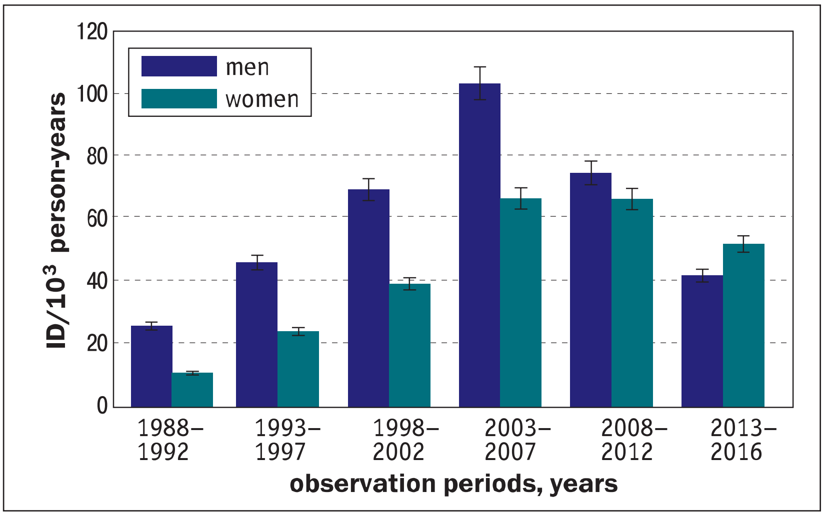

Figure 3.30. **Post-accident dynamics of mortality from non-neoplastic diseases of the evacuated population aged 40–60 years on the date of the accident, depending on gender**

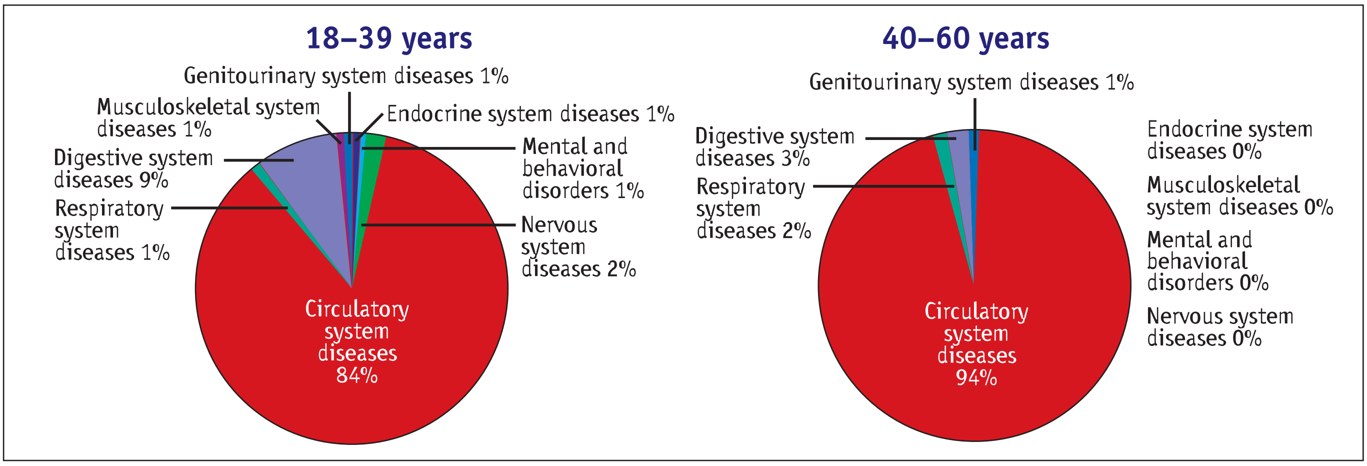

Figure 3.31. **Structure of mortality from non-neoplastic diseases of the population evacuated from the 30-km zone of the Chornobyl NPP by disease classes for the observation period (1988–2016) depending on age at the date of the accident**

3.1.3. Non-tumor effects in the adult population of radioactively contaminated areas of Ukraine

Introduction

Cohort-epidemiological studies of the health of residents of RCT of Ukraine were conducted. The cohort of subjects consisted of 65,189 people aged 18–60 years on the date of the Chornobyl accident, who lived and still live in RCT Zhytomyr, Kyiv, Chernihiv, Rivne Oblasts, respectively Ovruch, Ivankiv, Kozelets, Rokytne districts. More detailed characteristics of the numerical composition of the cohort by age, gender and total individual dose of ionizing radiation (external and internal) are given in section 3.1.1. Source of information – data from the State Register of Ukraine of persons affected by the Chornobyl disaster of the Ministry of Health of Ukraine. The period of research and analysis was 30 years (1988–2016). Subject of research: non-neoplastic morbidity, disability, mortality, effects of the total effective dose of ionizing radiation from the isotopes ^{131}Cs, ^{134}Cs, accumulated in 1988–2012.

Non-neoplastic disease

As a result of an epidemiological study of the development of non-neoplastic morbidity in residents of RCT, aged 18–60 years on the date of the Chornobyl accident, for the first time in 1988–2016 90,590 cases were detected (Table 3.18).

Residents of RCT aged 18–39 years have a lower incidence (97.33 ID/10^3 person-years), compared with 40–60-years-old (111.24 ID/10^3 person-years). Among younger men the incidence is lower than among older ones ($p < 0.05$), and among women, depending on age, there were no significant changes in morbidity levels (Fig. 3.32). Women were sick more often than men, regardless of age ($p < 0.05$).

According to the dynamics of the incidence of non-neoplastic diseases among residents of RCT aged 18–39 years on the date of the accident, the incidence rate over 16 years (1988–2002) gradually

Table 3.18
The number of newly detected non-neoplastic diseases among residents of radioactively contaminated areas by gender and age on the date of the Chornobyl accident for the period of the study 1988–2016

Age, years	Rezidents of RCT, abs. value (%)		
	men	women	total
18–39	16 474 (52.05)	29 381(49.85)	45 855 (50.62)
40–60	15 179(47.95)	29 556 (50.15)	44 735 (49.38)
18–60	31 653 (100)	58 937 (100)	90 590 (100)

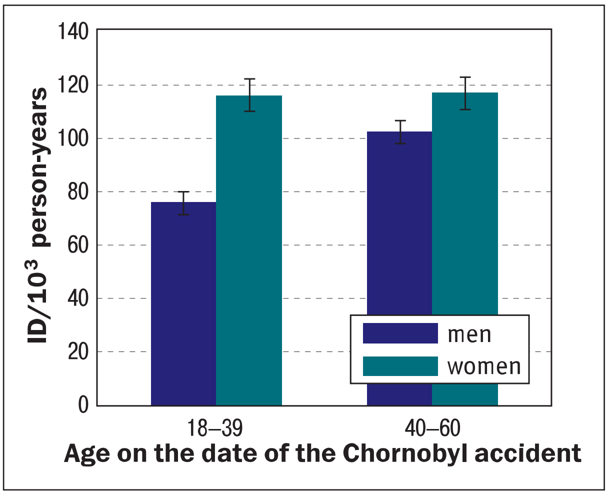

Figure 3.32. Levels of non-neoplastic morbidity of RCT residents depending on age at the date of the Chornobyl accident and gender for the years of observation 1988–2016

increased, and in subsequent years decreased, in 40–60-years-old, on the contrary – the incidence from the highest level in the first period decreased in the following five-year periods to the lowest level in 2013–2016 (Fig. 3.33, 3.34). Particularly sharp decline in morbidity, almost two or three times, occurred during the period 2008–2012 compared to previous five-year periods, regardless of gender and age on the date of the Chornobyl accident.

The nature of changes in morbidity levels among men and women in age groups is identical to the general cohorts. Among women of both age cohorts, the incidence exceeded the incidence of men during the thirty-year follow-up period.

According to the indicators of the structure of non-neoplastic morbidity, the dependence of disease development on gender and age on the date of the Chornobyl accident was noted. Among the younger residents of RCT at the first three places were diseases of the respiratory system, digestive system, circulatory system, among the older – diseases of the circulatory system, respiratory system, digestive system. Diseases of the respiratory, endocrine, nervous, and genitourinary systems were significantly more prevalent among the younger ones, and diseases of the circulatory and musculoskeletal systems were significantly more prevalent among the older ones (Table 3.19).

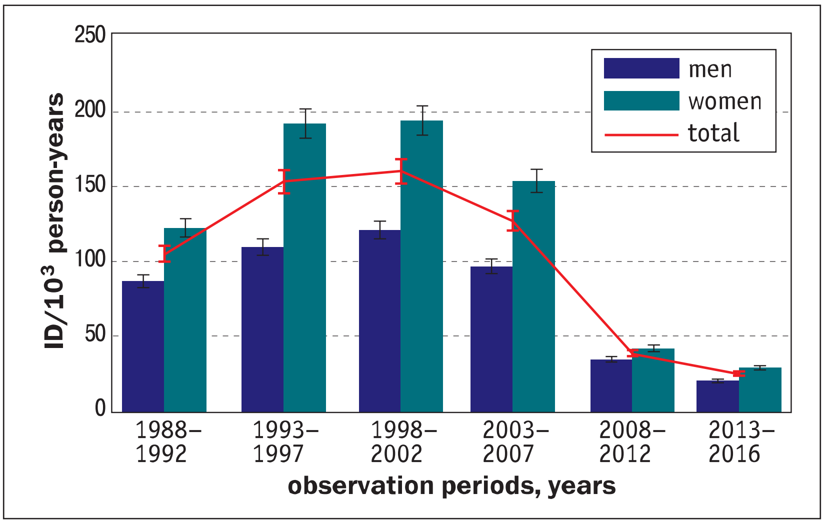

Figure 3.33. Dynamics of the overall incidence of non-neoplastic diseases among residents of RCT, aged 18–39 years on the date of the Chornobyl accident, depending on gender for the years of observation 1988–2016

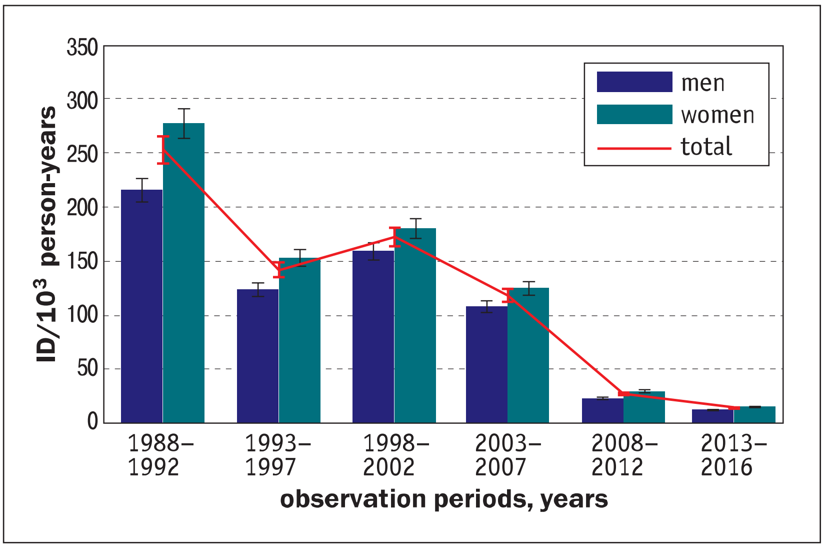

Figure 3.34. Dynamics of the overall incidence of non-neoplastic diseases among residents of RCT, aged 40–60 years on the date of the Chornobyl accident, depending on gender for the years of observation 1988–2016

Table 3.19

The structure of non-neoplastic morbidity of RCT residents depending on the age at the date of the Chornobyl accident and gender for the period 1988–2016 (%)

Classes of diseases to ICD–10 (code)	Age at the date of the Chornobyl accident, years					
	18–39			40–60		
	men	women	total	men	women	total
Diseases of the endocrine system (E00-E90)	2.22	3.00	2.72	1.13	2.10	1.77
Mental and behavioral disorders (F00–F99)	1.14	0.91	0.99	0.61	0.83	0.76
Diseases of the nervous system (G00–G99)	7.99	8.63	8.40	6.75	6.91	6.85
Diseases of the circulatory system (I00–I99)	11.93	12.95	12.58	26.89	28.42	27.90
Respiratory diseases (J00–J99)	43.38	32.35	36.31	23.78	19.32	20.84
Diseases of the digestive system (K00–K93)	22.79	18.08	19.77	19.91	17.95	18.61
Diseases of the genitourinary system (N00–N99)	3.88	14.72	10.83	4.37	6.63	5.87
Diseases of the musculoskeletal system (M00–M99)	12.36	9.36	10.44	16.55	17.84	17.40

Disability

As a result of an epidemiological study among residents of RCT, aged 18–60 years on the date of the Chornobyl accident, for the first time in 1988–2016 revealed 11,153 cases of disability from non-neoplastic diseases (Table 3.20).

Residents of RCT aged 18–39 years have a higher disability from non-neoplastic diseases (14.62 ID/10^3 person-years) compared to 40–60 years old (10.59 ID/10^3 person-years) ($p < 0.05$). There is a dependence of the level of disability on gender – among younger people the disability is higher among women than among men, among older people – among men (Fig. 3.35).

Residents of RCT, regardless of gender and age at the date of the accident, had a significant increase in disability until 1993–1997 (7–11 years), compared to the first 7 years after the accident. The second significant increase occurred during 2008–2012 (21–26 years after the accident) and remained at high levels until 2016 (Fig. 3.36, 3.37). Among men and women aged 18–39 and 40–60 years, the dynamics of disability is identical to these mixed cohorts. Among women aged 18–39, the dis-

Table 3.20

The number of first-established cases of disability from non-neoplastic diseases among residents of radioactively contaminated areas by age at the date of the Chornobyl accident and the article for the observation period 1988–2016

Age, years	Rezidents of RCT, abs. value (%)		
	men	women	total
18–39	2 468 (57.91)	4 423 (64.19)	6 891 (61.78)
40–60	1 794 (42.09)	2 468 (35.81	4 262 (38.22)
18–60	4 262 (100)	6 891 (100)	11 153 (100)

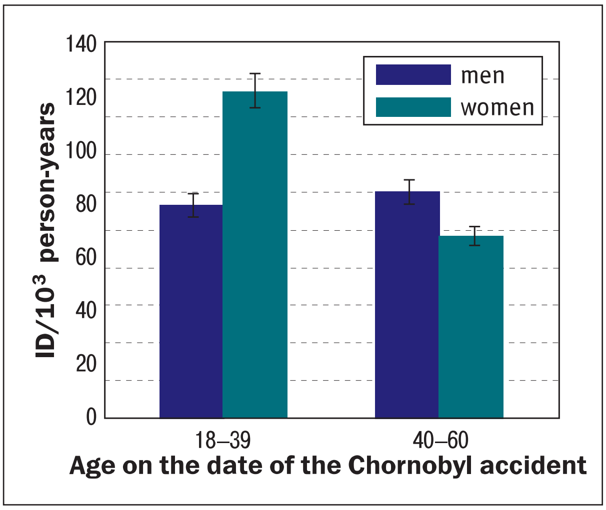

Figure 3.35. Levels of disability from non-neoplastic diseases of RCT residents depending on age at the date of the Chornobyl accident and gender for the years of observation 1988–2016

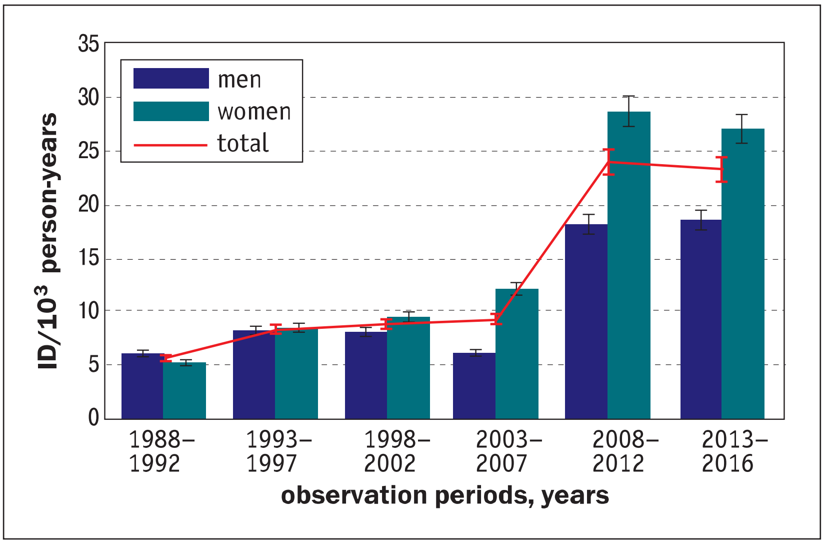

Figure 3.36. Dynamics of the general level of disability from non-neoplastic diseases among residents of RCT, aged 18–39 years on the date of the Chornobyl accident, depending on gender for the years of observation 1988–2016

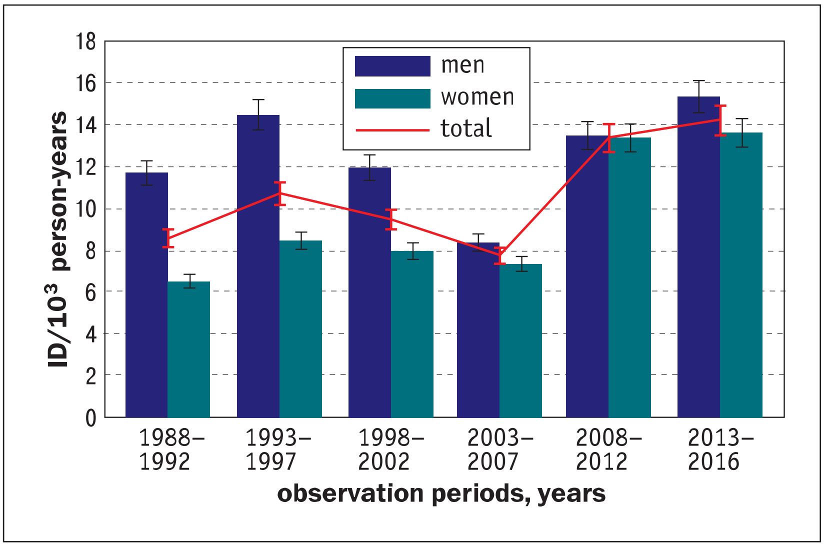

Figure 3.37. Dynamics of the level of disability from non-neoplastic diseases among the residents of RCT, aged 40–60 years on the date of the Chornobyl accident, depending on gender for the years of observation 1988–2016

ability significantly exceeded the disability of men from 2003 to 2016, in 40–60 years old, disability prevailed among men in almost all five-year periods.

The structure of disability from non-neoplastic diseases among residents of RCT during the study period is given in Table 3.21.

Among the residents aged 18–39, the first three places of diseases-factors of disability were diseases of the circulatory system, endocrine and nervous systems, which accounted for 89.37 % of the structure of disability. A significant contribution to disability was in mental and behavioral disorders, diseases of the digestive system.

Table 3.21
The structure of disability from non-neoplastic morbidity among residents of RCT depending on age at the date of the Chornobyl accident and gender for the period 1988–2016 (%)

Classes of diseases according to ICD–10 (code)	Age at the date of the Chornobyl accident, years					
	18–39			40–60		
	men	women	total	men	women	total
Diseases of the endocrine system (E00-E90)	30.23	25.65	27.41	4.08	8.12	6.42
Mental and behavioral disorders (F00–F99)	7.72	5.91	6.60	1.36	1.43	1.40
Diseases of the nervous system (G00–G99)	8.83	19.88	15.62	5.15	6.72	6.06
Diseases of the circulatory system (I00–I99)	49.08	44.62	46.34	69.31	75.00	72.61
Respiratory diseases (J00–J99)	5.78	4.58	5.04	5.72	2.09	3.61
Diseases of the digestive system (K00–K93)	12.61	8.31	9.99	10.25	3.24	6.18
Diseases of the genitourinary system (N00–N99)	1.26	1.75	1.56	0.91	1.19	1.07
Diseases of the musculoskeletal system (M00–M99)	3.69	1.87	2.57	3.23	2.21	2.64

Among men and women, the structure of disability is identical to the structure of a mixed cohort. It should be noted that men in this age group have a greater number of disabled people than women in almost all diseases, except for diseases of the nervous and urogenital systems. Among 40–60-year-old residents of RCT, both men and women, in the structure of disability, the greatest indicators are found in diseases of the circulatory system. A significant role in the development of disability of residents of this age can be traced to diseases of the endocrine system, diseases of the digestive system. There is a difference in the diseases-factors of disability: among men the disability occurred mostly due to diseases of the respiratory system, digestive and musculoskeletal systems, among women – mental and behavioral disorders, diseases of the circulatory, nervous, genitourinary, endocrine.

Mortality

As a result of an epidemiological study of mortality from non-neoplastic diseases among residents of RCT, in 1988–2016, 11,586 cases were identified (Table 3.22). Mortality due to non-neoplastic diseases among RCT residents differs significantly by age: the younger ones are much lower (5.28 ID/10^3 person-years) than the older ones (22.61 ID/10^3 person-years).

Residents of RCT of the older age category have a higher mortality rate compared to the younger one

Table 3.22
Number of deaths from non-neoplastic diseases among residents of radioactively contaminated areas depending on age at the date of the Chornobyl accident and gender for the observation period 1988–2016

Age, years	Rezidents of RCT, abs. value, (%)		
	мen	women	total
18–39	1 727 (69.41)	761 (30.59)	2 488 (100)
40–60	4 115 (45.23)	4 983 (54.77)	9 098 (100)
18–60	5 842 (50.42)	57 44 (49.58)	11 586 (100)

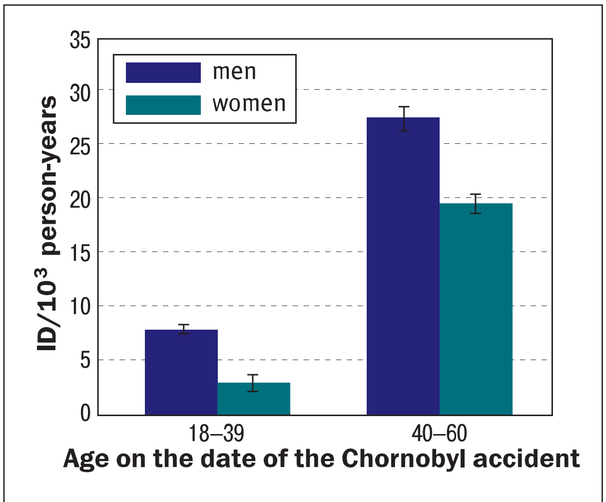

Figure 3.38. **Mortality rates from non-neoplastic diseases of residents of radioactively contaminated areas depending on age at the date of the Chornobyl accident and gender. Years of observation 1988–2016.**

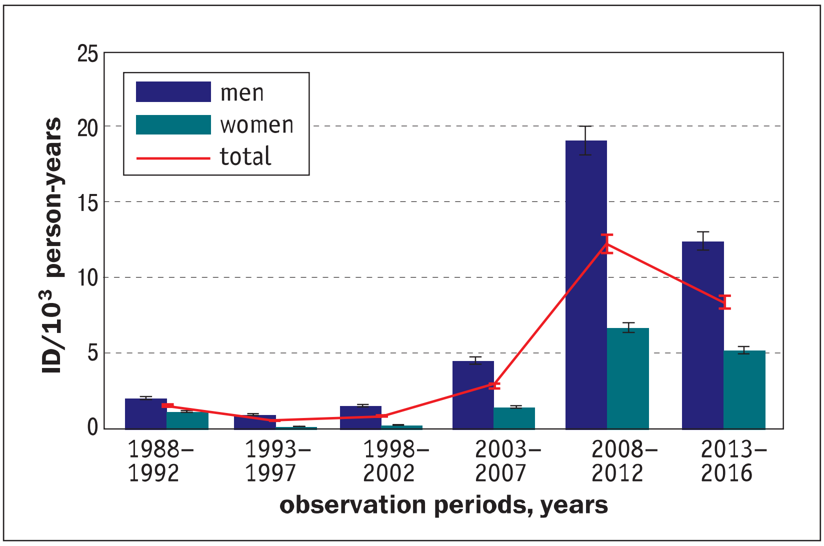

Figure 3.39. Dynamics of mortality from non-neoplastic diseases of RCT residents, aged 18–39 years on the date of the Chornobyl accident, taking into account gender and time after the accident

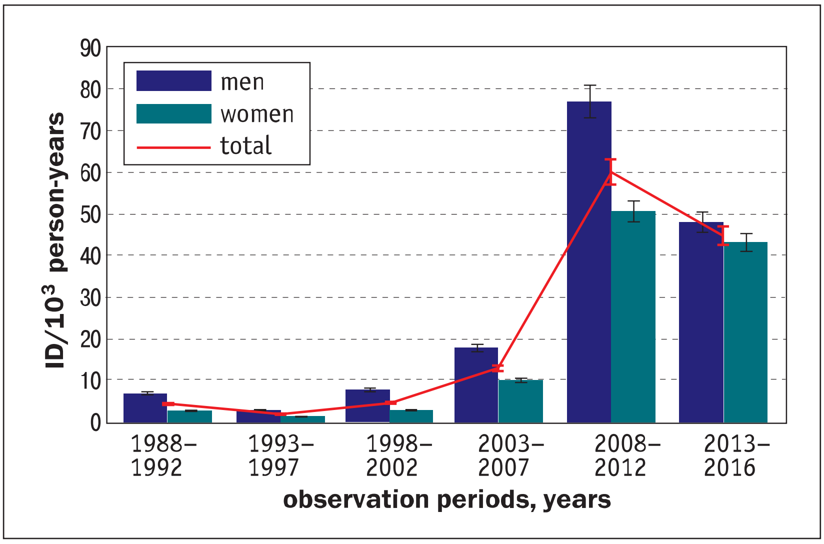

Figure 3.40. Dynamics of mortality from non-neoplastic diseases of RCT residents, aged 40–60 years on the date of the Chornobyl accident, taking into account gender and time after the accident

(Fig. 3.38). Mortality is higher among men than among women, regardless of age.

Mortality from non-neoplastic diseases of RCT residents aged 18—39 and 40—60 years on the date of the Chornobyl accident, taking into account gender and time after the Chornobyl accident, has been increasing since 1988 in the following five-year observation periods. Most deaths were registered in 2008—2012 (Fig. 3.39, 3.40).

In the following years (2013—2016), mortality decreased, but remained high compared to previous five-year periods. In the age cohorts of 18—39 and 40—60 years on the date of the Chornobyl accident, the dynamics of mortality from non-neoplastic diseases is similar, regardless of gender. In 2008—2012, the mortality of women and men was the highest compared to other five-year observation periods.

In the last period there was a significant decrease in mortality compared to the penultimate, but the mortality rate remained significantly higher than in 1988—2007.

The structure of mortality from non-neoplastic diseases of RCT residents by gender and age on the date of the Chornobyl accident for the observation period 1988—2016 is given in Table 3.23.

In 18—39-years-old and 40—60-years-old, the first three places are occupied by diseases of the circulatory system, respiratory and digestive organs (94,38 % and 98,90 %, respectively). Among younger people, the mortality rate exceeds the mortality rate of older people in all classes of non-neoplastic diseases, in particular diseases of the circulatory system and respiratory system.

Mortality is higher among men aged 18—39 than among women, due to mental and behavioral disorders, diseases of the nervous system, respiratory system, among women, mortality from diseases of the circulatory, endocrine, digestive and genitourinary systems prevailed. Among 40—60-year-old men among the causes of death prevailed diseases of the respiratory system, digestion, among women — diseases of the circulatory system.

Table 3.23
The structure of mortality from non-neoplastic diseases of RCT residents depending on gender and age on the date of the Chornobyl accident for the period 1988–2016 (%)

Classes of diseases according to ICD–10 (code)	Age at the date of the Chornobyl accident, years					
	18–39			40–60		
	men	women	total	men	women	total
Diseases of the endocrine system (E00–E90)	0.81	1.71	1.09	0.36	0.40	0.38
Mental and behavioral disorders (F00–F99)	2.26	0.53	1.73	0.05	0.02	0.03
Diseases of the nervous system (G00–G99)	2.20	1.45	1.97	0.32	0.30	0.31
Diseases of the circulatory system (I00–I99)	77.82	80.95	78.78	89.65	94.70	92.42
Respiratory diseases (J00–J99)	7.35	2.76	5.95	7.58	3.05	3.10
Diseases of the digestive system (K00–K93)	8.80	11.56	9.65	1.70	1.12	1.38
Diseases of the genitourinary system (N00–N99)	0.69	1.05	0.80	0.29	0.38	0.34
Diseases of the musculoskeletal system (M00–M99)	0.00	0.00	0.00	0.05	0.02	0.03

Effects of ionizing radiation

On the basis of risk analysis, significant dose-dependent effects of ionizing radiation were found in the dose range of 13 – ≥ 40 mSv in the development of certain non-neoplastic diseases of the circulatory system, respiratory system, digestion, which mainly formed non-neoplastic morbidity among RCT residents (Table 3.24, 3.25).

At the date of the Chornobyl accident, the development of diseases of the circulatory system has detected among persons aged 18–39 and 40–60 years, namely: among younger people – diseases of veins, lymphatic vessels in the dose range 26 – < 40 mSv, among older – diseases of veins, lymphatic blood vessels, essential hypertension, other heart diseases, endocardial diseases in the range of 13 – < 40 mSv.

In the dose range of 13 – ≥ 40 mSv in 18–39-year-old and 40–60-year-old residents of RCT from respiratory diseases there was a dose-dependent effect of development on chronic laryngitis and laryngotracheitis, chronic rhinitis and nasopharyngitis, simple chronic bronchitis, chronic obstructive pulmonary disease.

Under the influence of radiation in the dose ranges of 13 – < 26 mSv and ≥ 40 mSv in 18–39-year-old and 40–60-year-old residents of RCT among the diseases of the digestive system the dependence revealed gastritis and duodenitis, liver fibrosis and cirrhosis, pancreatic diseases.

High indicators of the effect of ionizing radiation were found on respiratory diseases in the dose range of 13 – ≤ 26 mSv, regardless of the age of RCT residents at the date of the Chornobyl accident, and on the digestive organs in the dose range of ≥ 40 mSv in persons at the age of 40–60 years.

In view of the above, it should be noted that in the changes in the health of the adult population of

Table 3.24
Relative risks of non-neoplastic morbidity of RCT residents aged 18–39 as of the date of the Chornobyl accident for 1988-2016, depending on the accumulated effective doses of ionizing radiation from ^{134}Cs, ^{137}Cs (cohorts with doses < 13 mSv) (RR ± CI)

Classes, groups of non-neoplastic diseases according to ICD–10 (code)	13 – < 26 mSv			26 – < 40 mSv			≥ 40 mSv		
	RR	CI -95 %	CI +95 %	RR	CI -95 %	CI +95 %	RR	CI -95 %	CI +95 %
Total cases	0.92	0.90	0.94	**1.23**	**1.19**	**1.26**	**1.14**	**1.10**	**1.18**
Diseases of the circulatory system (I00–099):	0.47	0.44	0.50	0.57	0.52	0.62	0.54	0.47	0.61
➢ diseases of veins, lymphatic vessels (I80–I89)	1.11	0.93	1.34	**2.67**	**2.17**	**3.27**	1.12	0.78	1.61
Respiratory diseases (J00–J99):	**1.85**	**1.78**	**1.92**	**2.52**	**2.41**	**2.65**	**2.54**	**2.39**	**2.70**
➢ chronic rhinitis, nasopharyngitis,pharyngitis (J31)	**1.73**	**1.32**	**2.28**	**3.04**	**2.20**	**4.20**	**2.25**	**1.44**	**3.52**
➢ chronic laryngitis and laryngotracheitis (J37)	**6.78**	**4.04**	**11.39**	**3.91**	**2.02**	**7.54**	**3.25**	**1.39**	**7.59**
➢ simple chronic bronchitis (J41)	**1.80**	**1.56**	**2.08**	**2.81**	**2.37**	**3.34**	1.05	0.77	1.45
➢ chronic obstructive pulmonary disease (J44 –J44)	**1.18**	**1.06**	**1.31**	**1.46**	**1.27**	**1.68**	0.60	0.46	0.79
Diseases of the digestive system (K00–K93):	0.89	0.85	0.93	0.64	0.59	0.69	1.08	1.00	1.18
➢ gastritis and duodenitis (K29)	1.03	0.96	1.10	0.68	0.60	0.77	**1.32**	**1.16**	**1.50**
➢ fibrosis and cirrhosis of the liver (K74)	0.61	0.45	0.83	0.72	0.46	1.13	**1.95**	**1.30**	**2.93**
➢ diseases of the pancreas (K85. K86)	**1.28**	**1.10**	**1.48**	0.69	0.53	0.91	**1.82**	**1.42**	**2.32**

Table 3.25
Relative risks of non-neoplastic morbidity of RCT residents 40–60 years old on the date of the Chornobyl accident for 1988-2016, depending on the accumulated effective doses of ionizing radiation from ^{134}Cs, ^{137}Cs (cohorts with doses <13 mSv were accepted for control), (RR ± CI)

Classes, groups of non-neoplastic diseases according to ICD–10 (code)	13 – < 26 mSv			26 – < 40 mSv			≥ 40 mSv		
	RR	CI -95 %	CI +95 %	RR	CI -95 %	CI +95 %	RR	CI -95 %	CI +95 %
Total cases	1.02	1.00	1.04	0.92	0.89	0.94	0.69	0.66	0.73
Diseases of the circulatory system (I00–099):	0.99	0.96	1.03	0.70	0.65	0.74	0.38	0.34	0.43
➢ diseases of veins, lymphatic vessels (I80–I89)	**1.76**	**1.61**	**1.94**	0.87	0.73	1.03	0.84	0.65	1.08
Respiratory diseases (J00–J99):	0.96	0.91	1.02	0.75	0.68	0.82	0.38	0.31	0.46
➢ chronic rhinitis, nasopharyngitis, pharyngitis (J31)	**1.95**	**1.70**	**2.24**	**1.38**	**1.12**	**1.71**	0.96	0.68	1.37
➢ chronic laryngitis and laryngotracheitis (J37)	**10.01**	**1.23**	**81.35**	4.23	0.26	67.57	9.90	0.62	15.35
➢ chronic obstructive pulmonary disease (J41)	**1.66**	**1.58**	**1.74**	**2.24**	**2.11**	**2.38**	**2.01**	**1.85**	**2.19**
➢ simple chronic bronchitis (J44)	**2.60**	**2.27**	**2.97**	**1.75**	**1.43**	**2.13**	0.75	0.50	1.12
Diseases of the digestive system (K00–K93):	**1.55**	**1.17**	**2.04**	1.00	0.64	1.58	1.33	0.74	2.37
➢ gastritis and duodenitis (K29)	**2.35**	**1.60**	**3.45**	**2.42**	**1.46**	**3.99**	**3.30**	**1.80**	**6.04**
➢ fibrosis and cirrhosis of the liver (K74)	**3.31**	**2.96**	**3.70**	**2.23**	**1.91**	**2.61**	**1.78**	**1.40**	**2.26**
➢ diseases of the pancreas (K85, K86)	**1.53**	**1.42**	**1.66**	1.01	0.89	1.15	0.75	0.61	0.93

RCT in the remote period of the Chornobyl accident, there were three main periods:

➢ the first period, tentatively called «early» falls on the first seven years from the date of the accident – 1988–1992 – and was characterized by an increased incidence among people aged 18–39 years, and 40–60 years, mainly endocrine, respiratory, digestive, circulatory systems diseases against the background of low levels of disability and mortality;

➢ the second period, distant in time – «the period of increasing levels of chronic forms of somatic diseases» falls on 1998–2007, against the background of increasing disability and mortality;

➢ the third period – «late» falls on 2008–2016 and is characterized by a gradual decrease in the level of non-neoplastic morbidity against the background of a significant increase in disability and mortality.

Thus, based on the risk analysis, significant dose-dependent effects of ionizing radiation in the dose range of 13 – ≥ 40 mSv in the development of certain non-neoplastic diseases of the circulatory, respiratory and digestive systems were found. These diseases mainly formed non-neoplastic morbidity among residents of RCT. Individual non-neoplastic diseases from these classes with dose-dependent effect in the dose ranges13 – < 26 mSv, 26 – < 40 mSv, ≥ 40 mSv were identified. Based on risk analysis, dose-dependent effects of the development of certain non-neoplastic diseases in RCT residents depending on age at the date of the Chornobyl accident were established, namely: 18–39-years-old have dose-dependent effects in the development of respiratory diseases, 40–60-years-olds – circulatory system diseases.

3.1.4. The damages of bronchopulmonary system in the clean-up workers of the Chornobyl accident (1988–2021)

As a result of the Chornobyl NPP accident a huge amount of radioactive substances came into the environment and were spread by the airborne-dust flows that caused external and internal exposure (primarily inhalation) of the large contingents of population in low doses. According to various estimates at least 200,000 survivors of different categories had undergone an inhalation of radionuclides. The clean-up workers of Chornobyl NPP accident are the most vulnerable and one of the largest categories among them. Especially it concerns those who were involved in the post-accident work in April and May 1986, and during the period prior to completion of the «Shelter» object – spring 1987 [12–14].

Under such circumstances the radionuclide inhalation was one of the main ways of their intake in the clean-up workers who worked in the 30-kilometer zone around the plant. A very wide range of radioactive isotopes, including those belonging to the «hot» particles, causes a certain difficulty of prognostication the remote radiation effects.

Results of the long-term (1996–2015 years) pulmonology investigation of more than 16 thousand

(16,133) participants of the liquidation of the Chornobyl NPP accident consequences in 1986 at the Out-Patient Clinic of Radiation Registry of NRCRM testify to the reliable incessant increase of morbidity with chronic bronchitis and chronic obstructive pulmonary disease (COPD) among this contingent of patients [15, 16].

Analysis of the relative risks of radiation exposure, based on the clinical and epidemiological study (1992–2004 years) in NRCRM of 7,665 male COPD patients – clean-up workers of the Chornobyl NPP accident in 1986–1987 showed an evidence link of this disease with radiation exposure at doses higher than 0.25 Sv (control group have doses below 0.05 Sv) (Fig. 3.41).

These data are generally coincided with the clinical-epidemiological study results at the SRU and the Ministry of Health of Ukraine statistics, that confirming a leading place of bronchopulmonary diseases in morbidity structure of this contingent.

Thus, the Chornobyl accident significantly contributed to the growth of morbidity and prevalence of lung diseases among the clean-up workers, evacuees and inhabitants of contaminated areas.

In the group of patients with radiation exposure over 500 mSv in the remote post-emergency period a probable increase in the frequency of lung cancer was established (2.43 % vs. 0.60 % for the doses under 500 mSv ($p < 0.01$)). Radiation dose in the male clean-up workers, who further developed lung cancer, was significantly higher (368.7 ± 90.8) mSv than in those with no lung cancer – (204.2 ± 5.6) mSv ($p < 0.05$) [17].

As a result of long-term (1987–2005) complex clinical and morphological study of the 2,736 COPD patients, namely in the 2,427 clean-up workers of the Chornobyl accident of 1986 (including 11 persons with documented incorporation of «hot particles» (mainly ^{137}Cs, ^{60}Co) and external radiation doses in the range of 2–76 cSv (I group), and 309 COPD patients without a history of radiation exposure (II group, nosology control – NsC), confirmed the presence of COPD pathomorphosis under the effect of external irradiation and dust radionuclides inhalation [12, 15, 16].

The manifestation of bronchopulmonary diseases in the early period after radiation exposure was characterized by the complex of symptoms, that characteristic feature was the presence of distinct irritation of the upper respiratory tract. Overall, the «poverty» and «blurriness» of clinical symptoms with dyspnea at the beginning of the disease preceded the appearance of other symptoms and was typical for the clean-up workers of the Chornobyl NPP accident. A hypo-reactive nature of COPD exacerbations prevailed[12, 15, 16].

The performed studies demonstrated a preference of COPD in the structure of chronic nonspecific bronchopulmonary morbidity in the clean-up workers. Its share is about 77 %, along with up to 15 % of chronic bronchitis, and more than 8 % of bronchial asthma [12, 14–16].

High level of comorbidity, i.e., the presence of multiple concomitant diseases, is typical for the victims of the Chornobyl catastrophe who have COPD. Concomitant diseases were registered in all the clean-up workers but only in 35 % of patients with COPD, who had not been linked with participation in the Chornobyl NPP accident clean-up activities (NsC group). Combined involvement of cardiovascular and nervous systems was traditional (early emerging of vegetative disorders followed by arterial hypertension and coronary heart disease; early cerebral arteriosclerosis, encephalopathy), which during

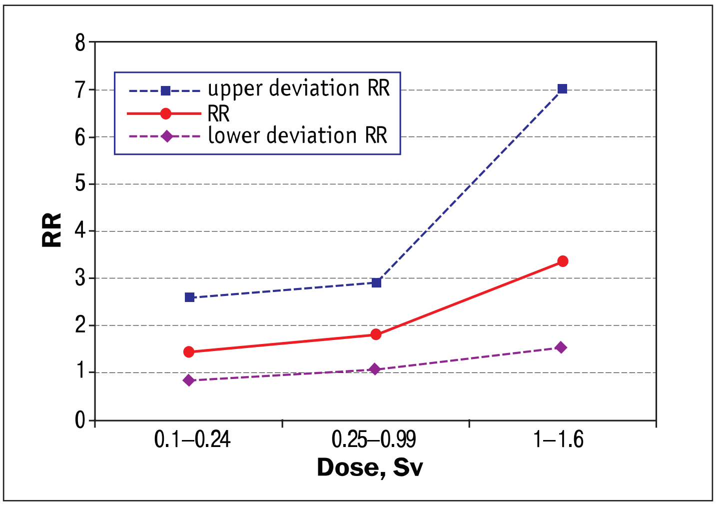

Figure 3.41. Relative risks and 95 % CI (RR) the incidence of COPD in the clean-up workers of 1986–1987 period (Buzunov VP, Krasnikova LI, NRCRM, NAMS of Ukraine, 2005)

the first years was manifested in the 63.4 % of cases, and today is diagnosed almost in 100 % of the patients.

Concomitant diseases of the endocrine system (first of all chronic thyroiditis and hypothyroidism) found in 15 % of patients, as well as disorders of pituitary-thyroid and hypothalamic-pituitary-adrenal regulation links have an intensive impact on development and progression of COPD in the clean-up workers.

Digestive system diseases were diagnosed in more than 90 % of COPD patients. Impact of duodeno-gastric (18 %) and gastro-oesophageal (44 %) reflux, liver and biliary ducts diseases (43 %), diseases of the upper respiratory tract (42 %) was especially important. It should be mentioned that the majority of patients (87 %) have increased titers of antibodies to the persisting cytomegalovirus infection (87 %), and also during 2011–2021 to the Epstein-Barr virus (68 %) [12, 15, 16].

It is proved that course of COPD in the Chornobyl clean-up workers in a remote post-emergency period is more severe compared to the nosology control group, as is evidenced by higher rates of assessed complaints on dyspnea, cough with purulent mucous sputum, and frequency of exacerbations per year [18–19].

For the clean-up workers the gradual transformation of bronchial obstruction syndrome was also characteristic, namely at the beginning of the disease a hypotonic dyskinesia of membranous part of the trachea and small bronchi obstruction was detected, which later turned into a total bronchial obstruction with a low level of its recoverability. Disease deterioration is also confirmed in the study of lung function: if the 2nd degree of pulmonary insufficiency during exacerbation of COPD was detected in 4 % of patients in 1996, almost half of the COPD patients among clean-up workers (study group – 46 % control – 34 % of patients) had a severe pulmonary insufficiency in 2005, which was associated with development of emphysema and pneumofibrosis [12, 15, 16].

Spirometry results in the COPD clean-up workers when compared with the group of nosology control patients indicated a significant decrease in the maximum volumetric rate at 75 % FVC (FEF_{75}), with no change in average group values of other volume and speed indicators.

The body plethysmography indicators in COPD clean-up workers compared to the nosology control patients showed the significant violations of lung volumes ratio due to significantly higher levels of residual volume (RV), internal volume of gas in the chest (ITGV) and expiratory reserve volume (ERV), which proved the more severe respiratory problems in the main study group of patients due to pulmonary emphysema and lung hyperinflation that was accompanied by development of pulmonary hypertension, right ventricular dilatation and formation of its diastolic dysfunction [18, 19].

New data are available about the presence of dose relationship between respiratory function indicators and dose of irradiation in the range of more than 500 mSv for COPD clean-up workers in the remote period after exposure. This is shown by a significant decline in levels of forced vital capacity (FVC) and FEF_{75} for the clean-up workers with a highest level of deviation in individuals who have been exposed to doses in the range of more than 500 mSv and a significant decrease in the vital capacity of lungs parameter (VC). FEF_{25} in the main groups of the clean-up workers and NsC group did not differ, while an exhaling at 50 % of FVC and 75 % of FVC were significantly reduced in comparing with NsC group data [18, 19].

It is proved that the reduction of diffusion capacity of lungs (DLco) in the group of COPD clean-up workers is one of the hallmarks of ionizing radiation and inhalation exposure of emergency-originated radionuclides, that also confirming more severe course of the disease and meeting more frequently the signs of pneumofibrosis and emphysema at the X-ray examination [18, 19].

At endoscopic examination of the 877 COPD clean-up workers and 116 representatives of the NsC group, the chronic atrophic endobronchitis with significant fibrotic changes of bronchial mucosa were revealed as a rule. Endoscopic mucosal signs of tracheal and bronchial involvement in the patients – clean-up workers had a typical pattern featuring, in general, the relevant atrophic form of endobronchitis and significant catarrhal-sclerotic changes. Since 1996 they were accompanied by a severe deformation of the bronchial tree. In the NsC group a level of atrophic and sclerotic changes in bronchial mucosa was significantly lower. During the first years of observation (up to 1996) the patients of main clinical group were characterized by a low level of endobronchial inflammation activity, while patients of the NsC group demonstrated a complete inflammatory response.

Since 1996 the significantly purulent forms of endobronchitis began to rise in the patients-clean-up workers and decreased severity of atrophic changes emerged. At present we didn`t fix significant difference in the endobronchial inflammation activity between the groups. Number of catarrhal-sclerotic endobronchitis cases was and remains significantly higher in the clean-up workers of Chornobyl NPP accident than in NsC group [12, 15, 16].

The X-ray symptoms were characterized by rapid development of pneumofibrosis and progressive bronchi deformation. The diagnosis of chronic bronchitis in patients among the clean-up workers was confirmed by an X-ray during the first years of observation. In some cases the X-ray symptoms were ahead to clinical symptoms. However, in some patients they became significant only at the 10^{th} year after the accident. In addition, by the X-ray examination was revealed the progressive development of emphysema and pneumophibrosis, moreover for those who suffered COPD from 6 to 10 years or more such complications were occurred significantly more often than in NsC group [12, 15, 16].

Pathomorpological analysis of endobronchial biopsy in the clean-up workers having COPD (n = 416) allowed to verify the regenerative transformation processes in bronchial mucosa, origination of microvascular lesions, violation of fibers genesis, and characteristics of inflammation chronicity. For the clean-up workers who had suffered from radionuclides inhalation were typical the signs accelerated cell populations renewal (abnormal proliferation of main cell types) and featuring the appearance of epithelial cells with modified phenotype in the mucous membrane of bronchi, significant expression of squamous metaplasia and distinct basal cell hyperplasia of the surface epithelium as well as surface epithelium dysplasia of varying degrees. There were deformation, sclerosis and hyalinosis of the epithelial basal membrane of the bronchi as well. At the same time in clean-up workers a significant range of pathologies of the ciliary apparatus of ciliated cells was established [12, 15, 16].

A range of microorganisms belonging to the resident and pathogenic microflora was identified in sputum and endobronchial content of clean-up workers. A set of microorganisms in associations of 2–4 species of different genera that have different sensitivity to antibiotics were identified in endobronchial washouts from all examined clean-up workers of the Chornobyl NPP accident. *Staphylococcus aureus* ranked the first place by frequency of detection in sputum of clean-up workers (47.43 %). Second place was occupied by the yeast-like fungi of *Candida genus* (26.97 %). *Streptococcus pneumoniae* (5.58 %), *Haemophilus influenzae* (4.65 %), *Klebsiella pneumoniae* (2.79 %) were present much less frequently. Other microorganisms, such as *Moraxella catarrhalis, Proteus vulgaris, Proteus mirabilis, Streptococcus viridans, Streptococcus faecium, Neisseria perflava, Neisseria sicca, Enterobacter aerogenes, Enterobacter Iwoffi* were met sporadically.

An atypical availability of the *Escheria coli* for the bronchi content was noteworthy. It can be associated with a significant frequency of gastroesophageal and duodeno-gastric reflux and digestive tract components entry to the bronchial tree accompanied with vegetative regulation disorders and dysbiosis in these patients. It should also be noted that the study of endobronchial washouts usually defined microorganisms of several (2–4) genera and species with frequent association of *Haemophilus influenzae* and *Streptococcus viridans, Neisseria perflava* and *Streptococcus faecium* with different sensitivity to antibiotics. Moreover, according to morphological and ultrastructural analysis in particular the clean-up workers present deep penetration of microorganisms in the lamina propria of bronchial mucosa [12, 15, 16].

The dose-dependent changes in cellular immunity were established in the COPD clean-up workers exposed in dose ranges of less and more than 500 mSv. Namely, there was a significant reduction in the number of $CD3^+$ T-cells, mainly by $CD8^+$ subpopulation, while the number of $CD4^+$ cells probably was higher compared with the NsC group throughout the whole range of doses. A decrease of the cytotoxic $CD3^+16^+56^+$ T-lymphocytes, increase of $CD3^-16^+56^+$natural killer cells, an increase of the $CD3^-19^+$B lymphocytes, and changes in humoral immunity were found indicating a dependence of the immune status on absorbed radiation dose [18].

The direct relationship of respiratory disorders in COPD patients such as FEV_1, FEF_{25}, FEF_{75} and DLco with the level of $CD3^+16^+56^+$ of cytotoxic T lymphocytes was defined, that is the cause of severe clinical course [18].

Results obtained in the study of bronchoalveolar washouts showed a redistribution of cells in the T-link with a decrease in the relative content of major subpopulations of T-cells. At the same time a relatively high number of cytotoxic cells with high expression of functionally active surface antigens was discovered [12, 15, 16].

There were stages of the immune mechanisms formation in COPD after exposure with the predominance of radiation-caused immune deficiency at the first stage and the cytotoxic and immunocomplex reactions during the formation of long-term effects [12, 15, 16].

In the study of the relationship between the condition of the bronchopulmonary system and the length of the telomer in 113 clean-up workers of the Chornobyl NPP accident in 1986–1987, radiation exposure from 1.0 to 880 mSv, in the remote postaccidental period, a decrease in the relative length of telomer (RTL) was found for main clean-up workers group patients with COPD compared to clean-up workers who had no pathology of the bronchopulmonary system. Significantly shorter RTL (M ± SD) values were determined in COPD patients who were exposed more than 500 mSv (13.6 ± 2.5) compared to COPD patients who were irradiated at a dose of less than 100 mSv (15.3 ± 2.3) [20].

Conclusions

1. Bronchopulmonary system became one of the main «target» tissues for a combined action of external exposure and inhalation of the fission-fragment mixture of radionuclides after the Chornobyl NPP accident, that hereinafter realized in chronic obstructive pulmonary disease, manifestation of which occurred during the first 3–5 years after the patients' participation in the clean-up work.
2. The Chornobyl accident contributed to the growth of incidence and prevalence of the pulmonary diseases among the clean-up workers of the accident.
3. The course of COPD in clean-up workers in early years upon the accident was characterized by minimal clinical symptoms, followed however by the rapid development of fiber-plastic changes in the lungs and bronchial mucosa with progressive deformation of them, hypo-reactivity of exacerbations and disorders of bronchial secretion. More severe clinical course was observed in remote period after exposure.
4. Broncho-obstructive syndrome in the clean-up workers of the Chornobyl NPP accident is modified in a range from hypotonic dyskinesia of membranous part of the trachea and small bronchi obstruction to a total low-reverse obstruction. For the clean-up workers of the Chornobyl the significantly lower values of volume and speed indicators by spirometry results were established. Significant violations of lung volumes ratio due to significantly higher levels of residual volume were found. A dose relationship between the respiratory function indicators and radiation dose for the patient group among was established in the clean-up workers of the Chornobyl NPP accident exposed at doses more than 500 mSv compared with exposed at doses less than 500 mSv and the nosology control. Significantly lower rates of lung diffusion capacity (DLco) in the group of COPD clean-up workers of the Chornobyl NPP accident consequences with regard to nosology control were revealed, confirming the severity of the disease, more frequent detection of signs of emphysema and pneumofibrosis by X-ray examination in patients of the main group.
5. Clean-up workers patients with COPD have several concomitant diseases, namely the COPD is a component of multiple organ pathology which caused great violation in function of integration systems providing homeostasis.
6. Chronic diffuse atrophic endobronchitis with significant fibrotic changes in bronchial mucosa morphologically relevant chronic inflammation disorders with distinct regeneration, damage to the mucociliary apparatus ciliary epithelial disorders of microcirculation and epithelial-connective relationships, transformed fibril-genesis, inability of local protection mechanisms and signs of the intensity of aging reactions in the bronchi mucosa were verified according to endoscopic studies in clean-up workers with COPD.
7. Endobronchial environment in the COPD clean-up workers of the Chornobyl NPP accident was contaminated preferably by representatives of 2–4 types of resident and pathogenic microorganisms with different sensitivity to antibiotics and typical invasion of microorganisms in the lamina propria of bronchial mucosa.
8. In the groups of COPD clean-up workers of the Chornobyl NPP accident exposed to dose ranges of less and more than 500 mSv the dose dependence of changes in cellular immunity, including significant

reduction in the number of $CD3^+$ T cells, mainly by $CD8^+$ subpopulation was found, while the number of $CD4^+$ cells probably were higher compared with the control group throughout the all range of doses. Decrease of the cytotoxic $CD3^+16^+56^+$ T-lymphocytes, increase of $CD3^-16^+56^+$ natural killer cells, $CD3^-19^+$ B lymphocytes and changes in humoral immunity was established indicating the dependence of the immune status from absorbed radiation dose. A direct relationship of respiratory disorders (indicators FEV_1, FEF_{25}, FEF_{75} and DLco) in COPD patients was defined with level of $CD3^+16^+56^+$ of cytotoxic T-lymphocytes, that is the basis of severe COPD clinical course. In the remote postaccidental period, the reduction of RTL was detected in the clean-up workers – patients with COPD compared with the clean-up workers group that have not pathology of the bronchopulmonary system. Significantly shorter RTL (M ± SD) values were determined in COPD patients who were exposed more than 500 mSv (13.6 ± 2.5) compared to COPD patients who were irradiated at a dose of less than 100 mSv (15.3 ± 2.3).

3.1.5. Diseases of cardiovascular system in emergency workers of the Chornobyl accident. Radiation exposure as a risk factor.

During long term period cardiovascular diseases have high prevalence and remain the leading cause of death among the population of European countries, including Ukraine. According to statistics [1], in Ukraine the age-standardized prevalence rate (per 100 thousand population) of cardiovascular diseases in 2015 was 8801 for men and 6499 for women, and coronary heart disease (CHD), which is the leading cause of death from all diseases of the circulatory system, respectively, 5852 and 3146. The age-standardized mortality rate per 100 thousand population was 1102 for men and 727 for women.

Emergency workers (EW) of the accident at the Chornobyl NPP (ChNPP) have the same mortality statistics as in the non-irradiated population: according to the latest data [2], in 2012 the non-neoplastic mortality rate in EW from 18 to 60 years was 10.6 ‰, i.e., 1060 people per 100 thousand. The share of deaths from cardiovascular disease was 82 %.

Previous studies have revealed some differences in the development and course of cardiac pathology in EW and non-irradiated individuals of the same age. The date of the Chornobyl accident was used as the starting point from which the time before the diagnosis of disease was counted. The patients who were examined, EW and persons who were not exposed to radiation, were practically healthy people before the accident.

After the accident, the most common diseases of the circulatory system, namely hypertensive heart disease (HHD) and CHD developed in EW earlier and at a younger age. Thus, according to the Kaplan-Meyer median survival, 50 % of EW became ill with HHD at (9.7 ± 0.7) years after the accident at the age of (49 ± 0.7) years, while non-irradiated patients at (19, 7 ± 1.1) years ($p = 0.000$) at the age of (58.5 ± 0.9) years ($p = 0.000$). EW became ill with CHD after (11.7 ± 0.5) years at the age of (57 ± 0.6) years, while in the group of non-irradiated persons these indicators were (20.7 ± 1.0) and (62.2 ± 0.7) years.

Analysis of non-radiation risk factors (RF) showed that there was no significant difference between EW and non-irradiated patients in the incidence of hypercholesterolemia (HC), overweight, tobacco smoking (TS) and type 2 diabetes mellitus (DM), which preceded the development of HHD and CHD. HC was found in 60 % of EW and 53.5 % of non-irradiated controls, overweight in 39.2% and 38.9 %, respectively, smoking in 40.7 % and 38.9 %, DM in 11% and 7.3 %.

The relative number of patients in both compared groups differed almost insignificantly in most clinical forms of CHD. It was obvious that these data would fluctuate with the number of examined patients.

In the last 5 years, due to current and retrospective analysis, the EW group at the Chornobyl NPP and non-irradiated control (CG), which were included in the study by simple random sampling, increased to 535 (EW 1986–1987) and 204 CG people, respectively. In EW, a combination of HHD and CHD was diagnosed in 412 patients, only HHD in 85 people, and only CHD in 38 people. In the CG, this proportion corresponded to 155, 24 and 25 people. The age of EW on the date of the accident and the date of the last examination did not differ significantly from the age of CG patients: (37.6 ± 8.9)

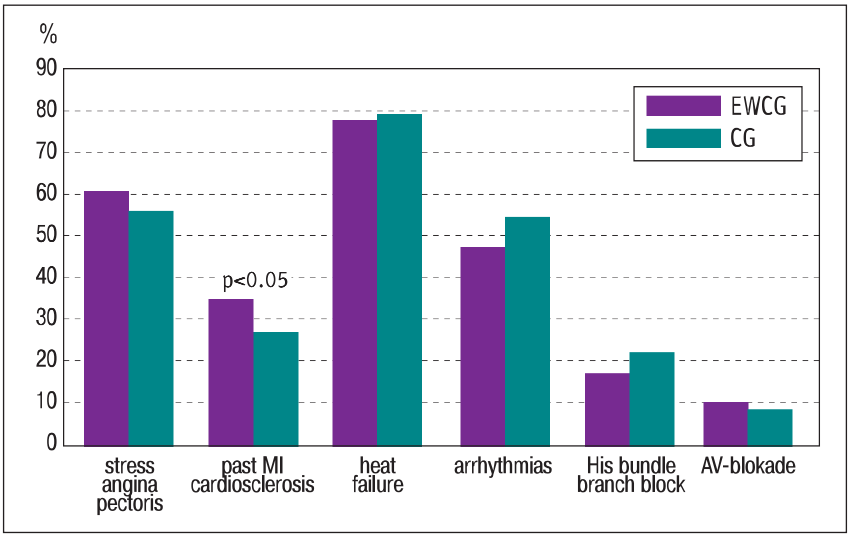

Figure 3.42. Frequency of CHD clinical forms, arrhythmias and blockades

against (35.5 ± 9.8) and (65.4 ± 11.0) against (66.1 ± 10.0) years.

EW and CG patients were distributed according to the stage of severity of HHD as follows: I stage 7.1% vs. 2.8 % at p <0.01, II stage 52.9 % vs. 65.4 % at p <0.01, III stage 40.0 % vs. 31.8 % at p < 0.05. Thus, among EW there were more patients with HHD I and III stages, and HHD II stage were more common among non-irradiated controls. Stress angina and past acute myocardial infarction (MI) were the most common CHD clinical forms in EW and CG patients (Fig. 3.42). The relative number of patients in both groups with arrhythmias (atrial fibrillation, ventricular and supraventricular arrhythmias), complete and incomplete blockade of the His bundle legs and AV blockade did not differ significantly.

The study of traditional RF showed that, as in previous years, the frequency of their occurrence in EW and CG did not differ significantly. The analysis of each FR contribution in the development of HHD and CHD was performed using the Cox regression method or the model of proportional risk [3]. Independent variables were: participation in the Chornobyl accident, the presence of hypertension and DM before the development of CHD, burdened heredity (BH), TS, total cholesterol, body mass index (BMI) and age of patients at the time of the Chornobyl accident. The first five indicators were dichotomous, i.e., they had only two values: the presence of the sign was equal to 1, and its absence to 0. Other indicators belonged to the interval scale. The patient's age in years was used as a time scale.

It was calculated that the development of HHD was significantly influenced by three factors: participation in clean-up work, age of a patient at the time of the accident and the content of total cholesterol (Table 3.26). Thus, in the EW cohort the risk of developing HHD was 2.2 times higher than in non-irradiated individuals. Elderly patients had a lower chance of HHD development. The age of a person older than 1 year reduced the risk by 8 %, and by 10 years by 56.6 %. With an increase in total cholesterol by 1 mmol/l, the risk of HHD development increased by 20.7 %.

The risk of CHD was determined by the same factors as HHD but with minor numerical differences.

Table 3.26
Influence of different independent variables on the risk of HHD development

Indices	Coefficient of regression (B)	Standard error of (B)	p	OR	95% CI lower	95% CI upper
Participation in clean-up work	0.795	0.166	**0.000**	2.215	1.601	3.066
Patient's age, years	-0.084	0.010	**0.000**	0.920	0.902	0.938
BH	-0.241	0.169	0.153	0.786	0.565	1.094
BMI, kg/m^2	0.026	0.019	0.172	1.027	0.989	1.066
total cholesterol, mmol/L	0.188	0.057	**0.001**	1.207	1.080	1.349
DM type 2	0.263	0.242	0.277	1.301	0.809	2.093
TS	-0.050	0.196	0.801	0.952	0.648	1.398

Table 3.27
Influence of different independent variables on the risk of CHD development

Indices	Coefficient of regression (B)	Standard error of (B)	*p*	OR	95 % CI	
					lower	upper
Participation in clean-up work	1.251	0.176	**0.000**	3.493	2.472	4.935
Patient's age, years	-0.126	0.013	**0.000**	0.882	0.860	0.904
BH	-0.120	0.173	0.489	0.887	0.631	1.246
BMI, kg/m^2	0.035	0.020	0.084	1.036	0.995	1.078
Total cholesterol, mmol/L	0.114	0.051	**0.026**	1.12	1.013	1.239
DM type 2	-0.344	0.265	0.194	0.709	0.422	1.192
TS	-0.359	0.207	0.084	0.699	0.465	1.049
Arterial hypertension	-0.307	0.156	0.050	0.736	0.542	1.000

Participation in the clean-up work increased it 3.5 times (Table 3.27). The younger the patient was, the greater were his chances of developing CHD: one year of an age difference increased the risk by 11.8 %. The difference of one mmol/l of total cholesterol increased the risk of CHD by 12 %.

Our researches have shown that in the combination of RF analyzed by Cox regression, participation in clean-up work poses a much higher risk of HHD and CHD onset than traditional risk factors. These results allow to attribute such a risk factor as participation in emergency work, to the proven cardiovascular RF. We are talking about not only ionizing radiation but of chemical, temperature, dust and other harmful factors that also impact on humans during emergency work.

In the period from 2016 to 2018, for the first time during entire post-accident years, the state of cardiovascular system was studied in 145 women who participated in emergency work during 1986–1987 (group EW-f), and in 120 non-irradiated females (group CG-f) [4].

Analysis of HHD development after the Chornobyl accident in EW and in the CG of men and women using the Kaplan-Meier method showed that a faster accumulation of HHD new cases and, consequently, a decrease in the proportion of people without symptoms of this disease was revealed in EW-men (Fig. 3.43A). These data once again confirmed the results obtained 2 years later in a study with fewer subjects [5]. HHD developed in EW-m at a younger age compared to EW-f and non-irradiated men (CG-m), as evidenced by the median survival (Table 3.28).

In the age range from 53 to 75 years, the accumulated incidence of HHD in EW-f was slightly higher than in EW-m. The Breslow test showed a significant development of HHD on 2–3 years later in

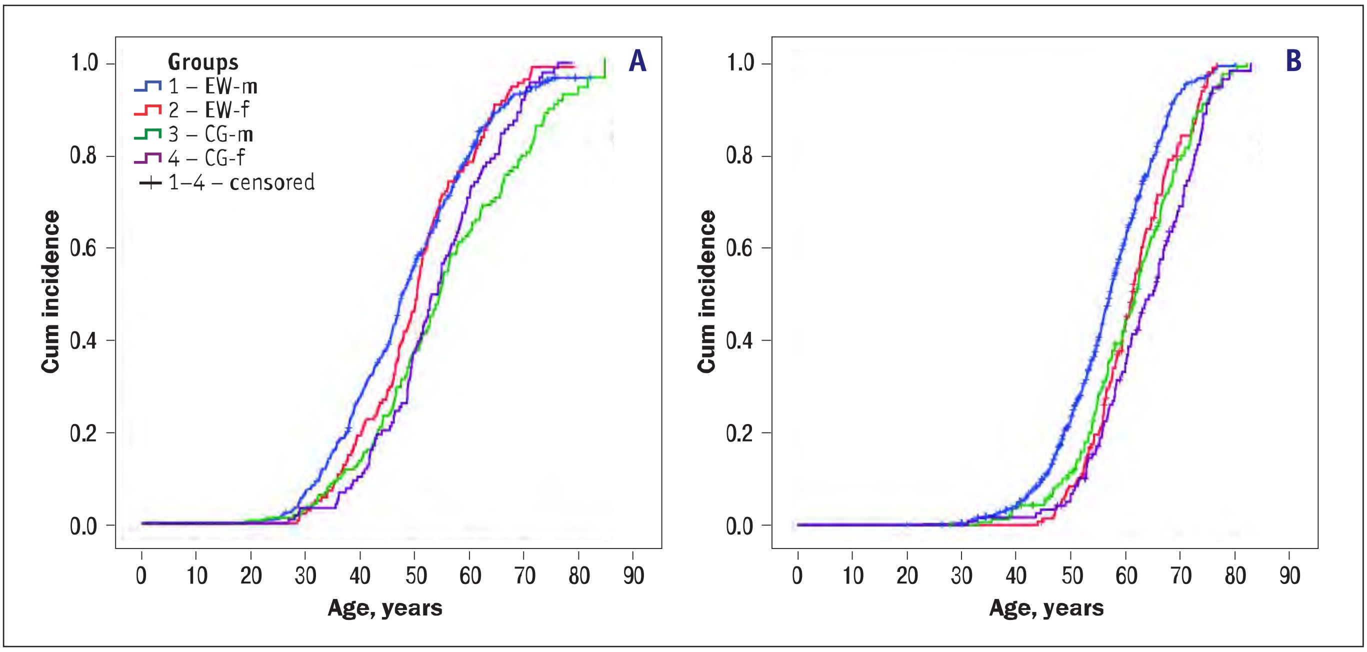

Figure 3.43. **Cumulated incidence of HHD (A) and CHD (B) in EW and CG of males and females depending on age**

EW-f group compared to EW-m ($\chi^2 = 4.298$, $p = 0.038$). The median survival in irradiated men and women was 7.4 and 3.7 years lower than in the corresponding control groups (Table 3.28).

The accumulated frequency of CHD in EW-m in the age range from 23 to 74 years was the highest in comparison with other groups (Fig. 3.43B, Table 3.28). The median survival in EW-m was 4.8 and 4.4 years lower than in CG-m and EW-f, respectively, and in CG-m and EW-f it was on 3 years less than in CG-f. In order of increasing values of the average survival rate the groups were as follows: EW-m, CG-m, EW-f and CG-f. According to the results of the log-rank test, the dynamics of the accumulated disease curves had significant differences between EW-m and EW-f ($\chi^2 = 19.172$, $p = 0.000$), EW-m and CG-m ($\chi^2 = 27.323$, $p = 0.000$) and EW-f and CG-f ($\chi^2 = 7.024$, $p = 0.008$).

During the post-accident period in EW-m and EW-f the development of HHD was faster than in the non-irradiated control (Fig. 3.44), as evidenced by the median survival rate, which in EW-m was 11 years, and in EW-f 7 years less than in the corresponding control (Table 3.29). The log-rank test confirmed the significance of the differences between the curves of the accumulated incidence of HHD between EW-m and CG-m ($\chi^2 = 59.857$, $p = 0.000$) and EW-f and CG-f ($\chi^2 = 10.729$, $p = 0.001$). Curves of HHD accumulated incidence in EW-m and EW-f did not differ ($\chi^2 = 0.004$, $p = 0.949$).

Table 3.28
Median (index ± standard error) survival time (patient age) in the development of HHD and CHD in male and female EW and CG

Groups	HHD		CHD	
	median	95 % CI	median	95 % CI
EW-m	47.5 ± 0.6	46.3–48.7	56.8 ± 0.5	55.8–57.8
EW-f	50.7 ± 0.7	49.4–52.0	61.2 ± 0.8	59.6–62.8
CG-m	54.9 ± 1.1	52.7–57.1	61.6 ± 1.0	59.6–63.6
CG-f	54.4 ± 1.1	52.3–56.7	64.2 ± 1.4	61.5–66.9

Table 3.29
Mean and median (index ± SE) survival time (years that have passed since the accident) in the development of HHD and CHD in male and female EW and CG

Groups	HHD		CHD	
	median	95 % CI	median	95 % CI
EW-m	8.7 ± 0.6	7.5–9.9	17.7 ± 0.7	16.4–19.0
EW-f	9.7 ± 1.3	7.2–12.2	21.7 ± 1.0	19.8–23.6
CG-m	19.7 ± 1.0	17.8–21.6	25.7 ± 0.7	24.3–27.1
CG-f	16.7 ± 1.7	13.7–20.0	25.7 ± 0.8	24.2–27.2

The rate of accumulated CHD in EW-m throughout the post-accident period was higher than in other groups (Fig. 3.44B). The log-rank test revealed the significant differences between the EW-m and EW-f curves ($\chi^2 = 16.350$, $p = 0.000$) and CG-m ($\chi^2 = 47.872$, $p = 0.000$). According to the median survival, in EW-m the accumulated frequency of CHD reached 0.5 values on 4 years and 8 years earlier than in EW-f and CG-m (Table 3.29), and in EW-f on 4 years earlier, than in CG-f. The curves of CHD accumulated incidence in EW-f and

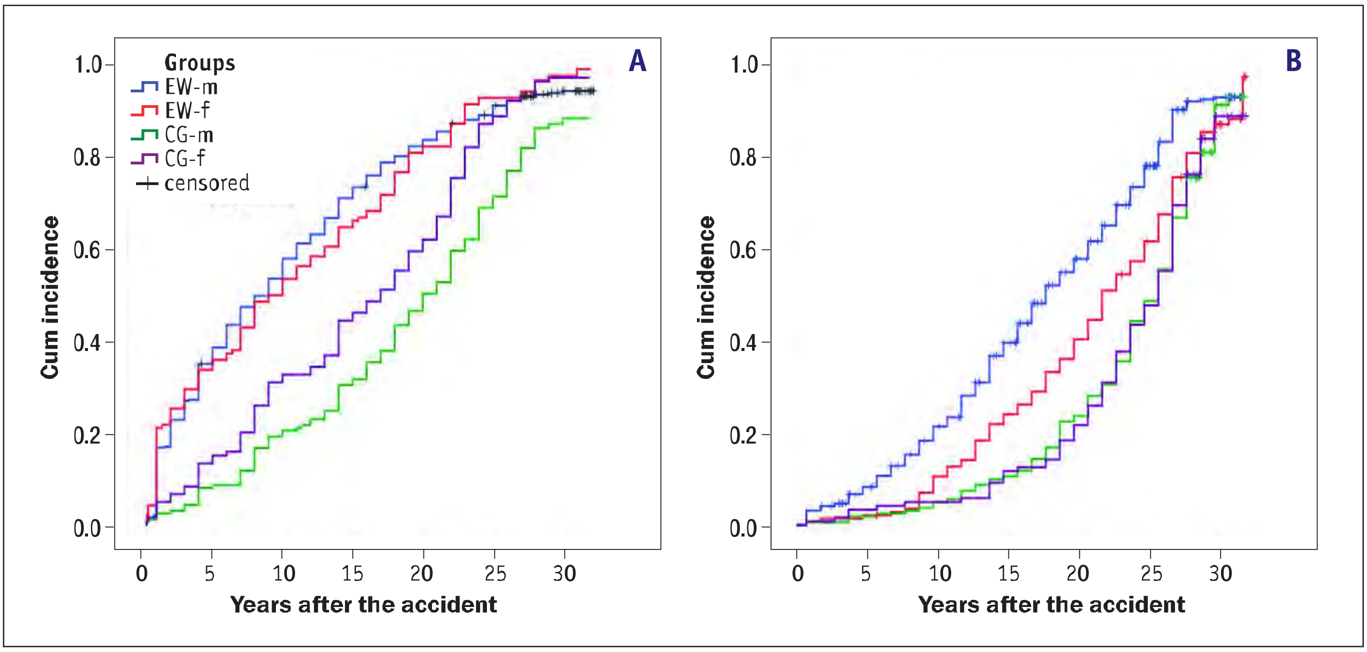

Figure 3.44. **Cumulated incidence of HHD (A) and CHD (B) in male and female EW and CG depending on the time past after the accident**

CG-f also differed significantly (χ^2 = 4.116, p = 0.042), especially in the range from 10 to 27 years after the accident.

Another area of research was the study of genetic predisposition to the development of cardiovascular diseases in persons who took part in emergency work. According to various publications, polymorphic variations of various genes associated with HHD and CHD are known. The SNP83 polymorphism (single nucleotide polymorphism) rs966221 of the phosphodiesterase (PDE) 4D gene belongs to one of them. An interest to the polymorphous variants of the *PDE4D* gene, and in particular to the SNP83 is due to the role of phosphodiesterase 4D in human metabolism. PDE4D selectively inactivates the secondary messenger cyclic adenosine monophosphate (cAMP), converting it into AMP. The cAMP as a secondary messenger, along with cyclic guanosine monophosphate (cGMP) regulating a wide range of cellular functions and morphological processes in a heart, including inotropism, chronotropism, apoptosis and hypertrophy. It is able to inhibit the proliferation of smooth muscle cells, and therefore its low level in the smooth muscle cells of vascular wall leads to an increase in their proliferation and migration. It can be expected that an increase in the activity of *PDE4D* and, consequently, a decrease in the cAMP content in these cells, will lead to the development of an atherosclerotic plaque or its instability. It should also be noted that atherosclerotic lesion of the arterial wall is accelerated by the effects of proinflammatory cytokines that induce an increased endothelial permeability, accumulation of fluid in extravascular space, and adhesion of leukocytes and monocytes on endothelium. Cyclic AMP limits the effect of cytokines and reduces the permeability of endothelial layer. However, it should be noted that the high content of cAMP along with low activity of *PDE4D*, on the one hand, inhibits the progression of atherosclerotic plaques, but, on the other hand, leads to amplified myocardial contraction, which in the presence of its ischemia can result in MI.

SNP83 rs966221 of the *PDE4D* gene was characterized by the presence of the following genotypes: CC, CT and TT. Our studies in men showed that EW and CG did not show significant differences in the development of HHD and CHD depending on genotype. However, in a separate group of men with a history of MI and genotype TT and CC + CT dynamics of the curves of cumulated morbidity for this pathology differed significantly in groups EW-m (Fig. 3.45A) according to log-rank test – χ^2 = 8.495 at p = 0.004. In carriers of the TT genotype, the development of MI was observed on average at (66.7 ± 2.8) years, and in carriers of the CC or CT genotypes at (73.9 ± 1.1) years.

In the CG male population, carriers of TT and CC + CT genotype, the dynamics of MI cumulated incidence did not differ significantly (log-rank test: χ^2 = 1.425, p = 0,233), but the graph (Fig. 3.45B)

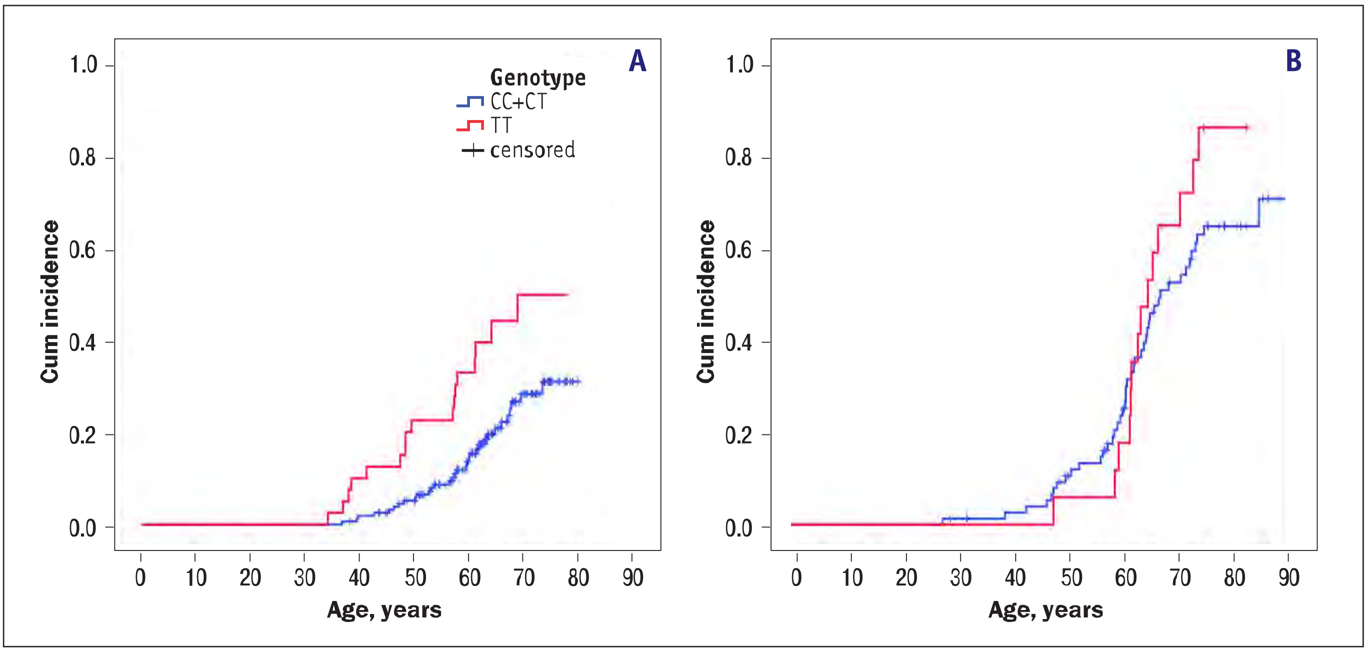

Figure 3.45. **Cumulated incidence of MI depending on age in EW-m (A) and CG-m (B) with different SNP83 genotype of the *PDE4D* gene**

shows that after the age of 65, patients with the TT genotype had an increased rate of cumulated morbidity than those with the CC and CT genotypes. The statistical confidence of these differences in the age group after 65 years was confirmed by the log-rank test: $\chi^2 = 6.535$ at $p = 0.011$). The development of MI in non-irradiated individuals occurred on average in (67.8 ± 4.6) years in carriers of the TT genotype and in (73.0 ± 2.5) years in carriers of the CC or CT genotypes.

Thus, the presence of TT genotype in polymorphism rs966221 of the *PDE4D* gene is associated with the development of MI at an earlier age in both EW and non-irradiated individuals.

3.1.6. Non-malignant diseases of endocrine system in adults and children irradiated as a result of the ChNPP accident

The accident at the Chornobyl Nuclear Power Plant (ChNPP) was followed by the release of a spectrum of radioisotopes, primarily radioactive iodine and cesium, being tropic to many tissues of the human endocrine system. These isotopes upon incorporation had become the main dose-forming factors, and their total damaging effect on hormone-producing cells was enhanced by the external γ-radiation. Thus, there was a combination of radiation factors (incorporated radionuclides and external exposure) that had made a negative impact on the state of central and peripheral endocrine organs in persons affected as a result of the accident at the ChNPP (the ChNPP accident survivors), namely the residents of radiologically contaminated territories (RCT), 30-kilometer exclusion zone evacuees, accident clean-up workers (ACUW), and children irradiated in utero. This events promoted the development of a range of clinical and functional disorders, non-malignant endocrine diseases featuring thyroid (nodular goiter, autoimmune thyroiditis, hypothyroidism), parathyroid, and non-thyroid diseases (prediabetes and diabetes mellitus, pre-obesity and obesity, metabolic syndrome, hypothalamic dysfunction etc.). Incidence of the stated health effects is statistically significantly (several times) higher than in the general population of Ukraine.

The short-term (in the ACUW of 1986 period and evacuees) or long-term (in the ACUW 1986–1990 period and RCT residents) radiation impact on central and peripheral hormone-producing tissues had led to a significant prevalence of nonmalignant diseases of endocrine system and related comorbid conditions among survivors who were exposed to a complex of unfavorable factors during and/or after the ChNPP accident. Emergence of such a range of disorders has caused a decrease in the working capacity of this category of population and a decrease in the quality and duration of their life. The latter require significant financial expenditures for the treatment, rehabilitation and social adaptation of the patients. Our studies have shown that in adult and childhood accident survivors, including the ACUW and their descendants, a progressive increase occurred during the post-accident years in the incidence and prevalence of thyroid disorders (hyperplastic, hypertrophic, and autoimmune ones), prediabetes, type 2 diabetes, pre-obesity, obesity, and metabolic syndrome with a peak period of manifestation 10–20 years upon radiation exposure, while onset of parathyroid disorders and associated conditions occurred 20–30 years later.

Exposure to ionizing radiation (IR) is currently thought to be proven only for the induction of thyroid cancer in children, which in some cases is life-threatening, yet being a rare disease (incidence 9 : 100,000 or 0.00001 % in children and 0.07 % in adults) compared to other endocrine diseases including malignancies. However, during the previous years, a very common (incidence 13,000–52,000 : 100,000) class of endocrine system diseases i.e., non-malignant ones were neglected, as evidenced by the limited number of available publications based on the results of scientific research. Nevertheless, the long-term clinical observations (1986–2021) conducted by scientific staff of the National Research Center for Radiation Medicine (NRCRM), and updated scientific analysis of data by years (1992–2015) from the NRCRM Clinical and Epidemiological Registry (CER) using contemporary international diagnostic criteria indicates to a high overall prevalence (up to 85 % among adults and up to 76 % in children and adolescents) of non-malignant endocrine disorders in most categories of the accident survivors, which statistically significantly exceeds the respective value in the average population of Ukraine who had escaped the accidental exposure.

Stages of occurrence of endocrine system changes after exposure to radiation factors

After the ChNPP accident the largest part of absorbed dose affecting the endocrine system was formed in the first days or months, while the rest was formed over a long period of time, which makes it difficult to assess its negative impact. The airborne iodine isotopes had occurred in extremely high concentrations in the first days and weeks upon the accident at a background of natural iodine deficiency both with lack of vitamin D in the exposed population. Both the latter are triggers of a multifunctional strain in thyroid (named a «starved thyroid») and other endocrine glands, which predisposed to a significant accumulation of radioactive iodine in glandular tissues provoking the onset of acute effects i.e., the destruction of a part of hormone-producing cells in the immediate post-accident period (acute radiation thyroiditis with transient hyperthyroidism, insulitis, hypophysitis etc.), as well as certain types of cancer of hormone-producing tissues due to the induced mutations. When exposed to medium and low doses the radiation damage was delayed for years and decades, manifesting in the survived persons in the form of chronic non-malignant diseases, primarily nodular goiter (NG), chronic autoimmune thyroiditis (CAT), obesity, insulin resistance, and type 2 diabetes mellitus due to the changes in tissues of the central and peripheral endocrine glands.

During the initial reaction to the complex of unfavorable factors of the accident, which lasted from April to August 1986, there was a temporary increase in serum concentration of peripheral hormones due to the partial destruction of endocrine cells. Increase in the levels of peripheral hormones against the background of no central hypothalamic-pituitary response was a sign of disordered reverse-feedback hormonal relations due to insufficient synthesis of the releasing factors and pituitary tropic hormones, which was characteristic for the period of compensatory hyperproduction of peripheral hormones since September 1986 till about 1989.

During the period of subclinical hormonal disorders (1990–1994) the central regulation of hormone synthesis was restored along with decreased functional capacity of peripheral endocrine tissues and development of subclinical disorders of thyroid hormone synthesis and function of other endocrine organs.

In subsequent years (1995–1999) the risk of thyroid disease developing in the ChNPP accident survivors gradually increased by approximately 9 times, while of type 2 diabetes – by ~2.5 times in all age groups. The annual growth rate of endocrine diseases in the ACUW was ~3–5 times higher than among the unaffected adult population of Ukraine of similar age. The «rejuvenation» of endocrine diseases, being generally more characteristic for elderly people, was noted.

Non-malignant thyroid disorders

According to the State Registry of Ukraine (n = 68,145 records, 1988–2009 observation period), an increase in the incidence of non-neoplastic thyroid diseases was established, mainly due to the CAT, NG, and primary acquired hypothyroidism (Fig. 3.46).

Over the period since 1997 till now, the prevalence of CAT among ACUW is still increasing, while its stable level remains among residents of the Kyiv

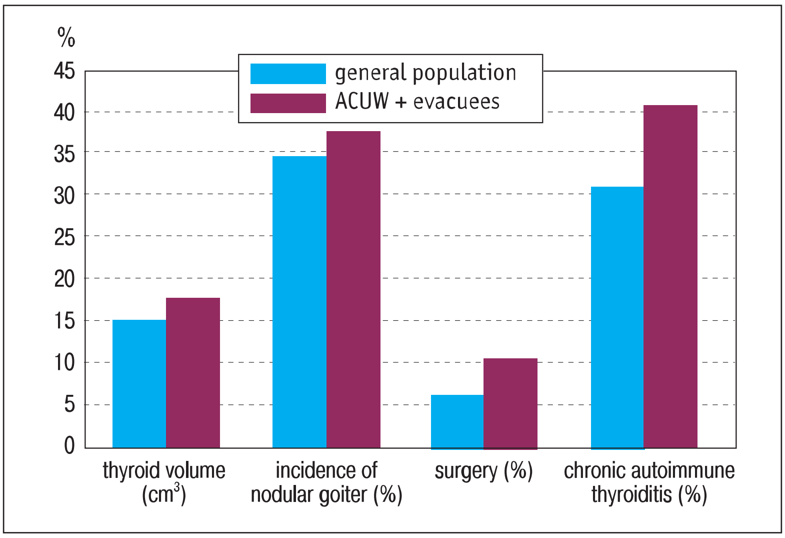

Figure 3.46. **Frequency of diagnosed thyroid disorders in the ChNPP ACUW (1986–1987 period of works) and evacuees from the 30-km exclusion zone in comparison with the general population of Ukraine not exposed to IR**

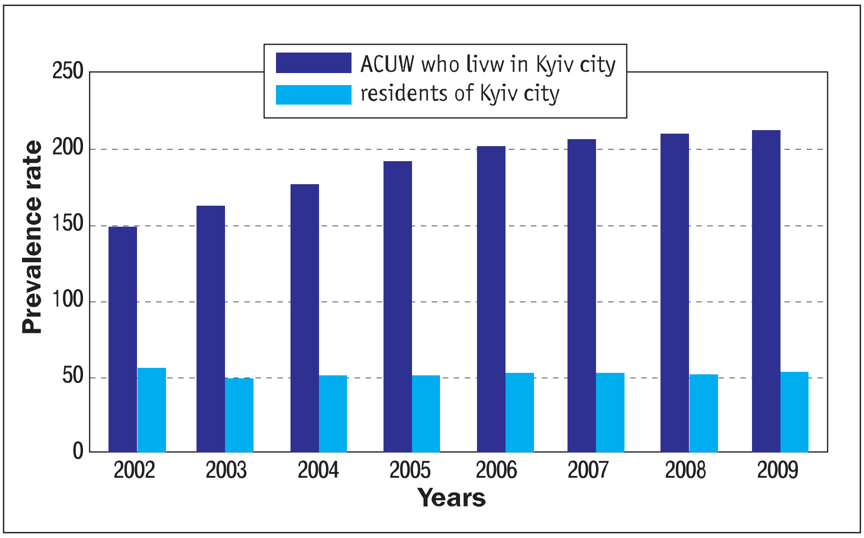

Figure 3.47. **Prevalence of chronic autoimmune thyroiditis among the ChNPP ACUW compared to unexposed residents of the Kyiv City (per 10,000 population**

City (Fig. 3.47). Rapid increase in the prevalence of thyroid disease was registered in ACUW, whose age in 1986 was under 20 years. External (whole body) radiation exposure in dose range of 0.25–1.0 Gy is a significant risk factor for the development of CAT and acquired hypothyroidism in ACUW of 1986–1987 working period and population evacuated from the 30-km exclusion zone.

Hormonal disorders in the period of 1986–1989 were not clinically reflected in any changes of endocrine morbidity among children and adolescents. Primary thyroid reaction to radiation, immune disorders in the first years upon accident, and structural changes that were later revealed on diagnostic ultrasound of thyroid (starting in 1990–1991) indicated the onset of the CAT development, while significant increase in thyroid antibody titer was delayed by 2–3 years. Decreased serum level of the free thyroxine was revealed only in 0.8 % of cases and the increased level of pituitary thyroid-stimulating hormone (TSH) with no any clinical manifestations – in 0.2 % within 1992–1996 survey period.

Strain of the central regulation from hypothalamic-pituitary system, found in 35.5 % of the examined children born from the ACUW (first generation), was a feature of thyroid system functioning in children surveyed in 2004–2006. The latter indicated a hypersecretory reaction of TSH under the thyrotropin-releasing hormone challenge test being probably a sign of a functional defect of cerebral neuroendocrine structures, capable of provoking further manifestation of thyroid disorders.

During the 2007–2014 period, clinical and hormonal study results indicated the role of functional lability of the hypothalamic-pituitary system, which can be either congenital or acquired, in the formation of an unfavorable premorbid background for the occurrence of various neuroendocrine syndromes in children born to parents irradiated as a result of the ChNPP accident. The established strain in hypothalamic-pituitary functioning was of great importance in the formation of thyroid disorders. Long-term strain leads to a decreased production of thyroid hormones, which causes an increase in TSH secretion. Under the influence of TSH the mass of thyroid gland increases leading to the formation of sporadic diffuse goiter. Stable and permanent thyroid enlargement most often leads to the activation of hyperplastic processes i.e., formation of a NG and immunoinflammatory processes, namely CAT.

A retrospective review of data on 24,588 adults from the NRCRM CER database showed that the incidence of thyroid disease among all the ChNPP accident survivors in 1992–2014 period averaged 40.29 %, which was significantly higher ($p < 0.0001$) than in the general population (3.9 %) of Ukraine (Fig. 3.48A).

Among various categories of the accident survivors the thyroid diseases were found most often in 35.37 % of ACUW ($p < 0.0001$) (Fig. 3.48B), as well as in 27.24 % of evacuees from the exclusion zone ($p < 0.0001$) (Fig. 3.48C), 28.6 % of residents of RCT ($p < 0.0001$) (Fig. 3.48D) and 46.74 % of children (Fig. 3.48D).

Over the years, the frequency of thyroid disease detection in adults varied from 17 % to 53 %, with the greatest increase 10–15 years after exposure to IR. NG and CAT prevailed in the accident survivors (all categories), ACUW and irradiated children being observed more often than in a group of unex-

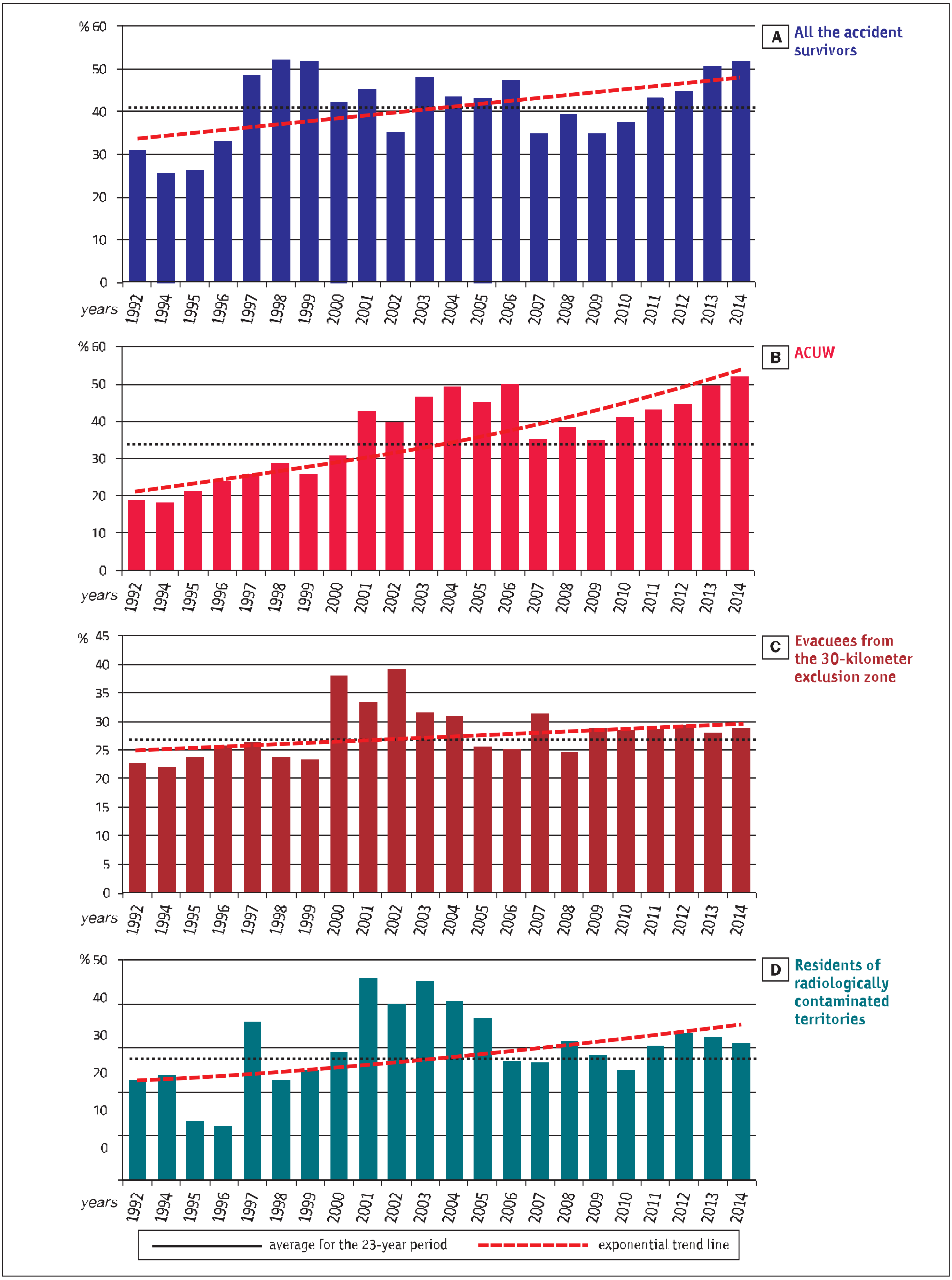

Figure 3.48. **Patterns of the thyroid disease incidence among different categories of the ChNPP accident survivors (24,588 adults, according to the data of NRCRM CER for 1992–2014 period)**

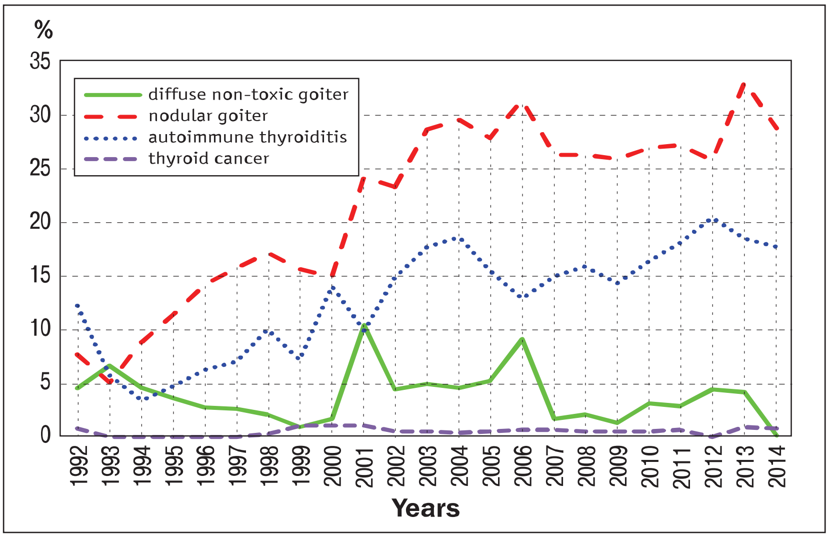

Figure 3.49. **Structure of thyroid morbidity in the ChNPP ACUW (10,771 persons, NRCRM CER data**

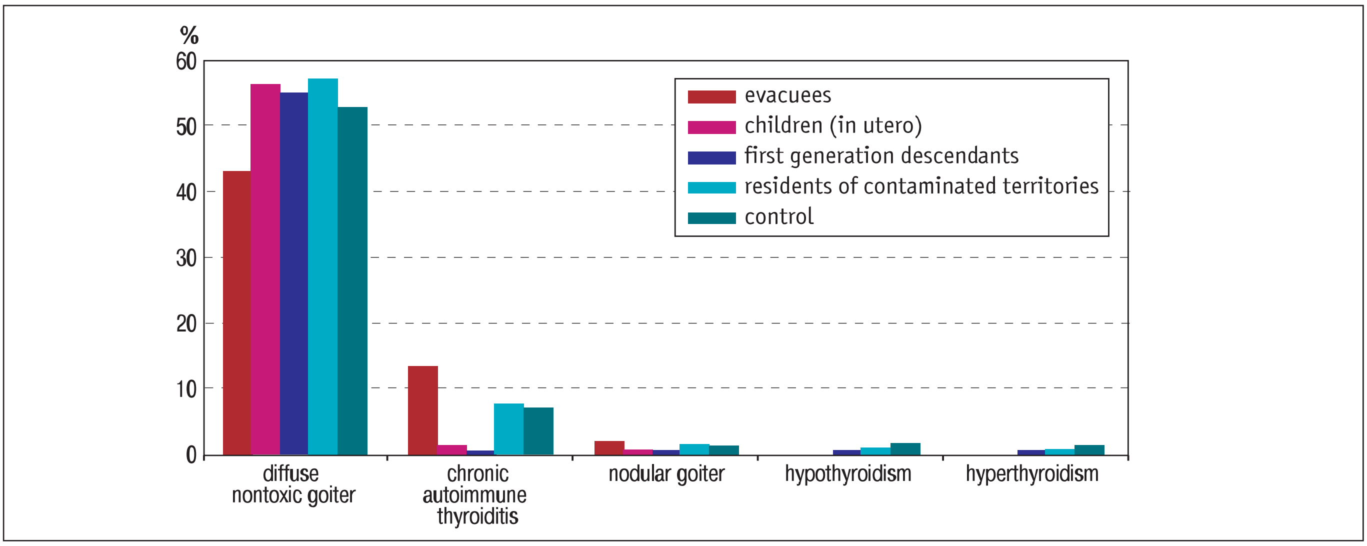

Figure 3.50. **Incidence of thyroid disease among 20,087 children survived after the ChNPP accident (NRCRM CER data for 1992–2012 period)**

posed persons from the general population of Ukraine (control group).

Incidence of NG in the accident survivors was on average 14.35 % and of CAT was ~8.0 % in the structure of thyroid morbidity over the years. According to the CER data the lowest prevalence was characteristic for diffuse non-toxic goiter (DNG) and disorders of thyroid function (hypothyroidism and hyperthyroidism), including their subclinical forms (Fig. 3.49). The obtained data indicate an exponential trend towards a significant increase in the incidence of NG and a moderate one for CAT in subsequent years.

DNG was found in 50.5 % of children in the most of study groups when reviewing the CER data on the thyroid disease incidence for 20 years (period 1993–2012) among children (Fig. 3.50).

Check-up of children irradiated as a result of the ChNPP accident (the CER data) revealed the most critical group of them, namely evacuees from the 30-km zone, exposed at the age of 3–6 years. Exposure to IR in them predisposed to the onset of DNG with 43.68 % incidence ($\chi^2 = 23.9$; $p < 0.0005$ vs. control group), CAT – 1.74 % ($\chi^2 = 31.6$; $p < 0.0005$ vs. the control), primary hypothyroidism – 0.96 % ($\chi^2 = 28.6$; $p < 0.0005$ vs. the control), and NG – 2.57 %. The peak prevalence of CAT occurred in 2001–2003, mainly during the period of active puberty (Fig. 3.51).

Thyroid disease in children born to irradiated parents (first generation) was detected in 42.64 %, which exceeded the value in control ($\chi^2 = 10.6$; $p < 0.002$), while CAT occurred significantly less often – 0.45 %, even in comparison with the control group ($\chi^2 = 8.68$; $p < 0.004$).

Among the ChNPP ACUW the NG and CAT prevailed in the structure of thyroid morbidity according to CER data, compared to official data for the gener-

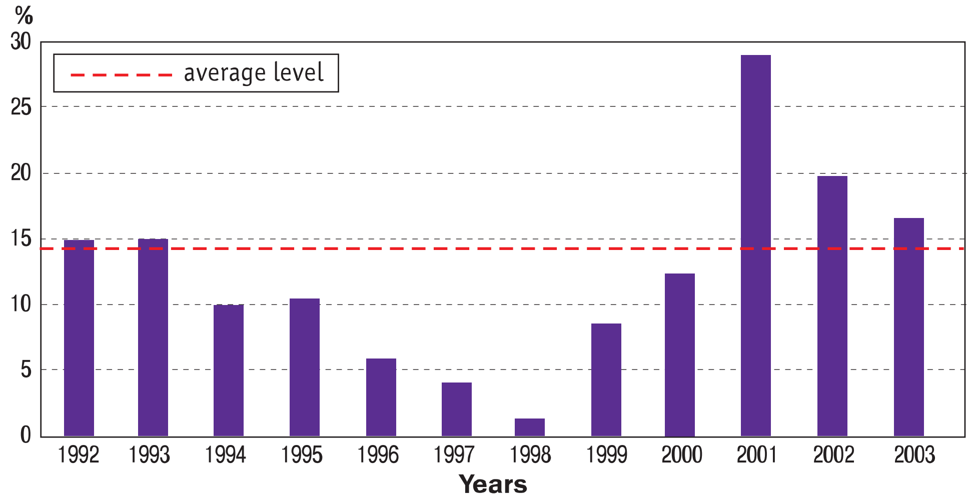

Figure 3.51. **Incidence pattern of chronic autoimmune thyroiditis in children evacuated from the 30-km exclusion zone at the age up to 18 years (20,087 subjects, NRCRM CER data for 1992–2012 period)**

al population of Ukraine, namely 21.8 % ($\chi^2 = 9602$, $p < 0.0001$) and 12.95 % ($\chi^2 = 5381$, $p < 0.0001$) respectively. DNG is of a lower share (3.94 %) among thyroid diseases. Thyroid dysfunction and thyroid cancer have made the lowest health impact in the ACUW.

When reviewing data on the ACUW of the «iodine» period (emergency work in April-July 1986) according to the spectra of external radiation doses in the range of 1.0–7.1 Gy, a statistically significant correlation was found with the occurrence of NG ($r = 0.883$; $p \leq 0.05$), both with a weak positive correlation in lower doses. According to the clinical study data, a correlation was established between the state of thyroid gland and effect of external γ-irradiation in the dose range of 0.2–0.49 Gy, accompanied by an increase in thyroglobulin antibody titer ($p \leq 0.01$) and predisposing to decreased thyroid function. In clinical settings these diseases correlated with external radiation doses in the range of 0.2–0.5 Gy. In this group of ACUW (average radiation dose 0.3 Gy) the highest frequency of CAT was observed, which can be considered a result of exposure to γ-radiation.

Thus, the combined effect of IR on thyroid cells led to a statistically significant ($p \leq 0.01$) increase in the incidence of hypertrophic (DNG, $p \leq 0.01$) and hyperplastic (NG, $p = 0.0002$) thyroid diseases among all population groups survived after the ChNPP accident, while incidence of CAT had increased only in ACUW of the «post-iodine» period of August 1986–1987 ($p = 0.003$). The increased probability of CAT had emerged in ACUW beyond the threshold of external radiation dose of 0.32 Gy, of hypothyroidism – above 0.41 Gy, of NG – above 0.37 Gy, and of obesity – above 0.7 Gy respectively. The maximum detection of CAT took place in 2002–2005 i.e., 15–20 years upon exposure to IR. Just this post-accident period can be considered the peak for CAT occurrence, which was associated with the impact of radiation factor.

Non-malignant parathyroid disease

Parathyroid injury is a newly emerged effect of IR on human body in the late terms upon exposure (more than 20–30 years). Parathyroid disease occurs here against imbalance in the vitamin D system through the emergence of resistance to its nuclear VDR-receptors and membrane MARRS-receptors, some gene mutations, as well as subsequent development of secondary hyperparathyroidism and gradual genesis of parathyroid adenomas. Radioactive iodine and cesium were main dose-forming isotopes during the ChNPP accident. At that it was established previously that incorporated isotopes of radioactive iodine, cesium, and strontium are tropic to parathyroid cells, as well as the latter are sensitive to irradiation of the neck area, which contributes to their dysfunction.

It is a well known that the thyroid is capable to accumulate various isotopes, including radioactive ones. The latter leads to the fact that it itself becomes a secondary source of α-, β- and γ-radiation

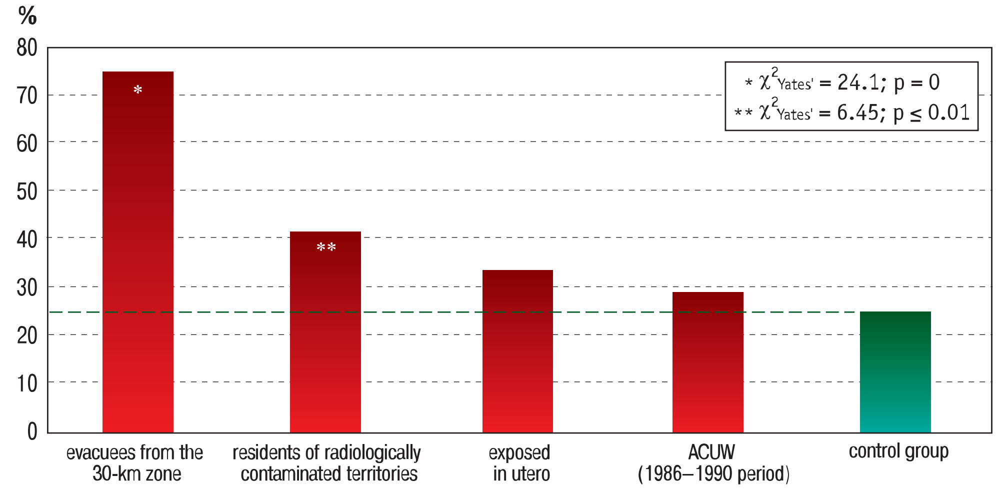

Figure 3.52. **Frequency of detection of parathyroid hyperplasia on diagnostic ultrasound in the adult ChNPP accident survivors vs. controls (n = 1,534)**

for the surrounding cells and tissues. Parathyroids are anatomically close to the thyroid, and that's why they not only accumulate tropical isotopes (iodine, strontium, cesium, and some others), but also experience an additional effect of the «thyroid-born» radiation, which together significantly increases the effective radiation doses for them, leading to parathyroid cell damage and glandular dysfunction.

Parathyroids are the main physiological regulators of calcium-phosphorus metabolism, consequently regulating and significantly influencing, directly or indirectly, the state of bones, muscles, kidneys, cardiovascular, nervous, digestive and other systems. Therefore, under and upon the parathyroid exposure their structural and functional state may be disturbed, which contributes to formation of the related disorders of other systems (i.e., comorbid conditions). This is not obvious to many doctors and specialists, as these issues only recently have come to the attention of scientists and expert clinicians.

Primary hyperparathyroidism is a rare complication after the radioactive iodine therapy. Commonly its latent period is more than ten years after radiation exposure [16]. Hyperparathyroidism was diagnosed after exposure to external beam radiotherapy for the head and neck cancer or some non-cancer disorders [17, 18]. Several studies indicate that parathyroid exposure leads to the occurrence of hyperparathyroidism upon a certain time. In particular, it was previously shown that the increased incidence of hyperparathyroidism in the irradiated persons is 2.5 times higher than in the general population, with a latent period of 20–46 years [16]. According to our data, the secondary (normocalcemic) hyperparathyroidism on a background of parathyroid hyperplasia, diagnosed 23–35 years after exposure, is the most frequent consequence of parathyroid irradiation.

An increased risk of hyperparathyroidism was established by Fujiwara (1992) among survivors of the atomic bombing in Hiroshima [19]. Some studies of the effects of radiotherapy indicate the development of persistent hypoparathyroidism [20]. According to one estimate, the critical doses for hypoparathyroidism after radiotherapy of Graves' disease (doses 2–38 mCi) are 140–750 cGy [21].

Therefore, previous studies, including ones in the survivors of atomic bombing in Hiroshima, indicate that accidental or iatrogenic irradiation of parathyroids can lead to both hyperparathyroidism (primary, secondary, tertiary) and persistent hypoparathyroidism with a latent period of more than 20 years.

Our studies in their turn have shown that parathyroid hyperplasia is detected 23–35 years after irradiation among persons having no primary or tertiary hyperparathyroidism, namely in the 28.8 % of ChNPP ACUW, 71.4 % of evacuees from the 30-kilometer exclusion zone, 41.7 % residents of RCT, and 33.3 % of irradiated in utero, which is more than in the non-irradiated residents of Kyiv City and Kyiv Oblast (24.3 %, the control group) (Fig. 3.52). The 58 % of children living on RCT have parathyroid hyperplasia.

Thus, there is a high prevalence of parathyroid hyperplasia among the population of Ukraine exposed to IR in different doses from tropic isotopes of iodine, cesium, and strontium, among other in a low-dose range. Such population groups primarily include the evacuees from the 30-km exclusion zone (71.4 %; $\chi^2_{Yates'}$ = 24.1, $p = 0$) exposed to a significant combined short-term impact of radioactive isotopes and external γ-radiation. Another critical group of affected persons, in whom a significant frequency of parathyroid hyperplasia was found, are residents of RCT, who are for a long time (years and decades) living under exposure to radiological contamination (air and food products) with cesium and strontium. A statistically significant (41.7 %; $\chi^2_{Yates'}$ = 6.45, $p = 0.009$) increase in parathyroid hyperplasia frequency was revealed in them.

The average serum level of parathyroid hormone in the ChNPP ACUW of the «iodine» period with diagnosed parathyroid hyperplasia was significantly higher ($p < 0.05$) than in the control group.

Non-cancer non-thyroid endocrine diseases

Clinical and epidemiological data accumulated at this time indicate that the exposure of population as a result of the ChNPP accident has led to a high prevalence of not only thyroid and parathyroid disorders, but also of other non-malignant endocrine diseases in adults and children. Such diseases are diagnosed many times more often than in persons who have not been exposed to accidental impact of IR.

Specifically, the incidence of pre-obesity and obesity in the accident survivors is 41.9 % and 36.8 % vs. 24.6 % and 31.1 % in control ($p \leq 0.001$), respectively. The total excess of body weight above the norm is observed in the majority of persons survived after the ChNPP accident (78.7 %) vs. 55.7 % in the control group. This is due to the prolonged effect of IR on the neurocrine cerebral structures (area of hypothalamic arcuate nuclei), which leads to the breakdown of protective regulatory mechanism in the proopiomelanocortin system, specifically in the synthesis of α-melanocyte-stimulating hormone (α-MSH). In persons not involved in the ChNPP accident the increase in blood levels of α-MSG occurs in proportion to the increase in body weight and serum leptin concentration, which can be considered a positive and physiological phenomenon directed at reducing of food consumption. Under the same conditions, but with more pronounced hyperleptinemia, the secretion of α-MSG was unchanged in the ChNPP accident survivors having the excess body weight or obesity ($p \leq 0.05$). Such events cause an excessive accumulation of adipose tissue in the body with onset of tissue leptin resistance, concomitant insulin resistance and hyperinsulinemia, formation of metabolic syndrome and associated morbid conditions. Central disturbances lead to disorders of integral regulation of energy balance and eating behavior in the ChNPP accident survivors. At that, among other, the decreased serotonin and melatonin concentrations occur, contributing to emergence of major depression, against a background of which the treatment of obesity can hardly be effective.

Such a situation is also typical for the onset of prediabetes or type 2 diabetes mellitus i.e., the median values are 15.5 % (up to 18.44 % in recent years) and 21.4 % respectively for all survivors, 8.6 % and 12.15 % for all ACUW, and 23.5 % for ACUW of the «iodine» period of 1986 ($p < 0.001$ vs. control) (Fig. 3.53). These values significantly exceed the data stated by the International Diabetes Federation for the residents of Ukraine. We support the opinion of Vathaire et al. [22] about hypersensitivity of endocrine cells of the tail part of the pancreas to the impact of IR, in contrast to 99 % of other cells of pancreatic head and body, which mostly represent the glandular exocrine part.

When comparing the incidence rate of endocrine disorders in the ChNPP ACUW of the iodine period in 1986, a two-way pattern can be observed between the external radiation doses and manifestations of disorders of the hormone-producing tissues. Their frequency is increasing in proportion to the external radiation dose of up to 0.99 Gy for almost all nosologies (diabetes mellitus, thyroid disease, obesity), but with radiation doses above 1.0 Gy, on the contrary, it is tending to decrease (Fig. 3.54).

During the ChNPP accident the children were irradiated mainly due to ^{131}I, that's why the highest prevalence of radiation thyroid effects was established just in them. Comparing their clinical data (including children born to ACUW i.e., first generation), obtained during a thorough clinical examination in hospital conditions, with data of their age-mates, there was found a functional lability of hypothalamic-pituitary system with the formation of unfavorable premorbid background for the emer-

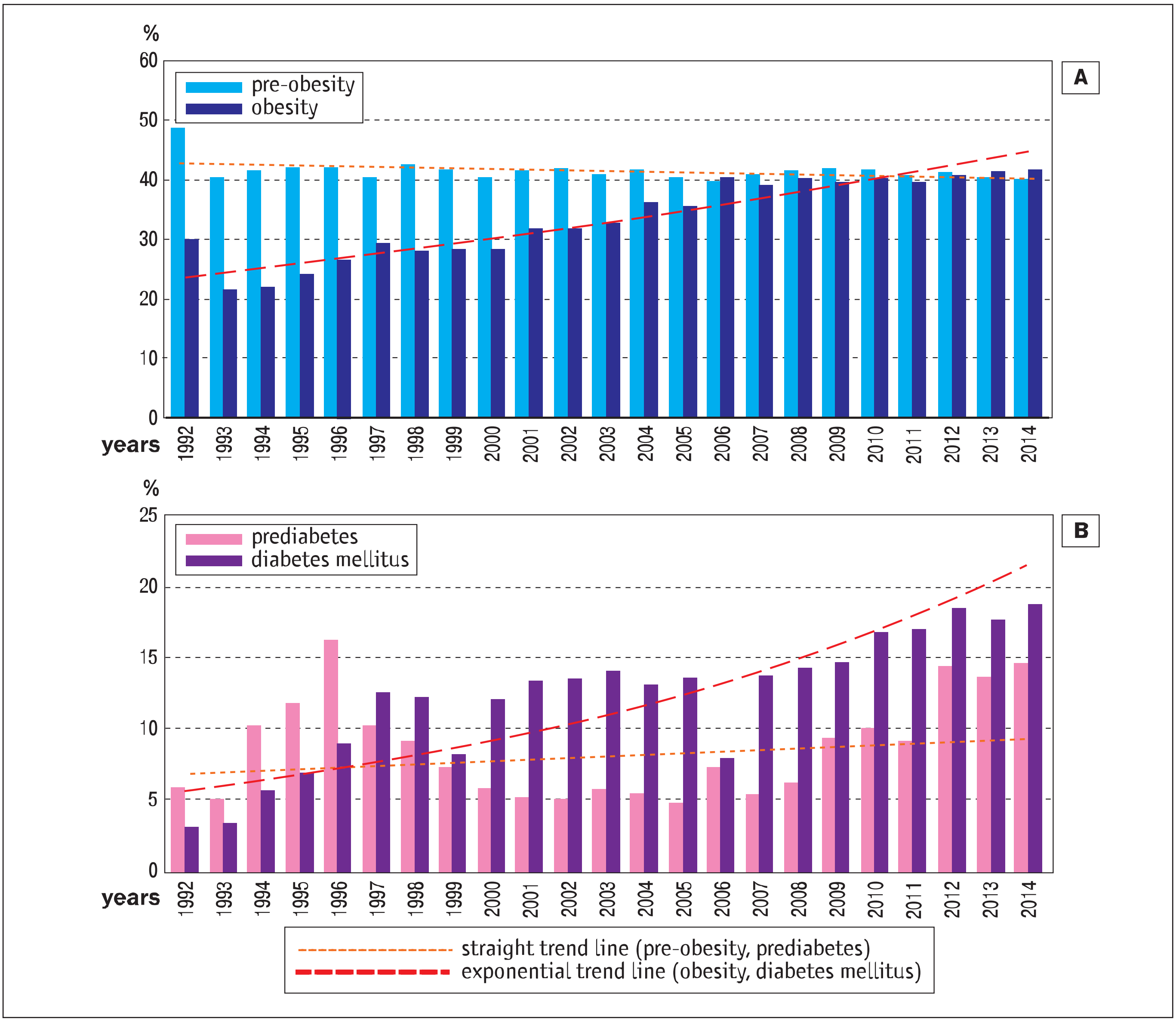

Figure 3.53. Incidence pattern of overweight/obesity (A) and pre-diabetes/diabetes (B) among the ChNPP ACUW (NRCRM CER data for 1992–2014 period, n = 10,798)

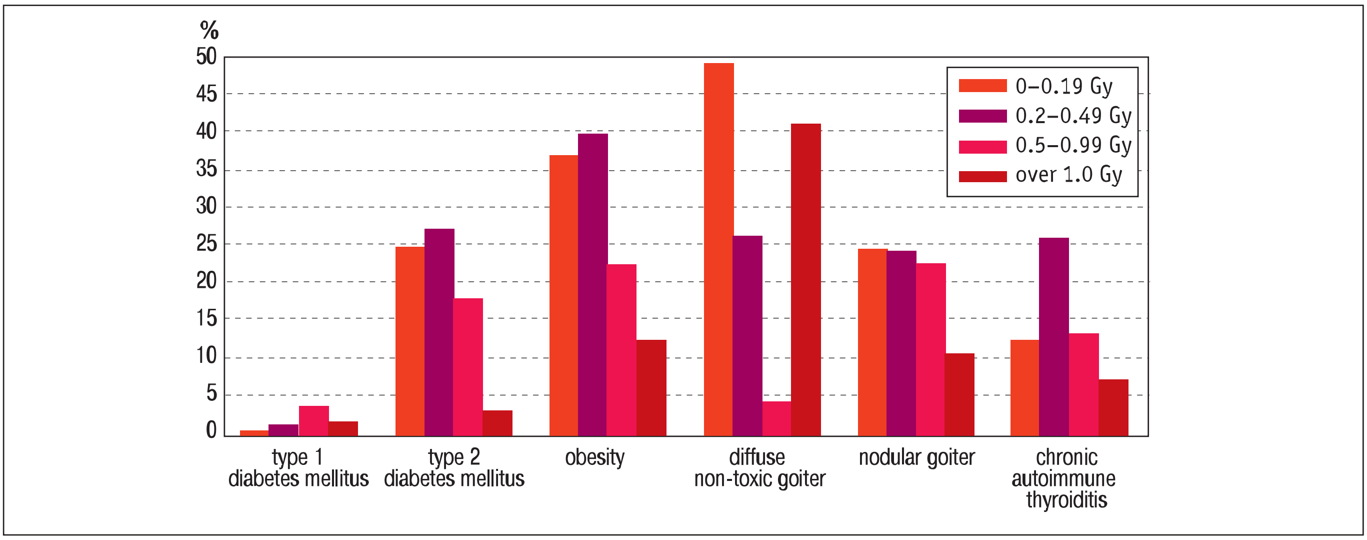

Figure 3.54. Incidence rate of endocrine disorders depending on external radiation doses in the ChNPP ACUW of the «iodine» period in 1986 (clinical research data)

gence of various neuroendocrine syndromes and subclinical resistance to a number of hormones. The long-term existence of such a strain leads to the decreased peripheral synthesis of hormones, resulting in abnormal secretion of tropic pituitary hormones, which is observed in 26 % of the examined children. The non-malignant disorders of endocrine system in the irradiated children include hypothalamic and metabolic syndromes, changes in sexual development and differentiation, and carbohydrate metabolism disorders. Clinical examination of children irradiated as a result of the ChNPP accident shows the prevalence of hypothalamic syndrome of the pubertal period in 25.4–28.9 % of them, accompanied by the presence of multiple striae (stretch marks) (83.0 % of cases), and asymmetry of arterial blood pressure (36.8 % of cases). In the first generation of children born to irradiated parents these disorders are determined much more often i.e., in 41.5–52.3 % of cases. It is impossible to diagnose such disorders conducting a simplified screening procedures for thyroid and other non-thyroid endocrine disorders without use of the challenge tests. Prevalence of pre-obesity and obesity in irradiated children is significantly lower, namely 3.2 % and 1.1 % respectively, than among adults, which corresponds to the different nature of their exposure to IR.

Today, we do focus our research to elucidate these features.

3.2. Mental health and neuropsychiatric effects

3.2.1. Background experience

Impact on mental health

The UN Chornobyl Forum has identified the impact on mental health as a major health and social problem following the Chornobyl disaster. The stress-related disorders, effects on developing brain, organic mental disorders and suicides, as well as cardiovascular diseases (including cerebrovascular ones) represent the spectrum of key health problems in the clean-up workers (CUW) of the ChNPP accident aftermath [4].

In terms of mental health impacts, the radiation emergencies are significantly different from natural disasters, other anthropogenic accidents and war conflicts if the weapons of mass destruction were not used. Significantly more people occur being involved thereat in their scope than those been directly affected. Inadequate perception of radiation risk is an important factor in mental health disorders, including the psychosomatic ones. A long-term impact of the Chornobyl disaster on mental health of survivors was surveyed. An epidemiological study in the CUW using a standardized psychiatric interview showed an increase in the incidence of mental disorders 18 years upon the accident, featuring depression, anxiety, post-traumatic stress disorder (PTSD), suicidal ideation, and severe headache.

Results of studies in Kyiv, Norway and Finland held in children exposed to ionizing radiation *in utero* indicate to the certain neuropsychological disorders associated with radiation, while other studies have found no significant effect on cognitive function or mental health. Only the higher rates of low self-esteem, clinical and subclinical depression, anxiety, and PTSD were identified in children and mothers. Mothers of younger children and CUW are subject to the highest risk of negative effects on mental health.

It was noted that further clinical and epidemiological psychiatric studies with dosimetric support, assessment of somatoneurological health, possible cognitive and psychotic symptoms are needed [32, 33].

Neuropsychiatric effects

Several mechanisms of radiocerebral effects have been identified, namely the impaired neurogenesis in hippocampus, changes in gene expression profile, neuroinflammatory response, abnormal neurosignaling, apoptotic cell death, cell death and their damage mediated by secondary injury, «vascular-glial union», etc.

Study results in the spectrum of potential radiation neuropsychiatric effects in children irradiated *in utero* were highly controversial. Some researchers have found no any cognitive or other neuropsychiatric effects in persons irradiated *in utero* and explained the subclinical mental disorders by social and psychological factors. At the same time, other studies have shown the neuropsychological and neurophysiological effects that depended on the intrauterine radiation doses on thyroid and fetus.

Radiation risks for cerebrovascular disease in the CUW were registered at radiation doses > 0.15 Sv, and for mental disorders and mortality from stroke at doses > 0.25 Sv. The CUW and evacuees have been found having a significantly elevated incidence of mental and behavioral disorders, vascular dementia, alcohol abuse, depression, and PTSD. The CUW feature an increased incidence of organic mental disorders, i.e., depressive, anxiety, emotionally labile (asthenic), and personality ones. Prevalence of alcohol dependence and alcohol abuse syndrome in the CUW is significantly increased. These syndromes develop secondarily due to the mental disorders that had occurred earlier.

Hypotheses were introduced on the role of ionizing radiation in development of disorders of schizophrenia spectrum and multiple sclerosis, which requires further clinical and epidemiological studies with estimation of radiation doses.

The dose-dependent cerebral disorders that occur after exposure to external irradiation at doses > 0.3 Sv and biological markers of radiation damage to the brain at doses > 1 Sv were identified. The radiation-associated cortico-limbic dysfunction of the left dominant hemisphere was revealed. Potential radioinduced neuropsychiatric effects may include the accelerated aging and neurodegeneration.

It has been suggested that chronic fatigue syndrome is a characteristic consequence of the impact of radiation in low doses and stress. A prospective study of personnel working on the transformation of the «Shelter» unit at the ChNPP into an environmentally safe system showed that the impact of low doses (0–56.7 mSv, M ± SD: (19.9 ± 13.0) mSv) and industrial risk factors can lead to the cognitive syndrome of chronic fatigue.

The neurocognitive deficits in survivors of the ChNPP accident suffering PTSD are higher than in veterans of the Soviet–Afghan War. The «post-radiation» PTSD is characterized by a projection of fear and uncertainty to the future (i. e. «anticipatory stress») regarding cancer, congenital malformations in offspring, etc. Risk of stroke and atherosclerosis is increased in the CUW suffering PTSD. Dysfunction of neocortex, hippocampus, and midbrain structures has also been identified.

Thus, the impact on mental health and neuropsychiatric consequences of the Chornobyl disaster were outlined as: 1) psychological and psychosomatic disorders; 2) long-term mental health disorders, including depression, PTSD, and alcohol abuse; 3) cerebrovascular and other organic disorders of the central nervous system, 4) cognitive disorders; 5) effects on the developing brain; 6) potential radiocerebral effects; 7) chronic fatigue syndrome; 8) suicide. Further neuropsychiatric studies with a perfect dosimetric support based on the analytical epidemiology with radiation risk assessment are required [32, 33].

Results received for the recent 5 years

Long-term effects on mental health and well-being

The long-term impact on mental health is the utmost medical and social consequence of the Chornobyl disaster featuring the excess of depression, anxiety disorders, stress-related symptoms (including PTSD), and medically unexplained physical symptoms (*i. e. psychosomatic disorders – ed. K.M. Loganovsky*). Females from the Chornobyl region who were pregnant or had young children in 1986 and CUW, especially those who worked since April till October 1986 are the most vulnerable subpopulation of survivors [34].

The impact on mental health was fueled by an excessive sense of health hazards from anticipated exposure, often caused by information from the local medical community and government officials. The CUW, evacuees and people living in radiologically contaminated areas have been officially labeled as «survivors» or «victims of Chornobyl». Mass-media had adopted these terms. Recognized as the Chornobyl victims, they receive a right to receive financial, health, and educational compensation, which, combined with ongoing monitoring by local and international organizations, can have an iatrogenic effect on psychological well-being. The psychological consequences, especially for mothers and CUW, continued to be a concern, while the mental health protection of survivors was inadequate to meet their needs [34].

Current planning of the nuclear disaster response in European countries is largely technical in nature, with less attention paid to social, psychological and ethical issues. The SHAMISEN consortium (Nuclear Emergency Situations – Improvement of Medical and Health Surveillance) with participation of 50 experts from 10 countries has critically reviewed the current recommendations and experience on dose assessment and reconstruction, evacuation decisions, long-term health surveillance programs and epidemiological research. The case studies and lessons learned from the living conditions and health of population affected by the Chornobyl and Fukushima accidents were assessed using an integrated approach to the health and well-being. A set of comprehensive recommendations have been developed to improve the preparedness, response, long-term observation and living conditions of populations that were affected by the past radiation accidents or may be harmed by such accidents in future with the purpose to meet their needs while minimizing an unnecessary anxiety [35].

The WHO believes that the experience of Chornobyl and Fukushima accidents clearly demonstrates that nuclear emergencies can lead to low and very low levels of radiation exposure, in which the psychological and social effects in the affected population will dominate over the actual biological effects of ionizing radiation itself. According to the international protection standards and guidelines it is required that both radiological and non-radiological health effects should be considered in the readiness and response to the real emergencies. There is an urgent need to expand the philosophy of radiological protection system beyond the metrics of radioactivity and radiation dose. Over the last decade, a number of multidisciplinary projects have been set up to assess the management options according to the social, economic and ethical criteria, in addition to the technical capacity of achieving this goal. The WHO and partners from the Intergovernmental Standing Committee on Mental Health and Psychosocial Support in Emergency Settings have developed a comprehensive framework and guidelines that can be applied to any type of emergency or catastrophe, regardless of its origin. There is a need to include available scientific expertise and technical, managerial, and personal resources what will be considered in a similar «decision-making structure» to be applied to the radiation emergencies. The radiological protection, medical support (especially primary care and emergency care, mental health support), social sciences (anthropology, psychology, ethics) and communication issues are the key areas of knowledge required to develop such a system. The implementation of such a multidisciplinary concept in operational terms requires the pesonnel extra education and training, which significantly exceeds current level of knowledge and experience [36].

According to the diathesis-stress model of radiation exposure and catastrophic stress effects, their combined action can result in deterioration of the mental health in survivors. The exacerbated symptoms of stress, substance abuse, anxiety and depression were revealed, although often at a subclinical level. People living in the Chornobyl Exclusion Zone have lower level of somatic and mental health [37].

The CUW in Estonia were found to have an increased odds ratio of current depressive disorder (OR = 3.07, 95 % confidence interval CI: [1.34; 7.01]), alcohol dependence (OR = 3.47, 95 % CI: [1,29; 9,34]) and suicidal ideation (OR = 3,44, 95 % CI: [1,28; 9,21]) [38].

At the same time, there is a discussion. To date the epidemiological studies indicate an increased long-term risk of cardiovascular disease in survivors. Impact on mental health is the most important consequence of the accident for public health in the three most radiologically contaminated countries, i.e., Ukraine, Republic of Belarus and the Russian Federation [39]. Some incidence excess of mental disorders and cerebrovascular disaese, including mortality from the latter with certain radiation risks, was revealed in the CUW [40]. The lifelong clinical and epidemiological psychiatric studies in all categories of the Chornobyl disaster survivors with reliable dosimetric support are required. The extreme urgency of environmental psychiatric problems in contemporary world has led to the establishing of a separate section «Ecology, psychiatry, mental health» on these issues within the World Psychiatric Association (WPA) (https://www.wpanet.org/ ecology-psychiatry-mental-health), where Ukraine is engaged, and Dr. Prof. Mr. K.M. Loganovsky as the representative of the state is a member of the Council of WPA Section of Environmental Psychiatry (https://3ba346de-fde6-473f-b1da-536498661f9c.filesusr.com/ugd/e172f3_93e54376b70c4d808c5b6bddbb3fec61.pdf).

3.2.2. Radiation risks of neuropsychiatric effects

A retrospective-prospective cohort clinical and epidemiological study for neuropsychiatric effects in the CUW with dosimetric monitoring of external radiation doses and external and internal control has been conducted over the previous five years. The randomized sample of male CUW participated in emergency works in 1986–1987 (n = 198) from the NRCRM Clinical and Epidemiological Registry (CER) aged 39 to 87 years (M ± SD: (60.0 ± 8.5) years), and been exposed to external radiation doses of 0.60–5900.00 mSv (M ± SD: (456.0 ± 760.0) mSv) was surveyed. The unexposed patients from the Department of Radiation Psychoneurology of the appropriate age and gender (n = 110, external control) were the comparison group. The CUW irradiated in doses < 50.0 mSv (n = 42) were recruited as an internal control. Standard diagnostic neuropsychiatric scales, psychodiagnostic questionnaires and tests, neuropsychological methods (including the Wechsler Intelligence Scale for Adults (WAIS) with a premorbid assessment), neuro- and psychophysiological methods (computer EEG and cognitive auditory challenges) were used. Methods of the descriptive and variational statistics, nonparametric criteria, regression-correlation analysis, Keplen-Meyer survival analysis, and risk-analysis were applied [41, 42].

Currently the cerebrovascular disease both with organic mental and depressive disorders mainly of the radiation-stress nature dominate in the CUW. The overall risk of neuropsychiatric disorders increases with the radiation dose (Pv < 0.001). Verbal memory and learning are impaired, IQ is reduced due to verbal component. There is an increased incidence of mild cognitive impairment and dementia. Cognitive impairment at doses > 0.3 Sv depends on the radiation dose (r = 0.4–0.7; p = 0.03–0.003). The affective disorders (depression) and neurocognitive deficits are more prevalent at higher radiation doses (≥ 50 mSv). The EEG parameters in the left posterior temporal area (Wernicke's area) depend on the dose value if the irradiation occurred at doses above 0.25–0.3 Sv. The cerebral information processes are disrupted with lateralization to the Wernicke's area at doses > 50 mSv. The radiation-induced dysfunction of cortico-limbic system of the left dominant cerebral hemisphere with a specific involvement of hippocampus is a key cerebral basis of the organic brain damage upon irradiation [41, 42].

Time (in years) of the debut of any neuropsychiatric disorder after the Chornobyl disaster, i.e., the period after which the disease arose upon disaster were used as an event for the analysis of survival (according to Kaplan and Meier). Neuropsychiatric disorders in the CUW emerged much earlier, namely 3–5 years after the catastrophe, and only approximately 30 years later these disorders appear almost equally in the CUW and unexposed control (Fig. 3.55). In addition, more neuropsychiatric disorders began to occur 7–10 years after the catastrophe in the CUW, which were also evacuated from the Chornobyl Exclusion Zone, than in those CUW who were not evacuated. This, of course, indicates the negative role of evacuation to the mental state. During the first 15 post-accident years a dose-dependent effect of the onset of neuropsychiatric disorders was detected, namely at doses greater than 300 mSv they appeared at the earliest terms, i.e., almost immediately after the catastrophe, while at doses of 50–300 mSv they emerged after 2 years, and at doses less than 50 mSv – after 10 years. Later there was no more this dependence [41, 42].

Figure 3.56 shows the quadratic dependence of the relative risk (RR) of neuropsychiatric diseases on radiation dose in the ChNPP accident CUW, odds ratio (OR) and 95 % confidence intervals [41, 42].

There is a significant excess of cognitive disorders, namely 99 (50.0 %) in the CUW vs. 20 (18.1 %) in unexposed (external) control (p = 0.04), affective disorders (depression) – in 96 (48.3 %) vs. 36 (32.7 %) (p = 0.007), and stress-related disorders – in 115 (58.4 %) vs. 8 (7.3 %) (p < 0.001), respectively. In the CUW irradiated at doses ≥ 50 mSv compared with the internal control group (exposed at doses < 50 mSv) the affective disorders were, respectively, in 89 (56.4 %) vs. 7 (19.1 %) (p < 0.001), and stress-related disorders – in 98 (62.8 %) vs. 17 (40.4 %) (p = 0.009). The relative risks (RR) and 95 % confidential intervals (95 % CI) of the incidence of neuropsychiatric disorders in the CUW of 1986–1987 period relatively to the internal control (< 50 mSv doses) are as follows: organic psychoses (RR = 3.15, 95 % CI: 2.6; 3.7), non-psychotic organic brain damage (RR = 1.99; 95 % CI: 1.6; 2.5); acute cerebrovascular disorders (RR = 1.40, 95 % CI: 1.3; 1.5), and chronic cerebrovascular disorders (RR = 1.23; 95 % CI: 1.0; 1.5). The neuropsychiatric diseases feature strong, increasing and

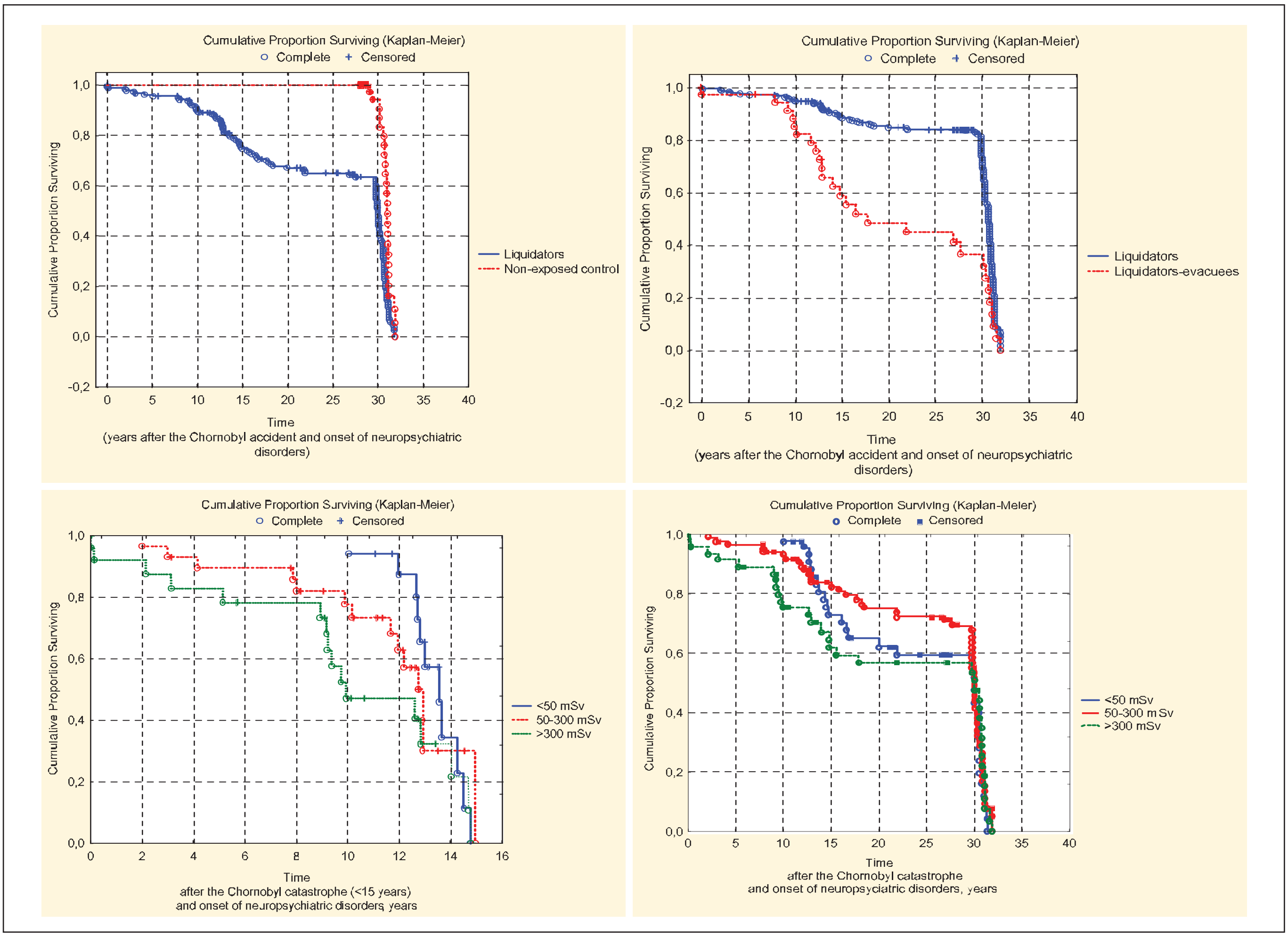

Figure 3.55. **Survival curves (Kaplan & Meier) for the onset of neuropsychiatric disorders after the Chornobyl catastrophe [32, 33]**

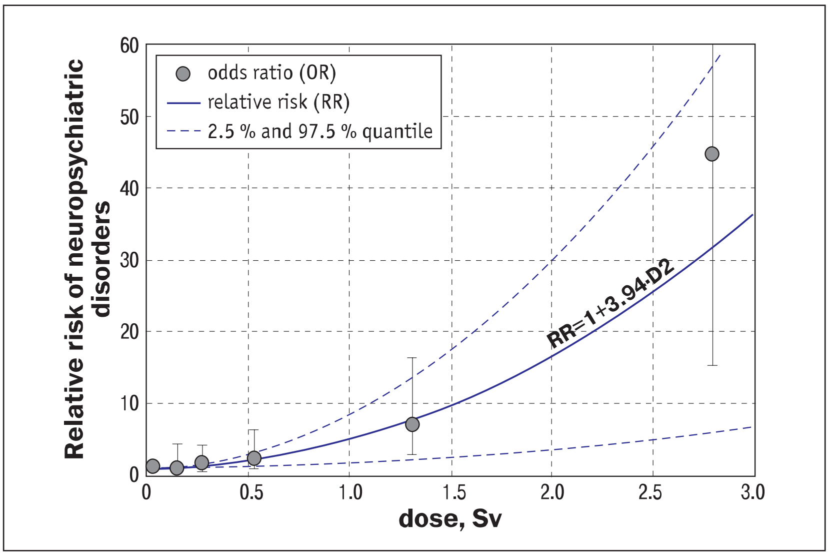

Figure 3.56. **Dose-effect dependence of neuropsychiatric disorders in liquidators (CUW) [41, 42]**

statistically significant quadratic (Pv < 0.001) dependence on the individual radiation dose, which leads to an excess of relative risk ERR = 2.76 Sv^{-2} (95 % CI: 1.06; 7.15) [41, 42].

It should be noted that the excess of morbidity and mortality from cerebrovascular diseases in employees of the manufacturing facility «Mayak» (USSR–RF) was detected at doses > 100 mSv [43]. This is the lowest dose offered as a threshold for neuropsychiatric (cerebrovascular) radiation effects. At the same time, according to the current concept this is just a «medium» but not a «low» dose. At the same time it is necessary to consider a quite other scenario of irradiation in the Southern Urals. The alpha-emitter plutonium was a principal dose-forming element there. We (V.O. Buzunov and K.M. Loganovsky) suggested that certain neuropsychiatric disorders could be considered not as the deterministic radiation effects (tissue reactions), but the stochastic effects of radiation. That is, for which there are no radiation dose thresholds, but the risk of their occurrence increases with the dose.

There is an excess of cognitive, affective, and stress-related disorders in the CUW. The risk of disease increases with increasing radiation dose. Radiation risks for organic psychoses, non-psychotic organic brain lesions, acute and chronic cerebrovascular disorders have been identified [41, 42].

Extensive review of the literature on epidemiological studies suggests that exposure to low doses of ionizing radiation (LDIR) ($\leq$ 100 mSv) or low dose rate ionizing radiation (LDRIR) (< 6 mSv/year) may cause negative or positive health effects. The latter may depend on genetic origin, age (especially prenatal), gender, nature of radiation exposure (i.e., acute or chronic irradiation), and radiation sources (such as atomic bombing, nuclear test drop, nuclear accident, buildings contaminated with radioisotopes, cosmic radiation, high natural radiation, medical examinations or procedures). The epidemiological and clinical studies indicate that exposure to LDIR or LDRIR can provoke cancer, congenital malformations, cardiovascular and cerebrovascular diseases, cognitive and other neuropsychiatric disorders, cataract and a range of ophthalmic and somatic disorders (endocrine, bronchopulmonary, digestive, etc.). At the same time, there is some evidence that exposure to LDIR or LDIR can also reduce the mutation rate and cancer mortality. Mechanisms of LDIR or LDIR health effects have not been sufficiently studied. Further research is required to determine under what circumstances the exposure to LDIR or LDRIR may cause positive or adverse effects, which may contribute to the development of new therapeutic approaches in prevention or management of radiation-induced human diseases or enhance the radiation-positive health effects [35].

3.2.3. Radiation–associated neurophysiological and neurocognitive disorders in the long–term period upon accident under different irradiation scenarios

The long-term radiation-associated neuro-psychophysiological and neurocognitive disorders (memory loss, deterioration of individual mental abilities in relation to the initial (premorbid) level, microfocal neurological symptoms, etc.) were detected under different irradiation scenarios after the Chornobyl disaster, namely the acute radiation sickness (ARS), exposure to radiation in low doses, intrauterine irradiation and irradiation under 1 year of age [45].

It is well known that the brain is extremely radiosensitive during its development. Intrauterine irradiated children still have a dose-dependent disharmony of intelligence due to the reduced verbal component, as well as neurophysiological disorders. These effects were observed upon irradiation at the 8th and later weeks of gestation at fetal doses > 20 mSv and thyroid doses *in utero* > 300 mSv, while when irradiated at weeks 16–25 of gestation then – at > 10 mSv and > 200 mSv doses, respectively. Despite the conflicting research results the prenatally irradiated children anyway require mandatory lifelong neuropsychiatric monitoring [45, 46].

The radiation-associated neurocognitive deficit in the CUW is largely associated with cerebrovascular disease, but neurodegenerative and autoimmune processes are certainly involved there, however this requires further research [47]. Deficiency of total IQ due to the decreased verbal IQ can be considered as a neuropsychological marker of cognitive impairment in the CUW, which reflects damage of the left (dominant) cerebral hemisphere [48].

Spontaneous and evoked bioelectrical activity of the brain is extremely radiosensitive and can be used as an economical and non-invasive biological dosimeter in the future [49], which can be applied in a wide range of exposure scenarios and dose ranges. In particular a decrease in the spectral power of the theta range of electroencephalogram (especially in the left frontotemporal region), increased beta activity and its lateralization to the left dominant hemisphere, and imbalance of normal asymmetry of visual evoked potentials to the reverse chess pattern and vertex wave can be considered the neurophysiological markers of prenatal irradiation [45, 46].

Using the actual non-invasive technology of cognitive auditory evoked potentials (Event Related Potentials, ERP, P300) their radiation-associated changes at doses > 50 mSv were identified, namely an increase of latency periods and decrease of amplitude of P300 component in Wernicke's area. Damage to the Wernicke's area impairs perception and understanding of language/conversation, namely the comprehension of words, instructions, addressed speech, etc. and leads to the patient's disability. At the present state of evidence, a radiation dose of 50 mSv can be considered as a threshold of radiation neurophysiological and neurocognitive disorders under the total whole-body external irradiation. This is critically important for the long-term spaceflights and in the field of interventional radiology, as well as, of course, in radiation emergencies [41].

Long-term radiation-associated neuro-psychophysiological and neurocognitive disorders due to the Chornobyl disaster are a significant scientific, practical and medical-social problem that requires further national and international research with an adequate dosimetric support.

3.2.4. Molecular-biological and genetic basis of cognitive and affective disorders

New data on neurobiological mechanisms of cerebral radiosensitivity and pathogenesis of radiocerebral effects are accumulating, featuring the inhibition of neurogenesis, mainly in hippocampus, changes in telomere and gene expression, apoptosis, neuroinflammation, autoimmune processes, «gliovascular complex», multiorgan dysfunction, etc. The 7th Framework Program of the European Union «Nuclear Fission and Radiation Protection» has implemented a joint European project CEREBRAD («Cognitive and Cerebrovascular Effects Induced by Low Dose Ionizing Radiation»), in which the NRCRM was participating. Clinical and new molecular-biological features of cognitive and cerebrovascular effects of irradiation in low doses were established there [50–53].

The *TERF1*, *TERF2* and *TERT (GE)* gene expression study by means of RT-PCR and relative telomere length (RTL) assessment using the flow FISH was performed in the CUW (n = 258, 22–2800 mSv radiation dose range) and the control group patients with vascular cognitive deficits (n = 78). Contemporary psychometric tools have been used to obtain the quantitative data on a degree of cognitive deficit. A statistically significant shortening of telomeres in the CUW upon irradiation at 100–500 mSv doses was established. The decreasing of RTL correlated with radiation dose increase and overexpression of negative telomere length regulators. The study results indicate the parallel changes in decrease of cognitive functions and telomere length, as well as features in the *TERF2*, *TERT* and *TERF1* gene regulation in the late period upon irradiation at doses above 500 mSv [50–52].

There is a large role of serotonin transporter gene (*SLC6A4*) in the pathogenesis of depressive states. Depression was more common in the patients with acute radiation sickness than in the CUW ($p = 0.006$). An increase in the number of *S/S SLC6A4* genotype carriers was found ($p = 0.03$) in the CUW compared with a large group of Europeans having no mental disorders. However, only for the S/S genotype carriers there was established a link between depression and patient's age ($r = 0.503$; $p = 0.033$), time after accident ($r = 0.581$; $p = 0.011$), both with a positive correlation between development of depression and radiation dose ($r = 0.515$; $p = 0.025$). Development of depression was associated with an incidence decrease of the highly functional *LA/LA* genotype to 4.76 % versus 31.25 % in the absence of depressive symptoms ($p = 0.042$) among persons 55 years of age and older. There was no difference in distribution of genotypes depending on the signs of depression ($p = 0.476$) in the younger patients. A pilot analysis of distribution of the *SLC6A4* gene genotypes for *HTTLPR* and *rs25531* polymorphisms in the CUW showed a need of further studies of the LA/LA and S/S genotype contribution to the development of depressive states associated with irradiation [54].

Cerebrovascular diseases, organic mental and depressive disorders, mainly of radiation-stress nature predominate in the CUW. The overall risk of neuropsychiatric disorders increases ($Pv < 0.001$) with radiation dose. Verbal memory and learning are impaired, IQ is reduced due to the verbal component. There is an increased incidence of moderate cognitive impairment and dementia. Cognitive impairment at doses > 0.3 Sv depends ($r = 0.4–0.7$; $p = 0.03–0.003$) on the radiation dose. Affective disorders (depression) and neurocognitive deficits are more prevalent at higher radiation doses ($\geq$ 50 mSv). In the left posterior temporal area (Wernicke's area) the EEG parameters depend on the dose value upon irradiation at doses above 0.25–0.3 Sv. The cerebral information processes are disrupted with lateralization to the Wernicke's area at doses > 50 mSv. Carriers of intermediate and low-activity genotypes (*L_A/S, L_A/L_G, L_G/L_G, L_G/S, S/S*) of the *SLC6A4* serotonin transporter gene more often have depressive disorders, especially severe ones, and a trend to increase the incidence and severity of cognitive and stress disorders. The radiation-induced dysfunction of cortico-limbic system of the left cerebral dominant hemisphere with a specific involvement of hippocampus is a key cerebral basis of organic brain damage after irradiation. Association of the *SLC6A4* gene *5-HTTLPR* and *rs25531* polymorphism genotypes with affective and cognitive disorders indicates the presence of neuropsychobiological characteristics of these disorders associated with the impact of ionizing radiation, depending on a certain gene polymorphisms [41].

At the end of this section we provide the most advanced unique study results on health and biological effects of low radiation does as biomarkers of external and internal irradiation. Cellular, molecular, genetic, and noninvasive (including neurophysiological) functional occupational biomarkers were studied in workers exposed to a combination of external gamma radiation and transuranic elements (alpha emitters). The study was conducted in personnel (n = 688) working on the Project of «Shelter» unit transformation into an environmentally safe system. An average external radiation dose was 26.06 mSv (0.1–113.35 mSv range) at the background risk of internal exposure to transuranic elements (plutonium and americium). Several biological parameters can be applied as biomarkers of irradiation at radiation doses under 100 mSv and even in the range of 20–50 mSv. Parallel changes were observed in the decrease of cerebral electrical activity, telomere length, and difference in *CCND1, CDKN1A, CDKN2A, VEGFA, TP53,* and *DDB2* gene expression. Increase in the number of such chromosome aberrations as dicentrics and paired fragments both with TCR-variant lymphocytes at doses exceeding the established occupational limits indicates the requirement in biological dosimetry. TCR-CD4$^+$, γ-H2AX$^+$ and the number of Cyclin D1$^+$ cells are the most sensitive markers here. Introduction of the flow cytometry technique for these markers allows obtaining the quantitative data in a shot time frame. Concomitant factors here included the respiratory dysfunction and smoking. Study of workers with a history of chronic irradiation in the exposure zone for 3–5 years showed the changes of compensatory origin, i.e., no shortening of telomeres, an increase in the number of NK-cells in combination with lower expression of intracellular γ-H2AX. Presence of radiation-induced changes in the regulation of cell proliferation genes, telomere function, and apoptosis was confirmed in nuclear workers [55].

In the recent decades there has been an increased concern about possible effects of ionizing radiation in low and moderate doses on cognitive function. An interdisciplinary group of experts (biologists, epidemiologists, dosimeters and clinicians) in this field have met in a framework of the European seminar MELODI on non-cancerous effects of radiation to summarize the state of knowledge on this topic and make recommendations for the future research in this field. In general, there are data on the cognitive effects of low doses of radiation, both in biology and epidemiology, although better characterization of the effects and understanding of the mechanisms are needed. Better description is required for the particular cognitive function or disease that may be affected by radiation. Such a kind of characteristic of cognitive deficits is to take into account the person's life expectancy, as the effects may vary depending on the age at exposure and/or at the evaluation of results. Evaluation of biomarkers, including neuroimaging, will help us understand the mechanism of cognitive deficits caused by radiation. Identifying loci of individual genetic susceptibility and studying gene expression can help identify the individuals who are at a greater risk. Mechanisms of cognitive effects caused by radiation are unclear being likely to involve both several biological pathways and different cell types. There is a need in the well-conducted studies in large epidemiological cohorts and experimental studies in appropriate animal models to better understand the cognitive effects caused by radiation. This done the results should be translated into recommendations for clinical radiation therapy and decision-making processes in the field of neuroimaging [56].

3.2.5. Posttraumatic stress disorder

Post-Traumatic Stress Disorder (PTSD) is a debilitating mental health condition that can develop after exposure to traumatic events. PTSD and substance abuse often occur together. It is widely recognized that comorbid conditions are difficult to treat being associated with worse treatment outcomes than any other disease. Several psychological treatments have been developed for the management of comorbid conditions, but there is no consensus on which therapies are most effective [57].

Excess of PTSD incidence of 4.1 % in the CUW vs. 1.0 % in unexposed control was found previously in the epidemiological study [58]. The «radiation» PTSD is distinct in the so-called «flashforward» phenomenon, i.e., predictive stress or anticipatory stress (prediction of fear and danger for the future due to cancer and non-cancerous diseases, congenital anomalies, etc.), comorbid disorders, somatoform disorders, depression, anxiety, neurocognitive deficitis and cerebrovascular disease [59].

3.2.6. Pathological personality changes (personality disorders)

In radiation emergencies a person is exposed not only to ionizing radiation, but also to a strong distress as the result of peculiarities of the perception of radiation, and beyond that acquires a traumatic experience. The latter affects the effectiveness of adaptation and risk of emotional and behavioral disorders, psychosomatic and other diseases [60, 61].

Retrospective-prospective data evaluation on the CUW and evacuees from the Chornobyl Exclusion Zone showed that the premorbid personality of all study subjects was characterized by the high working capacity, discipline, perseverance, stable views, optimism, energy, openness to new information, high motivation to achievements, propensity for empathy, altruism, and autocriticism [60, 61].

Upon the traumatic events the pathological personality changes occurred in the form of increased introversion and neuroticism, exacerbation of personality traits and increase in the number of accentuations of emotional, pedantic, anxious, cyclothymic, excitable and dysthymic type. All that was manifested in the introjectivity, pessimism, amplified emotional reactivity, passivity, isolation, slow thinking, irritability, hypersensitivity with tearfulness, weakening of volitional control and impulsivity, irresponsibility primarily to the own health, increased anxiety suspiciousness, touchiness, and panic response to the social changes [60, 61].

Such personality traits as extraversion, neuroticism, emotionality, pedantry, cyclothymism, demonstrativeness, anxiety, excitability and exaltation contribute to the formation of inadequate, hypertrophied perception of the radiation threat. All that is exacerbated by the high external reactivity, emotional instability, tendency to excessive vulnerability and sensitivity, inertia of mental processes, weakened self-control, tendency to panic reactions and subjectivity of assessments, lack of boundaries between fiction and reality, low tolerance to stress and feeling of helplessness being peculiar to the stated above psychological types. Hypertrophied perception of radiation risk contributes to the mental health disorders, such as low self-esteem, somatic uneasiness, social dysfunction, anxiety, sleep disturbances, low stress resistance and increased frequency of emotional and behavioral signs of distress that are most common in the ChNPP accident CUW and evacuees from the Chornobyl Exclusion Zone. Worse general health and higher levels of psychological distress are observed in persons affected by the two traumatic events (emergency work and evacuation) [62–64].

3.2.7. Cerebroophthalmological effects

Recently, there has been a growing research interest in the effects of ionizing radiation on brain and visual organ. These effects are thought to be a result of the combination of atherosclerotic, cardiovascular, cerebrovascular, and neurodegenerative processes. In addition, there is an ongoing discussion about possible abnormalities in the cerebral and visual function due to medical X-ray exposure within interventional radiology and nuclear medicine procedures involving both patients and healthcare professionals [53].

Ionizing radiation can affect brain and visual organs resulting, among others, in the onset of cognitive and visual disorders, behavioral disorders and reduced performance under occupational exposure in medical radiology, in particular within interventional radiological procedures, long space flights and possible radiation accidents [65, 66].

Potential cerebroophthalmic effects include specific neurocognitive deficits in a variety of neuropsychiatric disorders, including cerebrovascular and neurodegenerative diseases, radiation cataracts, radiation glaucoma, radioinduced visual neuropathy, and retinopathy. Particular attention is paid to the possible stochastic nature of many such effects. Individuals who have been exposed to ionizing radiation in utero and in childhood are a special target group with a higher risk of possible radiation effects, such as neurodegenerative and ophthalmic diseases. Experimental, clinical, epidemiological, anatomical and pathophysiological substantiation of radiosensitivity of the central nervous system and visual analyzer are given. Further studies are needed with adequate dosimetric and long-term medical and biophysical monitoring of the high-risk cohorts [65, 66].

3.3. Pathology of the digestive system and violation of oxidative homeostasis in the post-accident period as the basis of the development of pathological states

The results of previous studies

The gastrointestinal tract in the conditions of the Chornobyl accident belongs to the main target tissues of the action of damaging factors of radiation and non-radiation nature. Monitoring of the state of digestive organs in clean-up workers showed that the most common were erosive-ulcerative pathology of the stomach and duodenum and liver disease (Fig. 3.57).

Epidemiological «case-control» study revealed a high risk of erosive-ulcerative pathology in clean-up workers at the Chornobyl NPP with an absorbed dose > 25 cGy (OR = 4.67 with SI 2.84–7.71) in a wide age range).

Ionizing radiation and other negative factors of the Chornobyl accident affect the organization of all structural components of the gastric mucosa in clean-up workers of different ages [67]. These changes can be characterized as induced pathomorphosis, characterized by an atypical clinical course with a predominance of astheno-vegetative syndrome, association with *Helicobacter pylori*, altered

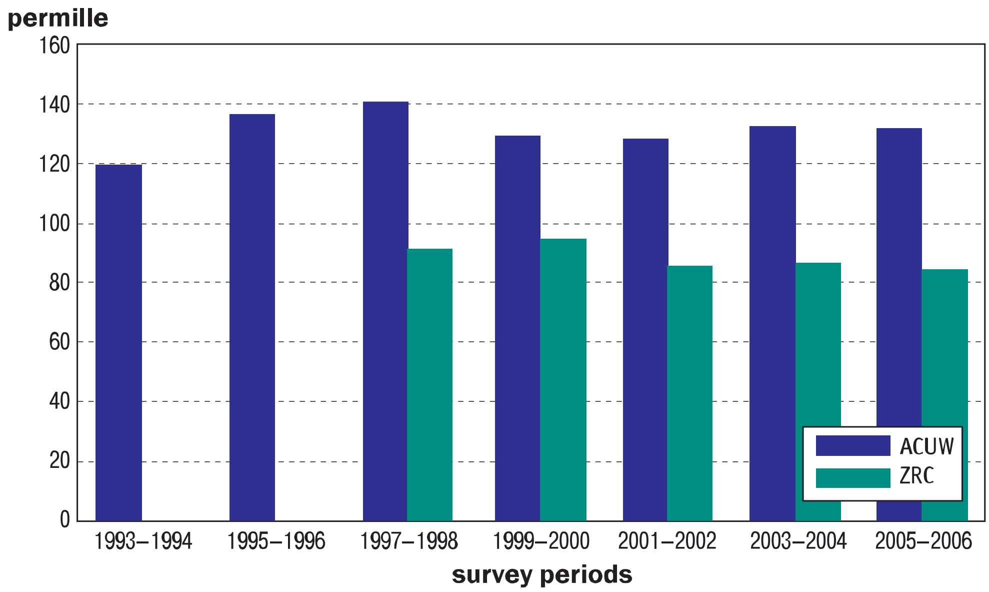

Figure 3.57. **The incidence of erosive-ulcerative pathology of the stomach and duodenum in clean-up workers at the Chornobyl Nuclear Power Plant (ACUW) and the inhabitants of the 4th zone of radiation contamination (ZRC) at the stages of observation**

secretory function and autonomic regulation, the presence of concomitant pathology [68]. Regularities of dose-dependent and age-related disorders of hormonal regulation of functional activity of the gastroduodenal zone and changes in psychological status were found.

Clean-up workers modifed the course of erosive-ulcerative pathology of the stomach and duodenum over time. Indicators of basal concentration of cortisol, adrenocorticotropic hormone (ACTH) and gastrin were in direct correlation with the level of absorbed doses over 25 cGy, which indicated a violation of local self-regulation of the gastroduodenal zone with a predominance of gastrin acid production mechanism.

In the remote period after the accident (2004–2008) in clean-up workers with erosive-ulcerative pathology of stomach and duodenum pronounced atrophic changes of the gastric mucosa were revealed, conditionong a high percentage of hypo- and anacid conditions.

The decrease in gastrin levels and acidity of gastric juice occurred with increasing dose, starting with 25 cGy; the lowest values of these indicators were registered in irradiated in the range of 50.0–99.9 cGy. Changes in the structure of the personality, characterized by a high level of anxiety, the presence of psycho-emotional stress and lack of neuro-psychological mechanisms that relieve anxiety were found.

The effect of ionizing radiation on the state of the human hepatobiliary system remains an unsolved problem of radiation medicine. The dominant position is the resistance of liver tissue to the influence of ionizing radiation. Since the second decade after the accident, there has been an increase in the number of detected cases of chronic hepatitis and liver cirrhosis.

According to epidemiological studies, 6–10 years after the accident, there was an increase in the incidence of chronic hepatitis among various categories of sufferers: the disease was found in 4.8 % of evacuees, 7.9 % of contaminated areas residents, 13.0 % of clean-up workers.

During the second decade after the accident, these figures increased to 16 % in evacuees and 36 % in clean-up workers. Between 1992 and 2004, 70 cases of liver cirrhosis were detected among 2,881 patients of Clinical-Epidemiolgical Registry with chronic hepatitis. There was a high risk of developing chronic hepatitis among those irradiated with an absorbed dose of more than 40 cGy [67].

A clinical study showed that the most numerous nosological group in the structure of chronic diffuse liver disease was non-alcoholic fatty liver disease (86.6 %). In the analysis of risk factors for the development of the disease, it was found that irregular diet and latent addiction to alcohol in clean-up workers were less important for the development of hepatitis than in the comparison group ($p < 0.05$). The activity of the inflammatory process in the liver in clean-up workers increased with the level of absorbed radiation dose: a direct correlation was found with the activity of gamma-glutamyl-transpeptidase ($r = 0.6$, $p < 0.02$), alanine aminotransferase ($r = 0.39$, $p < 0.02$) (Fig. 3.58). The

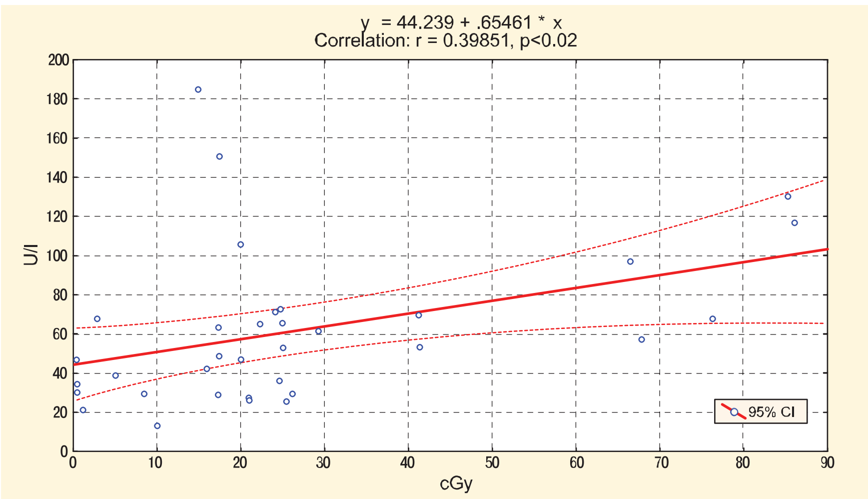

Figure 3.58. **Regression-correlation analysis between the level of absorbed radiation dose and serum ALT activity in clean-up workers with non-alcoholic steatohepatitis and steatohepatosis**

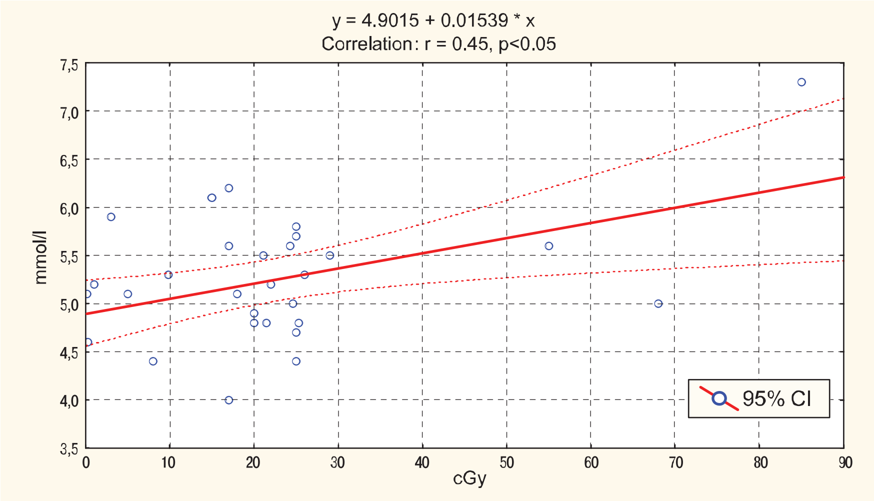

Figure 3.59. Regression-correlation analysis between the level of absorbed radiation dose and serum glucose concentration in clean-up workers with non-alcoholic steatohepatitis and steatohepatosis

observed increase in serum glucose, which is one of the main manifestations of the metabolic syndrome, was also associated with the radiation dose ($r = 0.5$, $p < 0.03$) (Fig. 3.59).

The results of research over the past 5 years

At the present stage of the study, results have been obtained on the peculiarities of metabolic changes in non-alcoholic fatty liver disease (NAFLD) in sufferers of the Chornobyl accident [68].

This group of patients was more likely to have high values of total blood cholesterol ((6.1 ± 0.1) mmol/l, $p < 0.05$), impaired lipid peroxidation and reduced antioxidant protection, as well as a large number of comorbid pathology (5.2 ± 0.2, $p < 0.05$), which was dominated by hypertension — (71.3 %, $p < 0.001$), cerebrovascular disease (73.5 %, $p < 0.05$), thyroid disease (47.1 %, $p < 0.05$).

The study of the persistence of hepatotropic viral infection showed a high incidence of viruses of the family Herpesviridae: herpes simplex type 1/2, cytomegalovirus and Epstein-Barr in non-alcoholic fatty liver diseases. Patients affected by the Chornobyl accident had a higher proportion of seropositive results with higher antibody titers. Most patients have been diagnosed with herpes simplex virus and cytomegalovirus mixed infection with a correlation between anti-HSV-1/2 IgG and anti-CMV IgG levels. A strategy of diagnostic and therapeutic measures to prevent the development of hepatocellular insufficiency in sufferers of the Chornobyl accident has been developed [69].

The effectiveness of hepatoprotectors of different groups in non-alcoholic steatohepatitis in sufferers of the Chornobyl accident was studied by assessing the functional status of the liver, changes in the proxidant-antioxidant system and persistent herpesvirus infections. The use of hepatoprotectors improved the state of antioxidant system (AOS) with an increase in the integrated index from (1433.1 ± 215.6) c.u. to (1649.1 ± 302.6) c.u., reduced the number of patients with decreased AOS, $p < 0.05$. Significant improvement in liver function, fat and carbohydrate metabolism, reduction of lipoperoxidation, increased activity of the antioxidant system, as well as a decrease in antibody titers to Epstein-Barr virus, ($p < 0.01$) in sufferers of the Chornobyl accident was found in the treatment of patients with NAFLD based on amino acids.

Complex therapy of NASH with the use of antiviral drugs in the sufferers of the Chornobyl accident had a positive effect on the processes of lipid peroxidation and the state of the antioxidant system with an increase in the integrated state of AOS from (1534 ± 237) c.u. to (2117 ± 431) c.u., decreased activity of the cytolytic syndrome and the frequency of detection of cholestasis syndrome, cholesterol level decreased too. Decreases in IgG antibody titers to herpes viruses were found in 58.3 % of patients, to cytomegalovirus in 54.5 % of patients, to core antigen of Epstein-Barr virus in 36.3 % of cases and to nuclear antigen in 33.3 % of cases [70].

3.4. Medical and biological effects of the Chornobyl disaster in children

The results of long-term observations indicate that one of the most unfavorable medical and biological consequences of the Chornobyl disaster is the deterioration of the children's health [71, 72].

Analysis of the data of the Clinical and Epidemiological Registry (CER) of State Institution «National Research Center for Radiation Medicine of National Academy of Medical Sciences of Ukraine» indicates that the number of children with chronic diseases among the affected contingents remains high and ranges from 70 to 74 % in recent years and the index of pathological lesions varies from 5 to 6, i.e., on average, children have 5–6 diseases and their level of health remains quite low. The structure of the detected pathology almost was unchanged for recent years, and the first places among somatic diseases are consistently occupied by diseases of the respiratory and digestive systems according to the CER data (Fig. 3.60).

It is known that as a result of the Chornobyl catastrophe in Ukraine the vast areas, which currently have the population of 2,235,365 people, including 464,568 children, were affected with radioactive contamination. A long-term source of radiation has been formed due to the entry of radionuclides into crops, dairy, meat and fish foods, and with them – to the human body [73, 74].

^{137}Cs is the most biologically dangerous among them. It is actively involved in the circulation of substances in nature, migrates through biological chains and reaches the human body. The contribution to the dose of internal irradiation of food is 98–99 %; from food milk provides about 80 % of a dose; meat – 5–10 %, potatoes – 5–6 %; vegetables – 1–6 %; fish – 1.2 %; mushrooms – 2–12.5 %; bread – 1–1.4 %. In individual farms of some districts of Zhytomyr, Kyiv and Rivne Oblasts, the problem of obtaining «pure» dairy products remains relevant today.

^{137}Cs, absorbed in the gastrointestinal tract, accumulates mainly in soft tissues and forms a dose of internal radiation, which in combination with food ration disorders can promote increase in morbidity of the digestive organs.

Some studies have revealed that the pathology of the digestive system had certain features in children living with long-term intake of ^{137}Cs in food chains. It was characterized by involvement of several regions of the digestive tract (66.20 % of children) in the pathological process. Atypical children diseases of the digestive tract, namely, a significant frequency of subatrophic (22.6 %) and mixed (26.4 %) disorders were identified, while hyperplastic (9.3 %) and catarrhal changes (8.3 %) were noted much less often [72].

The role of radiation factor in the deterioration of health and the growth of chronic somatic diseases in children remains controversial, although the increase in non-cancer diseases in survivors of the atomic bomb in Hiroshima and Nagasaki was noted by Y. Shimizu et al. [75].

A number of epidemiological studies on the effects of low doses of ionizing radiation on some systems of the child's body in recent decades have been pub-

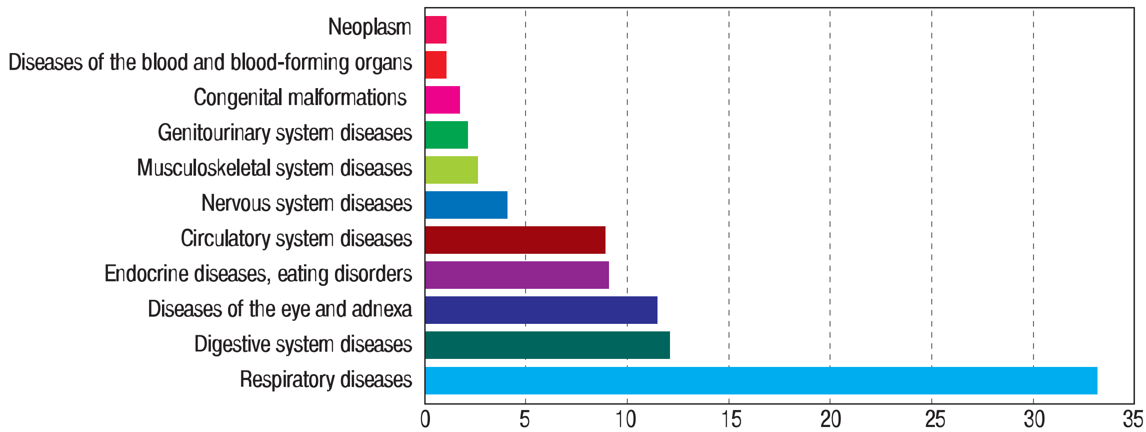

Figure 3.60. **The structure of the detected pathology in the affected pediatric contingents, according to CER of State Institution «National Research Center for Radiation Medicine of National Academy of Medical Sciences of Ukraine» (in %)**

lished. So, the data of longitudinal observations of the children cohort numbering 1,247 people indicate the dependence of the levels of hemoglobin, erythrocytes, leukocytes, and platelets on ^{137}Cs soil contamination density in settlements where children lived. There was an improvement in hematological parameters during a 6-year follow-up period [76] (Fig. 3.61).

The expediency of further studies, including the measurement of individual whole-body concentration of ^{137}Cs, was determined by the obtained results. A one-time study for the period 2008 to 2010 covered 590 children aged 0–17 years. In this study, children who were born at least 4 years after the accident were involved. It was found that children with higher individual values (logarithmic values of the human radiation meter – logHLM) of body ^{137}Cs activity had significantly lower hemoglobin, erythrocytes and leukocytes. The dependence of platelet depletion on logHLM was observed only in children older than 12 years. Thus, in this study it was shown that the decrease in the number of formed blood elements was associated with the level of incorporated radiocaesium, but blood parameters could be affected by other negative factors [77] (Fig. 3.61).

Analysis of the concentration of immunoglobulins of the main classes (IgG, IgA, IgM) in the serum of children from settlements with different ^{137}Cs soil contamination densities showed that children living in areas with higher levels of ^{137}Cs soil contamination showed lower serum IgG and higher – IgM. These results indicate certain changes in the content of immunoglobulins in children living in settlements with different ^{137}Cs contamination densities [78]. Decreased levels of immunoglobulins of the main classes (IgG, IgA), imbalance of immunoregulatory subpopulations of T-lymphocytes, inhibition of phagocytic function of neutrophils with the development of secondary immunodeficiency in children living in radioactively contaminated areas were confirmed in futher studies [79, 80]. Given the significant protective role of IgA on the mucous membranes of the respiratory tract, children and adolescents with low IgA levels were classified as at increased risk for respiratory pathology, the steady growth of which was observed throughout the period after the Chornobyl disaster [81].

Epidemiological analysis showed that children living in settlements with the highest quintile of soil contamination with ^{137}Cs were characterized by 2.6-fold decrease in forced vital capacity (FVC) < 80 % of predicted [95 % confidence interval (CI) 1.07–6.34] and 5.1-fold decrease in the ratio of forced expiratory volume per 1 second (FEV_1) to FEV < 80 % (95 % CI 1.02–25.19). Statistically significant evidence of both airway obstruction (FEV_1/FVC, peak expiratory flow, maximum expiratory flow at 25 %, 50 % and 75 % of FVC) and restriction of forced vital capacity with increasing soil contamination with ^{137}Cs [82].

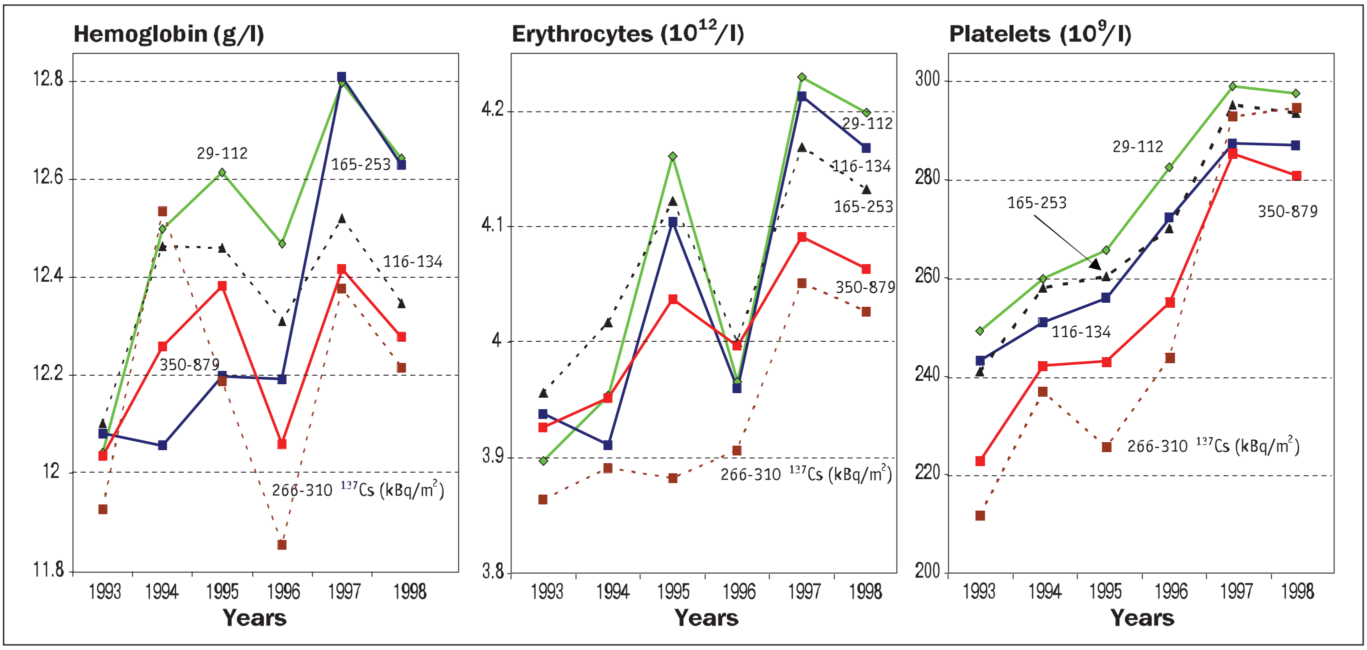

Figure 3.61. **Dynamics of hemoglobin, erythrocyte and platelet content in children permanently living in areas with different ^{137}Cs contamination densities [79]**

The above mentioned results were confirmed by the data of our next study, which showed that children with higher levels of incorporated radiocaesium have more pronounced disorders in the functional state of the bronchopulmonary system (Fig. 3.62) [83].

Impaired ventilation capacity in children residents of radioactively contaminated territories (RCT) was combined with changes in a number of indicators of non-respiratory lung functions, which were determined by exhaled breath condensate (EBC): decreased in lung excretory function and excretion of aerosols by respiratory organs, accompanied by fall in respiratory surfactant consentration, decreased content of phospholipids and total lipids in EBC. Intensification of free radical processes in EBC was revealed, as evidenced by an increase in light sum and rapid flare amplitude initiated by chemiluminescence of EBC, suppression of EBC antitryptic activity, which indicates a decrease in local protective factors of the respiratory system [84–86].

The tendency to a long course of respiratory diseases in children residents of RCT paid attention. The background for this was the presence of bronchial hyperreactivity, dysfunction of the lung surfactant system, the intensification of free radical processes and a decrease in the factors of local respiratory protection, which were found in children living in RCT. Studies of fatty acids in exhaled breath condensate by gas-liquid chromatography have shown activation of lipid peroxidation processes against the background of reduced antioxidant properties of lung surfactant and metabolic disorders of polyunsaturated fatty acids at the stage of bioregulation – eicosanoid formation [87].

Functional changes in the heart were observed in 40.0 % of children. The ECG registered sinus tachyarrhythmia in 32.0 % of cases, bradyarrhythmia – in 45.0 %, moderate metabolic disorders – in 42.4 %, and severe metabolic disorders in the heart muscle – in 3.8 %. When assessing the indicators of central hemodynamics and external respiration with the use of dosed physical exercise of medium intensity the decrease in stroke and minute blood volumes, a significant frequency of hypotonic (22.3 %) and dystonic (31.5 %) reactions to exercise, more intensive and less economical work of the ventilation apparatus, reduction of some indicators of general physical working capacity were found in a «stable state». This was evidenced by an increase in oxygen debt (by 14.8 %, $p < 0.05$), total oxygen demand for work (by 22.6 %, $p < 0.01$), periods of recovery of baseline pulmonary ventilation indices (by 18.6 %, $p < 0.02$) and oxygen consumption (20.1 %, $p < 0.01$) after exercise [72].

Vegetative support of the cardiovascular system in children was characterized by insufficient connection (rapid depletion) of the sympathoadrenal system during exercises, which can be attributed to the characteristic features of autonomic homeostasis for this period [88].

The permanent residence of children in radioactively contaminated areas is associated with a certain degree of risk for additional internal exposure due to the entry of radionuclides, primarily ^{137}Cs, with locally produced foods that form the basis of the diet of these children' contingents [74, 76, 89].

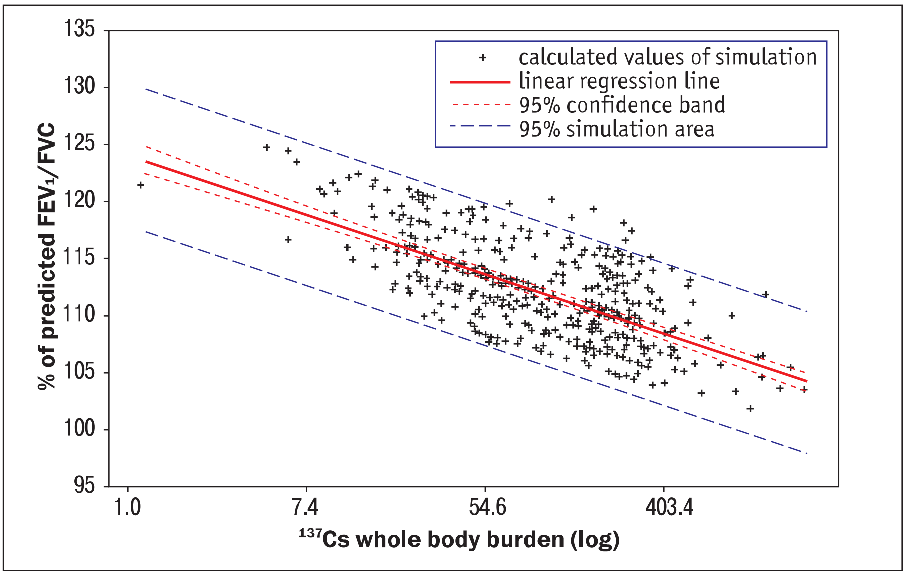

Figure 3.62. **The relationship between the FVC_1/FVC ratio and the logarithm of the ^{137}Cs content per unit of body weight (Bq/kg)**

Incorporation of radionuclides activates the processes of free radical and lipid peroxidation (LPO). Reactive oxygen species and LPO products destroy cell membranes, intracellular organelles, change metabolism, lead to a lack of antioxidant protection, which is considered one of the key mechanisms of damage to cells and tissues, including vascular endothelial cells [90].

It is known that the cell ability to perform specific functions is closely related to the condition of its surface cytomembrane. Radiation exposure causes numerous structural changes in cell membranes that persist for a long time after irradiation and lead to changes in the functional activity of cells [91].

In a model of peripheral blood erythrocytes, it has been shown that prolonged entry of radiocaesium into the body leads to significant damages of their cytomembranes, which is a sign of destabilization of membranes not only of these cells, but also a reflection of damage to cell membranes of the body as a whole [92].

Significant changes in the submicroscopic organization of intracellular organelles of blood cells, especially mitochondria, have been established. The most pronounced changes were observed in children with an active level of incorporated ^{137}7Cs exceeding 6845 Bq. When mitochondria are damaged, the activity of key enzymes of mitochondrial energy metabolism decreases, secondary mitochondrial insufficiency develops, which leads to systemic dysfunction of various cells, tissues and organs [93]. So, the consequences of the action of small doses of ionizing radiation on the human body are systemic (syndromic) in nature, a common feature of the pathogenesis of which may be, including energy mechanisms associated with impaired mitochondrial activity [94].

Disorders of nitric oxide metabolism can play a significant role in the pathophysiological mechanisms of medical and biological effects, and the formation of multifactorial pathology in children residents of RCT.

Recent studies have shown that one of the targeted objects of the damaging action of free radicals that are formed as a result of exposure to low doses of ionizing radiation is the vascular endothelium, which leads to the development of endothelial dysfunction, causes significant changes in the nitric oxide metabolism and can cause disorders of NO-dependent physiological functions of the body [95–97].

In the regulation of nitric oxide production by endothelial cells, an important role belongs to endothelial NO synthase (eNOS), the activity of which is associated with certain polymorphic variants of the gene – *eNOS*, including *4a/4b VNTR*-polymorphism in the 4th intron [98]. Although the polymorphism in intron 4, represented by two alleles (*4a/4b*), is not structural, obtained scientific data suggest the biological and functional roles of polymorphic variants in noncoding regions, which opens up the new possibilities for studying the pathogenesis of many diseases [98]. The presence of allele 4a is associated with decreased *eNOS* gene expression, which leads to a decrease in NO production and is considered as a risk factor for bronchopulmonary, cardiovascular pathology and other multifactorial diseases.

There is evidence that the presence of the a allele in the 4th intron of the *eNOS* gene in heterozygous and homozygous states is associated with increased individual radiosensitivity and more pronounced effects of radiation exposure [99].

It was found that in children living in RCT in the presence of the minor allele a in the genotype, there was a more significant inhibition of NO-synthase activity of the endothelium than in homozygotes with allele b, with a linear dependence on ^{137}Cs in the body (Fig. 3.63).

These children were 1.5 times more likely to have impaired ventilation capacity, the decrease in elasticity and extensubility indices of the lung tissue, decreased integral index of respiratory permeability – $FVC_1/PFVC_1$ (93.3 ± 2.8) % and (100.8 ± 2.1) % ($p < 0.05$). The feed back between the allele a carrier, the size of $FVC_1/PFVC_1$ indices, $r = 0.2590$ ($p < 0.05$) and of $FVC_1/PFVC_1$ indices, $r = 0.2627$ ($p < 0.05$) was revealed according to the data of correlation analysis [98].

Long-term monitoring of the health in children living at RCT under conditions of intakes of radionuclides with a long half-life indicates a high frequency of bronchial hyperreactivity, which is a risk factor for chronic bronchopulmonary pathology [72, 79, 100, 101].

It is now established that the etiology and pathogenesis of bronchoobstructive diseases are determined by the complex interaction of genetic features and adverse environmental factors. Modern research focuses on the study of the molecular and genetic basis of hereditary predisposition and is to

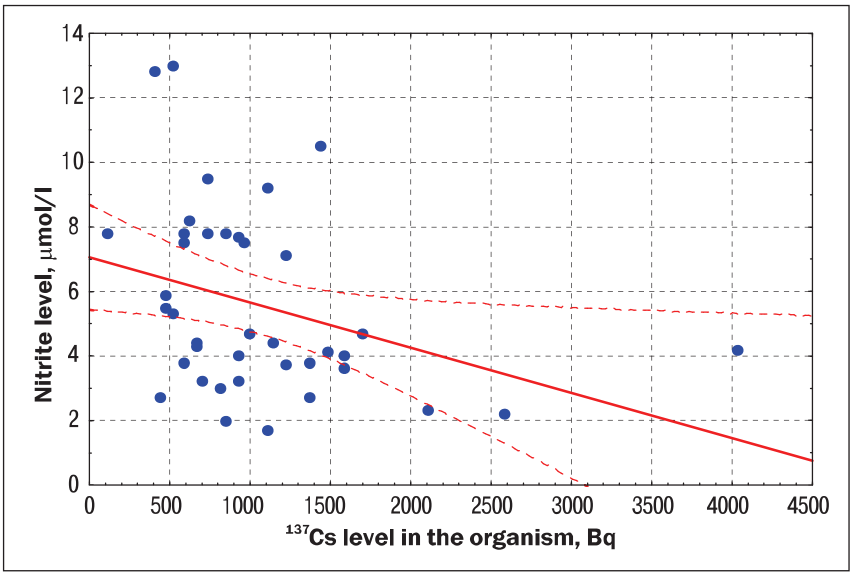

Figure 3.63. Dependence of serum nitrite level on the level of incorporated ^{137}Cs in children with genotype *4a/4b* of the *eNOS* gene

determine the role of certain genes and enzymes encoded by them in the pathogenesis of bronchoobstructive diseases.

The reaction of each individual organism to the influence of the environment depends on genetically determined features of the functioning enzyme detoxification systems. Among them, the most important role is played by glutathione-S-transferases (GSTs), which are directly involved in the second phase of biotransformation. A wide isomorphic spectrum of GST has been established, which is determined by the polymorphism of the genes encoding them. Differences in the structure of isoenzymes lead to different ability to metabolize xenobiotics and products of oxidative stress. This causes a different degree of susceptibility of each individual to the occurrence of multifactorial diseases, in particular, respiratory pathology [102].

The research results showed that in children from RCT with bronchial hyperactivity, the deletion polymorphism of the *GSTM1* gene and the *313AG* genotype of the *GSTP1* gene were found more often than in children without bronchial hyperreactivity, that is, an increase in early disorders of lung ventilation capacity was associated with the presence of a deletion polymorphism of the *GSTM1* gene and *313AG* genotype of the *GSTP1* gene, which may be a risk factor for further development of chronic pathology of the bronchopulmonary system [103].

Preliminary data on the contribution of hereditary predisposition, polymorphism of glutathione-S-transferase genes (*GSTM1*, *GSTT1*, *GSTP1*) and adverse environmental conditions in increasing the risk of bronchoobstructive disorders and their implementation in the form of bronchial asthma in children living at RCT were obtained too.

Even more complex and unresolved is the problem of genetic effects in the first and subsequent generations of offspring of irradiated parents.

Irradiation of pregnant women as a result of the atomic bomb explosion in Hiroshima and Nagasaki did not lead to an increase in congenital malformations in children, but there was an increase in the frequency of delayed physical and mental development of children (mostly irradiated at 8–15 weeks of gestation). In some children, mental retardation was combined with small head size. The conclusions of the Chornobyl Forum indicate that significant data on the presence of genetic abnormality excess in the affected child population have not been found [104].

In contrast, epidemiological studies by V. Wertelecki [105] showed that children born in the contaminated areas of the northern part of Ukrainian Polissya (Rivne Oblast) had one of the highest incidences of neural tube defects, blastopathy, microcephaly and microphthalmia in Europe [106]. The author believes that the obtained results justify the need to continue and expand the study of malformations under the influence of chronic radiation at low doses.

We assessed the consequences of intrauterine radiation on the children contingent with total number of 1,144 people, which included 3 groups: the I main group – children born to pregnant women at the time of the accident, women evacuated from Prypiat; the II main group – children born to pregnant women at the time of the accident and left to live in an area with a contamination density of ^{137}Cs over 555 kBq/m^2; the III – control group – children born in 1986, who were born and live in a radiation-safe regions of Ukraine.

Doses of total irradiation and equivalent doses of irradiation of the red bone marrow of the fetus in the I main group did not differ and ranged from 10.0 to 376.0 mSv. In the II main group, the total doses of general radiation in children, accumulated during the entire period of residence at RCT, including the antenatal period, amounted to 10.5–72.1 mSv; total equivalent radiation doses of red bone marrow were 14.1–81.7 mSv.

To assess the possible mutagenic and teratogenic effects of environmental factors, including radiation, it is proposed to use not only the frequency of congenital defects and sentinel phenotypes, which can be eliminated in the antenatal period, but also birth defects development (BDD) – small but persistent disorders of morphogenesis arising in the early stages of intrauterine development [107].

The results of researches showed that the action of medico-biological risk factors in combination with radiation in the period of organogenesis contributed to the formation of morphogenetic variants with multiple stigmas of dysembryogenesis. It was found that the smaller the gestational age of the fetus at the time of exposure to radiation and the higher the dose of radiation, the greater the number of BDD was detected in the child [107].

The presence of a direct correlation between the number of BDD in the child and the dose of total irradiation of the fetus (Ro = 0.61, $p < 0.002$) and the inverse correlation (Ro = -0.53, $p < 0.003$) with the gestational age of the fetus at the moment of radiation factor effect was found (Fig. 3.64).

The largest number of BDDs was registered in persons irradiated at 2 to 8 weeks of intrauterine development (Ro = -0.91, $p < 0.0001$).

It was established that in intrauterine irradiated children born to women evacuated from Prypiat (the I main group), there was a moderate correlation between the equivalent radiation dose of fetal red bone marrow and the number of aberrant cells (Ro = 0.50, $p < 0.02$), chromosome-type aberrations (Ro = 0.53, $p < 0.01$), number of translocations (Ro = 0.60, $p < 0.003$) and deletions (Ro = 0.60, $p < 0.003$) (Fig. 3.65).

In children who underwent prolonged exposure to radiation both during intrauterine development and in subsequent years of life (the II main group), there were significant correlations between the total equivalent doses of radiation to the red bone marrow, accumulated over the entire period of residence in the contaminated areas, and the number of aberrant cells (Ro = 0.62, $p < 0.002$), chromosomal aberrations (Ro = 0.72, $p < 0.0003$), stable (Ro = 0.64, $p < 0.003$) and unstable (Ro = 0.58, $p < 0.01$) damages to the chromosomal apparatus.

The dependence of the frequency of chromatid-type aberrations on the dose load on the red bone marrow has not been established.

Positive dynamics was showed by repeated cytogenetic examination at the age of 15–17 years. However, the frequency and spectrum of cytoge-

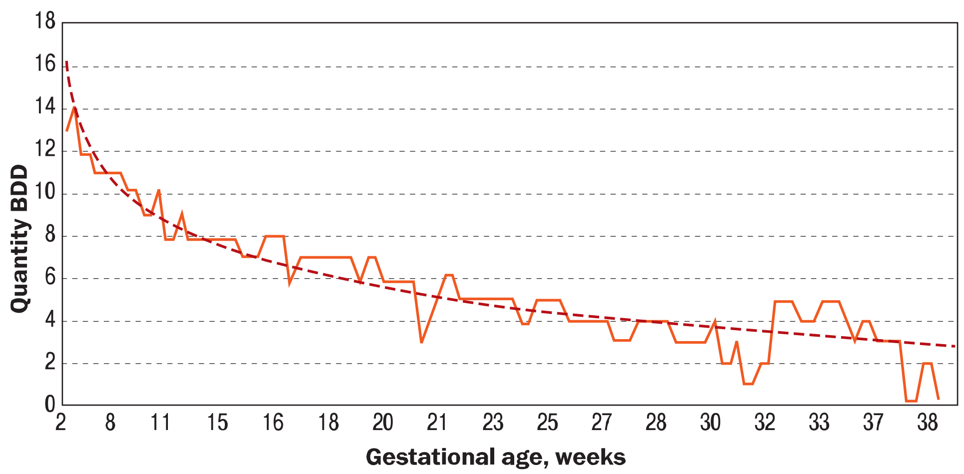

Figure 3.64. **The dependence of the number of birth defects development (BDD) on the gestational age of the fetus at the moment of irradiation**

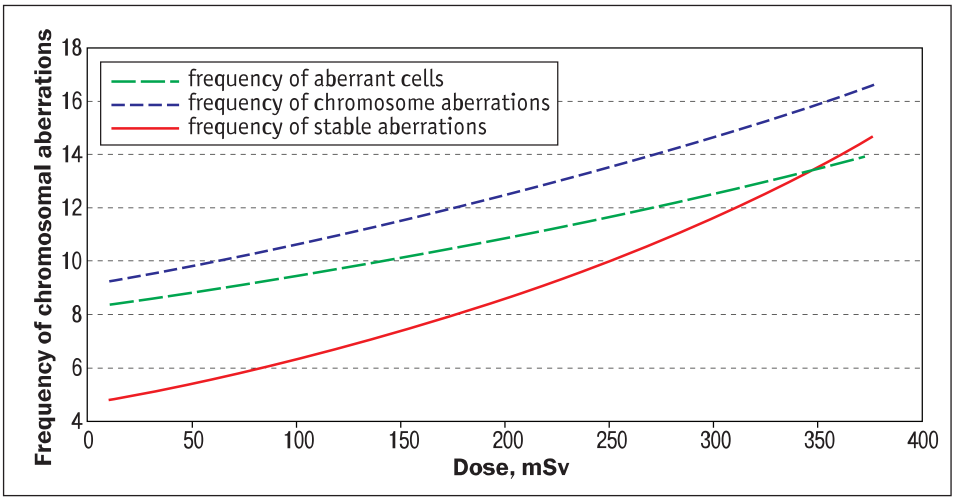

Figure 3.65. Frequency of chromosomal aberrations depending on the radiation dose of red bone marrow

netic abnormalities in 37.5 % of adolescents of group I and in 30.4 % of adolescents of group II continued to exceed the level of spontaneous mutagenesis [108].

These changes indicate destabilization of hereditary structures, which may be one of the risk factors that contributes to the development of multifactorial pathology, a high frequency of which we observed in children irradiated in utero.

To establish the possible consequences of irradiation of the father for his offsprings, 788 children from 394 families, which included a mother, father and two children, one of whom was conceived and born before the accident (sibs), the second – in the post-accident period (probands) were examined. The main group consisted of 297 families of clean-up workers of the Chornobyl accident. The main criterion for the selection of families in the main group was the fact of the impact of ionizing radiation on the father in the dose range from 100 to 1000 mSv due to his participation in the liquidation of the Chornobyl accident consequences. The control group consisted of 97 families in which parents and children were not exposed to radiation [109].

Studies have shown that the distribution of health groups among the siblings of the main groups was as follows: group I had 13.8 %, group II – 50.8 % and group III – 35.4 %. Among the siblings of the control group, these values were 15.5; 57.7 and 26.8 %, and among probands – 17.5; 52.6 and 29.9 %, respectively. That is, children born before the involvement of the father in the aftermath of the Chornobyl accident did not differ in health from children of the control group.

However, children conceived and born in the post-accident period in the families of clean-up workers of the Chornobyl accident had worse health than their older siblings born in the pre-accident period and children of the control group. The proportion of probands of the main group with chronic somatic pathology was 64.7 %, they often registered a combination of three or more nosological forms of pathology (57.3 %), in siblings – 23.8 %.

Children born in 1987–1988 had the lowest level of health – the number of practically healthy among them did not exceed 1.8 %, and the number of children with chronic somatic pathology was 92.8 %. In contrast, among the probands and siblings of the control group, the number of practically healthy children did not depend on the year of birth and ranged from 13.6 to 20.8 %.

Clinical and genetic studies have shown that morphogenetic variants with multiple minor developmental abnormalities were registered more often in probands than in siblings.

The use of mathematical apparatus, based on the method of group accounting of arguments, made it possible to identify a set of class-forming signs characterizing children born in the postaccidental period in the families of clean-up workers of the Chornobyl accident, and to single them out among all those examined. With the help of the instrumental-software complex designed to solve the problem of numerical assessment of the phenotype, it was found that morphogenetic variants were characterized in most probands by the presence of multiple stigmas of dysembryogenesis, and in 54.2 % of cases they included at least five MDAs with such complex of features: increased skin extensibility, telangiectasias, increased joint mobility, kyphoscoliotic posture, flat feet, dysplasia of connective tissue structures of the heart, gastrointestinal tract and abnormalities in the development of the renal pyelocaliceal system.

In siblings of the main group, siblings and probands of the control group, this phenotype occurred in no more than 13.5 %, i. e. four times less often than in children born to irradiated parents. The probability of correct recognition was 0.8030.

Comparison of cytogenetic analysis data showed that in children born after the Chornobyl accident in the families of clean-up workers, the frequency of chromosomal aberrations was higher (4.15 ± 0.03) % than in siblings – (2.81 ± 0.04) %, $p < 0.01$, mainly due to the increase in the number of chromosomal-type lesions – (3.19 ± 0.03) % and (1.88 ± 0.01) %, $p < 0.01$, while chromatid aberrations were recorded with the same frequency – (0.96 ± 0.13) % and (0.93 ± 0.14) %, $p > 0.05$. The probands showed stable chromosome damages (2.83 ± 0.03) % and (1.69 ± 0.04) %, $p < 0.05$ more often than the siblings [108].

Molecular genetic studies using the strategy of multilocus DNA fingerprinting allow to identify the emergence of new bands in probands, which were not observed either in parents or in siblings born to the father's clean-up workers of the Chornobyl accident [110].

An increase (by 5.6 times) in the variability of microsatellite-associated sequences in the genome of children born in the post-accident period in the families of clean-up workers of the Chornobyl disaster was revealed by comparative analysis of individual fingerprints RAPD-PCR and inter-SSR-PCR on DNA matrices of offspring [110].

The microsatellite loci themselves do not encode proteins, so most mutations do not significantly affect the viability of their carriers. However, it is logical to assume that if, as a result of exposure, the number of mutations in one part of the genome increased, then this, to a certain extent, may reflect changes in the entire hereditary apparatus.

Radiation disorders induced in the germ cells of the parents can be detected at different stages of the offspring ontogeny. In postnatal ontogenesis, presumably, «small» mutations that are in a heterozygous state are realized, the combination of which causes the destabilization of hereditary structures. It is possible that this phenomenon underlies the so-called «physiological inferiority» and reduces viability of the offspring of irradiated parents [111]. Signs of genome instability in the offspring of irradiated individuals may be the presence of multiple dysmorphias, organ dysplasias, increased frequency of chromosome aberrations and mutations in the DNA microsatellite fraction. All this contributes to the disruption of the processes of adaptation to the conditions of existence, an increase in the risk of development and realization of multifactorial pathology and a decrease in the level of health of children born to irradiated parents.

Possible mechanisms of transgenerational instability are currently being studied and widely discussed. However, the ability to predict the genetic consequences of ionizing radiation effect on humans, which has been the goal of genetics for the past 50 years, is still far from being resolved. But, it is already suggested that transgenerational instability may increase the risk of cancer and the development of congenital malformations in the offspring of irradiated parents. Perhaps, with the development of new, modern technologies, an answer will be found for many still unclear questions related to the occurrence of adverse effects in children exposed to low doses of ionizing radiation and children born to exposed individuals.

3.5. Study of inherited mutations in the genome of children whose parents were the liquidators of the Chornobyl accident (1986–1987)

One of the most pressing issues of concern to scientists, doctors and the public is the genetic effects of the Chornobyl accident and their consequences for the health of future generations. Obviously, the most complete and comprehensive answer to these questions could be given by large-scale long-term epidemiological studies of congenital and hereditary malformations conducted in the system of genetic monitoring of the population. Examples of such studies are observations of children who survived the bombing of Hiroshima and Nagasaki [112–114]. However, the authors themselves believe that a significant shortcoming of their research is the lack of results of such epidemiological studies before nuclear explosions, it the lack of an adequate control group. Similar epidemiological studies after the

Chornobyl disaster were conducted in Belarus, where genetic monitoring of congenital malformations was conducted before the Chornobyl accident. As a result of 10 years of research among the population living in areas contaminated with radioactive waste and received doses of radiation from 8 to 52 mSv, the authors note an increase in the frequency of congenital malformations compared to that observed among the population of these regions before the accident. Chornobyl, but based on the results of similar studies in other regions of Belarus conclude that such an increase «not only and not so much due to additional exposure of the population, but with a set of as yet unidentified factors, the most significant of which may be unbalanced nutrition» [115].

Recently developed methods for registering mutations in the human genome using DNA nucleotide sequence analysis, identification of mutations in genes that lead to the development of hereditary human diseases, opened a new era in the study of genetic effects of ionizing radiation on human heredity.

A number of studies have shown the influence of chemical contaminants in increasing the level of inherited mutations in minisatellites of birds (seagulls), as well as increasing the level of inherited mutations in minisatellite loci of mice after exposure to ionizing radiation [112, 113]. When studying the effect of radiation on the formation of mutations at different stages of gametogenesis in mice, it was shown that the most sensitive to mutagenesis is the stage of spermatids [114, 115].

In our study, the analysis of mutations was performed in two groups of families (mother, father, children). In the first group for the study were selected 183 children (from the 161 family) born to parents-liquidators (men) of the Chornobyl accident (1986–1987) (group of liquidators). The control group included 163 children (from 163 families) whose parents did not live in the Chornobyl accident zone and were not participants in the liquidation of the consequences of the accident. It should be noted that the assessment of the mutagenic effect of the factor involves a quantitative assessment of the dose and exposure to this factor. However, only the working conditions of the liquidators at the Chornobyl NPP did not allow to clearly record these parameters. Therefore, we tried to assess the dose and exposure during the analysis of the characteristics of the parents-liquidators during their work at the Chornobyl nuclear power plant.

As a result of the analysis of specially developed questionnaires, data were obtained characterizing the group of parents-liquidators: the period and nature of work, personal protective equipment, as well as radiation doses during work and their state of health. 89 % of parents-liquidators worked at the Chornobyl nuclear power plant since 1986 and only 11 % – since 1987. Only 4 % came to the Chornobyl zone for short-term work. 95 % of liquidators worked for a long time either directly on the territory of the Chornobyl NPP or in the cities of Chornobyl and Prypiat. According to the type of activity, this group was divided into 7 categories: 39 % worked directly at the nuclear power plant (firefighters, persons engaged in cleaning the reactor from radioactive contamination, repair work, construction of a sarcophagus, etc.); 14 % worked to neutralize radioactive contamination around the cities of Chornobyl and Prypiat; 14 % of liquidators were involved in the evacuation of the population in the Prypiat city (soldiers, police); 12 % – drivers who carried out regular transportation of people and goods between the station and neighboring cities; 7 % builders; 5 % – administrative staff and doctors who worked for a long time in the Chornobyl area; 5 % – helicopter pilots. About 3 % of liquidators who did not answer the questionnaire, we do not have some information about the nature of their work.

Of all the deviations of the health of liquidators registered since 1986, it should be noted that 40 % of liquidators noted chronic gastrointestinal diseases, 38 % – suffered from hypertension, 25 % – had vision problems, 23 % – heart disease (ischemic disease) and 15 % – neurological pathologies. Based on the obtained data, it is difficult to draw indisputable conclusions about which of these groups of diseases are caused directly by ionizing radiation, and which the result of severe stress and psychophysiological disorders, which in turn can be caused by ionizing radiation [116].

As a result of the survey of health and physical development of children, it was found that the share of almost healthy children from the families of liquidators was only 2 %, while in the control group – 26.7 %. Disharmonious physical development was observed in 30 % of children from liquidator families. Frequent infectious diseases (76 %) were observed in this group of children. In 62.5 % of children, the liquidators of the disease were accompanied by systemic lesions of the autonomic nervous system, they had a torpid course of the disease and their early chronicity. No hereditary pathology was detected in the group of children from the families of liquidators.

We created a collection of DNA samples of liquidator families (549 samples). Analysis of inherited mutations in minisatellite loci of different chromosomal regions was performed by blot hybridization with P32-labeled DNA probes kindly provided by Gilles Verne (IECH, Institut de Genetique et Microbiologie, France). An example of such an analysis for the CEB1 locus is shown in Fig. 3.66.

Table 3.31 presents the results of the analysis of mutations that occurred in the male gametes of liquidator parents in 7 minisatellite loci among children from liquidator families and control groups (mutations of maternal origin were not taken into account).

The highest mutability was observed in the CEB1 locus. For this locus the mutation rate in the control group was 14 % [117, 118]. In children of liquidators mutations in this locus were found a little more often: in more than 15 % of cases. The same trend was observed for mutations in loci B6.7 and CEB36. However, an increase in the level of mutations in children of liquidators in comparison with that in children from the control group is not statistically significant [119].

To assess the possible differential sensitivity of different stages of development of male gametes to the mutagenic effects of ionizing radiation, the group of children of liquidators was divided into two subgroups. The first included children who were conceived during the period, or no later than 2 months after the work of their parents at the Chornobyl nuclear power plant (hereinafter the group of conception «during»). The second group consisted of

Table 3.31
The level of inherited mutations in the control group and in the group of liquidators families

Minisatellite loci	Control group			Liquidators			The ratio of the mutations level	p^*
	I	II	III	I	II	III		
CEB 1(2q37.3)	163	23	0.1411	183	28	0.1530	1.08	0.115
CEB 15(1p36.33)	153	5	0.0327	169	2	0.0118	0.36	0.139
CEB 72(17q25.3)	161	4	0.0248	168	2	0.0119	0.48	0.225
CEB 42(8q24.3)	150	1	0.0067	171	2	0.0117	1.75	0.399
CEB 36(10q26.3)	160	0	0	181	4	0.0221	–	0.078
CEB 25(10q26.3)	123	8	0.065	138	3	0.0217	0.33	0.057
B6.7(20q13.33)	126	10	0.0794	144	12	0.0833	1.05	0.175
Total	1036	51	0.049	1154	53	0.046	0.94	0.075

Notes. I – the number of parental alleles, II – number of mutations, III – mutation level, p^* – probability by Fisher's test

Figure 3.66. **Analysis of inherited mutations in the locus CEB1 of the human genome using blot-hybridization**
1, 3, 4, 7 – parents;
2, 6 – children without mutations;
5 – a child with a mutant allele.

Table 3.32
The level of inherited mutations in the liquidators families (conception «During» and «After»)

Minisatellite loci	Conception «During»			Conception «After»			Ratio «During» / «After»	p*
	I	II	III	I	II	III		
CEB 1(2q37.3)	88	16	0.1818	95	12	0.1263	1.44	0.095
CEB 15(1p36.33)	85	2	0.0235	84	0	0.0	–	0.251
CEB 72(17q25.3)	78	3	0.0385	60	0	0.0	–	0.178
CEB 42(8q24.3)	88	1	0.0114	93	3	0.0323	0.35	0.264
CEB 36(10q26.3)	85	2	0.0235	86	0	0.0	–	0.245
CEB 25(10q26.3)	82	2	0.0244	86	0	0.0	–	0.237
B6.7(20q13.33)	80	6	0.075	64	6	0.0938	0.8	0.217
Усього	586	32	0.055	568	21	0.037	1.49	0.041

Notes. I – the number of parental alleles, II – number of mutations, III – mutation level, *p** – probability by Fisher's test

children conceived more than 4 months after the end of their parents' stay at the Chornobyl nuclear power plant (hereinafter the «after» conception group). This distribution was based on the fact that the period of spermatogenesis lasts from 64 to 73 days. The dates of birth of the children were indicated in the parents' questionnaires. The results of the analysis of mutations in minisatellite loci in children of these subgroups are shown in Table 3.32.

The results indicate that in the subgroup of children conceived during the work of their parents at the Chornobyl nuclear power plant, the total level of mutations of parental origin at all loci was 1.5 times higher than in the group of children where conception occurred much later after period of irradiation of their parents.

The results obtained by us do not allow us to unambiguously answer the question about the effect of ionizing radiation on the level of inherited mutations in minisatellite loci in children of liquidators of the Chornobyl accident, born after 1986. However, if the tendency to increase the level of mutations in the group of children conceived after fertilization of maternal oocytes by sperm exposed to ionizing radiation (during the work of parents-liquidators at the Chornobyl nuclear power plant) is not accidental, then, based on our data subgroups of families of liquidators, we can conclude that a possible mutagenic effect occurs during the period of spermatogenesis only, it does not affect the stem germ cells.

Under such conditions, it can be assumed that if there is any genetic effect of mutagenic action of ionizing radiation on the minisatellite loci of the germ cell genome, its action is limited to the transient period of spermatogenesis and is not significant for germ cells entering the meiosis phase after cessation of ionization. This is evidenced by the results obtained by Japanese scientists on the absence of an increase in the level of inherited mutations in the mini-satellite loci of offspring born several years after their parents survived the atomic bombing of Hiroshima and Nagasaki [120].

The current level of research of the human genome using the novel technologies of whole-genome sequencing significantly expands the possibilities of studying mutational processes in the human genome [121]. The use of such an approach to the analysis of induced by various mutagens and, in particular, ionizing radiation of inherited mutations opens new horizons in the study of the consequences of the Chornobyl accident for the health of future generations.

3.6. Morphological predictors of the placental complex, as prognostic criteria of health according to the «Certificate of the placenta» for 35 years after the Chornobyl accident (30 years)

I section – 30 years

The placenta is a unique organ in that it is a mixture of two genomic contributions and cells derived from the placenta to connect to the mother's tissue during pregnancy. It is known that the placenta is involved in systemogenesis, organogenesis and differentiation of internal organs of the fetus, performing the main functions associated with gas exchange, trophism, endocrine, immune, etc. [122, 123]

For more than 50 years, the State Institution «Institute of Pediatrics, Obstetrics and Gynecology of NAMS of Ukraine» (IPOG) has been studying the placenta in obstetric and extragenital pathology. The most pronounced changes in the placenta were observed in various types of hypoxia, which are caused by congenital and rheumatic heart defects of the mother; vascular pathologies; diabetes mellitus [124–130].

Since the beginning of the Chornobyl catastrophe in 1986 and until now, the staff of the Institute of IPOG and the Morphology Laboratory have been studying the placenta of the taphetoplacental complex, taking into account the indicators of internal radiation of small and super-small doses. Internal exposure is more dangerous than external. This is due to the fact that during the incorporation of radionuclides, cells are irradiated not only with gamma-ionizing radiation, but also with corpuscular radiation, as well as its significant non-uniformity. External and internal ionizing radiation acts on the structures of the tissue in which there are highly radiosensitive structures of capillaries of arterial and venous type, which includes the placenta [131–133]. Also, research scientists for the study of internal exposure was found to increase their role in fetal death in the early stages of gestation, infertility and cancer pathology in women after disasters large-scale world class (Three Mile Island Accident and Fukushima Daiichi Nuclear Power Plant Accident).

The aim of our study was to identify the role of internal placental irradiation associated with the Chornobyl accident, which had an impact on structural changes in the placenta, and to develop morphological predictors of the placental complex as prognostic criteria for health.

The studies were performed according to the «Placenta Certificate»*, which was created in the Laboratory of Pathomorphology to monitor changes in the placenta and was proposed for clinical studies based on radiometry, histological, histochemical, immunohistochemical and ultrastructural studies of placental lesions in women [134]. The «Placenta Certificate»* is copyrighted and accompanies the Placenta Protocol, which was included in Order of the Ministry of Health of Ukraine № 417 in 2004.

Joint studies of the internal irradiation of the placenta are being conducted with scientists from the Universities of Hiroshima and Shimano (Japan) to identify predictors of future health.

The material for the research was the placenta of women who were treated in the clinics of the institute from the regions of Ukraine (Kyiv, Chernihiv, Zhytomyr Oblasts). The analysis of the received data was carried out according to the computer program «Certificate of a placenta» created in laboratory. In total, more than 400 placentas were entered into the database by 2001. From 2002 to the present, 217 placentas have been examined, with an analysis of the results every 5 years and to this day.

The studied placentas, depending on the content of radionuclides, were divided into 3 groups:

➤ placenta of women with physiological course of pregnancy, without incorporation of radionuclides – comparison group (group I);

➤ placenta of women evacuated from the 30-kilometer zone, the content of radionuclides in the placenta is 0.5–4.8 Bq/kg (group II);

➤ placentas of women with a radionuclide content of 4.8 Bq/kg and more (group III).

The research methods were: radiometric, morphological, taking into account histochemical, immunohistochemical, ultrastructural.

Radiometry of the placenta was performed by methods using the following equipment:

➢ Selena Y-spectrometers;

➢ «Camberra» with scintillation detector;

➢ «Camberra» detector of well type;

➢ RC-101 isotope sample analyzer.

Radiometry was carried out in parallel in three laboratories: National Research Center for Radiation Medicine of the NAMS of Ukraine (Kyiv) (permanent); Laboratory of Radiometry of the IPOG (Kyiv) (permanent).

In parallel with radiometric measurements, morphological studies were performed:

➢ **histological methods** – staining with hematoxylin-eosin, picrofuxin according to Van Gizon;

➢ **immunohistochemical methods** – Detection of expression of PCNA-Anti-Rat Proliferating Cell Nuclear Antigen Clon proliferation markers: PC 10 (Dako); Anti-Human Antigen Ki67 Clone MIB-1 (Dako); markers of apoptosis – TUNEL (terminal

***«Certificate of placenta»**
1. Data of mother, newborn, stillborn, Apgar score, diagnosis.
2. Weight and size of the placenta.
3. Placental-fetal ratio.
4. Macroscopy of the placenta.
5. Anomaly in the development of the placenta, umbilical cord and membranes. Placental tumors.
6. Proliferation of cytotrophoblast, syncytiotrophoblast, stromal villi fibroblasts.
7. Structural features of placental dysfunction.
8. The results of radiometry of placental tissue.

deoxynucleotide transferase-mediated d UT Pnick-endlabeling); Anti Human Bax proapoptotic gene (Dako); onco-markers – Anti Human Bcl-2 onco-protein Clon 124 (Dako); Vascular endothelial growth factor – VEGF (Emergo Europe), CD-31, CD-105; marker of cell differentiation Anti-Human Cytokeratin Clone AE1 / AE3 (Emergo Europe) and mesenchymal factor – Mouse Anti-Swine Vimentin Clone: v9 (Dako);

➢ **electron microscopy method**.

The results and discussion of the study showed that during all years of studying the radiation factor, the presence of fluctuations of small and super-small doses of 0.5–4.8 Bq/kg and more in the placentas of women who lived and gave birth in Kyiv, Chernihiv, Zhytomyr Oblasts and Kyiv City (II–III groups) In comparison with placentas of women who lived in Poltava Oblast and Bristol (England) (I group Comparison).

Analysis of the obtained data revealed that 80 % of women gave birth to live babies (body weight from 2600–4000 g), and 20 % of women – stillborn. Analysis of the amount of incorporated radionuclides was mainly due to Cs-137 (Fig 3.67).

Thus, it can be considered that the placenta is an organ of biological monitoring, which revealed the presence of transuranic particles, which lead to internal irradiation of placental structures that develop during gestation, can affect its development, and therefore the development of the fetus and child.

Realizing that there may be more than just radionuclides in placental tissue, we conducted a joint study with European and American scientists under the ELSPAC program (European Longitudinal Study of Pregnancy and Childhood) on the content of heavy metals in placental tissues, the results of which were published in 2000 in Journal of Toxicology and Environmental Health. The placenta was examined in two cities of Ukraine – Kyiv (Left Bank district) and Dniprodzerzhynsk – during the full year of all births. Studies have shown that the concentration of lead, cadmium and mercury in the placenta is lower, or corresponds to the description of previous studies from other countries.

Therefore, we started the study of the placental complex with only the incorporation of small and super-small doses of radionuclides.

Morphological examination of the placenta of the first group (control) revealed changes that have been described in the work of the laboratory of morphology for a number of years since 1968.

In groups II and III, changes in the structures of the placental barrier depending on the accumulation of radionuclides were detected (Table 3.33). The largest structural changes were observed in group III, especially at the immunohistochemical level.

Peculiarities of changes in morphological studies in the presence of radionuclides in placental tissues greater than 4.8 Bq/kg in group III were revealed. A significant increase in markers of proliferation was found [immunohistochemically PCNA, Ki-67 2.8 times (Fig. 3.68).

Because cell proliferation underlies metaplasia, our findings may serve to further investigate perinatal oncogenesis and may be important in identifying the mechanisms of transplacental carcinogenesis. Radiation apoptosis was established and described (immunohistochemically) by the TUNEL method (Fig. 3.69). Apoptotic index exceeded in the structures of the nuclei of syncytia, cytotrophoblast and endothelium of fetal vessels three times than the control group. The so-called radiation apoptosis was

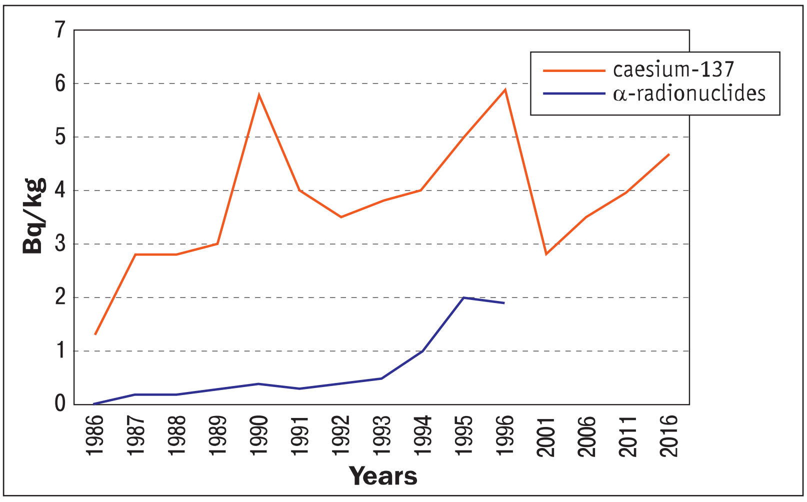

Figure 3.67. **The content of radionuclides in the placentas of women who lived in contaminated areas**

Table 3.33
Morphological features of the placenta of women with the incorporation of radionuclides

The content of radionuclides, Bq/kg	Circulatory disorders	Dystro-phic changes	Compensa-tory reaction	Prolife-rative changes	Ultrastructural changes			Immunohistochemistry		
					nuclei	EP	mitochondria	PCNA Ki-67	CEA	APO-1 TUNEL
I group – control comparison	20 %	20 %	48 %	1–2 %	2 %	без змін	1–2 %	1 %	–	2.5 %
II group, 0.5–4.8	Focal detachment of decidual membranes 25–28 %	25–28 %	30 %	30 %	32 %	10 %	10 %	25–30 %	1–2 %	15–18 %
III group, over 4.8	52 %	50 %	20–28 %	52 %		10 %	25 %	52 %	2–5 %	25–30 %

observed in the nuclei of endothelium fetal vessels and stromal cells, which is important for fetal embryogenesis.

Separately, we want to dwell on the expression of the tumor marker CEA (carcino-embryonic antigen) in the structures of the placental barrier, because according to the literature and our studies, this marker is not expressed in placental tissues in the dynamics of gestational age during physiological pregnancy. In III group in 25 % of the studied placentas with the incorporation of radionuclides more than 4–8.5 Bq/kg, positive expression of carcino-embryonic antigen (CEA) in the cytoplasm of stroma cells and the endothelium of fetal vessels of the chorionic villi (Fig. 3.70). This indicates the activation of the onco-perinatal process.

After 2000–2010 Ukraine, a significant increase in the incidence of thyroid tumors in 2.5 times was shown. We drew attention to pregnant women who underwent surgery for thyroid cancer and gave birth to offspring. In this study, we studied 100 placentas of women with thyroid tumors (malignant) in comparison with benign (uterine leiomyoma) in the clinics of the IPOG (department headed by Professor Y.V. Davydova). Morphological and immunohistochemical data on this were studied, published in the literature and reported at congresses.

In recent years, the literature found that the placenta is permeable to metastases in tumors that arose during pregnancy. It is shown and illustrated that most often metastases occur in malignant melanomas with possible metastasis to the fetus.

The placentas of women were also examined – (17 observations), which were operated on for papillary carcinoma (encapsulated), T 1NO.MO, including 1 observation with invasion of the thyroid capsule during pregnancy. Verification of the diagnosis was carried out in the laboratory of morphology of the Institute of Endocrinology and Metabolism of the National Academy of Medical Sciences of Ukraine, head – Professor T.I. Bogdanova, and in parallel was verified by international experts on the database of thyroid cancer.

We would like to draw attention to one observation, papillary carcinoma was detected and operated on in women during pregnancy. The detected

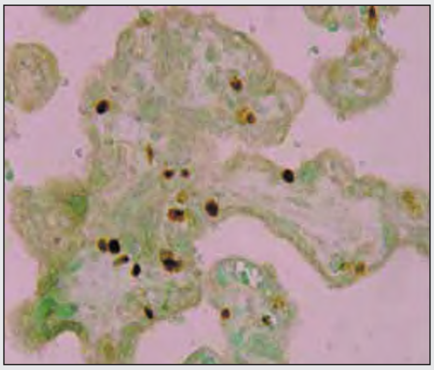

Figure 3.68. The placenta of a patient of group III.
Expression of Ki-67 in the nuclei of syncytia and villi cytotrophoblast. × 400.

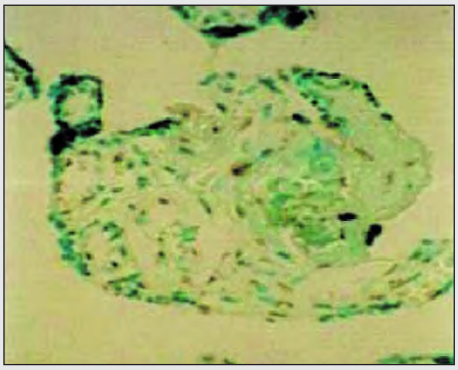

Figure 3.69. The placenta of a patient of group III.
Expression in the nuclei of apoptotic cells by TUNEL method. × 200

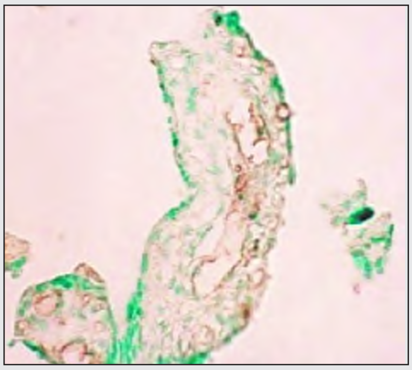

Figure 3.70. The placenta of a patient of group III.
Expression of carcino-embryonic antigen (CEA) in the stroma and fetal endothelium vessels. × 200.

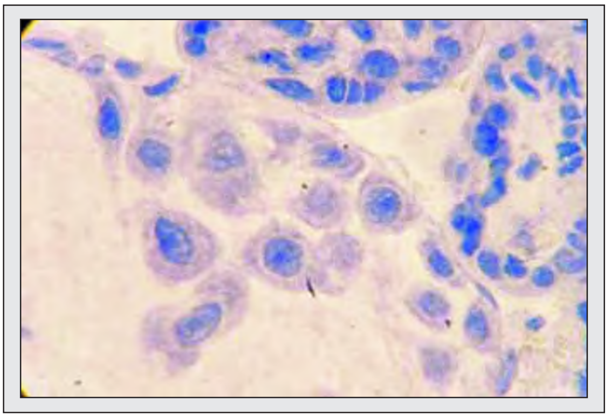

Figure 3.71. The placenta of a pregnant woman 21 years old
Papillary carcinoma of the thyroid gland revealed during pregnancy. She was operated on. The cell in the intervillous space of the placenta, consisting of epithelial cell structures. Hematoxylin-eosin. × 400.

focus, which was located in the intercellular space, consisted of epithelial cell structures and was treated by us as a metastasis of thyroid cancer (Fig. 3.71). These data were published and presented at the International Conference on Placentology in 2012.

Thus, summarizing the morphological, immunohistochemical data found by us it is possible to offer predictors of morphological researches of a placenta of women according to the «**Certificate of a placenta**»:

➤ the presence of internal irradiation according to placental radiometry > 4.8 Bq/kg;
➤ increase in markers of proliferation (in the study of immunohistochemical methods Ki-67, PCNA) in syncytia and stroma of villi;
➤ the appearance and increase of apoptotic cells of the stroma, endometrial villi (immunohistochemical study of apoptosis);
➤ positive expression of the prognostic onco-marker SER in the cytoplasm of the endothelium of fetal vessels and the stroma of the placental villi;
➤ in oncopathology in the mother, the placental tissues can serve as a organ of metastasis to detect further penetration of metastases to the fetus and child.

Stage II of 35 years (from 2016 to 2021)
Develop the latest and improve existing technologies for diagnosis, prevention and treatment of premature termination of pregnancy in women with miscarriage, taking into account the certificate (passport) of the placenta.
Fragment: «Morphological and immunohistochemical features of the placenta in women with miscarriage from 2016 to 2021.»

In the last 5 years, studies have been conducted in the placenta of women with miscarriage where we drew attention to the group of miscarriages and stillbirths.

Histologically and immunohistochemically examined placenta I, II group in comparison with the control group III. In place I and II, placentas with spontaneous abortions (I group) and miscarriage (II group) Were studied, in comparison with the control of group III.

The analysis of the obtained data was performed taking into account the indicators of the placenta certificate and the classification of placental damage (Amsterdam, 2015–2016). The studies were performed using histological and immunohistochemical markers, which are aimed at the study of vascular markers in placental tissues with the detection of the expression of MCAT (monoclonal antibodies) to the vascular endothelium of the placental barrier CD-31; vascular endothelial factor VEGF; transmembrane protein Type I, expressed in human vascular endothelial cells CD-105 or endoglin GP + 60. Markers of placental vascular damage have great potential for the development of modern technologies, as these processes are important in the pathology of the placenta.

Markers of inflammatory and immune processes CD-45, CD-56, family of the BCL-2 gene were also studied in order to identify their role in the processes of premature birth.

The study of radionuclides in the structures of the placenta on the apparatus of the analyzer of isotopic samples RC-101 (Japan) continues. In the placentas of women who gave birth to live babies, but with premature birth, found the content of radionuclides < 3 Bq/kg. These indicators coincide with the previous data (Table 3.33). In the studied placental tissues at stillbirth in some observations (up to 50 %) the content of radionuclides was 10.2 > Bq/kg and in the rest from 2.8 to 4 Bq/kg (Table 3.34).

Analysis of placental data from women with preterm birth revealed changes in the structures of the placental barrier in women of group I depending on the live birth of the child (group Ia) or death in the perinatal period (group Ib). These data are shown in Table 3.35.

As presented in Table 3.35, that in the placentas of women of group 1 (subgroup 1a), changes were mainly observed in the maternal vascular structures with a predominance of partial detachment of the decidual membrane (Fig. 3.72). Focal acceleration of chorionic villi maturation with fibrosis of their stroma and vessel walls was also detected in most cases – 60 % (Fig. 3.73). In subgroup Ia, maternal internal infarctions in 5 % of placentas were isolated. with the presence of avascular terminal and middle villi.

In some cases, focal lymphocytic infiltrates were noted in the decidual membrane and in the intervillous space. In group I, subgroup Ia (Table 3.35) revealed common foci of maternal internal infarctions and expressed structures of premature maturation and fibrosis of the stroma of villi, along with proliferation of syncytiotrophoblast. The detected changes lead to impaired perfusion in part of the placental barrier structures.

Table 3.34
The content of radionuclides in the placentas of women with miscarriage from 2016–2021

Groups	^{137}Cs content
Ia group – live births	< 3 Bq/kg in all cases
Ib group – stillbirths	> 10.2 Bq/kg – in 50 % of cases; in the rest – from 2.8 to 4 Bq/kg – less than 50 % of cases
III group – control	0–1.8 Bq/kg

Table 3.35
Morphological changes of placental tissue in women with premature termination of pregnancy and miscarriage in comparison with the control group (groups I–III)

Groups	Placental vascular processes						Placental inflammatory processes	
	Maternal				Fetal		Infectious	Immune
	Superficial implantation, decidual arteriopathy	Decidual membrane detachment	Perfusion disorders, accelerated maturation	Internal maternal infarctions	Increase in immature extravillous trophoblast	Perfusion disorders, immature villi, Delay of villi maturation		
Ia	0	90 % (parts)	60 % (parts)	5 % (partial)	0	1 % (single)	0	0
Ib	0	6 % (combination, complete)	3 % (complete, uneven)	8 % (expressed)	0	8 %	3	2
II	1 case	8 % (combined, complete)	5 %	90 %	Outbreaks, more than 90 %	Outbreaks, more than 90 %	4	0
III	0	0	Single villi	Single	Microfoci	Microfoci	0	0

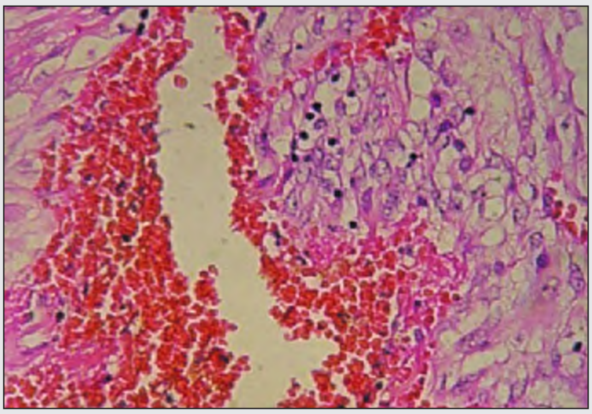

Figure 3.72. **Placenta of a woman with premature birth 29 weeks of pregnancy (1a subgroup)**
Partial detachment of the decidual membrane. Hematoxylin-eosin staining. × 200.

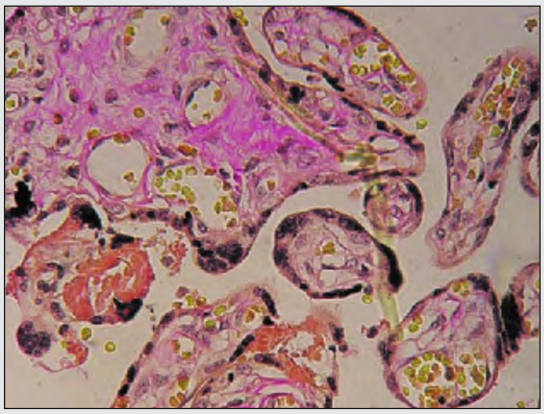

Figure 3.73. **Placenta of a woman with premature birth at 29 weeks of pregnancy (subgroup 1a)**
Stromal fibrosis of terminal villi and villi of medium caliber. Van Gizon staining. × 200.

In subgroup Ib in 9 cases of perinatal death perfusion disorders (complete) with detachment of the decidual membrane were found; small foci of avascular vortices and edema of the stroma of villi (Table 3.35). Internal maternal infarctions were detected in more than 90 % of cases with delayed villous maturation.

In group I in subgroup Ib (Table 3.35) in 4 cases the presence of widespread inflammatory-immune processes with chorionamnionitis combined with detachment of the decidual membrane was detected.

Analysis of the obtained data of group II placentas of women with abortion revealed irregular histological, which are associated with different gestational ages (5, 6, 8, 15, 19–20, 21–28 weeks). At the same time, histologically it was revealed in 90 % of cases of placental-vascular disorders of the maternal part of the placenta with the appearance of multiple internal maternal infarcts and with accelerated villi maturation and decidual arteriopathy (Table 3.35). These changes are revealed against the background of a clear violation of the perfusion of the villous structures (Fig. 3.74).

In all cases (Table 3.35) of the study group (II) there were changes in the maternal part of the placenta of the decidual membrane:

- ➢ uneven thickening with a violation of the architecture of the decidual shell;
- ➢ microfoci of multiple detachments of the decidual membrane with a decrease in the functionality of the placenta;
- ➢ foci of necrosis with different configurations of decidual cell nuclei;
- ➢ apoptosis and severe dystrophy of nuclei in decidual cells.

In the second group of placental studies at the gestational age of 15, 21, 30 weeks revealed inflammatory and immune processes of the maternal part of the placenta with chronic deciduitis (Table 3.35). There is a pronounced lympho-plasmacytic infiltration of the decidual membrane with adjacent parts of the chorion.

Immunohistochemical study (Table 3.36) revealed changes in the expression of vascular markers in the structures of the villous chorion in group I (subgroup Ia) with increasing expression of vascular markers (CD-31, CD-105, VEGF) along with a sharp decrease or absence of expression of these markers in groups Ib and II groups.

Immunohistochemical study of vascular markers (CD-105, VEGF, CD-31) showed negative expression of CD-105 and VEGF in the vessel wall with decidual arteriopathy (Fig. 3.75).

All these changes relate to disorders of vascular structures in the maternal part of the placenta, and then in the fetal structures of the manure.

Immunohistochemical studies of the villous chorion (Table 3.76) revealed:

- ➢ CD-105 – there is a weak positive expression (0-1 points) in the structures of the syncytia of the villi;
- ➢ VEGF – negative expression in all villi;
- ➢ CD-31 – positive expression in the epithelium of vascular villi;
- ➢ CD-56 – positive expression in NK cells in the stroma of villi 5–6 %, in decidual tissue – focal 15–20 %;
- ➢ CD-45 – uneven expression of 30–45 %;
- ➢ BCl-2 – positive expression in the syncytia of the villi – 3 points.

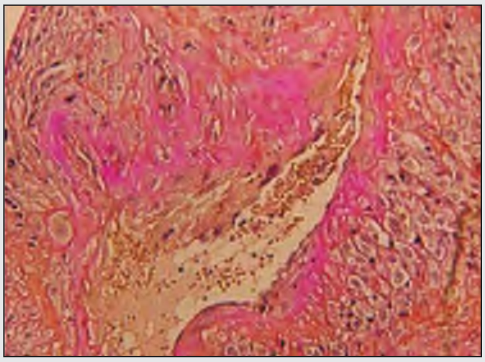

Figure 3.74. Placenta of a woman with abortion at 15 weeks (group II)
The decidual arteriopathy of superficial vascular implantation.
Van Gizon staining × 100.

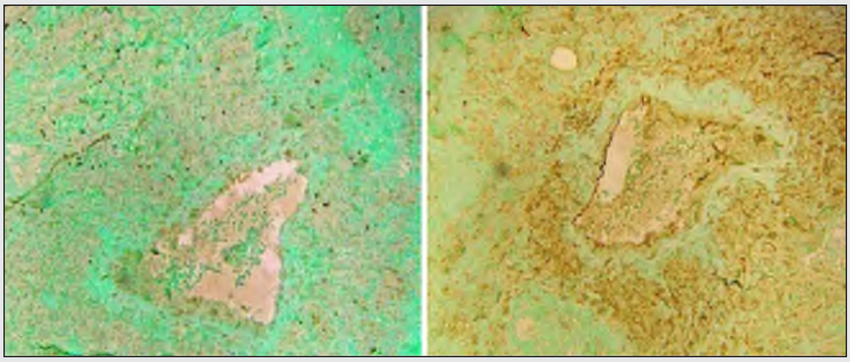

Figure 3.75. Placenta of a woman with abortion at 15 weeks (group II)
Immunohistochemical reaction of MKAT SD-105, VEGF. ×100.

Таблиця 3.36
Immunohistochemical features of the placenta of women of groups I–III (in points)

Group	CD-31		CD-105		VEGF	
	b. membrane	villi	syncytium	vas. villi ep.	syncytium	villi
I						
Ia	2–3	1–2	1–2	1б	2–3	3
Ib	–	–	0	0	0–1	0–1
II	0	0–1	0–1	0	0	0
		fet. m/s	thin syncytium	0	0	0
III (control)	3		1–2	single	1	1

Conclusion

The analysis of the obtained conclusions established that the histological and immunohistochemical features of placental factors in premature termination of pregnancy in women with miscarriage according to the placenta certificate:

➤ **Maternal** placental vascular processes

1. One of the most common (90 %) changes in the maternal part of the placenta during miscarriage – detachment of the decidual membrane (groups I, II); partially in group 1a and completely in group 1b with impaired perfusion.
2. Decidual arteriopathy with superficial implantation (II group of studies) and lack of expression of immunohistochemical vascular markers (CD-31, CD-105, VEGF) in the walls of blood vessels.
3. Internal maternal heart attacks: partially – group I and severe – group II.

➤ **Fetal** vascular processes

1. Delayed maturation of villi with the presence of immature avascular middle and stem villi of the chorion with impaired perfusion.
2. One of the factors of perinatal mortality in infertility is placental inflammatory processes (infectious and immune) (subgroup Ib; group II).
3. Immunohistochemical vascular markers in infertile (groups I, II) CD-105, VEGF – reduced expression compared with control in syncytia, which is involved in the process of perfusion of placental villi.
4. Immunohistochemical marker of endothelium CD-31 – reduced expression in the endothelium of fetal vessels (II group).
5. Immunohistochemical marker CD-56 – reduced expression in the decidual membrane.

Thus, the cause of perinatal miscarriage is placental factors such as impaired perfusion and decreased or no expression of immunohistochemical vascular markers (CD-31, CD-105, VEGF), which is important for diagnostic purposes for clinicians.

Summarizing the morphological, immunohistochemical data found by us **for 35 years** of research it is possible to offer **predictors** of morphological researches of a placenta of women according to the **«Certificate of a placenta»**:

1. The presence of internal irradiation according to placental radiometry > 4.8 Bq/kg;
2. Increase in markers of proliferation (according to the study of immunohistochemical methods Ki-67, PCNA) in syncytia and stroma of villi;
3. The appearance and increase of apoptotic cells of the stroma, endometrial villi, the so-called **«radiation apoptosis in the placenta»** (immunohistochemical study of apoptosis);
4. Positive expression of the prognostic onco-marker – cancer-embryonic antigen (CEA) in the cytoplasm of the endothelium of fetal vessels and the stroma of the placental villi, as a marker of perinatal oncogenesis;
5. In oncopathology in the mother, placental tissues can serve as an organ of metastasis to detect further penetration of metastases to the fetus and child;
6. Perinatal losses in miscarriages are accompanied by impaired perfusion of vascular factors of the placental barrier against the background of reduced or no expression of immunohistochemical vascular markers (CD-31, CD-105, VEGF).

3.7. The current system of medical expertise to establish causation of disease, leading to loss of health, disability and death with the action of ionizing radiation and other harmful factors of the Chornobyl accident in the remote post-emergency period

One of the key issues to minimize the consequences of the Chornobyl NPP (ChNPP) became the problem of medical and social expertise of victims [135, 136]. According to the decision of Government Commission № 539 from August 13, 1988 in agreement with the Trade-Unions and Goskomtrud of USSR the order of Ministry of Health No 731 from September 28, 1988 was issued «On the organization of the Central Interdepartmental Expert Council to establish causation of disease and disability with the works at the aftermath of Chornobyl accident and their professional nature» at the All-Union Research Center for Radiation Medicine Academy of Medical Sciences [140]. The basis of social protection of the Chornobyl accident victims is till our days with updating the of the Law of Ukraine «On the status and social protection of citizens affected by the Chornobyl catastrophe» ratified by the Verkhovna Rada (Ukrainian Parlament) on April 1, 1991 [138]. The 12th Article of this low is dedicated to «Establishing a causal link between the disease connected to the Chornobyl disaster, partial or complete disability of citizens affected by the Chornobyl disaster and the Chornobyl disaster». Of significant influence on making decisions in this issue are also articles 2, 14, 27 of this document.

Due to the ChNPP accident in Ukraine,1986, the largest man-made disaster in human history, 3,259,761 citizens of Ukraine and 2,293 settlements were affected.

On 01.01.2021 the status of victims of the Chornobyl Catastrophe in Ukraine had 1,718,113 persons, including 322,876 children. (Fig. 3.76).

The total number of affected adult citizens as on 01.01.2021, compared to 2008, decreased by 441,444 persons, or by 24.06 % (from 1,834,536 to 1,393,092 persons) (Fig. 3.75).

During this period, the number of clean-up workers of the accident decreased from 276,327 to 181,149, or by 95,178 people (34.44 %), that is, during the last 10 years, almost every third participant in the liquidation of the consequences of the accident at the ChNPP died.

The number of adult victims decreased from 1,558,209 in 2008 to 1,211,943 in 2021, or by 22.22 % (346,266 persons). The number of children affected by the ChNPP accident has decreased from 534,568 in 2008 to 322,876 in 2021, or by 211,692. Regarding the reduction of the number of this category, it is necessary to take into account the loss of the status of victims by children upon reaching the age of majority according to the current legislation.

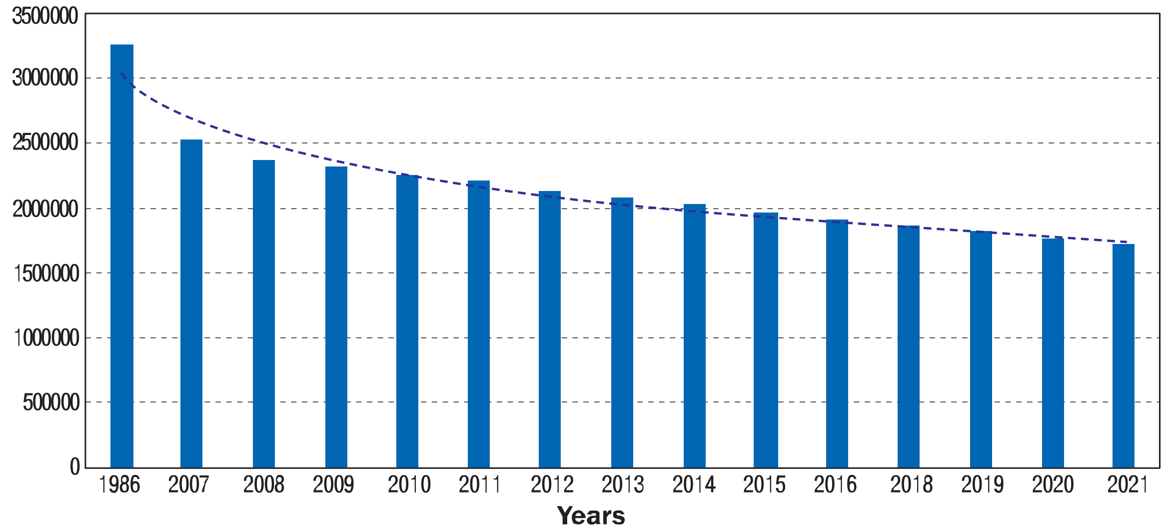

Figure 3.76. **Reducing the number of all categories of victims of the Chornobyl accident for the period of 1986–2021**

It is impossible to miss the characteristics of the victims of the ChNPP accident such a painful and socially important indicator as 41,165 people who have the status of wife/husband of the deceased citizen whose death was related to the Chornobyl catastrophe.

Expertise to establish the causal relationship of diseases, disabilities and causes of death with the action of ionizing radiation and other harmful factors of the ChNPP accident are persons who, according to current legislation, have the status of victims of the Chornobyl catastrophe [138].

The main regulatory documents governing the connection of diseases with the impact of the Chornobyl disaster for 1997–2011 years was the Order of the Ministry of Health of Ukraine No 150 from 17.05.1997 «On approval of regulations on diseases in which causal links can be installed with the action of ionizing radiation and other harmful factors due to the Chornobyl NPP accident» [139] and joint Order of the Ministry of Health and Ministry of Emergency of Ukraine No 166/129 from 30.05.1997 «On improvement of the system of expertise to establish causation of disease, disability and death with the effect of ionizing radiation and other harmful factors due to the Chornobyl NPP accident» [140]. By p. 3 of Decree of the Cabinet of Ministers of Ukraine No 1210 from 23.11.2011 «On improvement of social protection of citizens affected by the Chornobyl catastrophe» [141] and subsequent joint Order of the Ministry of Health and Ministry of Emergency of Ukraine No 789/1248 from 10.10.2012 «On introduction changes to the Order of the Ministry of Health of Ukraine and Ministry of Emergency of Ukraine from 30.05.1997 No 166/129» [142] regional interdepartmental expert commissions and regional medical treating expert commissions were eliminated except Central Interdepartmental Expert Commission (CIEC), Donetsk and Lviv regional commissions (Table 3.37), made changes to the procedure to establish causation of disease, leading to loss of health, disability and death with the action of ionizing radiation and other harmful factors of the Chornobyl catastrophe. The Order of Ministry of Health of Ukraine No 441 from 14.06.2012 «On amendments to the order of Ministry of Health of Ukraine No 150 from 17.05.1997» [143] defines the list of diseases for which can be determined relationship and instruction on its use.

Today, the components of the system of medical expertise to establish causation of disease, leading to loss of health, disability and death with the action of ionizing radiation and other harmful factors of the Chornobyl catastrophe for the adult population are the following expert commissions (Table 3.37): CIEC, which functions on the basis of NRCRM, and Lviv Oblast interdepartmental expert commission, which has the status of a communal enterprise. CIEC provides medical expertise to establish causation of disease, leading to loss of health, disability and death with the action of ionizing radiation and other harmful factors of the Chornobyl catastrophe with the impact of the radiation and nonradiation consequences of the ChNPP accident for all citizens of Ukraine who have the status of victims of the Chornobyl catastrophe and performs the role of a conflict appeal commission.

Lviv Oblast interdepartmental expert commission is responsible for conducting medical examinations for residents of Lviv, Vinnitsia, Volyn, Ivano-Frankivsk, Rivne, Ternopil, Khmelnytskyi and Chernivtsi Oblasts.

Category 1 of victims of the accident at the Chornobyl NPP is the most critical in terms of loss of health and work capacity, as it consists of persons who have the status of victims of the accident at the Chornobyl NPP and have lost work capacity due to diseases for which has been established a causal relationship with the impact of the consequences of the ChNPP accident.

During the period 1995–2014, there was a fast increase in the number of victims of category 1

Table 3.37
Distribution of regions from which persons affected by the Chornobyl disaster, documents submitted to the interdepartmental expert committees (IEC)

No	Commission	Regions
1	Central IEC	Zhytomyr, Kyiv, Cherkasy, Chernihiv oblast, Kyiv City and Donetsk oblasts that have been subordinated to Donetsk IEC – Dnipropetrovsk, Donetsk*, Zaporizhzhia, Kirovograd, Lugansk *, Mykolaiv, Odesa, Poltava, Sumy, Kharkiv and Kherson oblasts, the Autonomous Republic of Crimea* and Sevastopil City*, appeals and appellations from all regions
2	Lviv IEC	Lviv, Vinnitsa, Volyn, Ivano-Frankivsk, Rivne, Ternopil, Khmelnitsky and Chernivtsi oblasts

Note. *Provided that the citizenship of Ukraine, residence and registration on the territory controlled by Ukraine

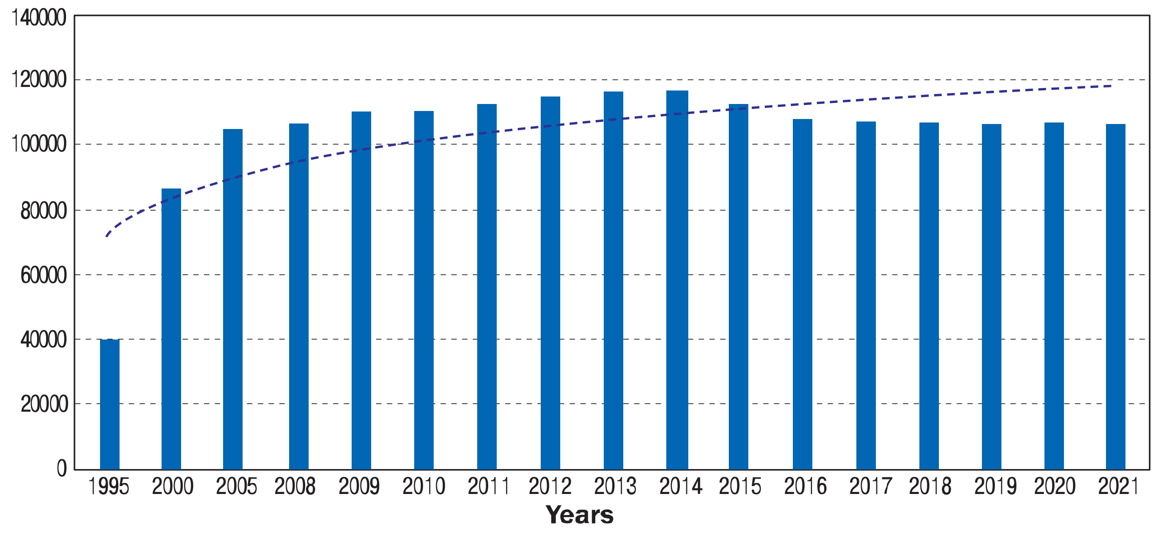

Figure 3.77. Dynamics of the number of ChNPP accident victims of the 1st category during 1995–2021

(from 40,106 to 117,158). During 2015–2021, there is a gradual decrease in the number of victims of this category from 113,268 on January 1, 2015 to 104,526 on January 1, 2021 (Fig. 3.77).

When significant decrease in the total number of clean-up workers of ChNPP accident taken place from 243,456 persons in 2013 to 181,149 in 2021 (or by 62,307 persons), the number of clean-up workers who have the 1st category decreased by 11,936 persons (from 67,509 in 2013 to 55,573 in 2021, or by 17.7 %). At the same time the relative number of clean-up workers who have the 1st category was 27.73 % in 2013 and 30.68 % in 2021.

The total number of adult victims also significantly decreased during 2013–2021: from 1,426,427 persons in 2013 to 1,211,943 in 2021 (or by 214,484), the absolute number of victims of the 1st category decreased by 236 people (from 49,249 in 2013 to 48,953 people in 2021). The relative number of victims who have the 1st category was 3.45 % in 2013 and 4.04 % in 2021 (Fig. 3.78).

Thus, during 2013–2021, there is a fast decrease in the total number of all categories of victims with a significant reduction in the absolute number of clean-up workers of ChNPP accident who have the 1st category and the relative stability of the number

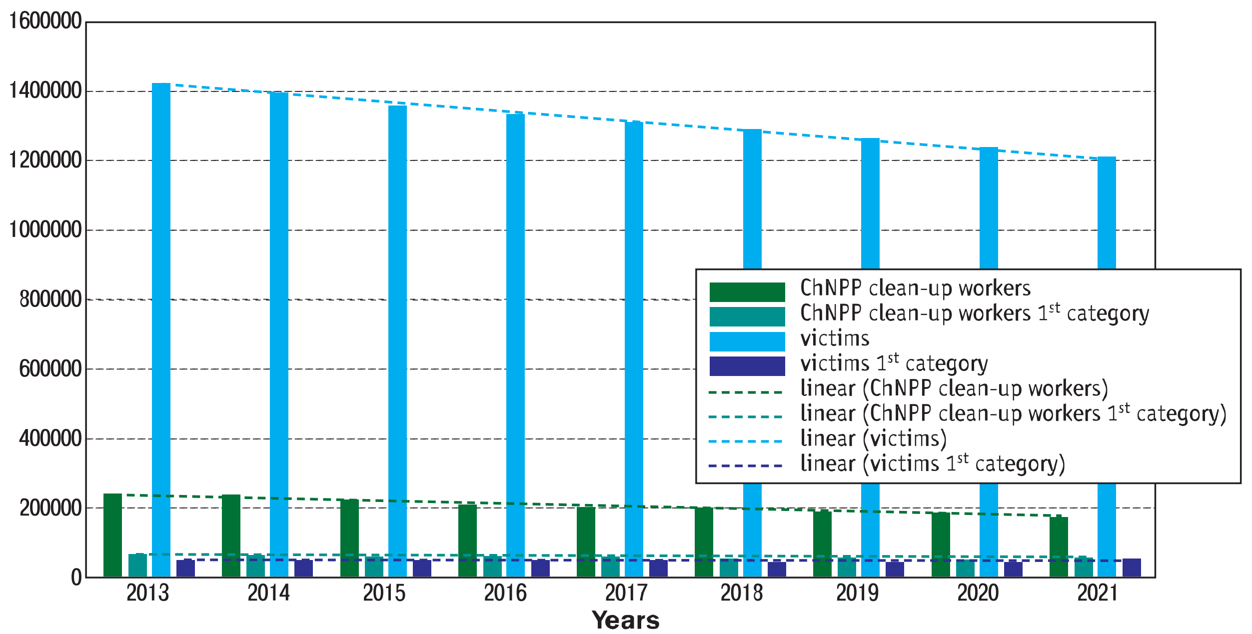

Figure 3.78. The structure and ratio of the number of main categories of victims and victims who have the 1st category during 2013–2021

of the cohort of adult victims of category 1. It should be taken into account that this relative stability of the number of victims of adult age who have the 1st category is formed from the ratio of losses of persons of this cohort and its replenishment due to the establishment of causation of disease, leading to loss of health, disability and death with the action of ionizing radiation and other harmful factors of the Chornobyl accident in the remote post-emergency period of categories 2B, 3B, 4B.

The average annual reduction in the absolute number of clean-up workers of ChNPP accident during 2013–2021 is about 7,790 people per year, adult victims – 26,810 people per year.

The main reasons leading to these changes are the increase in the incidence and prevalence of severe chronic disabling diseases, which quickly lead to a decompensated course and the development of complications, which, accordingly, leads to an increase in the mortality rate of the affected population [144].

As a result of the restructuring of the expert system in 2012, the volume of work of the CIEC increased threefold, during 2013–2020, 41,407 medical expert cases of victims were considered. The detailed scope of consideration by the CIEC for the medical cases of victims (by category) regarding the establishment for causation loss of health, disability and death with the action of ionizing radiation and other harmful factors of the Chornobyl accident in the remote post-emergency period is presented in Table 3.38.

In total, during 2013–2020, medical expert cases were considered: victims with disabilities – 29,856 cases, cancer patients – 22,283 cases, deceased – 14,456 cases.

The primary expertise was provided 78.21 % (32,381 cases) of the reviewed cases, including clean-up workers of ChNPP accident categories 2A and 3A – 27.91 % (11,555 cases), residents of the zone of enhanced radiological control (category 4B) – 32.28 % (13,367 cases), evacuees and residents of compulsory resettlement zone (category 2B) – 2.77 % (1148 cases), residents of the guaranteed free-will resettlement zone (category 3B) – 12.67 % (5,245 cases), victims category «D» – 2.57 % (1066 cases).

The part of medical expertise cases concerning clean-up workers and victims who have the 1st category (formed from all affected contingents) amounted to 21.79 % (9,026 cases) and in most cases it was postmortem – 73.55 % (6,639 cases), oncological diseases in this group accounted for 45.08 % (4069 cases).

A significant number of medical expert cases of oncology patients – a total of 22,283 cases (53.81 %) – causes concern. First of all, this applies to victims who live in the zone of guaranteed free-will resettlement (category 3B) – 72.98 % (3,828 cases). A large share of oncological cases is determined for residents of the zone of enhanced radiological control (category 4B) – 70.37 % (9,406 cases), as well as evacuees and residents of compulsory resettlement zone (category 2B) – 52.96 % (608 cases). It is difficult to ignore the high level of this indicator in relation to clean-up workers of ChNPP accident category 2A – 33.70 % (3360 cases). It should be noted that for victims of category D – 33.49 % (357 cases) are relatively young people – up to 40 years old.

Today, in the structure of medical expert cases, the leading place is occupied by oncological diseases – 60.3 %, cerebrovascular diseases and their complications make up 10.0 %, diseases of the cardiovascular system – 19.6 % [144], chronic diseases of the bronchopulmonary system – 1.6 %, endocrine diseases (without thyroid cancer) – 1.4 %, diseases of the digestive system – 1.1 %, other diseases in general – 6.0 %.

When analyzing the state of the medical and social expertise for establishment of causation loss of health, disability and death with the action of ionizing radiation and other harmful factors of the Chornobyl accident in the remote post-emergency period with the impact of the consequences of the ChNPP accident, it is necessary to pay attention to the fact that the normative and regulatory framework for certain issues remains incomplete and needs to be clarified and improved.

First of all, it is about making changes to the Law of Ukraine «On status and social protection of citizens affected by the Chornobyl catastrophe» [138] (Articles 4; 7, p. 7; p. 4 part 1 of article 11; p. 4. part 1 of article 14; part 1 of article 17) regarding the determination of the status of victims for children who, after reaching adulthood, lost this status and fell ill with oncological (primarily thyroid cancer) and oncohematological diseases, as well as regarding the guarantee medical care for the descendants of the victims of the second, third and subsequent generations. Insist on the clarification of this law, according to which the cancellation of the status of the territory that had a certain category of radiation contamination does not imply the cancellation or loss of the status of victims for the residents of this

Table 3.38

Volume and structure of providing CIEC medical expertise for the interdependence of the diseases that bring to the disability and death with the impact of the Chornobyl accident consequences during 2013–2021 years

Years	Characteristics of the cases under consideration	Category of victims (medical expert cases)							
		1st category formed from all categories)	clean-up workers 2A categories	clean-up workers 3A categories	evacuated and residing in the zone of compulsory resettlement (category 2B)	victims living in an area of guaranteed free-will resettlement (category 3B)	victims living in the zone of enhanced radiological control (category 4V)	victims category «D» (children)	Total
2013	**Total** incl.	**877**	**1168**	**193**	**117**	**596**	**2340**	**221**	**5512**
	patients with disability	865	717	171	86	308	2101	157	**4405**
	oncological patients	776	**311**	59	47	**487**	**1418**	90	**3188**
	cases of death	**662**	281	17	15	103	514	0	**1592**
2014	**Total** incl.	**1008**	**1212**	**182**	**128**	**619**	**2422**	**181**	**5752**
	patients with disability	958	728	139	90	330	1945	140	**4330**
	oncological patients	**544**	**348**	**64**	**74**	**428**	**1586**	**46**	**3090**
	cases of death	**825**	373	23	16	100	524	1	**1862**
2015	**Total** incl.	**1245**	**1199**	**194**	**154**	**736**	**1622**	**139**	**5289**
	patients with disability	1135	656	129	119	345	1274	99	**3757**
	oncological patients	493	485	104	87	**579**	**1045**	42	**2835**
	cases of death	**990**	431	45	20	165	433	0	**2084**
2016	**Total** incl.	**1215**	**1433**	**202**	**162**	**624**	**1271**	**125**	**5032**
	patients with disability	1058	742	150	120	279	920	92	**3361**
	oncological patients	474	**505**	89	90	**495**	**1010**	42	**2705**
	cases of death	**921**	481	34	18	90	303	0	**1847**
2017	**Total** incl.	**1155**	**1242**	**224**	**143**	**673**	**1013**	**107**	**4557**
	patients with disability	1065	718	140	108	346	794	93	**3264**
	oncological patients	423	451	106	71	**479**	**828**	36	**2394**
	cases of death	**955**	351	40	20	112	285	0	**1763**
2018	**Total** incl.	**1201**	**1309**	**232**	**175**	**747**	**1310**	**100**	**5074**
	patients with disability	1103	728	153	134	398	1026	89	**3631**
	oncological patients	492	466	102	94	521	1005	35	**2715**
	cases of death	974	438	36	20	126	237	0	**1831**
2019	**Total** incl.	**1184**	**1263**	**190**	**154**	**736**	**1874**	**99**	**5500**
	patients with disability	1042	648	122	110	395	1415	80	**3812**
	oncological patients	457	425	78	79	**482**	**1376**	28	**2925**
	cases of death	902	461	35	15	125	323	0	**1861**
2020	**Total** incl.	**1141**	**1145**	**167**	**115**	**514**	**1515**	**94**	**4691**
	patients with disability	1006	**629**	110	87	264	1117	83	**3296**
	oncological patients	410	369	53	66	357	**1138**	38	**2431**
	cases of death	**857**	357	28	15	90	268	1	**1616**
Total		**9026**	**9971**	**1584**	**1148**	**5245**	**13367**	**1066**	**41407**

territory who have lived under the influence of the radiation factor for the corresponding number of years.

A separate issue is the periodic updating of the scientifically based list of diseases, according to which the causal relationship of pathology (illness), disabilities and causes of death with the influence of the consequences of the ChNPP can be established. The latter requires taking into account many years of experience in minimizing the medical consequences of the ChNPP accident, the latest knowledge in the field of general and clinical radiobiology, radiation medicine, oncology and medical and social expertise, and conducting dosimetric passporting of populated areas of Ukraine that undergone radiation contamination.

In the case of examination of the connection of the disease that led to death, causation of the cause of death with the action of ionizing radiation and other harmful factors of the Chornobyl accident in the remote post-emergency period can be considered, if the diagnosis is included in the list and confirmed by the results of pathologic-anatomical, forensic medical research or, as an exception, clinically proven during an inpatient examination during the patient's lifetime. The direct, known cause of death may be related to the action of harmful factors as a result of the accident at the ChNPP accident without conducting a pathologic-anatomical or forensic medical examination, if it is the result of a disease that is included in the list and for which a causal relationship was established during life the patient.

In 2012, the reorganization of the system of medical and social expertise to establish the causal relationship of diseases, disabilities and causes of death with the impact of the consequences of the ChNPP accident proved its effectiveness and expediency in relation to the medical and social protection of victims of the Chornobyl catastrophe. There are unresolved issues (thyroid cancer in persons who have lost the status of victims in adulthood) that require changes and additions to the legislative framework. It is necessary to continue clinical and epidemiological studies of the regularities of the development and course of diseases in the affected contingents of the population in the remote post-accident period in order to develop scientifically based criteria for the causal relationship of diseases, disabilities and causes of death with the effects of ionizing radiation and other harmful factors of the Chornobyl catastrophe.

4. TRENDS IN MEDICAL AND DEMOGRAPHICAL INDICATORS IN THE RADIOACTIVELY CONTAMINATED TERRITORIES (1986–2016)

It is well-known that during the formation of the crisis demographic trend of any country, the key role was played by painful phenomena in the economic and social life, political and military conflicts. In the late 20th century, researchers began to acknowledge that ecological calamities also bring about corresponding changes in the demographic behavior of the population and have severe socio-psychological consequences.

Ukraine is not an exception. Its demographic situation is still being influenced by tragic events of the past century [1] and as well as there are still differences between the regions in reproduction and age structure of the population [2–4]. However, the Chornobyl NPP accident, that took place in April, 1986 and was recognized as the greatest anthropogenic radiation disaster in the human history, played a particular role in the formation of current demographic trends for some territories of Ukraine.

The previous National reports for the anniversary of the Chornobyl accident [5, 6] provided an in-depth analysis of the reasons for the accident, identified the amount of radioactive environmental contamination and contingents of irradiated, generalized the experience of removal of accident consequences and identified the environmental, economic and social consequences of the accident. Recently accumulated scientific knowledge on the implications of the Chornobyl accident for the health of people, who according to the current legislation were recognized as affected, prompts to further monitoring of their health [7, 8], including the medical and demographic indicators.

The previously conducted research on medical and demographical consequences of Chornobyl accident in Ukraine has evidenced that the latter became a catalyst for crisis changes, which in a short time have modified the existed demographic situation, created the current one and keep influencing the future of the territories that were radiologically contaminated. In particular, one could observe the process of depopulation of the exclusion area and unconditional (mandatory) resettlement in the first years after the accident due to evacuation of the citizens to «pure areas», which resulted in population crisis [9], decreasing the number of working-age population in the general structure of population, the change in gender balance [10], increasing level of overall [11] and premature death [12], change in reproductive pattern of the population [13]. Thus, owing to high migration activity of the youth and families with young children, during the post-Chornobyl period the age structure of the population of the most contaminated areas lost the potential of demographic growth and now one of the characteristics of these areas is high proportion of elderly [14].

The impact of the Chornobyl NPP accident on the birth rate in the radioactively contaminated territories (RCT) was also proven [15, 16]. It was shown [9], that with reproduction of population in the RCT being negatively low in the early 1990s (zone 2 – minus 5.3 ‰, zone 3 – minus 6.4 ‰, zone 4 – minus 9.1 ‰), in 2005 it became negatively critical (zone 2 – minus 18.6 ‰, zone 3 – minus 14.3 ‰, zone 4 – minus 26.3 ‰). According to the pattern of changes of demographic indicators, the most radiologically contaminated areas regardless of their zones are attributed to demographically depressive ones.

According to the studies [17], by the sum of medical and demographical indicators, the health status of the RCT residents was worse than that of the population living in non-contaminated areas. Moreover, the country experienced the agricultural reform that practically led to the collapse of the agribusiness and destroyed the rural social sphere, prompted sharp growth of unemployment among rural population and accelerated migration of rural youth to urban areas [18].

At the beginning of 2020, in the Ukraine State Registry there were 2.5 million people who suffered from Chornobyl accident, among them are: people who were engaged in eliminating the Chornobyl NPP accident consequences (13.3 %), residents of contaminated areas (64.2 %), evacuated or people who left the exclusion zone (3.4 %), people born from parents of 1–3 groups of initial records (3.4 %). It is known, that due to a number a reasons (reorganization of the health care sector, availability of health care institutions, financial constrains etc.) [19], not all the affected people undergo systematic medical examination. At the same time, all the categories of affected live in the RCT, thus we assessed the changes in the population number and reproduction that took place in the post-accident period, as per the information provided by State Statistics Service of Ukraine. The object of the study is the population of the administrative districts of Ukraine with the most intensive radiological contamination resulted from the Chornobyl NPP accident, namely: Korosten, Narodychi, Ovruch and Olevsk districts of the Zhytomyr Oblast, Ivankiv and Poliske districts of the Kyiv Oblast, Rokytne and Sarny districts of the Rivne Oblast, Kozelets and Ripky districts of the Chernihiv Oblast. The population of Ukraine as a whole was chosen for control group.

4.1. Population size, structure and age composition

For the period from 1986 to 2016 (Fig. 4.1) the number of population of the areas with the most intensive radiological contamination was dropping throughout all areas (with the exception of Sarny and Rokytne districts). The most significant decrease in population was in Kozelets (minus 32,930 people), Ovruch (minus 30,960 people), Korosten (minus 27,680 people) and Poliske (minus 25,060 people) districts. In Rokytne and Sarny, there was an increase in population by 5,280 people and 9,420 thousand people, respectively. As a percentage, the largest population losses are in Poliske (minus 81.32 % throughout the district, minus 95.91 % in the urban areas, minus 68.16 % in the rural areas) and Narodychi (minus 65.56 % throughout the district, minus 55.51 % in the urban areas, minus 68.40 % in the rural areas), which according to previous studies [20] is a consequence of organized ecological migration. During the specified period, the population of Ukraine decreased by 16.8 % or almost 8.8 million people. Thus, in comparison with the whole country, the percentage points of population loss of most of the studied RCT (total and rural areas – 8 out of 10 districts, urban areas – 6 out of 10) are higher, which is an evidence of more pronounced depopulation trends.

Whereas in the country the population decline began in the 1990s and the downward trend remain present till these days both in urban and rural areas, in the studied region it began immediately after the Chornobyl accident (with the exception of Rokytne and Sarny districts).

Women prevailed in the gender structure of the population of both the country (52.7 %) and the studied region in 2017 (from 50.4 % in Rokytne district to 56.7 % in Kozelets), with the exception of Sarny district, where the share of men is 1.5 percentage points higher. The ratio of gender and age groups of the RCT population, as well as in Ukraine, varies over time, but the ratio of male and female

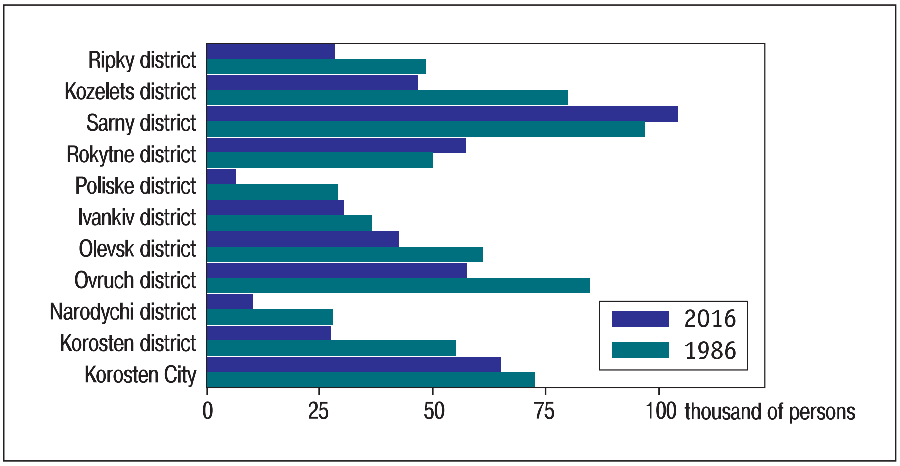

Figure 4.1. Average annual number of population at radioactively contaminated territories, 1986 and 2016

populations of different age groups has not changed significantly, and the imbalance remains especially noticeable in the age groups over 60 years.

Compared to 1986, in 2017, the population of Narodychi, Poliske and Ivankiv districts showed to have lacunae in certain age groups (children at the time of the accident), which indicates a disruption in the sequence of generational changes due to the elimination of the consequences of the Chornobyl accident (evacuation and organized relocation of residents). It is worth noting that a significant migration outflow of the population from the RCT in 1986–1995 did not «wash out» the entire population of the corresponding age groups, but the «demographic echo» will remain for many more years. In the population of Ukraine, no changes were found in the corresponding age groups.

In 2017, compared to 1986, there was an increase in the share of people aged 60 and older in the country's population, and their peers quickly «pass away» in the RCT. In the RCT, there is a significant regional variation in the levels of population ageing (Table 4.1). The ageing process of the population is typical for all European countries. But if in Europe a high proportion of older people is due mainly to high life expectancy (the so-called ageing «from below»), in Ukraine it results from lesser number of children (the so-called «ageing from above») [1]. In 2017, compared to 1986, there was a shift in the indicator of demographic ageing towards its increase, in Ukraine (+5.57 %), and in Korosten (+5.29 %), Ripky (+5.00 %), Kozelets (+3.07 %), Ovruch (+1.99 %) districts and in Korosten City (+1.63 %). In the rest of the territory, the share of people aged 60 and older decreased.

In Ukraine, the average population age for 2002–2016 grew by 2.2 year (men – 2.1 year, women – by 2.3 year), which indicates the demographic ageing of the population. The most RCT, on the contrary, are characterized by population rejuvenation (Table 4.2).

The data presented in Fig. 4.2 show that in Ukraine, over 15 years, the difference between the rate of ageing of men and women increased by 0.2 years. The RCT from Ivankiv, Rokytne and Ovruch districts proved to have value constancy, a decrease in indicators was noticed in Olevsk (minus 2.1 years), Narodychi (minus 0.9 years), Korosten (minus 0.3 years) districts, and an increase – in Korosten City (+1.1 years). At the same time, compared to the data for the country as a whole, the difference between the rate of demographic ageing of men and women is higher from by 1.0 (Poliske district) to by 2.5 (Ripky district) years, which indicates real and potential opportunities for extending the life expectancy for the RCT residents, including the labor-active period.

In accordance with the stable trend of population decline in Ukraine, the number of women of reproductive age is also decreasing: 1986 – 16.7; 1991 – 15.8; 2010 – 15.4; 2015 – 13.4; 2016 – 13.2 million, which cannot but affect the birth rate indicators (number of births, newborns and birth rates), since a small generation of those born in the late 1990s and early 2000s entered the reproductive age (the number of women aged 15–19 years is 1.6 (rural areas) and 1.9 (urban areas) times less than at the age of 45–49 years). The number of women at the most active age of childbearing (20–29 years) decreased from 3.9 million in 1986 to 2.9 million in

Table 4.1
Level of population ageing in Ukraine and studied RCT in 1986 and 2017 (%)

Studied administrative unit	1986			2017		
	ageing level at the age of			ageing level at the age of		
	60	65	70	60	65	70
Korosten City	20.17	9.34	5.65	21.80	16.23	10.53
Korosten district	26.78	17.93	11.60	28.06	21.82	16.46
Narodychi district	28.73	19.93	13.16	27.02	21.14	16.37
Ovruch district	23.65	15.49	9.72	25.64	19.34	13.86
Olevsk district	18.30	12.78	6.98	17.21	12.18	8.25
Ivankiv district	29.11	20.25	14.70	23.52	17.32	12.49
Poliske district	23.96	16.34	11.62	20.79	17.32	11.31
Rokytne district	12.19	9.16	6.56	11.94	8.38	5.34
Sarny district	13.11	10.19	7.38	13.44	9.43	6.19
Kozelets district	25.68	28.28	23.09	28.75	22.41	16.36
Ripky district	26.02	16.56	10.98	31.02	23.97	18.10
Ukraine	16.54	11.27	8.18	22.11	16.19	10.84

Table 4.2
Average population age in Ukraine and studied RCT as per All-Ukrainian census in 2001 and as of 01.01.2017 (%)

Studied administrative unit	2002			2017		
	all	male	female	all	male	female
Korosten	38.6	36.5	40.4	41.2	38.5	43.5
Korosten district	43.7	39.9	46.9	42.5	38.9	45.6
Narodychi district	43.5	39.4	46.9	42.1	38.7	45.0
Ovruch district	41.7	38.5	44.5	42.3	39.1	45.1
Olevsk district	36.5	34.1	38.8	37.2	34.6	39.6
Ivankiv district	43.7	39.5	47.1	41.3	38.3	43.8
Poliske district	42.3	38.0	45.9	39.2	36.1	42.0
Rokytne district	32.0	30.0	33.9	30.9	28.9	32.8
Sarny district	33.0	31.0	34.9	33.8	31.9	35.5
Kozelets district	45.5	41.0	49.3	44.5	40.7	47.7
Ripky district	45.9	41.9	49.1	45.9	41.7	49.4
Ukraine	38.9	36.2	41.2	41.1	38.3	43.5

2016, while their share in the number of women of reproductive age decreased by 1.9 percentage points. In both urban and rural areas of the country, almost 30 % of women of reproductive age were over the age of 40 and had the opportunity to fulfil their reproductive potential. In urban settlements, the women aged 34 (283,100 people), 33 (278,900 people) and 31 (266,000 people) years, in rural settlements – 30 (100,300 people), 31 (98,900 people) and 29 (98,200 people) years prevail.

A decrease in the number of women of reproductive age as of 01.01.2017 compared to 1986 was revealed in most of the studied districts of the RCT, namely: Ivankiv (minus 1,200 people), Ripky (minus 2,700 people), Narodychi (minus 2,800 people), Olevsk (minus 3,900 people), Korosten (minus 4,200 people), Ovruch (minus 4,800 people), Poliske (minus 5,000 people), Kozelets (minus 5,500 people) districts and Korosten City (minus 3,000 people). However, in Sarny and Rokytne districts, the number of women of reproductive age increased by 1,300 and 1,400 people, respectively. Every third or fourth woman of reproductive age in the RCT is of the most favorable age for childbearing (20–29 years). In 2016, compared to 1986, as in the country as a whole, the number of women aged 20–29 years in the RCT decreased from by minus 100 people (Sarny district) to by minus 2,000 people (Kozelets district). With the exception of Rokytne district, where this number increased by 300 people.

According to the national population projection [21], the number of women of reproductive age in 2020 will decrease by 6 % compared to 2015, and by 2025, this reduction will reach almost 11 %. With regard to changes in the quantitative and qualitative parameters of the female population of reproductive age in the RCT, data from literature sources on the state of their reproductive health [22, 23] and the

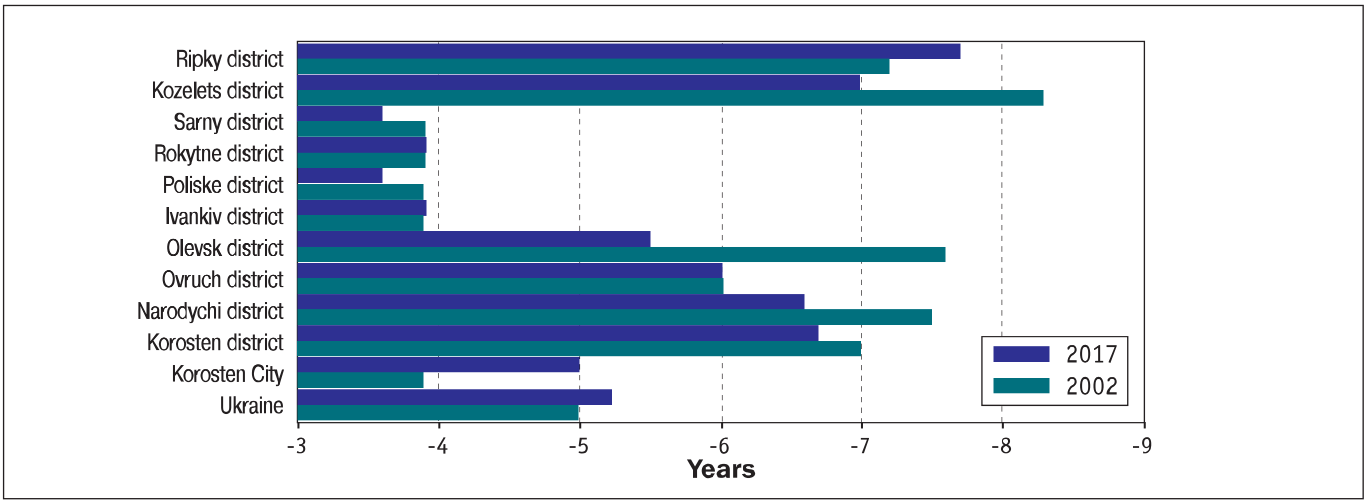

Figure 4.2. **Difference between the rate of demographic ageing of men and women living in radioactively contaminated territories and Ukraine, according to the All-Ukrainian census of 2001 and as of 01.01.2017**

high level of impoverishment [24], there is every reason to say that the indicators of population reproduction will continue to decrease.

According to the evaluation scale of E. Rosset [25], the population of the studied territories was still characterized by an extremely high level of demographic ageing in 2017. The most «old» (the share of people aged 60 and older in the total population exceeds 30.0 %) is the population of the Ripky district. The share of people of this age is 25.0–29.9 % in Kozelets, Narodychi and Ovruch districts; 20.0–24.9 % – Ivankiv and Poliske districts and in Ukraine as a whole. The most «young» population (the share of older people is up to 20 %) lives in the Rokytne, Sarny and Olevsk districts.

4.2. Reproduction of the population

The total decline in the population of the RCT and Ukraine during 1986–2016 was uniform neither spatially nor over time. Accordingly, the input to the total population decline of natural (result of the people birth/death processes) and migration movement (arrival and departure of people) differs significantly both in time and by territory. For example, in 1990, in Narodychi district, the input of natural loss to the total loss was 4.0 %, and in 2000 – 51.4 %. Meanwhile, in the Ripky district, it was minus 43.9 % and minus 74.6 %, respectively.

In the RCT and in Ukraine as a whole, migration processes (mechanical spatial movement of the population) for a long time were similar by the direction of flows (decline), but if Ukraine was losing its inhabitants mainly due to labor migrations [26], the RCT was experiencing environmental migration (in order to prevent irradiation exposure or reduce its levels) [27]. In total, according to official sources, more than 164,700 people migrated from the RCT due to the Chornobyl accident. A detailed overview of the spatial and temporal features of evacuation, organized voluntary and mandatory resettlement of residents of the areas of radiological contamination in Ukraine is presented in a number of publications [20, 27]. The current state of migration behavior in the RCT is characterized by the lack of regulatory intervention on the part of the State.

The information shown in Fig. 4.3 and 4.4 indicates the variability of the values of natural movement of the population during the observation period for all territories with a tendency to decrease in 2016 compared to 1986. The average values of natural movement coefficients for 1986–2016 are the highest in Rokytne and Sarny districts. Compared to changes in the control, a high level of correlation was found in all radiologically contaminated areas (with the exception of rural areas of the Poliske district, where the level of correlation is average).

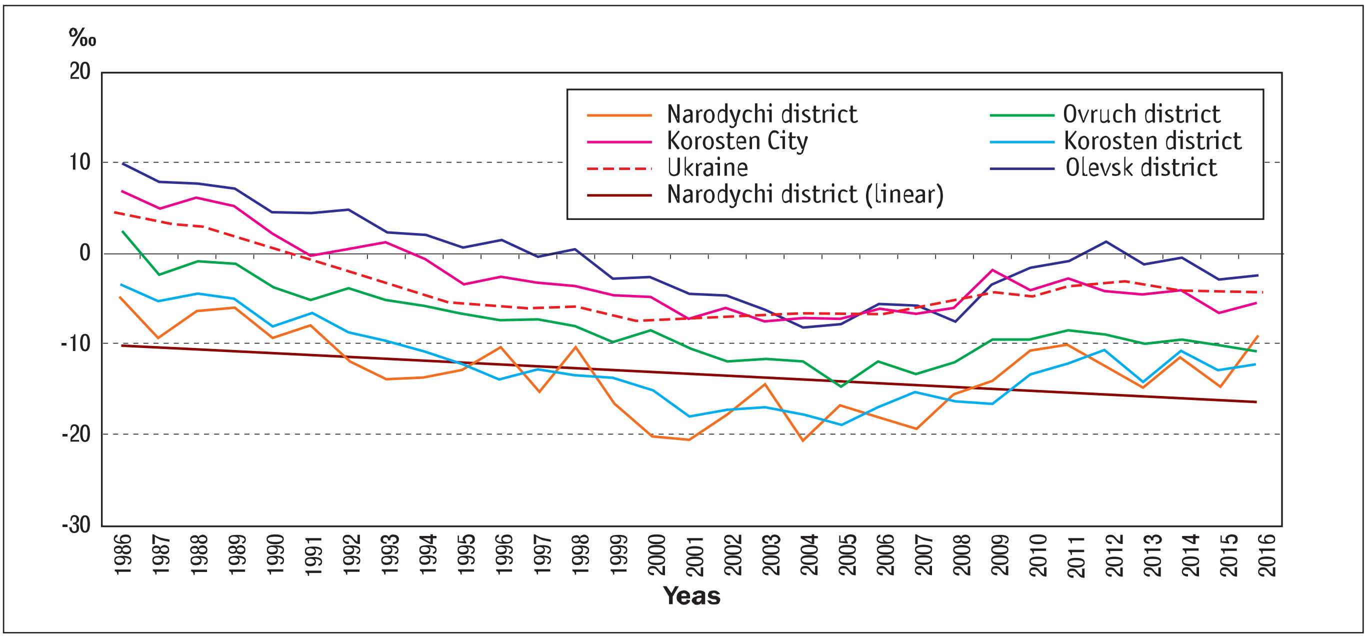

Figure 4.3. **Indicators of natural movement of population of Ukraine, Korosten City, Narodychi, Ovruch, Korosten, and Olevsk districts for 1986–2016**

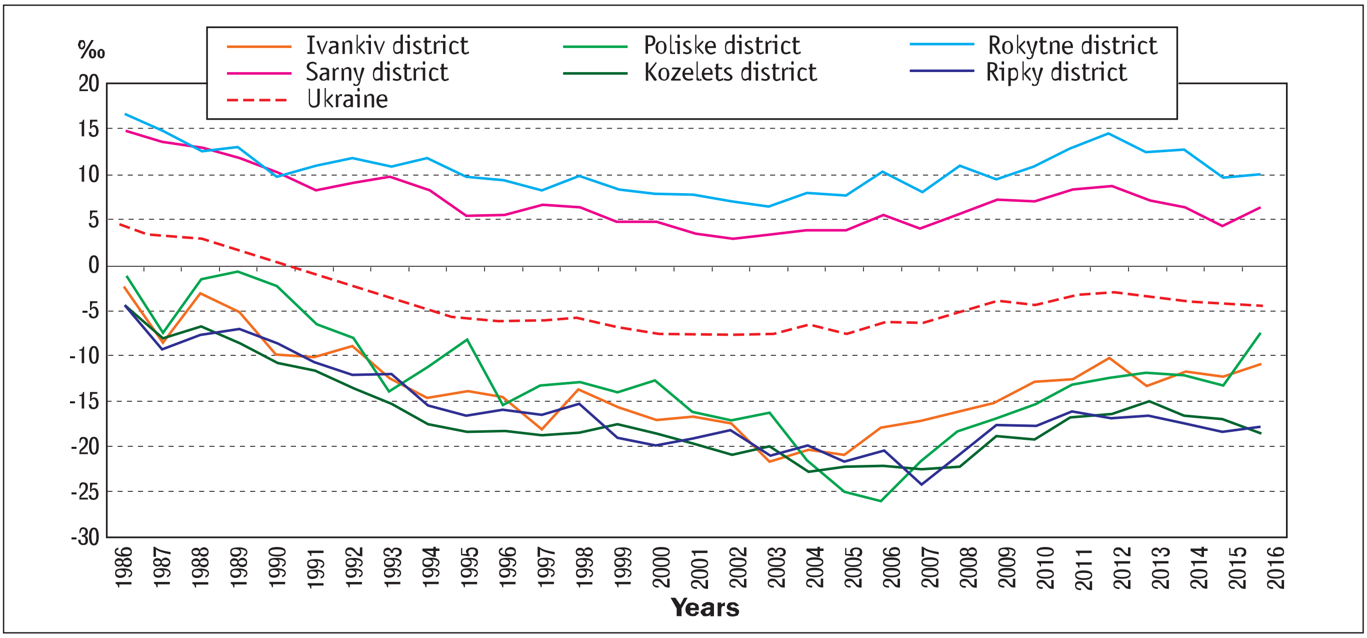

Figure 4.4. Indicators of natural movement of population of Ukraine, Ivankiv, Poliske, Rokytne, Sarny, Kozelets, Ripky districts for 1986–2016

In 2016, by the type of reproduction, the population of most RCT was attributed to a narrowed type (with the exception of Rokytne and Sarny districts, where it was expanded). And, according to the generic assessment of reproduction, it was negative low (Korosten as a town, Ukraine); negative threatening (Ovruch, Narodychi, Poliske, Ivankiv districts); negative catastrophic (Korosten, Kozelets, Ripky districts) and positive high (Rokytne and Sarny districts).

4.3. Birth rate

Analysis of data for 1986–2016 on the birth rate and its structure by the number of fetuses in Ukraine and the studied regions demonstrated that, compared to 1986, in 2016 the country experienced a decrease in the number of births by 2 times and an increase in the absolute number of births with three or more babies with a stable ratio of multiple pregnancies in the country. Meanwhile, in the RCT, there was a widespread decrease in the total number of births (from minus 1.0 % in Rokytne district to minus 7.4 times in Poliske district) and the number of births with twins, while there were no pregnancies with three and more babies.

From 1986 to 2001, the total number of births in the country fell by half, and after 2001 to 2012 inclusive, there was a gradual increase in the number of births, but the total number of births in 2012 and subsequent years did not exceed the number of births in 1986–1994. In 2016, in the country there were almost 397,000 babies born alive (urban areas – 258,700, rural areas – 138,300), which is by 14,700 less than in the previous year (urban areas – minus 7,400 babies, rural areas – minus 7,300 babies), and by 395,600 less than in 1986 (urban areas – 276,600, rural areas – 119,000 babies).

The studied RCT are characterized by national trends of decline in the number of births during the study period (Fig. 4.5 and 4.6) with a values variation for individual territories and years of research.

Despite the different profiles of statistical series in the RCT, the graphs clearly show the similarity of configurations of graphs of the relationship between the intensity of births and different stages of elimination of the consequences of the Chornobyl accident, namely:

➢ a sharp drop in the number of births in 1987 in the RCT recognized at that time (Ivankiv, Poliske, Narodychi, Ovruch, Olevsk and Kozelets districts);

➢ the process of compensation for postponed births in these areas in 1986–1987, which lasted for a limited period of time (1988–1989);

➢ an increase in the number of births in 1991–1996 (the period of active resettlement under the State program of mandatory and voluntary resettlement of the RCT residents).

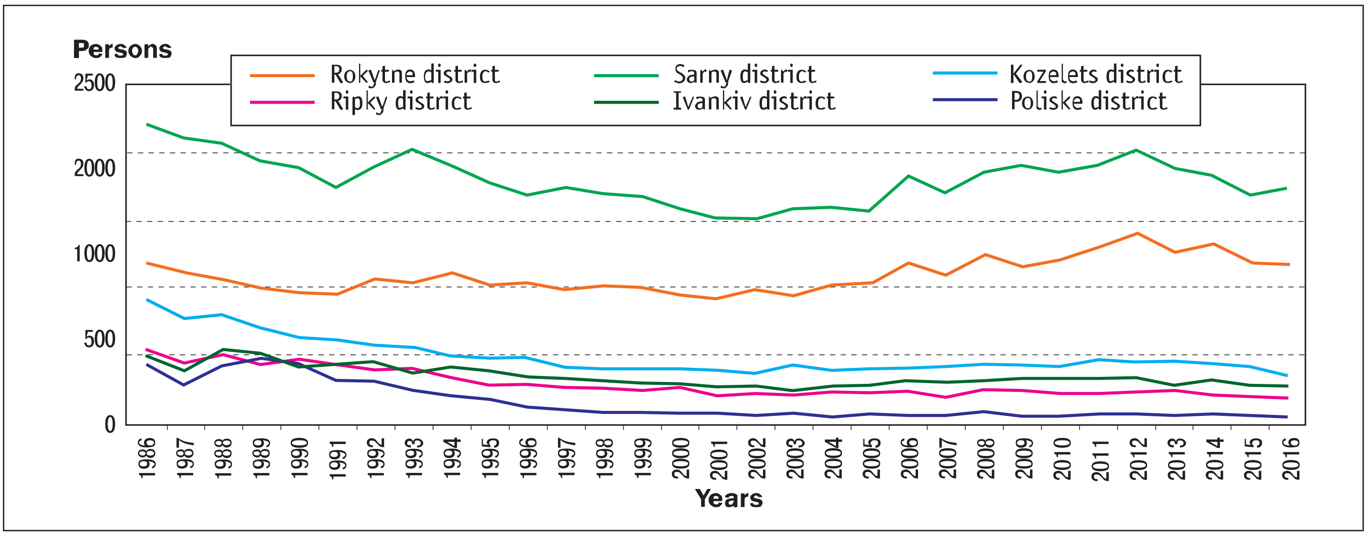

Figure 4.5. Number of persons born in Ivankiv, Poliske, Rokytne, Sarny, Kozelets, Ripky districts for 1986–2016

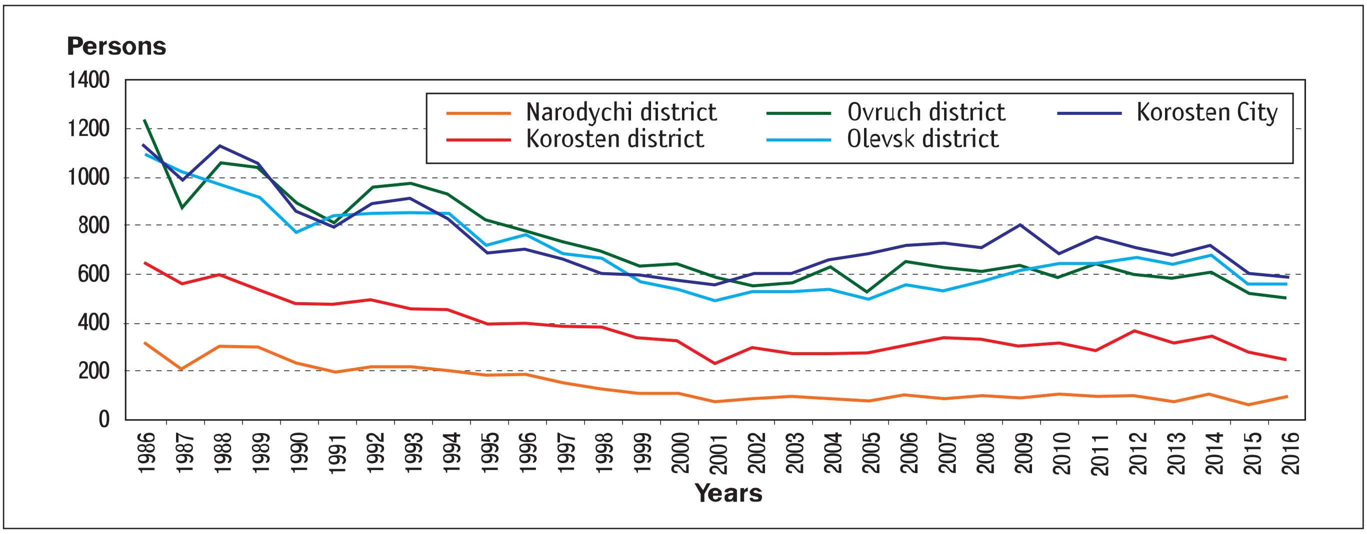

Figure 4.6. Number of persons born in Narodychi, Ovruch, Olevsk, Korosten districts and Korosten City for 1986–2016

Both in Ukraine and in the studied areas, the structure of newborns was dominated by boys (more than 51.0 % or 105–108 boys per 100 girls).

A decline in the birth rate in 2016 compared to 1986 was revealed both in the studied regions and in the country, regardless of place of residence. For example, in Ukraine, the birth rate decreased by 5.3 promille points, and the lowest birth rates were in 1999–2001.

In the RCT in 1986–2016 (Fig. 4.7 and 4.8) there was a significant differentiation of the birth rate with a minimum of values as in the country in 1999–2001. The initial birth rate (1986) was the highest in the districts of the Rivne Oblast, and the lowest in the Chernihiv Oblast. At the same time, the figures clearly show a decrease in the birth rate by 25–30 % in 1987 compared to 1986 («the effect of the Chornobyl accident» on the demographic process of birth rate) in the areas that in the first year after the Chornobyl accident were attributed to the areas of strict radiation control: Ivankiv, Poliske, Narodychi, Ovruch, Kozelets and Ripky districts (Table 4.3). In the country as a whole, there were no such sharp changes in the birth rate – the percentage of changes in 1987 compared to 1986 was minus 4.52.

Every year, the average indicator decreased from minus 0.5 % (Poliske and Narodychi districts) to minus 1.7 % (Kozelets district); in rural areas – from minus 0.2 % (Narodychi district) to minus 1.6 % (Ivankiv district), in urban areas – from minus 1.3 % (Ivankiv district and Kyiv Oblast) to minus 4.2 % (Poliske district).

The absolute decline in 2016 compared to 1986 in urban areas of the studied regions was from minus 4.9 ‰ (Narodychi and Ivankiv districts) to minus 12.2 ‰ (Poliske and Ovruch districts), in rural

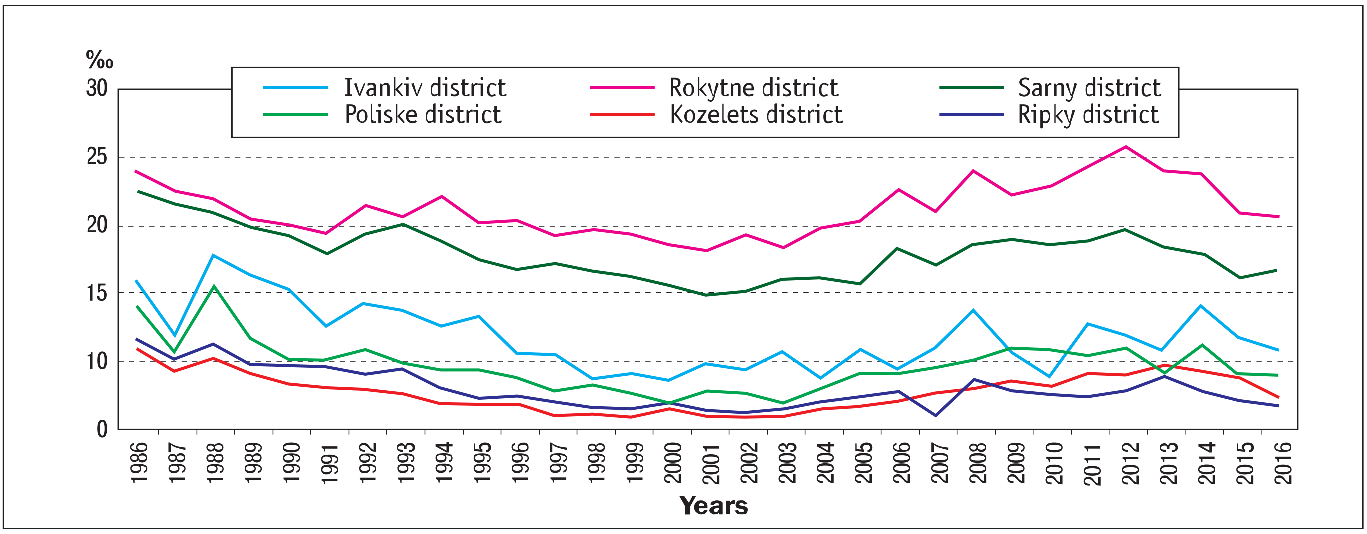

Figure 4.7. Birth rate in Ivankiv, Poliske, Kozelets, Ripky, Rokytne, Sarny districts for 1986–2016

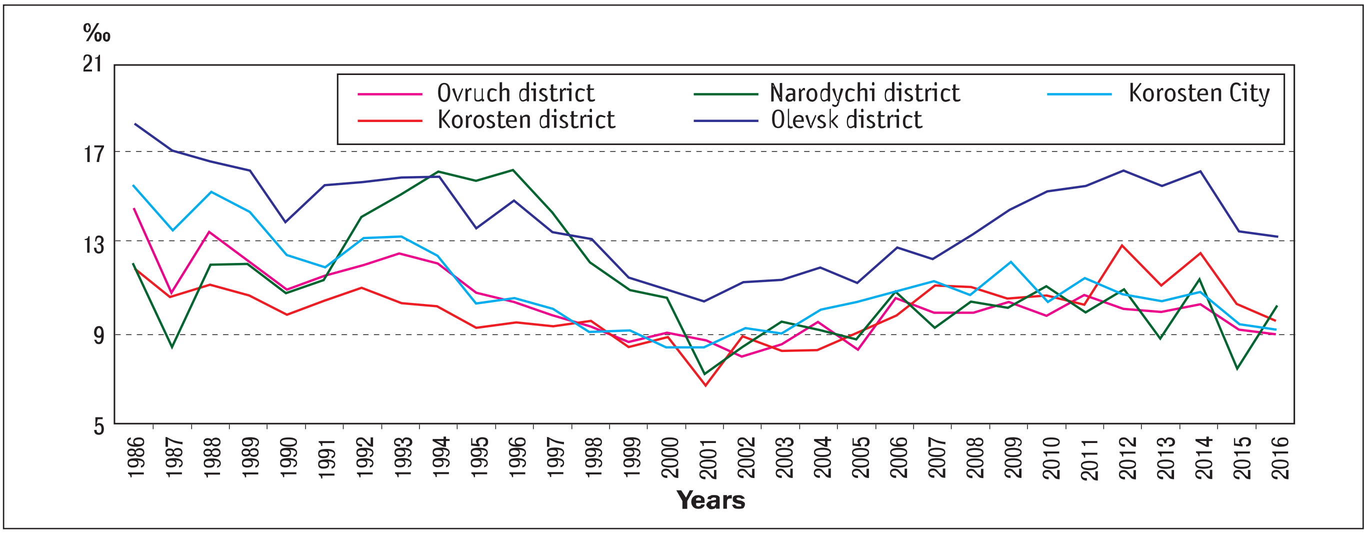

Figure 4.8. Birth rate in Korosten, Narodychi, Ovruch, Olevsk districts and Korosten City for 1986–2016

areas — from minus 0.7 ‰ (Narodychi district) to minus 5.4 ‰ (Ivankiv district). As a percentage, the maximum decrease in the indicator was in urban areas of the Poliske district (minus 72.6 %) and rural areas of the Ivankiv district (minus 38.9 %), and the minimum — in Rokytne (minus 31.5 %) and Narodychi districts (minus 6.2 %), respectively.

The calculated average values of the birth rate for 1986–2016 indicate that in all settlements of the RCT, its level was higher than in the country as a whole (10.54 ± 0.71) ‰ in Olevsk (14.20 ± 0.74) ‰, Poliske (11.96 ± 0.86) ‰, Sarny (18.15 ± 0.68) ‰ and Rokytne (21.32 ± 0.70) ‰ districts. In urban areas, the values were lesser than in the country as a whole (10.19 ± 0.80) ‰ in Ripky district (9.80 ± 0.90) ‰; in rural areas (11.35 ± 0.58) ‰ — in Ripky (6.79 ± 0.33) ‰, Kozelets (6.79 ± 0.37) ‰, Ivankiv (9.14 ± 0.70) ‰, Ovruch (9.97 ± 0.40) ‰, Korosten (10.12 ± 0.45) ‰, Narodychi (10.21 ± 0.64) ‰, Poliske (11.23 ± 0.85) ‰ districts.

The difference between the data for 1986 and 2016 reflects not only the process of reducing the birth rate over time across the studied areas (Table 4.3), but also allows (with significant differences in the birth rate) to differentiate the degree of changes by the level of indicators compared to the national level, namely: favorable indicators — values above the national level, average level — values close to the national level, unfavorable indicators — less than the national level. It is shown that both in 1986 and in 2016 the group with favorable indicators includes the districts of the Rivne Oblast, the second group — Korosten as a town and Poliske district, the third group — Narodychi, Kozelets, Ripky, Korosten, Olevsk, Ovruch, Ivankiv districts. Positive dynamics

Table 4.3
The difference in birth rate in 1986 and 2016

Birth rate, ‰	Areas with relevant birth rates	
	1986	2016
< 10.0		Korosten City, Ovruch, Kozelets, Ripky, Ivankiv, Korosten districts
10.1–12.0	Narodychi, Kozelets, Ripky, Korosten districts	Poliske and Narodychi districts, Ukraine
13.1–15.0	Ovruch and Ivankiv districts	Olevsk district
15.1–17.0	Korosten City, Poliske district, Ukraine	Sarny district
18.1–19.0	Olevsk district	
> 20	Rokytne and Sarny districts	Rokytne districts

of changes in indicators over time was only in the Olevsk district, stable – in Rokytne and Narodychi districts.

Calculated special birth rate coefficients (overall fertility coefficients) for the RCT and Ukraine for the period from 1986 to 2016 indicate that all statistical series are characterized by a tendency of fluctuating indicators (Fig. 4.9 and 4.10).

The minimum values of the indicator were throughout the areas in 1998–2003. The districts

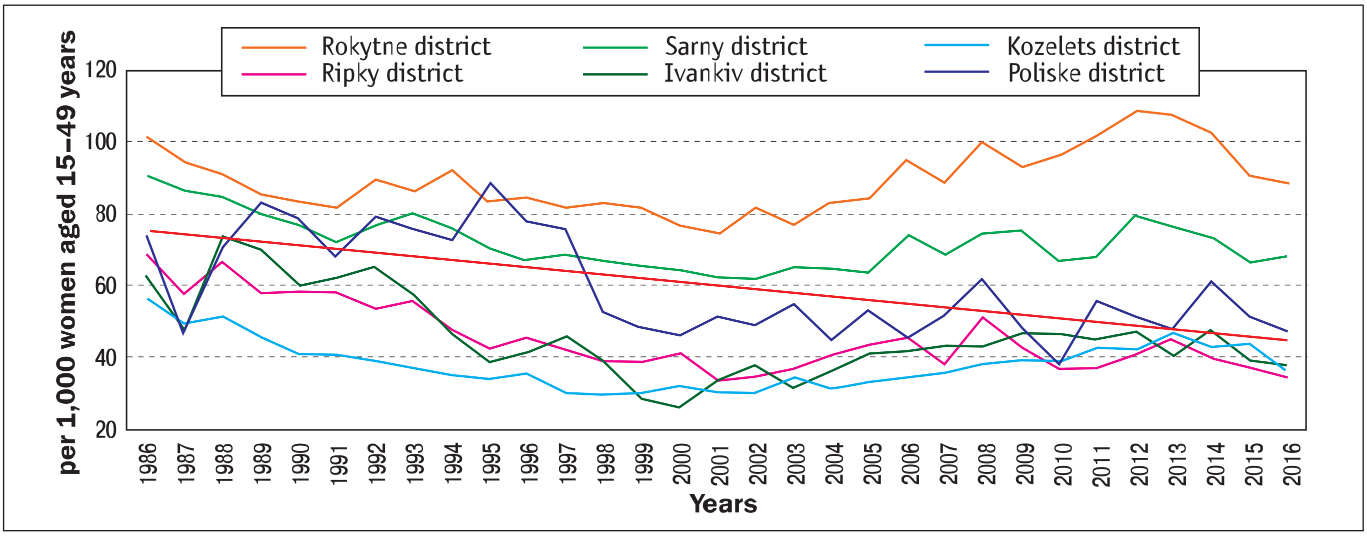

Figure 4.9. **Special coefficient of birth rate of population of Rokytne, Sarny, Kozelets, Ripky, Ivankiv and Poliske districts per 1,000 women aged 15–49, for 1986–2016**

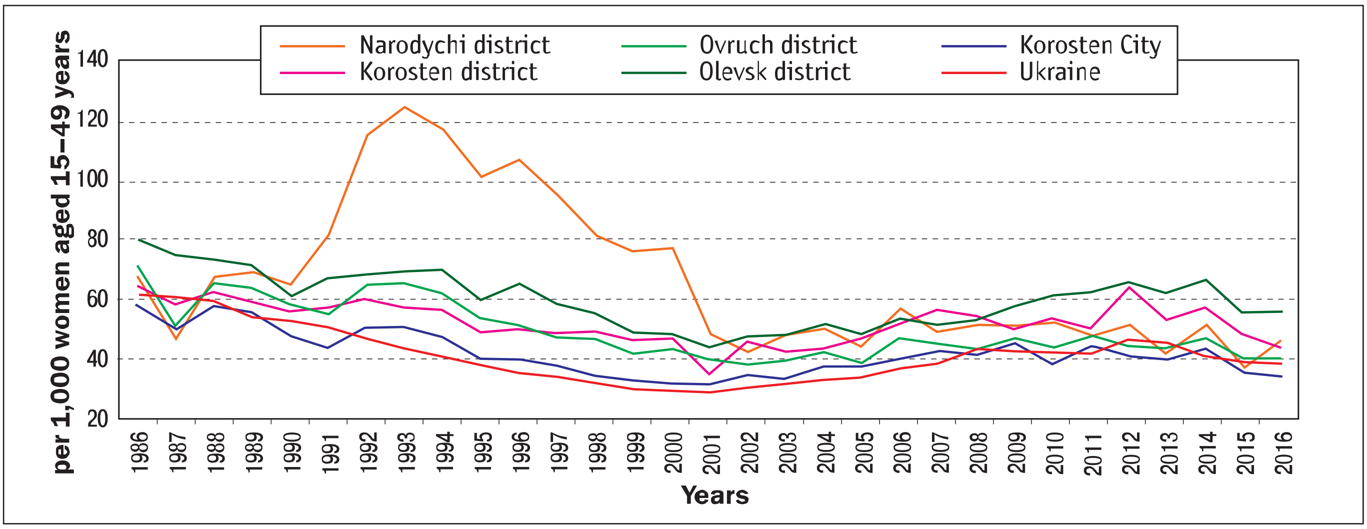

Figure 4.10. **Special coefficient of birth rate of population of Ukraine, Narodychi, Ovruch, Korosten, Olevsk districts and Korosten City per 1,000 women aged 15–49, for 1986–2016**

that experienced the intense migration of the residents under the program of mandatory and voluntary resettlement (Poliske, Narodychi, Ovruch and other districts) are characterized by a tendency to increase the levels of the special birth rate in 1991–1996. The trends of changes in indicators over time most similar to the national ones were found in Kozelets and Ripky districts.

It should be noted that in Ukraine, as in most European countries, society did not accept extramarital births for a long time, therefore marriage and birth rate were closely connected [28]. The liberalization of society's views on marriage and illegitimate children in the country allowed for an equalization at the legislative level of the rights of women and men to raise children, regardless of the marriage type, which also resulted in an increase in the number of illegitimate births. For example, in 1991 the share of extramarital births in the total number of live births in the country was 11.9 %, whereas in 2016 it was 20.5 %.

In the studied districts, in 2016, compared to 1986, the share of extramarital births increased throughout the country (with the exception of rural areas of the Rokytne district). The lowest percentage of extramarital births in 2016 was revealed in the districts of the Rivne Oblast, where the level of canonical marriages is higher and divorce rate is lower (Table 4.4)

Experts attribute the increase in the number of children born outside marriage in the country to the changes in moral standards regarding intimate relationships (mostly the spread of premarital relationships), the lack of readiness of young people to marriage, the irresponsibility of one/both parents to their parental obligations, excessive demands for a marriage partner, women emancipation, crisis of the modern family and weakening of its social prestige [24, 28, 29].

According to [30], the mother contingent in Ukraine is traditionally considered quite young, especially in comparison with other European countries. However, while in the 1980s about one out of five children was born by mothers aged 30+, in 2016 it was every third child (Table 4.5). In 2016, babies born by women aged 40+ were twice as often as in 2001, but their share in the structure of newborns is insignificant. Changes in the structure of live births by maternal age indicate that modern Ukrainian women postpone births to an older age.

Thus, the most active childbearing age both in the RCT and in the control group was and remains the age of 20–29 years (every second child). The number of newborns in mothers aged 45–49 years is minimal or, as in most areas, not observed. There was a decrease in births by mothers aged 20–24 years by minus 2.49–21.18 percentage points in all the studied districts and the country; 15–19 years – by minus 0.61–12.03 percentage points in all the studied districts (with the exception of Korosten district with +0.06 percentage points) and the country; 25–29 years – by minus 11.83 percentage points in Poliske, by minus 1.26 percentage points in Korosten and minus 1.05 percentage points in Narodychi districts and minus 1.26 percentage points in Korosten City; 40–45 years – by minus 1.23 percentage points in Ovruch and minus 0.82 percentage points in Rokytne districts. In other age groups, there was a widespread increase in the proportion of births in the total number of newborns.

In 2016, the average age of Ukrainian mothers reached 27.6 years, but remained younger compared

Table 4.4
Extramarital births in 2016 in radioactively contaminated territories and in Ukraine (%)

Areas	All population	Urban areas	Rural areas
Narodychi district	41.24	34.62	43.66
Ovruch district	22.49	17.44	25.07
Olevsk district	23.75	25.67	22.79
Korosten City	–	24.01	–
Korosten district	–	–	29.96
Ivankiv district	25.09	12.73	33.33
Poliske district	46.03	33.50	46.67
Rokytne district	6.37	10.64	5.79
Sarny district	8.09	11.25	6.67
Kozelets district	26.35	22.52	30.34
Ripky district	29.94	29.03	31.25
Ukraine	20.2	19.5	22.4

Table 4.5
Structure of live births per mother's age, for 2001 and 2016 (%)

Areas	Year	Mother's age, age groups						
		15–19	20–24	25–29	30–34	35–39	40–44	45–49
Ivankiv district	2001	15.56	38.83	23.37	14.09	4.12	0.69	0.00
	2016	8.35	27.64	26.18	23.64	11.64	2.55	0.00
Poliske district	2001	18.07	42.17	27.7	7.23	2.41	2.41	0.00
	2016	17.46	39.68	15.87	14.29	7.94	4.76	0.00
Narodychi district	2001	16.67	42.85	30.95	5.25	2.38	0.00	0.00
	2016	10.31	32.99	29.90	20.62	5.15	1.03	0.00
Ovruch district	2001	12.65	45.53	23.95	11.47	4.22	2.02	0.16
	2016	7.10	30.56	32.35	20.32	8.88	0.79	0.00
Korosten City	2001	12.30	41.65	31.28	10.90	3.34	0.35	0.00
	2016	5.66	31.39	30.02	21.61	9.26	2.06	0.00
Korosten district	2001	12.39	44.02	28.63	8.55	4.27	1.71	0.00
	2016	12.45	37.35	23.74	17.90	6.61	1.95	0.00
Olevsk district	2001	16.77	42.02	25.66	10.00	4.65	0.81	0.00
	2016	11.25	36.79	25.88	15.18	9.11	1.79	0.00
Rokytne district	2001	12.89	39.86	25.50	12.58	6.65	2.42	0.09
	2016	8.59	34.83	27.02	18.61	9.09	1.61	0.25
Sarny district	2001	11.62	39.04	28.01	12.62	6.87	1.59	0.25
	2016	5.51	34.73	30.83	17.91	8.50	2.30	0.22
Kozelets district	2001	19.80	43.15	22.59	9.39	3.30	1.78	0.00
	2016	7.77	21.97	33.78	24.66	9.12	2.70	0.00
Ripky district	2001	14.12	43.13	26.72	11.83	3.44	0.76	0.00
	2016	8.92	29.30	36.94	16.56	5.72	1.92	0.64
Ukraine	2001	14.57	41.50	26.45	11.82	4.25	0.98	0.04
	2016	5.52	25.14	33.37	23.61	9.96	2.07	0.13

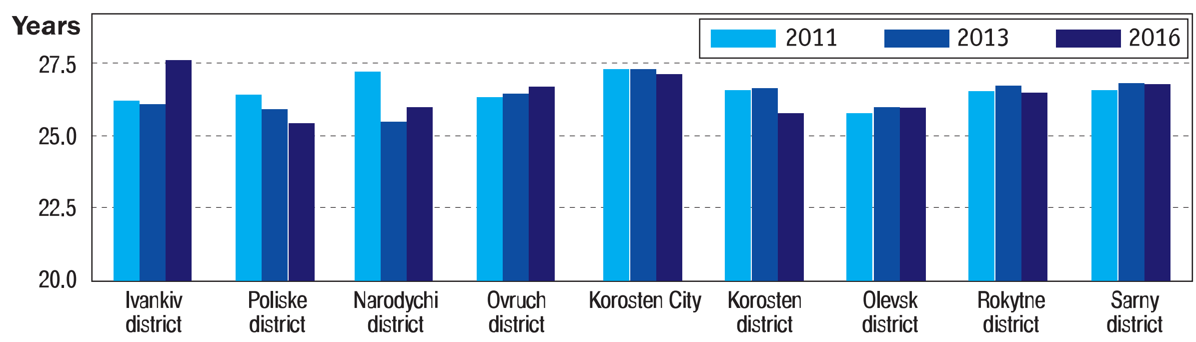

Figure 4.11. **Average mother's age at the birth of a child, for 2011–2016**

to European countries. And in recent years, the average age of a mother at the birth of a child in the RCT is younger than in Ukraine (Fig. 4.11).

During 1986–2016, there was a steady increase in the average age of mothers at the birth of their first child both in the country and in radioactively contaminated areas, which is obviously caused by the so-called «civilizational demographic changes.» In recent years (Fig. 4.12), in the RCT women gave birth to their first child at a younger age: in Rokytne (22.1–22.4 years), Narodychi (21.3–22.6 years) and Poliske (19.9–23.0 years) districts.

Compared to 2011, the share of births of first children decreased in 2016, while the share of births of third and subsequent children increased. However, researchers believe that if the socio-economic situation of families continues to worsen, it is likely that the process of shifting from having three children to having two children and from two children to one child will continue [31, p. 166–180].

In the structure of children born in radioactively contaminated areas (Table 4.6) in 2016, the share of first-born children ranged from 31.45 % (Sarny district) to 52.53 % (Korosten district), the second-born

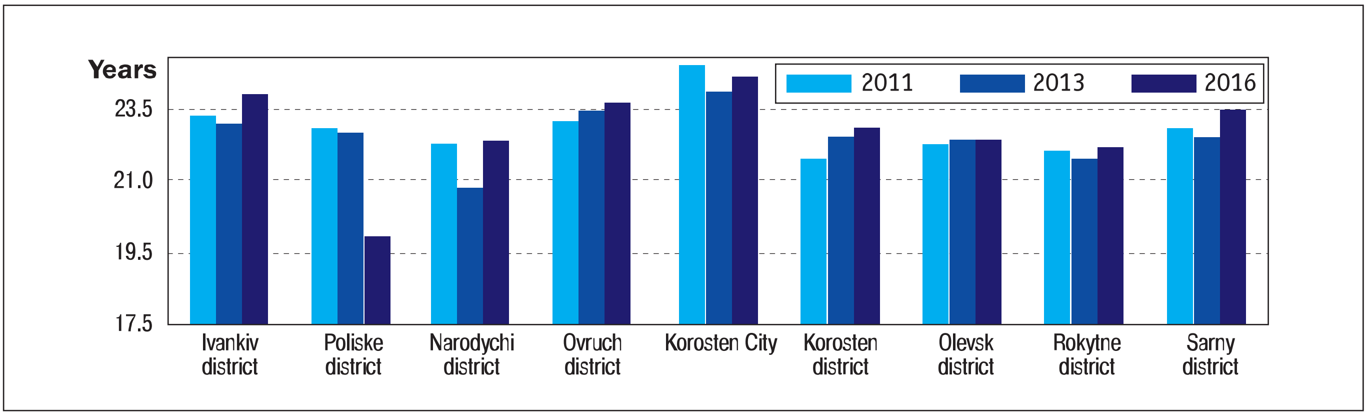

Figure 4.12. Average mother's age at the birth of a first child, for 2011–2016

Table 4.6
Structure of live births per the order of a child for a mother, for 2011 and 2016 (%)

Area	Year	The order of birth of a child for a mother				
		first	second	third	fourth	fifth and subsequent
Ivankiv district	2011	42.34	36.64	11.71	5.11	4.20
	2016	42.91	33.45	14.18	3.64	5.82
Poliske district	2011	37.18	33.33	17.95	2.56	8.98
	2016	42.86	26.98	17.46	9.52	3.18
Narodychi district	2011	30.93	35.05	14.43	10.31	9.28
	2016	44.33	29.90	18.56	2.06	5.15
Ovruch district	2011	42.95	37.93	12.54	3.76	2.82
	2016	46.94	31.16	13.41	4.54	3.94
Korosten City	2011	47.40	37.82	11.58	1.60	1.60
	2016	48.89	35.51	9.95	2.74	2.91
Korosten district	2011	37.84	30.74	16.55	5.41	9.46
	2016	52.53	26.46	13.23	4.28	3.50
Olevsk district	2011	40.85	34.15	16.77	5.03	3.20
	2016	45.54	32.32	11.43	5.89	4.82
Rokytne district	2011	27.82	25.45	18.26	9.63	18.84
	2016	32.12	25.23	16.31	10.28	16.06
Sarny district	2011	31.12	29.33	19.65	8.33	11.57
	2016	31.45	32.49	17.14	7.39	11.53
Kozelets district	2011	50.42	35.44	9.70	2.53	1.91
	2016	40.20	44.26	9.80	2.70	3.04
Ripky district	2011	42.17	38.26	12.17	4.35	3.05
	2016	52.23	30.57	9.55	4.46	3.19
Ukraine	2011	50.81	35.29	9.29	2.58	2.01
	2016	48.22	35.14	10.25	2.97	2.63

children – from 25.23 % (Rokytne district) – to 44.26 % (Kozelets district), the third-born children – from 9.55 % (Ripky district) – to 18.56 % (Narodychi district), the fourth-born children – from 2.06 % (Narodychi district) – to 10.28 % (Rokytne district), the fifth-born and subsequent children – from 2.91 % (Korosten City) – to 16.08 % (Rokytne district). Compared to the national values, for the RCT, the percentage of first-born and second-born children is lower (with the exception of Kozelets and Ripky districts, Korosten City), which indicates the orientation of families towards having many children and, accordingly, the possibility of replacing generations of parents with children. The leaders in the birth of fifth and subsequent children are residents of Rokytne and Sarny districts (up to 19.0 %).

Annually, from 1,800 (2001 and 2002) to 7,900 (1986) children in Ukraine are stillborn (losses are categorized as stillbirths if fetal death occurs in antenatal period, that is, before the start of labor, or in intranatal period, that is, during childbirth) [32].

Boys predominated among stillbirths: all settlements 51.7–56.7 %, urban areas 51.4–56.3 %, rural areas 50.8–58.7 %.

In Ukraine, during the studied period, there was a noticeable decrease in the number of stillbirths, namely: in 1986 there were 7,873 stillbirths, and in 2016 – 2,244 or by 4.2 promille points less or by minus 3.5 times (urban areas – minus 5.5 promille points or minus 2.0 times, rural areas – minus 1.1 promille points or minus 21.1 %), while the perinatal period expanded by 6 weeks (that is, from 22 weeks of pregnancy) [33, 34]. Average indicator for 1986–2016 is higher in urban areas (7.0 per 1,000 live and dead births) than in rural areas (6.0 per 1,000 live and dead births).

Studying the levels of reproductive losses in the RCT, it was found that the quantitative values of stillbirths differ both by year and by territory: from not a single incident, for example, in the Poliske district (1989, 1991–1996, 1997–1999, 2001–2008, 2009–2016) to 23–24 cases (1991 and 1986, respectively) in Sarny district.

A comparative analysis of the stillbirth rate for the RCT by average (1986–2016) values indicates the presence of a significant territorial differentiation of their levels: from 2.7 per 1,000 live and dead births in the Poliske district to 8.8 ‰ in Korosten City. In half of the districts, the stillbirth rate is higher than in the country as a whole (6.6 ‰) and reaches 7.7 ‰ (Sarny district) – 8.3 ‰ (Korosten district), in the rest of the districts it is lower, namely: Poliske – 2.7 ‰, Olevsk – 3.1 ‰, Ovruch – 4.0 ‰, Rokytne – 4.2 ‰, Ivankiv – 4.8 ‰ and Ripky – 6.1 ‰). It should be noted that having the same level of stillbirth by areas with very different socio-economic characteristics may indicate a different degree of reliability of records of stillbirths in the regions, which may be complicated by cases of underestimation or distortion of data (stillbirths can be attributed to late miscarriages or premature babies who died within the first seven days, recorded in the statistics as stillbirths, and not cases of born alive or dead). The lack of access to prenatal care, fetal monitoring, hospitals and safe prompt delivery, the quality of maternity care, education, general and sanitary culture of the population should not be underestimated. There is also a discrepancy between the current modern clinical protocols for providing care to pregnant women and newborns and the capabilities of maternity hospitals (which may be due not only to the outdated infrastructure and equipment, but also to insufficient training of personnel) [35].

4.4. Death rate

During 1986–2016, in the country, from 565,200 (2016) to 792,800 (1995) people died annually, in other terms, the death rate was at the level of 11.1 ‰ (1986) – 16.6 ‰ (2005). In rural areas, mortality rates for the entire observation period were significantly higher than in urban settlements (Fig. 4.13): rural areas – 14.7 ‰ (1986) – 20.5 ‰ (2005), urban areas – 9.2 ‰ (1986) – 14.8 ‰ (2005). In 2016, compared to 1986, there was an increase in mortality in Ukraine by +8.9 promille points or +32.4 % (urban areas +4.0 promille points or +43.5 %; rural areas +2.9 promille points or +19.7 %). The annual increase in the death rate was taking place until 2008 (with a slight slowdown in 1997–1999), and then there was a gradual decline (in 2016 to the level of 1999), which could not compensate for the long-term growth of the indicator. On average, the annual mortality rate for the entire population increased by 9.4 %: in urban areas by 14.2 %, in rural areas by 6.0 %.

National trends towards an increase in mortality rates in the dynamics of observation are also inherent in the studied districts, with the difference that the highest levels (Kozelets and Ripky districts) exceed the lowest (Rokytne and Sarny districts) by more than 2 times (Fig. 4.14). This situation resulted primarily from the age structure of the population.

Most of the studied territories show a significant range of indicators during 1986–2016, with minimal values in 1986 and maximum values in 2005–2008. Compared to 1986, there was revealed an increase in the indicator in 2016 for all settlements from 1.1 promille points or +6.4 % (Poliske district) to +9.8 promille points or +55.3 % (Kozelets district); in urban areas – from 1.0 promille points or +9.2 % (Narodychi district) to +7.1 promille points or +114.5 % (Rokytne district), in rural areas from 2.9 promille points or +10.2 % (Ivankiv district) to +9.8 promille points or +89.1 % (Kozelets district). It is shown that the largest range of indicators was in Poliske and Kozelets districts – 19.9 promille points (min = 15.9 ‰ in 1989, max = 35.8 ‰ in 2007) and 14.6 promille points (min = 15.9 ‰ in 1986, max = 30.5 ‰ in 2008), respectively.

Compared to the national indicators (14.5 ± 0.54 ‰), the average mortality rates for 1986–2016

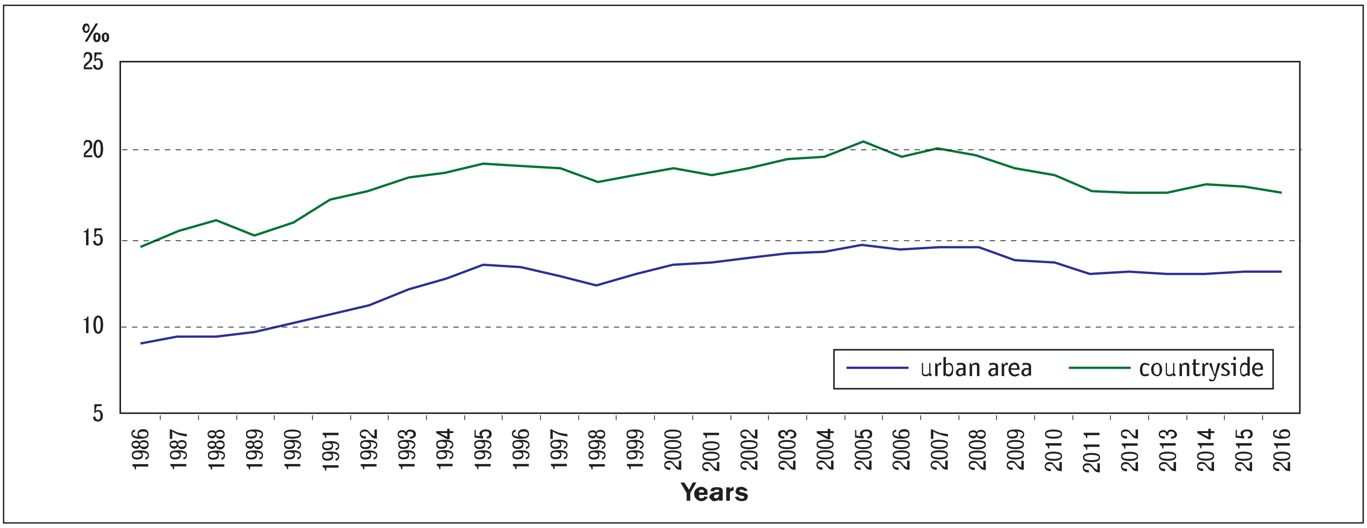

Figure 4.13. **Dynamics of death rate for urban and rural population of Ukraine, for 1986–2016**

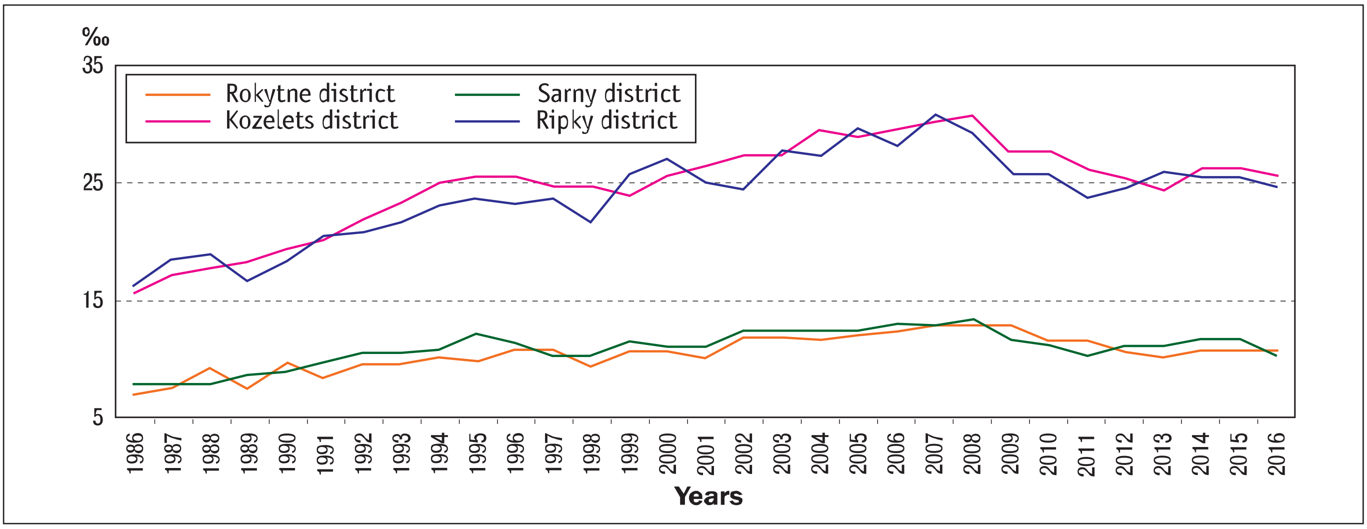

Figure 4.14. **Dynamics of overall death rate for population of Kozelets, Ripky, Rokytne, Sarny districts, for 1986–2016**

were higher in seven studied districts: Ovruch (18.5 ± 0.98) ‰, Korosten (22.5 ± 1.29) ‰, Ivankiv (23.2 ± 1.17) ‰, Ripky (24.0 ± 0.51) ‰, Narodychi (24.3 ± 1.45) ‰, Poliske (24.7 ± 1.76) ‰, Kozelets (24.8 ± 1.36) ‰; lower in two districts – Rokytne (10.7 ± 0.51) ‰ and Sarny (11.4 ± 0.52) ‰ ones and Korosten City (13.8 ± 0.88) ‰, close to the national ones – in Olevsk (14.7 ± 1.17) ‰ and they are statistically significant (significance level 0.05 %), except for Olevsk district.

Figure 4.15 reflects the dependence of the average mortality on the irradiation dose for 10 studied areas for 1991–2005. The average adult effective total dose accumulated in the period from 1986 to 2005 was used as the irradiation dose. The total average district mortality rate aggregated for 1991–2005 was used as the mortality indicator. The period for which the aggregated mortality rate was taken was shifted by 5 years relative to the period for which the dose was accumulated, since the latent period of stochastic effects associated with the irradiation dose for most diseases are approximately 5 years. The study did not reveal a statistically significant dependency between mortality and irradiation dose. Correlation coefficient between the average dose and mortality (Fig. 4.15) is $r = 0.18$ ($Pv = 0.67$).

In Ukraine, a comparative analysis of male and female mortality is of great medical and social interest, since the mortality rate of men significantly exceeds that of women, especially under the age of 40 [36]. Data from Fig. 4.16 clearly illustrate the dynamics of changes in the mortality rates of men and women in Ukraine over time and similar «waves» of growth in 1986–1995 and 1999–2008 and a decrease in 1997–1998 and 2009–2012 compared to 1986. The increase in the indicator in 2016 for

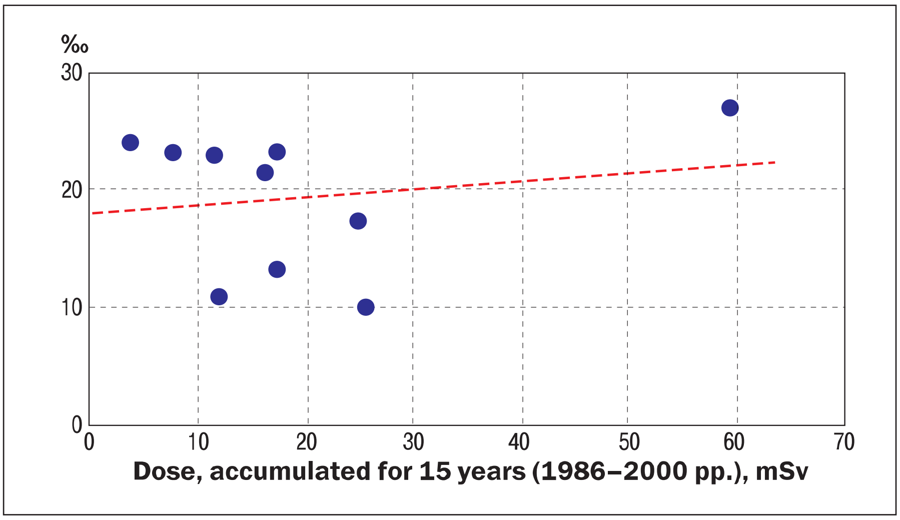

Figure 4.15. **Dependence of an average death rate of population of 10 studied districts from irradiation dose, 1991–2005**

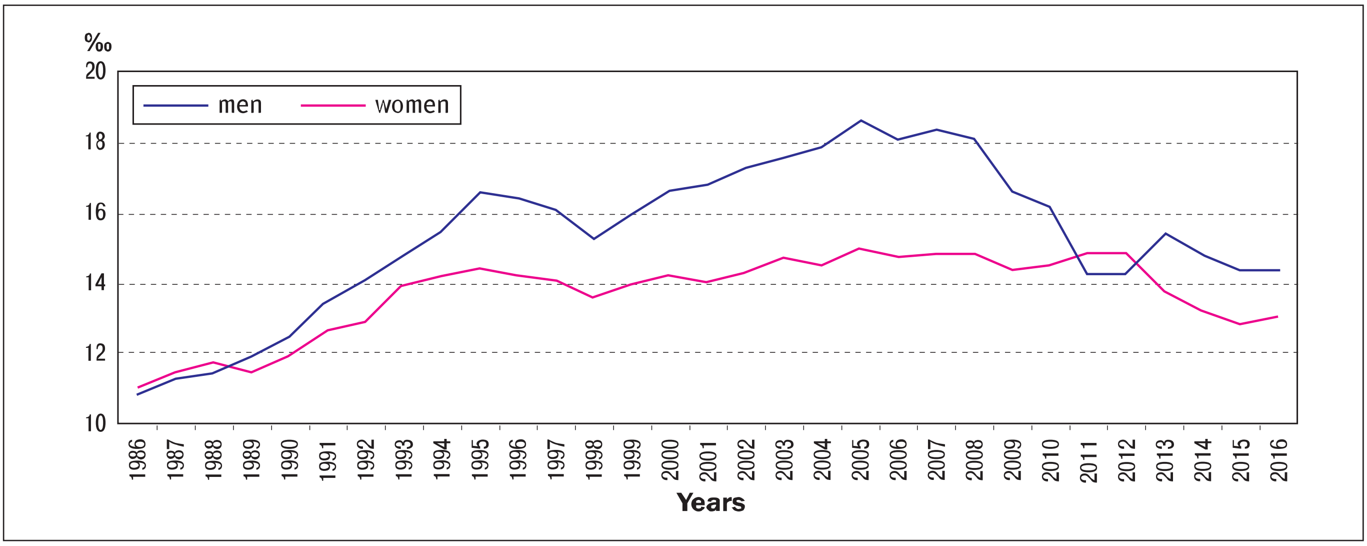

Figure 4.16. **Dynamics of death rate for men and women in Ukraine, for 1986–2016**

men was by 3.5 promille points or 31.5 %, and for women – by 1.9 promille points or 16.5 %. In urban settlements, by 3.6 promille points or 37.4 % and 1.2 promille points or 20.0 %, respectively, and rural – by 3.6 promille points or 30.0 % and 1.3 promille points or 19.0 %, respectively.

The dynamics of mortality rate of male and female residents of the RCT is similar to the national one (Fig. 4.17 and 4.18). It is shown that the average mortality rates for the period from 1986 to 2016 are lower than the national level only in Korosten, Rokytne and Sarny districts.

Estimates of the correlation coefficients between mortality rate and irradiation dose separately for men and women are statistically unreliable and are $r = 0.19$ ($Pv = 0.59$) and $r = 0.2$ ($Pv = 0.57$), respectively. This is because the RCT residents did not receive doses that could have caused deaths. We believe that the mortality rates of the adult population are more dependent not on the levels of ionizing irradiation, but on age, quality of medicine, social well-being and morbidity, which, in turn, in addition to the dose, depends on lifestyle, nutrition, ecology, heredity, etc.

Among the age-related mortality rates, the infant mortality rate (death of children under 1 year old) is of particular importance, since it is not only an important health indicator of this population group, but also a criterion for the socio-economic state of society and the health system, characterizes opportunities and real measures to ensure the life and health of future generations.

It is established that during 1986–2016, from 3,000 (2016) to 11,600 children under the age of 1 year died annually in the country (the average number for 1986–2016 – 6,000 children). Both in the urban areas (57.0–61.2 %) and in the rural areas (55.1–59.7 %), boys predominated among died children. The dynamics of infant mortality in Ukraine indicates its gradual reduction throughout the country (Fig. 4.19).

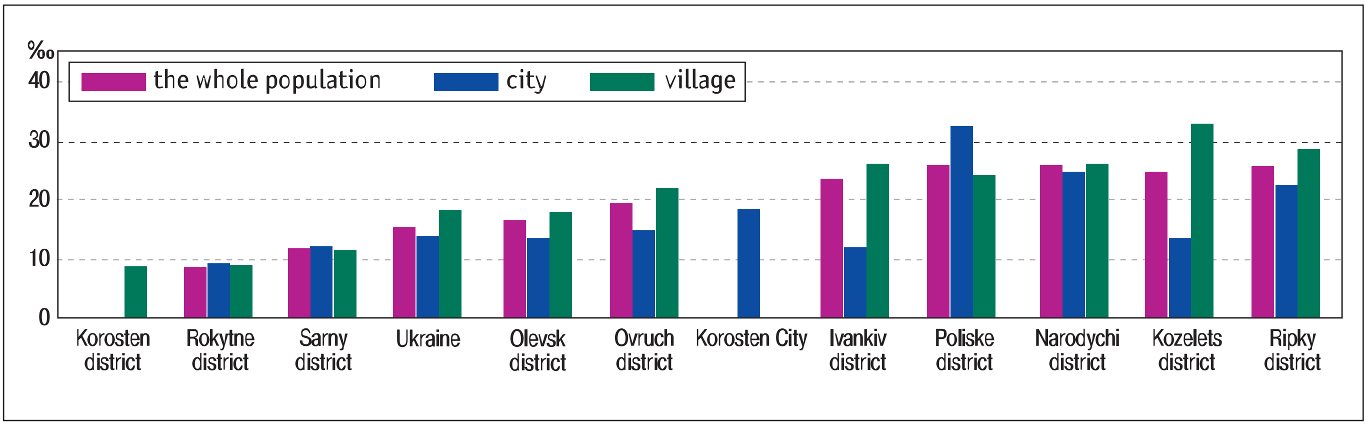

Figure 4.17. Average mortality death rate, for 1986–2016

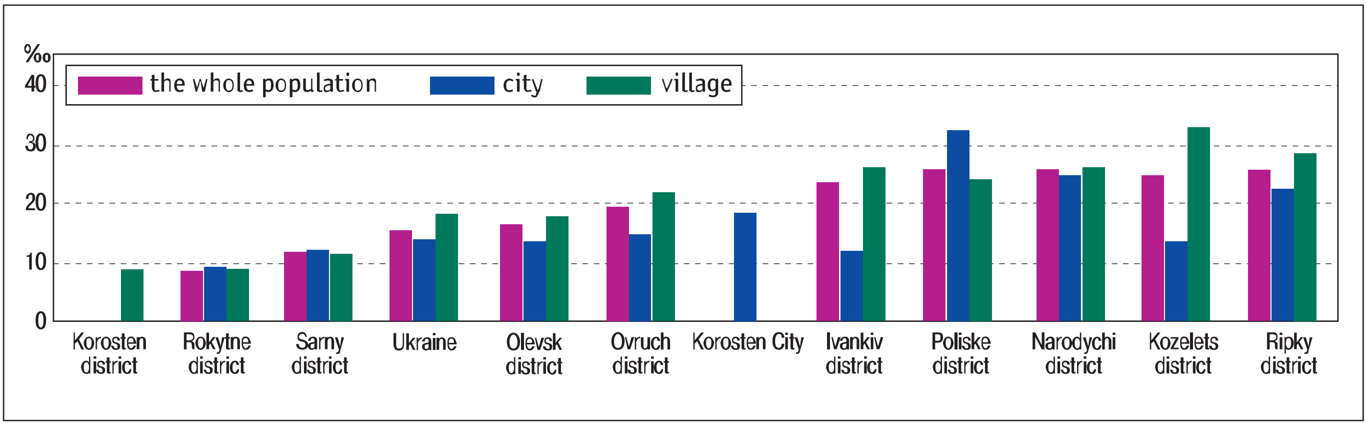

Figure 4.18. Average female mortality rate, for 1986–2016

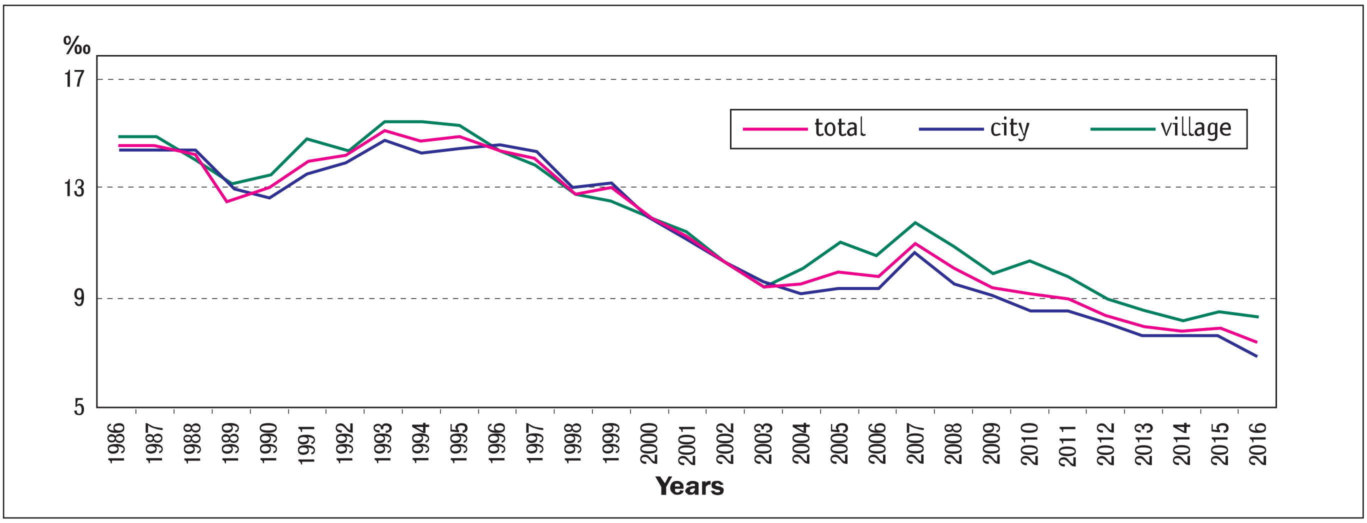

Figure 4.19. Dynamics of infant mortality rate in Ukraine, for 1986–2016

It is worth mentioning that the sharp increase in the indicator throughout the country in 2007 was a consequence of the transition of Ukraine to new standards for determining the perinatal period and live birth rate [33].

In 2016, compared to 1986, infant mortality decreased by 7.3 promille points or 49.5 % (urban areas – by 7.6 promille points or 52.4 %, rural areas – by 6.6 promille points or 44.0 %), but its level remains higher than in the countries of the European Union and Japan [37].

A positive downward trend in infant mortality, which is consistent with the national one, is also evident in the studied regions (Fig. 4.20), but significant changes were found only in Narodychi, Ovruch and Rokytne districts.

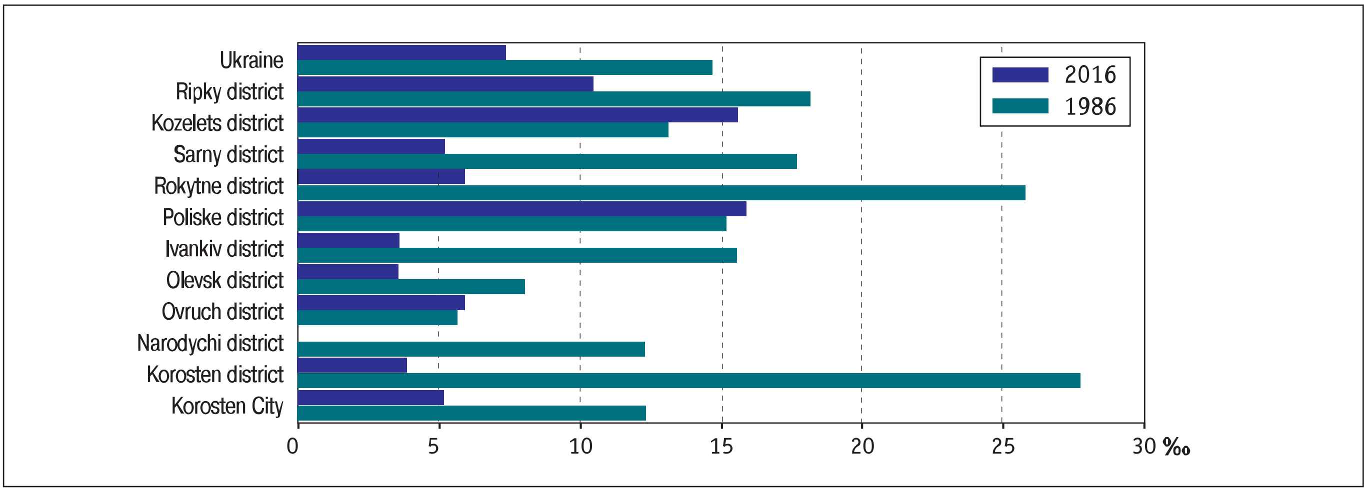

Figure 4.20. **Infant mortality rate for 1986 and 2016**

Significant fluctuations in values both in the dynamics of observation and between districts were revealed in the RCT. For example, in 1992 in Olevsk district it was 16.6 ‰, and in 1993 – 5.1 ‰; in Poliske district in 1995 – 5.2 ‰, and in 1996 – 30.5 ‰. Therefore, the range of variation (R) of values is significantly higher than in the country as a whole (R = 7.7) – from 13.7 (Sarny district) to 46.4 (Ovruch district).

Comparing the RCT data for 1986 and 2016, it is possible to reveal a decrease in the average annual growth rate for the entire population in most areas. With the exception of Kozelets (+5.7 %), Ovruch (+1.6 %), Poliske (+1.5 %) and Narodychi (0.0 %) districts.

Narodychi (18.92 ± 1.99) ‰ and Rokytne (14.3 ± 1.05) ‰ districts have the highest average infant mortality rates for 1986 –2016, the lowest – Ovruch (9.40 ± 0.86) ‰ and Olevsk (10.10 ± 0.72) ‰ districts. Thus, in comparison with the country as a whole – (11.53 ± 0.46) ‰ – it is possible to note different variants of changes in the indicator over time for the RCT: infant mortality can be either lower or higher than the national indicators. Different significance of the correlation (high, medium, low) and its absence were also revealed: Olevsk district (total, urban, rural areas), Ivankiv district (urban area), Kozelets district (urban area), Ripky district (rural area) and Narodychi district (rural area).

A statistically significant dependence of infant mortality on the maternal irradiation dose is presented in Fig. 4.21. Mortality rate was aggregated within 15 years (from 1991 to 2005). The cumulative effective dose accumulated by adult women in the first 15 years after the accident, i. e. from 1986 to 2000, was used as an irradiation dose. The correlation coefficient between infant mortality and maternal irradiation dose is significant r = 0.8 and statistically highly reliable (Pv = 0.006).

Also statistically significant is the dependence of infant mortality on the irradiation dose of 1986, aggregated over the period from 1987 to 1990 (Fig. 4.22). The correlation coefficient is r = 0.8 (Pv = 0.004).

For comparison, the dependences of infant mortality over other time periods were created. Fig. 4.23 shows the relationship between infant mortality in 1986 and maternal irradiation dose in 1986. There is no correlation between infant mortality and irradiation doses in 1986. The correlation coefficient is statistically unreliable and is r = -0.18 (Pv = 0.6). There is also no association between infant mortality 20 years after the accident and irradiation doses in 1986 (Fig. 4.24).

The correlation coefficient for this data is r = -0.13 (Pv = 0.71). Thus, the negative impact of the Chornobyl accident on the infant mortality in the 10 most radioactively contaminated districts of Ukraine has been proved. The negative impact of the irradiation dose started in 1987, since in 1986–1987, during pregnancy, the mother could accumulate a fairly high dose of radiation for both the whole body and the thyroid gland. Moreover, the baby was also irradiated in the womb (in utero). These combined factors, in our opinion, caused an increase in infant mortality in the RCT in the first 15–20 years after the accident.

However, 20 years after the accident, there is no statistically significant dependence on the mother's irradiation dose and infant mortality. This may be due to a significant reduction in the irradiation dose

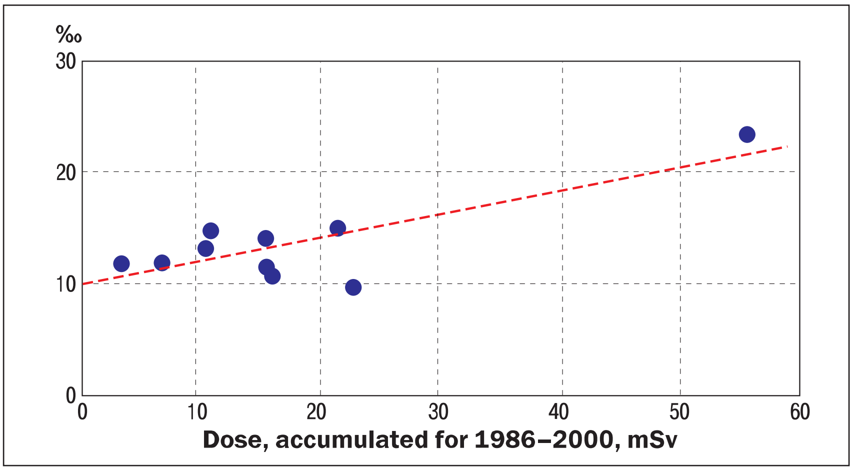

Figure 4.21. Dependence of average infant mortality rate from 10 studied districts from mother's irradiation dose (1991–2005)

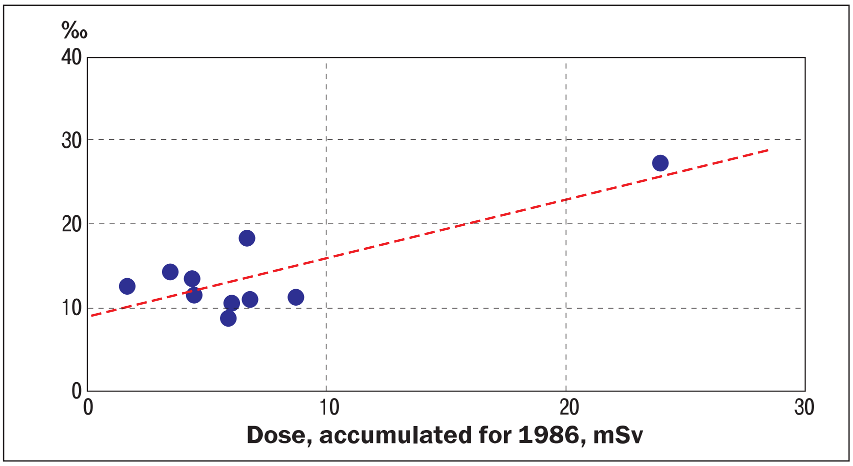

Figure 4.22. Dependence of average infant mortality rate from 10 studied districts from mother's irradiation dose (1987–1990)

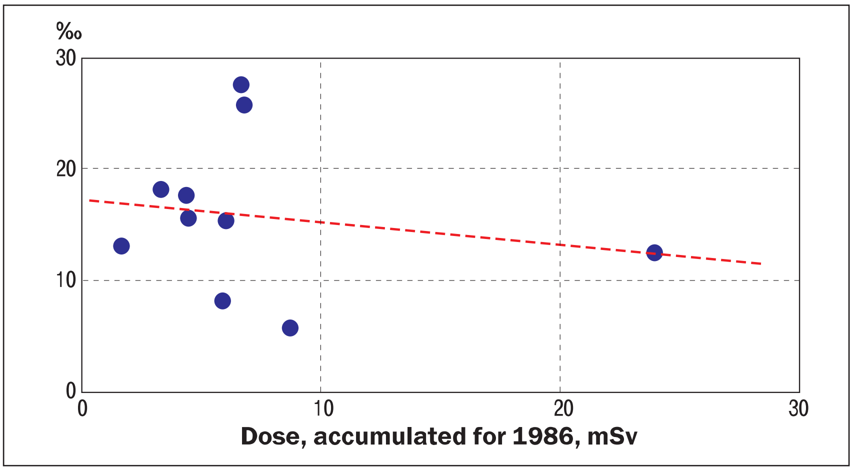

Figure 4.23. Dependence of average infant mortality rate from 10 studied districts from mother's irradiation dose (1986)

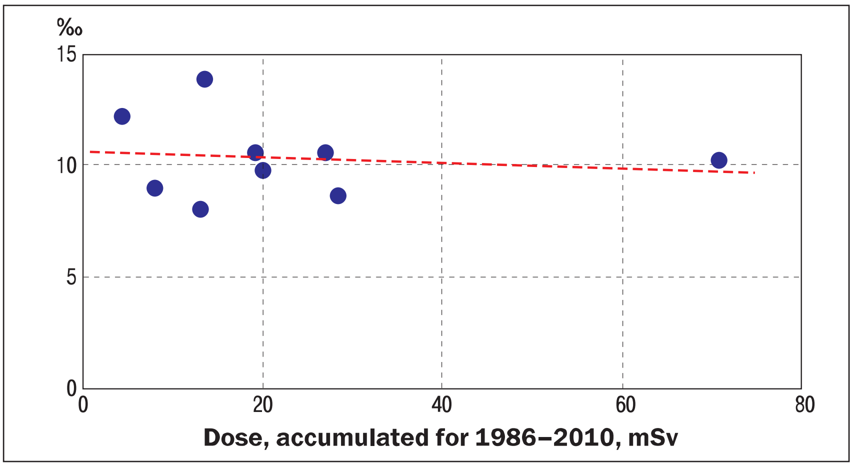

Figure 4.24. Dependence of average infant mortality rate from 10 studied districts from mother's irradiation dose 20 years after the accident (2006–2015)

of both mother and child during these years. Given the identified patterns, research needs to be continued for a more thorough study of this phenomenon. In addition, it is advisable to study the mechanisms of influence on the viability of a newborn of irradiation doses received by the mother before and during pregnancy, as well as irradiation doses of the child in the womb (*in utero*).

In Ukraine, people born in 1968–1986 (children at the time of the accident) were recognized as one of the risk groups due to the levels of irradiation to the thyroid gland with radioisotopes of iodine and general irradiation from other radionuclides, which made it advisable to further study their health status by mortality rates. The combination of information databases of the State Statistics Service of Ukraine and the Ministry of Justice of Ukraine made it possible to form a cohort of the study (more than 31,000 people who at the time of the Chornobyl accident were aged 0–17 years and lived in Ivankiv, Poliske, Narodychi and Ovruch districts) and collect depersonalized information about 2,100 deaths in 1986–2011. The control was the population of Ukraine of the appropriate age.

Comparison of survival curves (Fig. 4.25) using the logrank criterion [38] showed that with a proba-

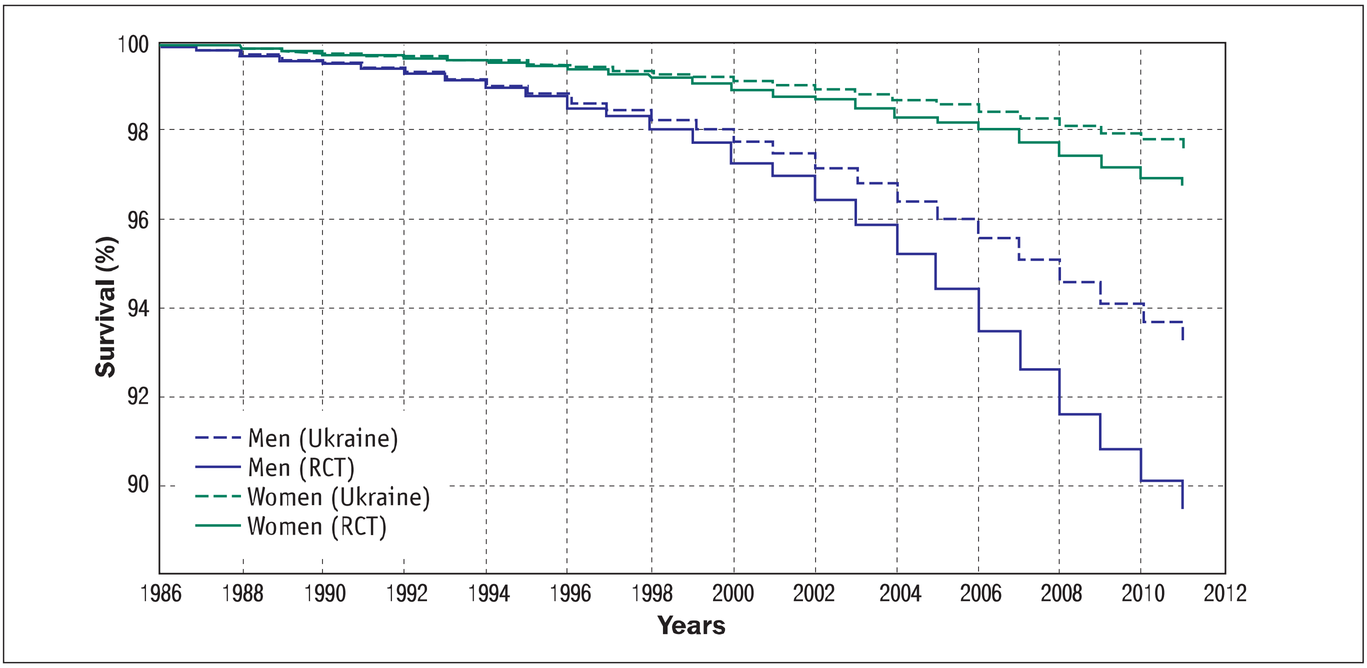

Figure 4.25. **Survival function for 1986–2011 created for people born in 1968–1986 who lived in Ukraine and studied areas**

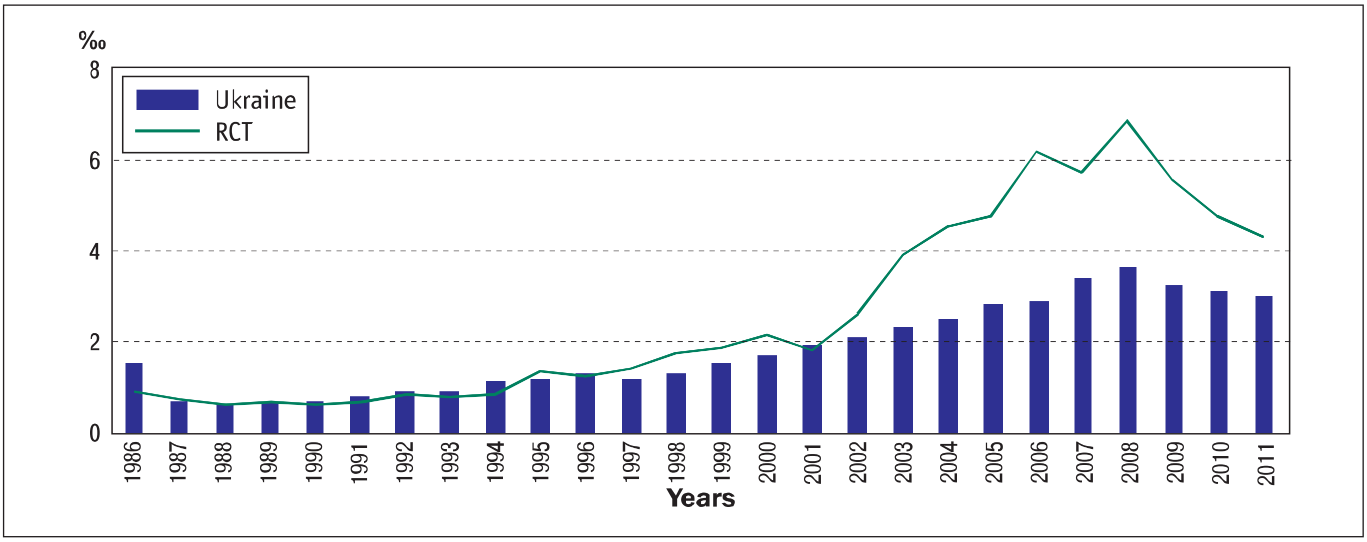

Figure 4.26. **Standardized mortality coefficients of people born in 1968–1986 who lived in the RCT per 1,000 people of the same age, for 1986–2011**

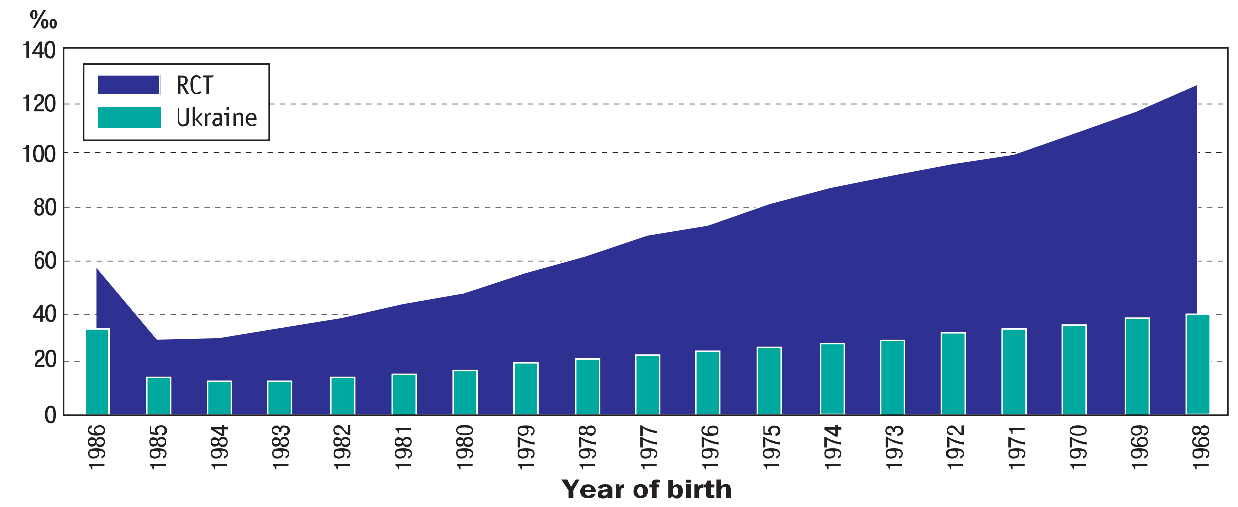

Figure 4.27. **Mortality coefficients of peers born in 1968–1986 who lived in Ukraine and in the RCT per 1,000 people of the same age, for 1986–2011**

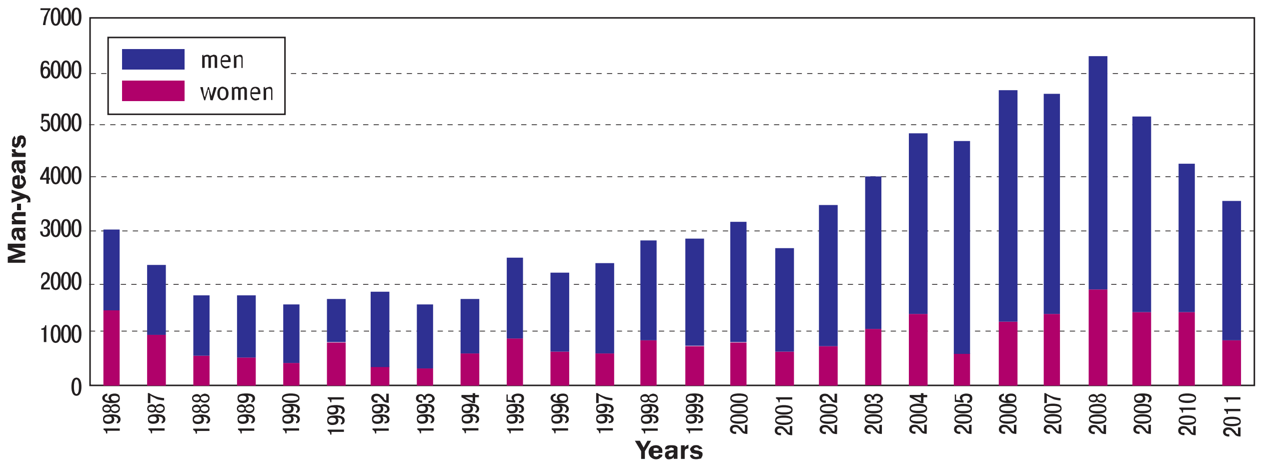

Figure 4.28. **Dynamics of potentially lost years of life for died people born in 1968–1986 who lived in the RCT, for 1986–2011 (person-years)**

bility of $P > 99.9$ % (significance level $\alpha < 0.1\%$), all curves differ from each other by statistical significance. This means that the mortality rate of both men and women born in 1968–1986 is statistically significantly higher in the RCT compared to Ukraine as a whole.

Age-standardized indicators (standard of the population of Ukraine of the corresponding age) for the RCT (Fig. 4.26) indicate higher mortality rates of their residents as early as 10 years after the accident.

According to the data provided (Fig. 4.27), mortality rates of peers living in the RCT are higher than in control area.

The average chronological mortality rate for 1986–2011 in the cohort of the RCT residents was (2.26 ± 0.37) ‰, and in Ukraine – (1.74 ± 0.74) ‰.

As a result of premature deaths from diseases of 2,060 people born in 1968–1986, who lived in the Ivankiv and Poliske districts of the Kyiv Oblast and Narodychi and Ovruch districts of the Zhytomyr Oblast during 1986–2011, 82,300 years of life were potentially lost (Fig. 4.28). The women's subcohort had the lowest losses in 1993 (300.3 person-years), the men's subcohort – in 1991 (847.3 person-years), the maximum losses – in 2008 (men – 4494.9 person-years, women – 1811.2 person-years). The average rate of potentially lost years of life for a deceased person was 39.7 years, men – 37.5 years, women – 48.5 years. In premature mortality, the key role (50.4 %) goes to external causes, 43.1 % – somatic pathology, 6.55 % – symptoms, signs and vaguely defined conditions.

4.5. Viability index

The negative dynamics of the viability index on the studied areas with radiological contamination persists to this day (Table 4.7). Major changes in the reproduction mode were found in urban residents.

The level of the indicator in 2016 ranged from 0.28 (Ripky district) to 1.93 (Rokytne district) – the entire population, urban areas – from 0.33 (Poliske district) to 1.25 (Sarny district), rural areas – from 0.18 (Ripky district) to 2.16 (Rokytne district). The decrease in 2016 relative to the level of 1986 for all settlements was from 1.4 times (Narodychi district) – to 2.6 times (Ovruch and Ripky districts), urban areas – from 1.6 times (Narodychi district) – to 5.4 times (Poliske district), rural areas – from 1.0 times (Poliske district) – to 2.6 times (Ripky district). At the same time, during the study period, the values of the population viability index in the districts of Zhytomyr, Kyiv and Chernihiv Oblasts were consistently lower than the All –Ukrainian level, in contrast to the regional indicators of the Rivne Oblast.

The processes taking place in the demographic sphere in the RCT cannot but cause deep concern, therefore, the demographic situation in the region is estimated based on calculations of territorial indices and a multidimensional average variable [39] for each district (Table 4.8).

Results of calculations of multidimensional average variable (*P*) and 11 medical and demographic territorial indices (among «positive» are the fertility rate of women aged 20–29, share of the reproduc-

Table 4.7
Dynamics of viability index for population of the studied areas for 1986–2016

Areas	Years							Decline in 2016 compared to level of 1986, in times
	1986	1991	1996	2001	2006	2011	2016	
All settlements								
Narodychi district	0.72	0.59	0.62	0.26	0.38	0.50	0.53	1.4
Ovruch district	1.19	0.66	0.59	0.45	0.46	0.55	0.45	2.6
Olevsk district	2.14	1.39	1.10	0.69	0.70	0.91	0.84	2.5
Ivankiv district	0.85	0.51	0.38	0.33	0.35	0.47	0.46	1.8
Poliske district	0.94	0.66	0.42	0.37	0.27	0.50	0.60	1.6
Rokytne district	3.23	2.28	1.87	1.75	1.81	2.12	1.93	1.7
Sarny district	2.96	1.83	1.50	1.32	1.42	1.78	1.58	1.9
Kozelets district	0.72	0.42	0.29	0.25	0.25	0.36	0.30	2.4
Ripky district	0.72	0.49	0.33	0.25	0.28	0.32	0.28	2.6
Ukraine	1.40	0.94	0.60	0.50	0.60	0.76	0.70	2.0
Urban areas								
Korosten City	1.77	0.98	0.80	0.53	0.64	0.81	0.63	2.8
Narodychi district	1.33	0.79	0.62	0.26	0.64	0.73	0.81	1.6
Ovruch district	2.18	1.18	1.04	0.62	0.65	0.94	0.64	3.4
Olevsk district	3.18	1.54	1.28	0.70	0.77	1.07	1.02	3.1
Ivankiv district	2.55	1.34	1.09	0.77	0.79	0.93	0.81	3.1
Poliske district	1.79	1.06	0.41	-	-	1.00	0.33	5.4
Rokytne district	3.58	3.92	1.75	1.36	1.29	1.58	1.14	3.1
Sarny district	3.14	1.92	1.24	1.00	1.23	1.47	1.25	2.5
Kozelets district	1.90	1.01	0.78	0.55	0.65	0.91	0.59	3.2
Ripky district	1.34	0.96	0.59	0.40	0.43	0.55	0.45	3.0
Ukraine	1.72	1.10	0.63	0.53	0.66	0.80	0.76	2.3
Rural areas								
Korosten district	0.77	0.61	0.41	0.28	0.37	0.46	0.44	1.8
Narodychi district	0.62	0.54	0.62	0.26	0.31	0.44	0.47	1.3
Ovruch district	0.97	0.55	0.48	0.40	0.40	0.45	0.40	2.4
Olevsk district	1.80	1.31	1.03	0.68	0.68	0.89	0.78	2.3
Ivankiv district	0.65	0.41	0.28	0.24	0.26	0.36	0.36	1.8
Poliske district	0.64	0.48	0.41	0.37	0.27	0.47	0.63	1.0
Rokytne district	3.17	1.98	1.89	1.83	1.93	2.22	2.16	1.5
Sarny district	2.86	1.78	1.66	1.52	1.54	1.96	1.80	1.6
Kozelets district	0.48	0.28	0.18	0.17	0.16	0.21	0.20	2.4
Ripky district	0.47	0.31	0.21	0.18	0.20	0.20	0.18	2.6
Ukraine	1.02	0.73	0.56	0.47	0.52	0.68	0.61	1.7

Table 4.8
Demographic parameters and integrated estimate of demographic state of the areas with the most intensive radioactive contamination in Ukraine in 2016*

Parameters	Ukraine	Rokytne district		Sarny district		Olevsk district		Ovruch district		Narodychi district	
	value	value	index	value	index	value	index	value	index	value	index
Share of people aged 0–14 in the population, %	15.25	30.27	1.985	27.57	1.8079	20.46	1.3416	15.17	0.995	15.70	1.0295
Share of women aged 15–49 in the population, %	23.976	23.14	0.965	24.25	1.0114	23.759	0.9909	22.5109	0.939	22.12	0.9226
Share of women aged 20–29 in reproductive population, %	27.8319	30.24	1.087	31.93	1.1472	31.17	1.1199	29.96	1.076	30.16	1.0837
Overall birth rate, ‰	10.3	20.70	2.01	16.80	1.6311	13.4	1.301	9.00	0.874	10.30	1.0000
Special birth rate, ‰	38.96	89.22	2.29	68.56	1.7598	56.29	1.4448	39.76	1.021	44.79	1.1496
Fertility rate of women aged 20–29, ‰	81.92	182.8	2.231	143.26	1.7488	114.65	1.3995	85.18	1.040	97.37	1.1886
Marriage rate, ‰	5.40	6.80	1.259	6.50	1.2037	5.30	0.9815	4.20	0.778	2.70	0.5000
Ageing level, %	15.89	8.36	0.526	9.39	0.5909	12.02	0.7565	19.17	1.2064	21.60	1.3594
Overall mortality rate, ‰	14.70	10.70	0.728	10.6	0.7211	11.9	0.8095	19.80	1.3469	19.40	1.3197
Infant mortality, ‰	7.40	5.94	0.803	5.23	0.7068	3.54	0.4784	5.92	0.8000	0.00	0.00
Divorce rate, ‰	3.30	0.10	0.03	0.20	0.0606	0.40	0.1212	0.60	0.1818	0.10	0.0303
Integrated estimate			1.249		1.112		0.947		0.719		0.742

Parameters	Ivankiv district		Korosten district		Poliske district		Ripky district		Kozelets district	
	value	index	value	index	value	index	value	index	value	index
Share of people aged 0–14 in the population, %	15.51	1.017	15.60	1.023	18.30	1.200	12.20	0.800	13.09	0.8584
Share of women aged 15–49 in the population, %	27.61	1.152	21.246	0.8861	22.87	0.954	19.279	0.8041	20.88	0.8709
Share of women aged 20–29 in reproductive population, %	31.21	1.121	32.67	1.1738	28.55	1.026	31.73	1.1401	30.39	1.0919
Overall birth rate, ‰	5.00	0.926	3.70	0.6852	4.50	0.833	4.20	0.7778	5.10	0.9444
Special birth rate, ‰	38.87	0.998	44.76	1.1489	47.80	1.227	35.97	0.9233	36.76	0.9435
Fertility rate of women aged 20-29, ‰	9.20	0.893	9.60	0.932	11.00	1.068	7.00	0.6796	7.70	0.7476
Marriage rate, ‰	68.36	0.834	85.44	1.043	91.89	1.122	62.61	0.7643	58.49	0.7140
Ageing level, %	17.61	1.108	21.87	1.3763	16.42	1.033	24.39	1.5349	22.59	1.4216
Overall mortality rate, ‰	3.64	0.492	3.89	0.5257	15.87	2.145	10.42	1.4081	15.56	2.1027
Infant mortality, ‰	0.70	0.212	0.80	0.2424	0.70	0.212	2.70	0.8182	3.00	0.9091
Divorce rate, ‰	19.80	1.347	21.80	1.483	18.30	1.245	25.00	1.7007	25.70	1.7483
Integrated estimate		0.707		0.660		0.618		0.402		0.363

Note. *Calculated according to the data of State Statistics Committee of Ukraine tive women in the overall population, share of people aged 0–14 in the overall population, marriage rate; among «negative» are ageing level, overall mortality rate, infant mortality rate, divorce rate) as an integral assessment of the demographic state showed that in 2016 the demographic situation in the Olevsk district of Zhytomyr Oblast ($p = 0.947$) was the closest to national one, which is due to similar values of the share of reproductive women (deviation – minus 0.2 percentage points) and marriage rate (minus 0.1 promille points), significantly higher coefficients of the total birth rate (+3.1 promille points), special birth rate (+17.3 promille points), fertility of women aged 20–29 (+32.7 promille points), share of people aged 0–14 in the overall population (+5.2 percentage points), lower share of people over 65 years (minus 3.9 percentage points) and divorce rates (minus 2.9 promille points), general mortality (minus 2.8 promille points) and lower infant mortality rate (minus 3.9 promille points).

The best situation was in Rokytne ($p = 1.249$) and Sarny ($p = 1.112$) districts of the Rivne Oblast. The positive deviation is due to both high fertility rates for women aged 20–29 and other age groups, marriage rates, share of women of active childbearing age (20–29 years) and share of the population aged 0–14 years, and the lowest share of the population over 65 years and divorce rates, total and infant mortality. The combination of the above parameters explains the highest values of the integral assessment.

However, in the Kozelets district, six out of seven «positive» parameters have the lowest values among all studied areas with the highest coefficients of total mortality and infant mortality, share of people over 65 years in the population, which led to the lowest integral assessment value ($p = 0.363$). The situation is similar in the Ripky district ($p = 0.402$), where high percentages of the population older than working age, high rates of total and infant mortality reduce positive deviations resulted from a higher share of women aged 20–29 in the reproductive contingent of women and lower divorce rates.

Such districts as Poliske, Narodychi, Ovruch, Ivankiv and Korosten occupy an intermediate place in comparison with the districts of Rivne and Chernihiv Oblasts ($p = 0.618$–0.742). However, having almost the same values, the share of children aged 0–14 in the population (deviation from the national average from minus 0.1 to +3.0 percentage points), share of women of reproductive age in the population (from minus 2.7 to +3.6 percentage points), share of women aged 20–29 years in the reproductive contingent of women (from +0.7 to +4.8 percentage points), total birth rate (from minus 1.3 to + 0.7 percentage points) they have significantly lower divorce rates (0.1–0.8 ‰ for the RCT compared to 3.3 ‰ for the country), lower marriage rates (from +2.7 to +5.0 ‰ for the RCT compared to 5.4 ‰ for the country) and higher special birth rate (from +0.8 to 8.8 promille points; with the exception of Ovruch district – minus 0.1 promille points), fertility rates for women aged 20-29 (from +3.3 to 15.5 promille points; the exception is Ivankiv district – minus 13.6 promille points) and total mortality (from +3.6 to 7.1 promille points) and share of people aged over 65 (from +0.5 to 6.0 promille points).

The studied areas of Ukrainian Polissya differ significantly: both in number and variability of values of other medical and demographic indicators; both among themselves and in comparison with the data for the whole country. However, if in the first years after the Chornobyl accident its impact on population health was not recognized, then modern medical, demographic and epidemiological studies confirm the presence of changes in the health of both certain categories of affected and residents of the most radioactively contaminated territories.

5. SOCIO-PSYCHOLOGICAL STATUS OF POPULATION LIVING ON RADIOLOGICALLY CONTAMINATED TERRITORIES

The socio-psychological consequences of the Chornobyl disaster in a context of thirty-five years of changes in Ukrainian society have significantly affected the social well-being of population living on radiologically contaminated territories (RCT). Imperfection of the legal framework for social protection and drawbacks in medical and psychological rehabilitation have accentuated the perception by the affected population of social and political changes taking place in the country. The stated above influenced the formation of social well-being, social activity and health of population [1–5].

Review of social well-being parameters with the use of factor analysis approach highlighted the groups of social needs that make greatest impact on the formation of integrated index of social well-being in RCT population. If in 1999 and 2005 there was prevalent a factor in which the main burdens were formed by socio-political and legal guarantees (socio-political, social security, social relations spheres; contribution of all features to the variance was 38.3 % and 22.60 %, respectively), then in 2013 the utmost factor (27.24 %) was formed due to material, professional-occupational, recreational-cultural, and information-cultural spheres. The social well-being of RCT population featured a steady trend to improve and in 2013 did not differ significantly from the social well-being of population of nominally clean territories (NCT). At run-time over the years there was a significant decrease ($p \leq 0.05$) in the number of respondents on RCT with an average level of integrated index of social well-being and an increase of those with enhanced and high level ($p \leq 0.05$). Improvement of social well-being over time indicates a gradual return of RCT population to the active life and ability to solve the essential vital problems [6, 7].

During 2013–2018 the socio-economic problems of the country, «exacerbated by the Chornobyl syndrome» were characteristic for the RCT population. Financial problem was the key one for majority of population in the studied areas. Low salaries along with growing household spendings and lack of additional earnings increase the level of social strain. The greatest dissatisfaction of RCT population in 2015 was in the socio-political sphere and sphere of social security.

The nation-wide employment issues were found also characteristic for the study area according to research in 2016–2018. The working population appreciates employment, despite low salaries. First of all, this is due to the low assessment of opportunities to get a job both in the region, in the country as a whole, and abroad. Estimates of employment opportunities in Ukraine and abroad ($r = 0.285$; $p \leq 0.01$) are increasing in the younger and middle age groups. Position of protection against unemployment received the worst assessment of population (45.6 points on a 100-point scale).

The level of well-being was estimated by population mainly as average (59.39 points). There was a significant difference between rural and urban population in terms of expenses and ability to meet their needs. Rural population satisfied only the needs related to material and household sphere of the first level, while some items of expenditure that go beyond the primary ones are excluded from the list at all. The best estimates of well-being among urban population were in the groups of young and middle age ($r = 0.307$; $p \leq 0.01$). Dependence on the level of education was revealed at that ($r = 0.269$; $p \leq 0.01$). There were also more optimists about improving the level of well-being among younger population ($r = 0.241$; $p \leq 0.01$).

Estimations of quality of life, according to the indices of security and safety, were 56.08 and 52.94 points (city and village, respectively) (Table 5.1). Among citizens it varied depending on the age of respondent and his/her well-being, while in rural population there was a significant dependence only on the level of well-being (r = 0.299; $p \leq 0.05$). Social protection for the persons with low income featured, firstly, the provision of social assistance to reimburse the costs of housing and communal services. Since 2015 the number of donated households increased 8.4 times in villages and 3.7 times in cities. However in 2016 the number of families receiving subsidies in rural areas decreased from 5,095 to 1,307, which is most likely due to an imperfect social assistance mechanism.

The state of environmental protection and human health were estimated at low scores among both urban and rural populations (55.8 and 47.8 points, respectively). Investments in the environment protection are increasing, but it is more about current expenditures rather than capital investments. Environmental research is in a broad sense excluded from the items of capital investment expenditures, which clearly has negative impact on ecological state of the region.

Medical provision was the factor influencing socio-psychological state of population. Issue of the public health service, according to the studied parameters, was estimated below average in the scope of possibility to buy pharmaceutical drugs, receiving medical care in rural areas, availability of healthcare specialists by profile, preventive work among children and adults. Availability of medical treatment for the affected population significantly depended on its financial capacity [8]. Lack of the required healthcare specialists, poor provision with diagnostic equipment (including doctors' offices in clinics) and necessary medicines utmost give rise to the complaints of population. Insufficient funding for the targeted medical examinations of people living on RCT, imperfect social security, and insufficient media coverage of the experience of medical professionals in health consequences of the Chornobyl Nuclear Power Plant (ChNPP) accident had a significant impact on reducing the efficiency of healthcare. According to experts the decentralization of funding from different ministries, misuse of funds, and lack of proper control by the state over the targeted use of funds were the main organizational shortcomings there [9].

The democratic system in the opinion of surveyed population was only declarative in nature with no positive development in all, without exception, branches of government and in providing any real freedoms to citizens. The satisfaction level was below average. Assessment of central authorities depended on the level of well-being and age of the respondent.

Integral indicator of the quality of life of RCT population was within average values (41–60 points). Level of satisfaction with the spheres of life (well-being, environment, democratic governance) among the urban population was significantly higher than in rural areas.

The quality of life of RCT population and factors influencing its formation fully reflected the processes taking place in the country (according to the Institute of Sociology, NASU), but differed in the hierarchy of negative components that shape them. Spheres of well-being and RCT environment were rated by population significantly lower [10].

Table 5.1
Average values of quality of life in urban and rural population of the NPP surveillance zone by spheres (in score points)

Spheres of assessment of quality of life	Urban population		Rural population	
	M±m	Rank	M±m	Rank
Health	56.63 ± 1.15	3	55.72 ± 1.26	6
Well-being	58.69 ± 1.32*	4	53.44 ± 2.06	3
Employment	59.31 ± 1.07	5	62.21 ± 2.42	7
Education	69.55 ± 0.86	8	68.73 ± 2.28	9
Housing	73.16 ± 1.22**	9	66.95 ± 1.66	8
Social life engagement	61.39 ± 1.01*	6	55.35 ± 1.79	5
Environment	66.91± 0.98**	7	54.41 ± 1.56	4
Democratic governing	45.41± 1.07	1	44.39 ± 1.95	1
Safety	56.08 ± 0.82*	2	52.94 ± 1.17	2

Notes. *Statistically significant difference ($p \leq 0.05$) between urban and rural population; **statistically significant difference ($p \leq 0.01$) between urban and rural population; NPP – nuclear power plant

Hierarchy of life values of the RCT population did not change over time remaining in the sequence of «health», «children», and «family well-being». The value of «family well-being» was related to a person's dominant need to create a comfortable microenvironment around him. The high value of «health» was not a feature of the population living under environmentally unsafe conditions, but was inherent to the majority of population as a way of survival. At the same time, the population's attitudes towards the value of health were gradually increasing [7].

Issue of public perception of radiation risk held a valuable place in the structure of social and psychological consequences of the ChNPP accident [11-15]. The risk situation that developed on RCT in 1986-1991 was due to a real risk factor of radionuclide contamination. It was characterized by a high level of public concern for their health and health of children and relatives due to the possible effects of ionizing radiation. In 1992–1994 there was a decrease in the number of respondents who considered the radiation situation dangerous to health, with a further tendency to its increase in 1997, and gradual decrease later. Increase in the headcount of this group was not due to deterioration of radiation situation, but to the sharp economic changes in the country.

Over time of 1999–2013 the number of respondents who considered the radiation situation at the place of residence being dangerous to health decreased. The calculated index of danger to public health in 2005 was 0.10, in 2010 – 0.16, in 2013 – 0.38 (with the optimal value of 1; scale from minus 1 to +1, where value 1 means no danger to health). In population of the NCT it was 0.32; 0.33 and 0.57, respectively [16].

In 2016-2018 the majority of population of zones 3 and 4 (64.4 %) of RCT assessed the ecological situation at the place of residence as «relatively favorable». According to population estimates, the radiation pollution of territories as a result of the ChNPP accident was a leading factor determining the ecological situation (4.2 points on a 5-point scale). Other factors were ranked at lower scores. Among them, the first place continued to be occupied by the NPP operation, namely the consequences of NPP function – 3.7 points, pollution from agricultural activities – 3.1 points, environmental pollution from industrial emissions – 2.8 points.

The state of mental well-being of RCT population over time of the post-accident period (1993–2005) differed significantly from the NCT population. After 2005 (2006–2013) the mean overall GHQ 28 index (characterizing the depth of minor mental disorders), mean ratings on scales of somatization, anxiety, social dysfunction, depression, and the situational anxiety index according to Spielberger Inventory were within the control (acceptable) values (Fig. 5.1).

Review of the GHQ 28 data structure by scales showed the somatization one being most relevant, taking the first place in the structure during the studied post-accident period (1993–2018). The alarm scale ranked second until 1995 and third upon. Since 1995 the socio-economic problems dominated in population, bringing to the second place a social component, namely the social dysfunction, as indicated by sociological research [17]. Somatization index, characterizing the state of somatic health, correlated at an average level with the rank of anxiety (r = 0.644; $p \leq 0.01$) and social dysfunction (r = 0.342; $p \leq 0.01$). Average ratings on scales of somatization and anxiety over time of 2005–2013 were slightly higher compared to those in NCT population.

The state of mental well-being of RCT population according to the GHQ 28 and Spielberger Inventory over time of 2016–2018 were within acceptable ranges, but significantly differed in urban and rural population (Table 5.2). Average ratings of somatization and anxiety were significantly higher in rural population compared to the urban one. Average ratings of social dysfunction and depression were close in values in urban and rural populations. Structure of the GHQ 28 scales was the same as in previous years, i.e., in the sequence of somatization, social dysfunction, anxiety, and depression. The reviewed parameters were different depending on gender, namely in females being higher than in males. There was a trend to increase of the measured mental health parameters in population at the age from 20 to 54. At the age of 60 and older both the GHQ 28 total score and ratings by scales were lower compared to other age groups. Regarding the hierarchy of average scales, in the age groups of 20–29 and 30–39 the first place was occupied by social dysfunction scale, in contrast to other groups, where somatization scale was at the first place. The latter indicated the predominance of social factors in the life of these groups. The State-Trait Anxiety Inventory (STAI) score (by C.D. Spielberger) was close to the level in

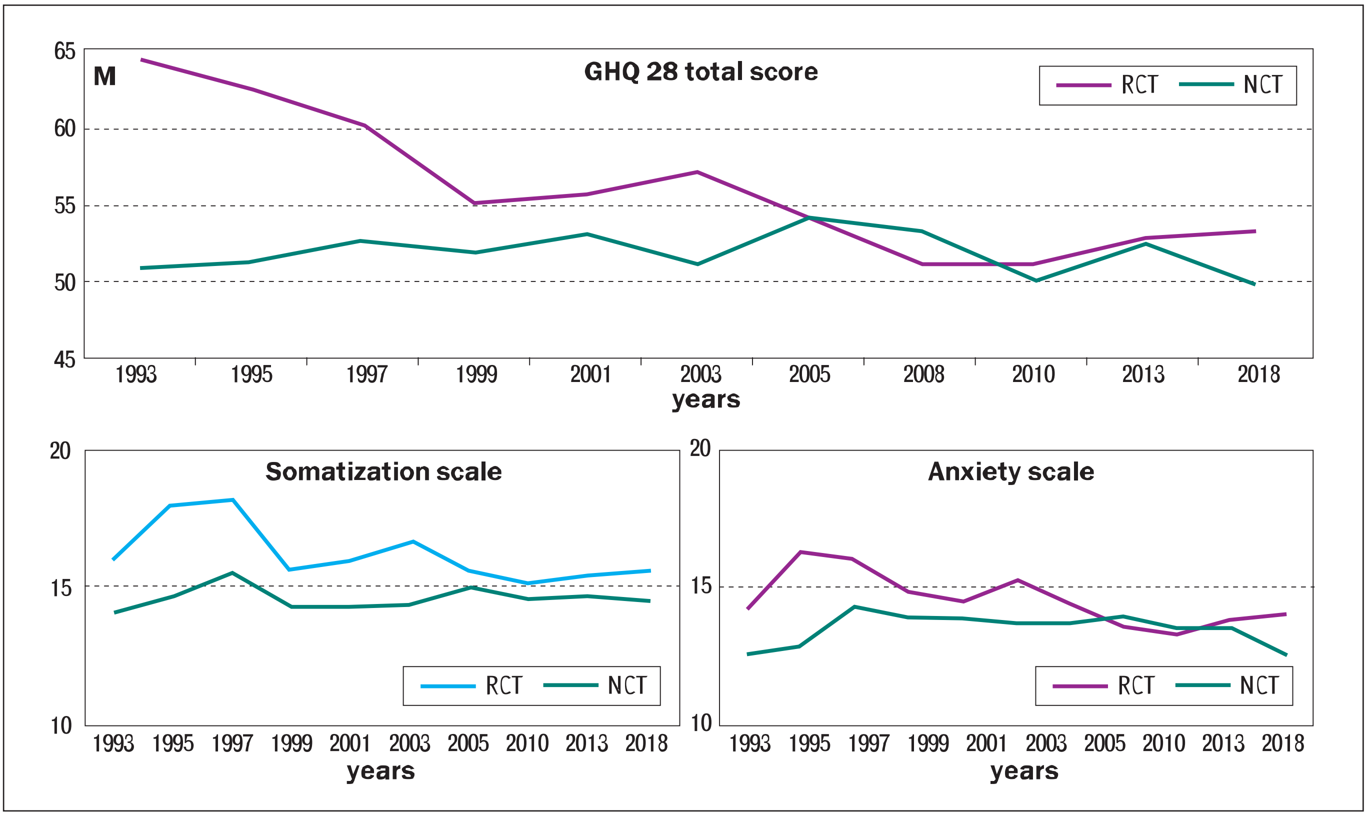

Figure 5.1. **Average ratings on somatization and anxiety scales and GHQ 28 total score in RCT and NCT populations over time**

Table 5.2
Average parameters of mental state in urban and rural population in surveillance zone (GHQ 28 scores)

Scores	Urban population			Rural population		
	males	females	all	males	females	all
Total	48.46 ± 1.14	54.80 ± 1.04	52.48 ± 0.81	50.39 ± 1.25	58.63 ± 1.72	54.66 ± 1.20
Somatization	13.38 ± 0.48*	16.45 ± 0.39	15.33 ± 0.32	14.89 ± 0.52	17.47 ± 0.62	16.22 ± 0.44
Anxiety	12.89 ± 0.49	14.32 ± 0.40**	13.80 ± 0.32***	12.71 ± 0.60	16.47 ± 0.70	14.66 ± 0.21
Social dysfunction	14.24 ± 0.33	15.31 ± 0.26	14.92 ± 0.21	13.89 ± 0.41	15.97 ± 0.83	14.97 ± 0.49
Depression	7.95 ± 0.22	8.72 ± 0.26	8.44 ± 0.18	8.89 ± 0.71	8.73 ± 0.45	8.81 ± 1.20

Notes. *Statistically significant difference ($p \leq 0.05$) between scores in urban and rural male population; *statistically significant difference ($p \leq 0.05$) between scores in urban and rural female population; ***statistically significant difference ($p \leq 0.05$) between scores in urban and rural population.

control population (12.34 ± 0.19; 12.04 ± 0.4, respectively). Higher average STAI scores were observed in persons with secondary education compared to the secondary special and higher school graduates (13.04 ± 0.56; 12.90 ± 0.33 and 11.83 ± 0.26, respectively) [18].

The most general trend over time of 1993–2018 characterizing a somatic well-being of people living on RCT was a reduced self-esteem of health compared to NCT population. The self-assessed health (SAH) index at runtime indicated the general trend of health deterioration since 1986 till 1997 (Fig. 5.2).

A two-peak curve was specific for RCT population with the maximum number of «sick» and «very sick» estimates in timeline of 1991, 1995, 1997, when the SAH indices were 0.43, 0.22, and 0.21, respectively.

There was a strong trend of somatic health improving in RCT population within 1997–2013 period. Over time of 2013–2018 there was a health deterioration of population according to the self-assessments. The SAH index in urban population in 2013 was 0.85, while in 2018 being 0.69. The SAH index of rural population was 0.74 and 0.55 in 2013 and 2018, respectively. We observed similar values throughout the post-accident period on the NCT. The self-assessment indices in males were higher compared to females (from 0.84 to 0.53). The SAH indices in population of the NPP surveillance zone decreased with age from 0.91 (20–29 years) to 0.25 (over 60 years).

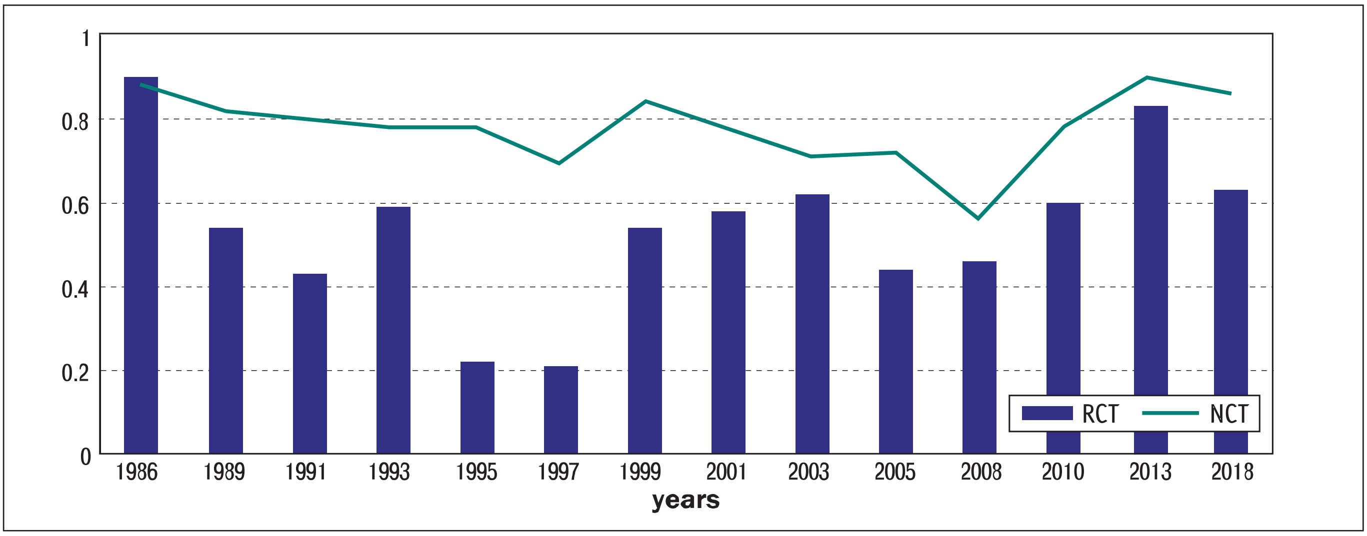

Figure 5.2. **Somatic health indices by self-assessment over time in RCT and NCT population**

Results of the conducted study showed a correlation of the somatic and mental health with factors characterizing quality of life in RCT population, namely the well-being ($r = 0.408$; $p \leq 0.01$), environment ($r = 0.311$; $p \leq 0.01$), security ($r = 0.299$; $p \leq 0.01$), democratic governance ($r = 0.272$; $p \leq 0.01$), etc. Correlation between the overall mental health index and integrated quality of life index in rural population vs. urban was higher ($r = 0.514$; $p \leq 0.01$ and $r = 0.320$; $p \leq 0.01$, respectively). The highest correlation coefficients of the GHQ 28 total score, somatization and anxiety scale scores with quality of life assessment components were in rural population compared to urban one. There were significant correlations between social dysfunction and well-being, state of the environment, expectations of change and quality of life in general in the urban population.

Social wellness, both with mental and somatic well-being were determined by the socio-economic and socio-political situation in the country. In resolving the social and health problems within consequences of the Chornobyl catastrophe the Ukrainian Parliament for a long time did not adopt any conceptually new changes to the legal framework on this issue, but only circumscribed the operation of a large number of articles of existing laws adopted in 1991. Now the coordinated actions of the Cabinet of Ministers and the Parliament of Ukraine are required to improve the situation. The state measures and means aimed at preserving and improving the health of population should be focused at optimization of legal and regulatory framework of the Chornobyl accident clean-up and recovery operations.

The main directions of advancing the health care system for the RCT population are: improving the financing level of primary healthcare, purchase of medical and diagnostic equipment, addressing the issue of staffing of doctors and paramedics, purchase of medicines, forming of understanding by RCT population of the need for systematic health monitoring with a real understanding of the value of health but not its declaration, informing the population about peculiarities of behavior and living on RCT. The current system of benefits and exemption practice does not fulfill most of the tasks assigned to it and needs to be revised.

6. EXPERIMENTAL SIMULATION OF THE CHORNOBYL DISASTER EFFECTS ON HUMANS

After the Chornobyl disaster the attention of specialists, among other, was focused on the issues of radiobiology and radiation medicine, within which the research into mechanisms of low-dose radiation effects, joint effects of ionizing radiation with other factors of the physical, chemical or biological nature, as well as the search and testing of tools with radioprotective and radiomodifying properties have become particularly relevant.

Numerous new data obtained in radiobiological studies of the radiation accident consequences forced to revise some paradigms in radiobiology and prompted the formulation of new paradigms. Radioadaptation, induction of genomic instability, loss of the ability of irradiated cells to adequately perceive positional information, cumulative nature of radiation dose impact under chronic exposure, and non-equivalence of external and internal irradiation were outlined among the key radiobiological effects that affect the content of paradigms. Since the reflection of radiation damage in the form of long-term epigenetic changes or the accumulation and delay of implementation of hidden radiation damage in the sequence of cell generations is a convincingly proven fact, the issue of dose calculating under chronic exposure, as well as transgenerational radiation effects, have been outlined [1].

Issues of biological effectiveness and mechanisms of the influence of low-dose ionizing radiation (IR) on the human organism are attributed to the most urgent radiobiological problems. For a long time, there was no generally accepted opinion about the reality of just the existence of such an effect, while among researchers who recognize the biological effectiveness of low-dose IR there was no common opinion about the mechanisms of its action.

Results of experimental research conducted after the ChNPP accident significantly contributed to the revision of some paradigms in radiobiology, and mechanisms of low-dose radiation effects in particular [2].

Simulation of radiobiological effects under the impact of low-intensity X-ray and gamma-radiation

Action of IR on living beings initiates the biological effects of various magnitudes and duration, localized in certain structures, systems, or organism as a whole. Over time, the realization of biological effects can occur immediately upon exposure to IR, in the long term, or in the generations of descendants of irradiated parents. The etiology and pathogenesis of specific late consequences of exposure to IR significantly depend on radiosensitivity, state of the organism and its individual systems, individual characteristics and living conditions. These main and many other factors are extremely difficult to take into account, so researchers, as a rule, analyze the statistically averaged stochastic or deterministic effects. At the same time, the assessment of early response to the IR exposure has certain advantages in terms of fundamental knowledge of the nature of radiation-induced disorders. In this field, a number of experiments were carried out to determine the regularities of radiobiological effects under the impact of low-intensity X-ray and γ-radiation. A comparative characterization of these effects in a wide dose range, including the low-doses of IR, was provided [3, 4].

The «dose–time–effect» dependence was determined by means of a comparative evaluation of radiation-induced changes in the content of lipids, lipoproteins and the intensity of lipid peroxidation (LPO) in the blood of laboratory rats after single, fractionated, and long-term irradiation with γ-quanta from ^{60}Co in the dose range of 0.1–6.0 Gy. It was found that irradiation of rats in different mode leads to specific features of the time patterns and dose dependence of radiogenic changes in the content of blood plasma lipids. It has been shown that fractional irradiation is more sparing for the body, and long-term exposure causes significantly greater radiation-induced changes than a single exposure to IR. At different stages of development of the body's reaction, the parameters of lipid content under investigation showed different sensitivity to the certain doses and regimes of irradiation. This indicates that at different stages of the body's reaction its individual components can participate in LPO at different rate [5].

Intensification of LPO as a result of irradiation in moderate and high doses is defined as a classic sign of radiation disorders. The LPO in blood under irradiation in low doses was noted by the majority of researchers, however, data on the activation in other organs and tissues are somewhat contradictory.

Results of an experimental study on the effect of prolonged low-intensity irradiation on the lipid-lipoprotein spectrum, state of LPO and antioxidant protection (AOP) system of blood plasma and liver of rats indicated the development of a long-term hypolipidemic effect due to the prolonged γ-irradiation at a total dose of 1.0 Gy. Decrease in the LDL/HDL ratio by 50 % as a result of prolonged γ-irradiation in low doses confirmed the possibility of a radiation modification of physicochemical properties of lipoproteins, capable of changing the serum and liver tissue lipoprotein spectrum with no additional impact [6].

Study of biochemical changes in the brain of rats (LPO parameters, content of biologically active compounds, structural and functional state of the brain cell nuclei chromatin) in the time course of observation during 1 month after a single total external γ-irradiation at a dose of 1.0 Gy showed the significant changes in organization of interphase chromatin of brain cell nuclei according to the DNA and histone H1 content in the chromatin fractions. Its decondensation was noted, which may cause a nonspecific expression of the genome. These processes were correlated with dynamic fluctuations in the activity and properties of histone-specific proteinases, which was probably a consequence of the studied processes [7].

Discoordination was identified in the isoenzyme spectrum of a number of enzymes (esterase, lactate dehydrogenase, malate dehydrogenase, and acid phosphatase), at that the recovery of the content of some isoforms does not occur even in the long-term observation period. Thus, the occurrence of significant changes in the structural organization of chromatin of the brain cell nuclei under irradiation at a relatively low dose may indicate the vulnerability of genome in postmitotic cells to IR in low levels of exposure [8].

Cytogenetic analysis of rat bone marrow stem cells on the 30th day upon total X-ray exposure in different doses showed that the number of cells with unstable chromosomal aberrations in cases of 0.1, 1.0, and 5.0 Gy dose was 1.88 %, 2.75 %, and 8.37 %, respectively (0.85 % in the control). Difference in the case of irradiation at a dose of 0.1 Gy was unreliable. It is believed that the replicative instability, caused by a disorder of normal mutation code, as a result of which chromosomes acquire the ability to be highly mutatable during hundreds of subsequent generations, is the reason for appearance of unstable chromosomal mutations in the long term. When IR affects cells that are at rest, the damage to chromosomal apparatus is not restored due to the very weak ability to repair in many types of stem cells, while failure to enter the mitosis does not give an opportunity to be realized in a chromosomal mutation. Thus, both individual cells and groups of cells can exist in bone marrow for a long time, the recovery of which from radiation damage or its realization into chromosomal aberrations does not occur [9].

Simulation of the effects of radiation exposure on hematopoiesis was carried out in a unique experiment. Lifetime observations were made of the growth of cultures of lymph nodes and thymus of experimental animals under conditions of the total X-ray irradiation in 0.3, 0.5, 1.0, and 2.0 Gy dose using the time-lapse microcinematography imaging method. The use of emperipolesis as a model for studying the IR effect on interaction of cells significantly expanded the understanding of mechanism of action of microenvironment on hematopoiesis, which opens up prospects for finding ways of rational influence on hematopoietic system of an irradiated organism [10].

Numerous experimental studies on animals have shown that there is no single and unidirectional effect of IR (one-time total X-ray and γ-radiation) on the structure and function of immune system. The first working classification of immune disorders in irradiated organism in the dose range of 0–8 Gy was created. It was determined that, depending on the IR dose, both reversible and irreversible changes in the functional activity of immune system develop in mice. Just irreversible changes can be considered the manifestations of secondary post-radiation immunodeficiency, the first signs of which appear in animals starting with IR doses of 2–3 Gy, which depends on radiosensitivity of mice lines and, probably, on genetic determinism. The conducted experiments showed that the post-radiation structural and functional changes of immune system depending on radiation dose are complex in nature, and the formation of immune response cannot be considered from the standpoint of linear dependence of the effect on the IR dose [11].

Different biological effectiveness of local (cerebral) X-ray irradiation in the pituitary-gonadal system, depending on the dose and mode of irradiation, was experimentally confirmed [12].

Morphofunctional abnormalities in the hormone-producing cells of the ovary and adenohypophysis of female rats in the late period upon single total external γ-irradiation at a dose of 1.0 Gy, depending on puberty period at the time of irradiation, were determined. Results of the electron microscopic and morphometric study of theca cells and FSH-gonadotropocytes indicated a decrease in protein synthesis, and also in energy- and hormone-producing functions by 1.5–2.0 times (vs. control) in sexually immature female rats one month after irradiation, and by almost three times in adult female animals of the early reproductive age. The experimental study data confirm the results of clinical-epidemiological and clinical-laboratory observations regarding features of the development of post-radiation hormonal disorders depending on the received dose and age at the time of irradiation [13].

Relationship between the exposure dose and exposure time on ovulation and superovulation was revealed. A comparative assessment was conducted of disorders of the oocyte functions caused by both direct and indirect impact of X-ray radiation in a wide range of doses from 0.5 to 2.0 Gy of total irradiation and from 0.5 to 10.0 Gy of local irradiation of the pelvis and head. It was established that with total irradiation at a dose of 0.5 Gy and local irradiation of the head at a dose of 5.0 Gy there was observed a radiostimulating effect of the quantitative output of viable oocytes II. A comparative review of the influence of exposure time and IR dose on distribution of the living and dead cells by different types was carried out, which prompted identification of the most damaging regime of IR irradiation of animals [14].

Role of the dose and mode of irradiation on fluctuations in the level of gonadotropic hormones in the post-irradiation period was studied. Study of the IR effects on the formation of offspring revealed a stimulating effect of IR on the number of offspring. Significant increase in the number of viable offspring occurred upon irradiation at a dose of 0.5 Gy. Study of the survival of isolated oocytes revealed a rather high their radioresistance to IR [15].

In experimental simulation of the Chornobyl disaster a special attention was paid to the study of radiobiological effects due to the incorporation of radionuclides, primarily ^{137}Cs. Review of the results of previous studies showed that the use of radiation sources with different quanta energy had caused different effects under equal dose load, which prompted us to investigate the effects of a one-time total exposure to IR with different quanta energy under the same absorbed dose (5.0 Gy) on oxidative phosphorylation in the liver of experimental animals. The soft X-ray radiation with a 0.095 MeV energy, γ-radiation from radioactive ^{137}Cs with a 0.66 MeV energy, and γ-radiation from radioactive ^{60}Co with a of 1.25 MeV were administered. X-ray radiation and γ-quanta from ^{137}Cs and ^{60}Co caused a reactive response in respiratory chain of mitochondria, consisting of phases of stimulation and inhibition of the oxidative phosphorylation. The higher the energy of IR quanta, the faster interphase transition occurred. Stimulation of the speed parameters in case of irradiation with γ-quanta from ^{60}Co significantly exceeded the changes occurring when ^{137}Cs was used. That is why the energy exhaustion of mitochondria was observed already one month after irradiation, as a result of which the rates of respiration processed were decreased in all metabolic states. At the same time, it was possible to observe the development of restorative processes in liver. It was established that under the conditions of this experiment the post-radiation changes in the indices of oxidative phosphorylation were reversible and not interfering with recovery processes [16].

Prenatal irradiation of rats by the incorporated radionuclide ^{137}Cs with an activity of 60 Bq per animal was carried out by administering the isotope on the 6th and 16th days of gestation. The accumulated radiation dose in the range of 0.5–1.0 cGy caused some changes (increased excitability) in behavioral reactions, which were determined even on the 4th month of the animals' life. Greater expressiveness of the changes was evident in animals irradiated on the 16th day of gestation, which corresponded to especial radiosensitivity of the central nervous system at the later stages of its intrauterine development [17].

Simulating the combined effects of the radiation accident factors

Numerous data were obtained in previous studies on the oxidative modification of plasma membrane lipids through the intensification of free radical reactions under the IR exposure, including the low-intensity irradiation in low doses and combined impact of IR with various factors of physical, chemical, and biological nature [18].

A comprehensive approach in the study of biological effects low-dose IR provides an opportunity to assess the biological feasibility of changes occurring at the membrane level featuring the processes of oxidative phosphorylation (OPh) (cells, exoergic reactions) and the processes of removal of xenobiotics and radionuclides (liver, body, endoergic reactions), which can serve an example of a radiobiological experiment planned according to the multilevel principle. It was established that previous (in relation to other experimental influences) single external irradiation (from the ^{60}Co source) had caused a non-specific activation in rats, which lead to accelerated elimination of xenobiotics (tetrachloroethane, nembutal) and ^{137}Cs radionuclides from the body. The functional strain of biological structures that affect the accelerated removal of ^{137}Cs, tetrachloroethane, and nembutal is provided with energy due to activation of the OPh at the succinate oxidase site of respiratory chain in mitochondria in the tissues of irradiated rats. The one-time external irradiation at a dose of 50 cGy (from the ^{60}Co source) had caused the adaptive changes in rats increasing body's resistance to subsequent exposure to higher doses of radiation and intensity of other factors. The conducted studies proved a fundamental possibility of using the one-time external irradiation at a dose of 50 cGy (^{60}Co source) in the cross-adaptation scheme [19].

In the selected model of experimental research, which is as close as possible to the conditions of an emergency situation, when external exposure precedes internal one, it was shown that the previous single external γ-irradiation modifies the kinetics of ^{137}Cs in the body of rats and specific organs and tissues, which depended on the absorbed dose of external exposure. Namely, the external exposure in a dose of 0.5 Gy accelerated the removal of ^{137}Cs (1.85 MBq/kg), reduced the effective half-life of radionuclide, significantly reducing the absorbed internal radiation doses. At the same time, it was established that previous external irradiation of animals in a dose of 1.0 Gy did not reliably affect the kinetics of ^{137}Cs (1.85 MBq/kg). Probably, irradiation in a dose of 1.0 Gy instead of a stimulating effect exacerbated the damage of cellular membranes, supresing the transmembrane ion fluxes, which reduced the rate of removal of radioactive cesium from the body [20].

According to hematological parameters, the combined external (0.5; 1.0 Gy) and internal (the ^{137}Cs source, 1.85 MBq/kg activity) irradiation had led to the more pronounced changes compared to the individual impact of radiation factors. In the range of low and medium doses, the internal irradiation was of a dominant role, suppressing the recovery of hematopoiesis [21].

It is known that in case of accidental exposure its effect on the body, in particular on the central nervous system, is most often combined with the impact of a number of different stressors. Such a combined impact leads to a somewhat uncertainty of the final effect, which was clearly manifested in the health consequences of the Chornobyl NPP accident. The matter was that the severity of consequences at relatively low radiation doses did not correspond to the expected responses, i.e., the psychoneurological disorders in persons, who were exposed to a complex of accidental factors, today still remains an important medical and socio-economic problem. Possibilities of determining the significance of radiation and non-radiation factors and interaction of their effects based on the dosimetry and clinical studies' data are quite limited. However, at least some key questions can be clarified in a model experiment taking into account the actual exposure dose and stress burden.

Dependence of the response of parameters of the conditioned reflex behavior in rats to non-radiation stress (footshock) on the level of previous irradiation at doses of 0.5, 1.0, 3.0, and 6.0 Gy was studied. Changes in behavioral reactions (shuttlebox and Skinner box settings) in the single totally γ-irradiated and non-irradiated rats, that were stressed (footshock), evidenced that the reactions to stress based on parameters of a conditioned reflex behavior were generally characterized by a direct stimulatory effect, which in the period after stress can evolve to depression. Changes in response to the stress detected in irradiated rats were nonlinearly dependent on the dose of previous irradiation featuring a slight increase in a dose of 0.5 Gy, significant increase in 1.0 Gy, slight decrease in 3.0 Gy, and significant decrease (to the level in the control) in 6.0 Gy.

According to the regression analysis results at the irradiation in doses of 1.0, 3.0, and 6.0 Gy, a probable interaction was found between the radiation impact and non-radiation stress [22].

Study of the interaction patterns of the impact of γ-irradiation and emotional-pain stress showed that the reaction of the higher nervous activity of rats to the combined influence of IR and stress was not additive characterizing a reliable interaction of the effects of both specified factors. Irradiation in doses of 0.5 Gy and 1.0 Gy and the applied emotional pain stress caused the unidirectional changes in higher nervous activity, while their interaction has had the opposite effect. It should be noted that the extrapolation to the humans of dose values used in the experiment (with all limitations and ambiguity of direct extrapolation), for example based on the known LD_{50} values, gives levels two to three times lower. With this approach, doses of 0.5 Gy and 1.0 Gy correspond to the human doses of 0.2–0.5 Gy, i.e., the level of exposure that was mostly experienced by the ChNPP accident clean-up workers [23].

Summarization of the results of years-long experimental research and observations of health in people who work with IR sources allow us to consider the lability of regulatory systems under conditions of relatively low-dose total radiation as adaptation-adaptive response, and to characterize the effects of high radiation burden as a narrowing of the range of adaptive responses due to disorders in neurohumoral regulation of the functions of irradiated organism up to the exhaustion of their reserves.

The functioning pattern of hypothalamic-pituitary-adrenal and sympathoadrenal systems (HPAS and SAS, respectively) under the impact of low-dose IR have been determined. The phasic nature of changes in the rat HPAS and SAS as a result of single external total γ-irradiation (1.0 Gy), single (1.85 MBq/kg mass) and long-term (0.6 kBq/animal/day, 270 days) ^{137}Cs incorporation was revealed according to the morphofunctional characteristics of the secretory cells in hypothalamic paraventricular nuclei (PVN), adenohypophyseal corticotropic cells, adrenocorticocytes of the adrenal cortical layer and adrenocytes of the adrenal medulla, and concentration of hormones in blood serum. Nature of changes in the rat HPAS and SAS under the low-dose irradiation, depending on the type of exposure, dose, dose rate, and duration of exposure, was clarified [24].

Effects of incorporated ^{137}Cs (a radioisotope was administered in the dose of 600 Bq/animal daily for 1, 3, 6, and 9 months) and one-time total external irradiation with γ-rays from ^{137}Cs in doses of 0.1, 0.5, 1.0, 2.0, and 5.0 Gy on the serum level of hormones, activity of membrane enzymes, intensity of LPO in blood, endocrine organs and the liver, intensity of oxidative phosphorylation and activity of microsomal hydroxydases in liver, activity of catalase and hemoglobin content in erythrocytes, and acid resistance of erythrocyte membranes were studied. Significant morphofunctional changes due to the long-term administration of ^{137}Cs radioisotope in low doses were established. However, under these conditions, the stress reactions with corresponding stimulation of SAS did not occur. At the same time, the effect of external irradiation in the dose range of 0.1–5.0 Gy was characterized by typical signs of a stress reaction, i.e., activation of the pituitary-adrenal system, increased secretion of corticotropin, hypertrophy of adrenal cortex, and hypersecretion of corticosteroids. No clear dose-dependent changes however were detected in quantitative terms. Therefore, response of the body, as well as of the endocrine system to chronic incorporation of ^{137}Cs and to acute one-time external irradiation differed significantly. A discrepancy between a low-dose internal irradiation and the severity of morphofunctional changes in the studied organs was noted. This inconsistency was most evident in the pattern of liver detoxification. The obtained data indicate that the total biological effect of the ^{137}Cs-radioisotope incorporation consists in its impact as an emitter and interaction with cellular structures as a chemical element [24].

Given the fact that: a) in persons who were exposed to the complex of negative factors of the ChNPP accident the diseases of cardiovascular system are among the most prevalent health disorders; b) incorporated heavy metals play a significant role in health deterioration of survivors along with the consequences of exposure to IR; c) highly prevalent arterial hypertension is the leading factor in pathogenesis of coronary heart disease, being in many cases the main cause of disability and premature death, an experimental model was created to clarify the patterns of the formation of the effects of separate and combined impact of IR, cadmium and lead salts on the functional and morphological state of cardiovascular system. Effect of a single total γ-irradiation (in the dose range of 0.5–6.0 Gy) and incorporation of cadmium and/or lead salts on cardiovascular system in rats was studied separately and under a functional load by ischemia of the left kidney, which caused the development of arterial hypertension. The direction of LPO changes and the activity of antioxidant protection enzymes, structural and functional changes in cardiovascular system depending on the radiation dose, exposure to metals, their combined action, kidney ischemia, and observation period were determined. The combined effect of γ-irradiation, cadmium and lead exacerbated the sclerosis of the aorta, arteries and reduction of myocardial capillaries, which indicated the potentiation by salts of heavy metals of the damaging effect of IR on the elements of the vascular wall. At the same time, cardiomyocytes are secondarily involved in pathological process, which is initiated in the vessels and finalized with accelerated development of cardiosclerosis and arterial hypertension. The radiation-induced disturbances of microcirculation lead to degenerative-dystrophic changes followed by sclerosis of the stroma of organs of cardiovascular system, which can be attributed to the non-stochastic (deterministic) effects of IR [25].

Study of the effectiveness of administration of anti-radiation agents

Today, the classification of anti-radiation agents reflects the history of formation and current state of radiation pharmacology. Since the discovery of the «chemical protection» phenomenon against the harmful effects of radiation (Bacq Z., 1951) and within further development of radiation pharmacology, a number of classifications of anti-radiation agents have been proposed, which reflects certain stages of the formation of theoretical ideas about possible mechanisms of their action and the requirement of these drugs in medical practice [26]. According to contemporary classification [27], the anti-radiation agents are 1) radioprotectors («chemical protection» agents), i.e., the anti-radiation drugs of short-term effect exerting it at physicochemical and biochemical levels in the process of absorbing the IR energy; 2) «radiomitigators», i.e., long-acting anti-radiation drugs that realize their effect at the systemic level by accelerating the post-radiation recovery of radiosensitive tissues due to a number of patterns of the immune system; they are used, among others, as drugs for emergency therapy of radiation damage in early days after irradiation before the development of clinical manifestations of acute radiation damage; 3) radiomodulators («biological protection» agents) i.e., medicines and food additives that increase the body's resistance to adverse environmental factors; 4) medicinal products for protection against the incorporation of man-made radionuclides; 5) drugs that prevent manifestation of the primary reaction to IR.

Practical need in anti-radiation agents for the specific scenarios of radiation exposure and the corresponding tactical and technical requirements for medicinal products are the key aspects of classification of anti-radiation agents.

In the post-Chornobyl period, the main attention was paid to decorporants, adaptogens, and biological radioprotectors i.e., drugs of natural origin with various pharmacological effects. Since 1986, the staff of the Institute of Experimental Radiology of the NRCRM has investigated the effectiveness of about 45 drugs and food supplements used to correct the radiation effects [28, 29].

Study of the properties of various thymic humoral factors under the impact of IR made it possible to significantly expand the understanding of their role in the body and indications for their use in healthcare practice. In addition to immunotropic, they have other functions i.e., activate and regulate hematopoiesis, participate in regulation of adaptive growth of cells of various organs and tissues, stimulate glucocorticoid activity of adrenals, and directly or indirectly determine their function under stress. Additionally to this spectrum they exert radioprotective properties and possible antimutagenic action. All this opens up the prospect of a comprehensive approbation of thymic hormonal factors as anti-radiation drugs, e.g. as radioprotectors, as means of treatment of radiation injuries, as drugs for pathogenetic therapy of the consequences of acute and chronic effects of IR [11].

Possibility to correct the changes in the rat higher nervous activity after irradiation in doses of 0.05, 0.5, and 5.0 Gy was shown. Medication complexes of antioxidants of artificial and natural origin were used. The received results indirectly indicate the significant role of oxidative stress component of the radiation effects' pathways in the studied range of doses. It was established that the use of agents with antioxidant properties (α-tocopherol, ascorbic acid) in rats exposed to combined impact of the IR in doses of 0.5 Gy and 1.0 Gy and the emotional and pain stress not promoted the normalization of behavioral reactions, but led to the increasing damage of central nervous system [30].

Quercetin is effective in significant reducing of negative effects of γ-irradiation on the rat higher nervous activity if administered before irradiation and to a lesser extent – in the near term upon exposure. However, no improvement was achieved in the conditioned reflex behavior of rats in case of use in later terms. Under non-lethal doses of irradiation and under additional stress the disturbances of higher nervous activity in relatively later terms were primarily due to the deep and long-lasting changes caused by oxidant stress induced by irradiation [31].

Under the combined effect of external IR and stress, as well as with internal irradiation of animals due to the incorporation of ^{137}Cs, the correction of radiation-induced disorders is one of the measures to prevent the disturbances in hormonal regulation system. First of all it is feasible through the consumption of safe food products not contaminated with ^{137}Cs, as well as application of means reducing the ^{137}Cs body burden and supplementing the body with micro- and macroelements, vitamins and biologically active substances. Use of the biologically active food additive elamine, which reduces the accumulation of ^{137}Cs in the body, has membrane-stabilizing and antioxidant properties, is experimentally justified for the correction of radiation-induced disorders and changes induced by a stress factor in HPAS and SAS. Elamine administration normalized the serum concentration of hormones and contributed to normalization of the morphofunctional parameters of cellular organelles in secretory cells in hypothalamus, corticotropic cells in adenohypophysis, adrenocorticocytes in cortical layer, and adrenocytes of the medulla of adrenal glands [32].

The radiomodifying and antitoxic ability of polymineral substances of natural origin «Minerol» and «Benta» was established in the test system of the culture of proliferating cells of the L_{929} line under the combined impact of IR and incorporated heavy metals. Use of both products increased the cell survival in monolayer cultures by 1.5–2 times and cellular mitotic activity by 2–6 times while simultaneously reducing the number of atypical polykaryocytes. The studied substances can be recommended for use as preventive tools to reduce the negative effects of the combined action of IR and xenobiotics [33].

Despite the detection of radioprotective properties in a wide range of compounds of different origins, the search for biologically active substances capable of increasing the body's resistance to IR remains an urgent problem in terms of their use in the event of the radiation damage threat associated with radiation therapy of cancer patients, nuclear facility accidents or use of nuclear weapons.

Recently, much attention has been paid in the world scientific literature to the study of biological effects of endocannabinoids, which exhibit high biological and pharmacological activity and are capable of modulating many functions of the body. Special attention should be paid to the low-polar biologically active substances, namely N-acylethanolamines (NAE), which have cannabimimetic properties and are able to influence the biochemical processes underlying the pathogenesis of many diseases. Created at the Institute of Biochemistry named after A. V. Palladin of the National Academy of Sciences of Ukraine, a drug based on NAE with saturated chains N-stearoylethanolamine (NSE) is capable of inhibiting the tumor growth, increasing the activity of enzymes of antioxidant system and accumulation of LPO products.

It was established that the preliminary oral administration of NSE 50 mg/kg for 7 days to the rats totally single-irradiated in a dose of 6.0 Gy had prevented changes in the activity of key antioxidant enzymes (superoxide dismutase, catalase, glutathione peroxidase) and of the increase in serum concentration of TBC-active products [34].

When the dose of NSE was reduced to 10 mg/kg with the same administration regimen before and after a single total irradiation of animals in a dose of 6.0 Gy, its radioprotective properties remained according to the blood plasma concentration of TBA-active products, nitrite anion and catalase activity, although according to the peripheral blood assay a slowing down of recovery processes was observed [35].

The protective properties of NSE were also revealed when it was administered in a dose of 10 mg/kg of animal weight before and after the induction of emotional and painful stress. However, under the administration of NSE before the combined impact of IR in a dose of 6.0 Gy and stress, the radiosensitizing properties of the drug were manifested through the increase in concentration of TBC-active products and nitrite anion [34].

Thus, with further improvement of knowledge of proper doses and modes of administration the NSE may be useful as a preventive drug for mitigating the intensity of radiation damage and treatment in the early period upon irradiation, as well as a radiosensitizing agent during radiation therapy of cancer characteristic for the late period after radiation exposure [36].

Application of bioindication methods on cell culture

At the current stage of development of experimental science, there is an urgent need to use some alternative models and methods of scientific research, among which experiments in vitro, which include method of bioindication using cell cultures, are prioritized. The specified method is defined as classic in radiobiology. Its use can successfully replace experiments on laboratory animals for the following reasons: 1) cheapness and availability of the material used (to cultivate the cell culture it is enough to remove organ cells from 1–2 animals; the obtained cell lines can be used for a long time period, in contrast to biomonitoring, in which dozens and hundreds of animals die); 2) possibility to quickly obtain results and maintain lifelong observation of the model throughout the experiment; 3) high correlation of in vitro and in vivo results; 4) the resulting cell lines preserve a high species and organ-tissue specificity throughout the experiment. The advantage of bioindicators lies in their adequate reflection of the state of natural environment and in the fact that mechanism of metabolic processes in them is close to a person's, and correlations are possible here. The use of bioindicators provides answers to the issues of toxicity and biological activity or protective properties of the investigated agent, both with viability of the biosystem in its presence. Method of bioindication on cell culture corresponds to the world level.

One of the emerging problems of modern radiobiology regarding the mechanisms of formation of late effects of exposure after the Chornobyl accident are the cellular aspects of late radiation effects.

One of the most important aspects of exposure to IR is the decrease in the functional capacity of descendants of irradiated cells, which in the future leads to manifestations of the late radiation damage, such as tumors, genetic changes, and disorders of embryonic development. As is known, the basis of radiation pathology at the cellular level features three types of disorders that arise as a result of the direct impact of radiation, namely the cell death, fixation of hereditary disorders, and non-lethal hereditary changes that are persistently reproduced during reproduction of somatic cells.

There was conducted a study of a cross-adaptive response using the combined effect of two adaptive modes, namely γ-irradiation and millimeter waves (MMW). It is known that every factor that acts in a low dose causes stimulation of the growth and development of living organisms. The radioprotective, activating cell division and ATP synthesis effect of MMW provides grounds for their use as an additional adaptation factor.

The separate and combined effects of short-term γ-irradiation and low-intensity non-thermal electromagnetic radiation on viability, radioresistance and adaptive response in a number of cell generations were studied on a transplanted culture of L929 line fibroblast-like cells. When subculturing cells were exposed to IR in 0-generation at a sublethal dose of 10.0 Gy and MMW, the ability of cells to reproduce had doubled, compared to a separate impact of IR. At that the viability of cells in such cultures was significantly higher. It was shown that additional γ-irradiation of cells in a dose of 5.0 Gy had led to increased radioresistance of descendants of cells irradiated in the 0-generation in doses of 0.1 and 1.0 Gy. It was established that in descendants of intact cells and those irradiated in the 0-generation in doses of 0.1 and 1.0 Gy in the 10^{th} passage, the ability of cells to radioadaptive response was observed, the value of which significantly increased under the combined effect of IR and MMW. Results of the conducted studies indicated the protective effect of MMW in relation to IR. This effect was «fixed» in the irradiated cells being observed during the 50 post-irradiation cell generations [37].

Increasing the effectiveness of radiotherapy (of radioresistant tumors also), necessitates application of the cutting-edge technologies, namely the neutron capture therapy and photon capture therapy, both with substantiating the regimes of their use in model experiments at the pre-clinical stage.

Experimental study of the modifying effect of magnetically controlled nanocomposites containing ^{157}Gd on the cellular morphofunctional characteristics in the L_{929} cell culture test system was conducted. It was established that magnetically guided nanocomposites with gadolinium modified with diethylenetriaminepentaacetic acid and meso-2,3-dimercaptosuccinic acid were more biocompatibile with cells, as incubation of cells with such neutron-capturing agents in the studied concentration range exhibited no toxicity, except for the maximum concentrations, at the same time reducing the adhesive cell properties. A decrease in mitotic activity was observed for all nanocomposites against a background of the control density value of cell population, which may indicate the synchronization of cell division. It was found that the ferrite stabilized with sodium oleate had caused the destructive changes in cell culture only at a concentration of 500 μg/ml, but a reduced mitotic activity in cell culture by 3–5 times over the entire concentration range. It was shown that the magnetically controlled nanocomposites had induced apoptosis in cell culture to one degree or another depending on the concentration of reagent [38].

Study of the combined effect of heavy metal salts and IR in the transplanted culture of proliferating cells of the L_{929} line showed a significant toxic effect of copper and nickel compounds on proliferative and mitotic activity of cells in vitro. Under the combined effect of γ-radiation and copper ions the cellular morphological and functional changes were observed, which were determined either by the radiation dose or by the concentration of trace element ions. Under the incubation of irradiated cells with nickel ions the sensitization of cells to irradiation at doses of 0.5 and 5.0 Gy and resistance of cells to irradiation at a sublethal dose of 10.0 Gy were observed [39].

Over the past 5 years

Over the past five years the studies were conducted to determine the specifics of radiobiological effects of ^{131}I in utero in sexually mature rats of the first and second generations, born from parents preconceptually irradiated by incorporated ^{131}I, as well as in animals irradiated in utero as a result of incorporation of ^{131}I at different gestational periods.

Development of experimental models of animal prenatal exposure to ^{131}I, calculation of absorbed thyroid doses for males, females and fetuses after a single oral administration of ^{131}I was carried out jointly with the staff of the Radiobiology and Radioecology Department of the Institute of Nuclear Research of the National Academy of Sciences of Ukraine.

On the basis of the developed experimental model of prenatal irradiation of rats as a result of preconceptional administration of ^{131}I to the parents one day before mating, there were identified peculiarities of radiobiological effects in the offspring of two generations due to tropism of the active factor to the thyroid tissue, structural and functional properties of the thyroid, time of radioisotope incorporation and radioiodine metabolism during pregnancy (gestational period), formation of a certain amount of the fetal thyroid dose, patterns of development of stochastic and non-malignant thyroid effects, mutational processes occurring against the background of mediated radiation-induced changes in the pro- and antioxidant systems, and in lipid-lipoprotein and carbohydrate metabolism.

It was shown that changes in the balance of thyroid and pituitary hormones in descendants of the first generation reflect the discoordination in pituitary-thyroid system function (with abnormal relationship between thyroid and pituitary hormones) indicating the presence of hidden hypothyroidism, while in descendants of the second generation the hyperthyroidism developed with preserved feedback thyroid-pituitary regulation, i.e., the increase in serum free thyroxine concentration naturally inhibited the secretion of pituitary thyroid-stimulating hormone [40].

Disorders of carbohydrate metabolism, pro- and antioxidant balance in the offspring of the first generation were determined, occurring due to the increased intensity of lipoperoxidation and decreased activity of antioxidant protection enzymes. Changes in the lipid-lipoprotein spectrum of blood serum were characterized by an atherogenic direction due to an increase in concentration of the main classes of lipids (total cholesterol and triglycerides) and cholesterol in the composition of the low-density lipoproteins [41, 42].

Studies of post-radiation effects in the offspring of the first generation of laboratory rats, which originated as a result of irradiation of the rat parents by incorporated ^{131}I in various combinations, showed the post-radiation effects in hematopoietic system of the offspring, caused both by intrauterine irradiation in the early stages of gestation and by the effects of transgenerational transmission of the genome instability [43–45].

Study of the patterns of hereditary post-radiation effects in the offspring of irradiated ^{131}I parents was carried out in order to detect the mutagenic effect of incorporated radioiodine on rat germ cells based on the parameter of genetic damage in rat germ cells by the method of dominant lethal mutations. It was shown that the ^{131}I incorporation leads to disorders of spermatogenesis, occurring due to mutagenic effect, and also leads to fetal death. The long-term effects in offspring of the first generation depend on the stage of spermatogenesis of germ cells that participate in fertilization and that have been irradiated. It was found that the stage of spermatogonia was of the sensitive ones to the effect of incorporated radioiodine [46].

Review and quantitative characterization of morphofunctional parameters in the primary culture of thyroid cells of the newborn rats, whose parents were injected with the radioisotope ^{131}I with an activity of 27.35 kBq per animal one day before mating, showed the destructive changes at cellular level in thyroids in animals of the first and second offspring generations, which had led to thyroid dysfunction. Signs of destructive-degenerative changes in thyroid were most pronounced in offspring of the first generation in case of irradiation of both parents [47].

In experimental study on the model of prenatal irradiation of male Wistar rats the peculiarities of neuroendocrine effects were established in the late period (10 months after birth, corresponding to the human age of about 31–32 years) due to the ^{131}I radioisotope incorporation (activity of 27.35 kBq per animal) on the 12^{th}, 13^{th}, and 14^{th} day of gestation, which formed the dose on fetal thyroid (0.19 ± 0.05), (0.37 ± 0.06) and (1.44 ± 0.09) Gy, respectively. Negative consequences of prenatal irradiation in the form of structural and functional disorders in the central nervous system as a result of ^{131}I incorporation on the 14^{th} day of gestation were revealed. According to the results of studies of animal behavioral reactions in the shuttle-box settings, a decrease in the number of produced conditioned reflexes, lengthening of latent period of conditioned reflex reactions, decrease in speed of animal learning and permanence of acquired stereotypes were determined, which indicated the presence of cognitive disorders [48].

Immunoreactive changes (increased number of apoptotic neurons in the cortical layer of cerebral hemispheres, increased concentration of neurospecific antibodies to the myelin basic protein) indicated the structural changes, namely the destruction of myelin sheaths [49].

Hypothyroidism (decreased serum concentration of free thyroxine), abnormal pro-antioxidant balance (decreased activity of catalase), changes in the lipid-lipoprotein spectrum (increased concentration of atherogenic fraction of LDL, decreased concentration of anti-atherogenic fraction of HDL and the main classes of lipids i.e., total cholesterol and triglycerides) manifested themselves more clearly with an increase in the ^{131}I radiation dose on the developing thyroid [50].

Method of obtaining a primary organotypic culture of thyroid cells of newborn rats was developed, structural and functional changes were investigated, and the assessment of cytotoxicity and mutagenicity of intrauterine exposure to ^{131}I with an activity of 27.35 kBq on a pregnant female due to radioisotope incorporation at different periods of gestation was provided. Cytotoxicity and mutagenicity of intrauterine exposure to ^{131}I was more pronounced when the radionuclide was administered earlier in pregnancy. In all thyrocyte cultures, regardless of the time of radionuclide administration, the same number of apoptotic cells was determined, being 12 % of the control, as well as cells with signs of neoplastic transformation, which may indirectly indicate the genetic instability [51].

The radiobiological effects of prenatal ^{131}I exposure must be considered in the field of both general patterns of reactions or responses of biological objects to the IR, and specific ones related to the physical and biological properties of active factor, first of all, the tropism of radioiodine to thyroid tissue. As a result of radioiodine incorporation the indirect radiation effects occur in addition to the direct ones in a form of complex integral reactions of the body due to involvement of regulatory systems and neuro-humoral mechanisms. Initiation and implementation of the process of neoplastic transformation of thyroid cells due to radioiodine incorporation occurred at the relatively low doses of intrauterine irradiation and were considered as deterministic effect [52].

Possible transgenerational effects were studied in offspring of the first generation of rats under a combined exposure to NSE 50.0 mg/kg and external total γ-irradiation of their parents in a dose of 2.0 Gy. The transgenerational effect of NSE was found manifesting through radiosensitizing properties in offspring of the first generation of rats in case of its administration before the irradiation of their parents [53].

The radioprotective properties of the organic compound 2-mercaptobenzothiazole (2-MBT) were studied according to morphological characteristics (proliferation, mitotic activity, apoptosis, differentiation) in a test system of cultures of proliferating mammalian cells (transplanted and embryonic) irradiated with sparsely ionizing radiation and densely ionizing radiation. The morphofunctional characteristics and cellular ability to differentiate in vitro upon exposure with γ-quanta of ^{60}Co and fission neutrons spectrum were studied. The dose limits of effective influence of 2-MBT were established. It was found that the radioprotective compound 2-MBT in physiological concentrations was characterized by a dose reduction factor (DRF) significantly higher than standard radioprotector cystamine, protecting the poorly differentiated somatic cells from radiation exposure, which makes further recovery and differentiation into complex multinucleated structures possible. Quantitative assessment of the radioprotective properties of 2-MBT in the L_{929} cell culture test system showed the highest values of the protection coefficient (0.31–0.36) at a concentration of 3 μg/ml when exposed in a dose of 1.0 Gy. At the same time, the DRF, calculated according to the LD_{50}, at 2-MBT concentrations of 0.03 and 0.30 μg/ml was 1.5 and 1.8, respectively, and at concentrations of 3.0 μg/ml was the maximum, amounting to 4. Application of the model tests systems of transplantable cell cultures (fibroblast-like transformed, epithelial non-transformed, myogenic embryonic animal cells, etc.) allowed, in a certain approximation, to extrapolate the results of comprehensive assessment of a whole range of parameters of cell survival and viability in determining the radioprotective and/or radiomodifying properties of factors of various origins to the organism level [54].

Significance of the medico-social problem of cancer emerged in the Chornobyl NPP accident survivors and the need to solve it determines the priority tasks for increasing the effectiveness of its management including radiotherapy. Binary radiation therapy is a type of radiotherapy where the special drugs are used to enhance the effect of IR, but themselves have no pronounced biological activity. Currently, such types of binary radiation therapy technologies as the neutron capture therapy and photon capture therapy are intensively developing. For neutron capture therapy the primary radiation is a flow of thermal (epithermal) neutrons absorbed by the ^{10}B or ^{157}Gd elements. For photon capture therapy, the primary radiation is photons from X-ray equipment and medical accelerators, and the absorbing chemical elements have atomic numbers greater than 53. Binary therapy allows increasing significantly the dose up to the lethal level for malignant cells without harm or with minimal harm to normal cells.

Nature and features of the combined effect of IR (fission spectrum neutrons and γ-quanta of ^{60}Co), red light (630 nm wave length), and neutron-capturing agents with a molecular and nanostructure containing boron or gadolinium on the morphofunctional characteristics of cells in vitro were determined in previous studies in the test-system culture of the L_{929} line proliferating cells [38].

Currently, a prospective study is being conducted to determine the dose dependence of morphofunctional changes in the culture of malignant human cells under the X-ray irradiation and use of photon-capturing agents, to identify the possibility of enhancing the biological effect in cells using a combined effect of ionizing (neutrons and photons) and non-ionizing (630 nm light of the red range) radiation involving drugs that can be used in binary technologies. All of the above will allow to deepen the knowledge about pathogenetic mechanisms of combined effect, increase the effectiveness of binary therapy at the stages of pre-clinical and clinical trials.

Conclusion

Radiobiologists and radiologists have been trying to assess the health risks of low-dose IR in human for decades. Health risks are associated not only with cancer, but also with somatic mutations that may contribute to other diseases (including birth defects), and inherited mutations that may increase the risk of disease in future generations. The induced by low-dose IR human malignancies depend on several variables, most of which cannot be adjusted for in any epidemiologic or clinical study. Some confounding factors include the interaction of IR with other physical, chemical, and biological mutagens and carcinogens in a synergistic mode, variation of reparation mechanisms, which depends on the dose, fluctuations in sensitivity of the bystander cells to further exposure, which depends on previous exposure, variation of adaptation reactions, which depends on radiation doses and endogenous protective substances.

In parallel with epidemiological and clinical studies on determination of the late health consequences, a significant improvement in solution of the mentioned fundamental and applied problems was obtained due to experimental modeling of radiobiological effects of the Chornobyl disaster. In particular, the application of methodology inherent in radiobiology as an integrative interdisciplinary science has contributed to the deepening of knowledge about peculiarities of radioadaptive response and possibilities of its modification due to incorporation of radionuclides, chronic and/or prolonged action of sparsely and densely ionizing radiation, as well as the effectiveness of the use of existing and new radioprotectors and radiomodifiers.

It should be noted that all experimental studies were performed in accordance with the International Principles of the European Convention for the Protection of Vertebrate Animals used for Experimental and other Scientific Purposes (Strasbourg, 1986), Law of Ukraine # 3447 IV «On the Protection of Animals from Cruelty» (2014), and were confirmed by the relevant decisions of the Committee on Bioethics of the NRCRM regarding the regulation of the implementation of planned research including dissertations.

The use of adequate experimental models in vivo and in vitro in the studies of biological effects of the Chornobyl disaster factors will contribute to the further development of experimental science, which has an exact manifestation in understanding and explanation of medical consequences and solving the urgent tasks of protecting people from the effects of IR.

7. CHORNOBYL EXPERIENCE AND ROLE IN THE GLOBAL PRACTICE OF RADIATION SAFETY PROVIDING

7.1. Experience of medical and biophysical support of the Shelter Implementation Project regarding the construction of the New Safe Confinement and the transformation of object «Shelter» of the SSE Chornobyl NPP into an environmentally safe system (2004–2019)

Transformation of object of «Shelter» (OS) of the SSE Chornobyl NPP into environmentally safe system is one of the most important state programs in Ukraine. Both medical and dosimetric measures aimed on health protection of personnel participating in these works is at the top place among the most actual problems of modern clinical radiobiology, radiation hygiene and radiation protection [1, 2].

The OS is a destroyed by the off-design accident at a power unit #4 of the SSE Chornobyl NPP (ChNPP) being a building located on a ground surface and specially designed equipped to provide and maintain a durable protective isolation of radioactive waste (RAW) from contact or release to the biosphere. In its present state the OS should be characterized as a «place of superficial storage of unorganized RAW (temporal depository of unorganized RAW that is in a stage of stabilization and reconstruction)». This qualification of OS is obligatory for use in the field of adjusting and management of radiation safety of personnel and population [3]. Nowadays the «Shelter Implementation Project» (SIP) aimed for transformation of OS into the environmentally safe system is realized at the OS. The unicity of conducted works lies in a fact that personnel is essentially executing the work tasks under the impact of high-activity open radionuclide sources of ionizing radiation within doors of the destroyed unit #4 of the ChNPP or in a direct closeness to it on a heavily radioactively contaminated territory. According to existent statutory practice the works with such class of sources should to be performed in the sealed rooms («hot chambers») with application of the distance controlled manipulators. It provides a substantial decline of levels of doses of external irradiation of personnel both with complete exception of contact of personnel with radioactive materials and possibility of their incorporation. Due to unique origination of the OS the radiation-hygienic conditions in the work execution zones cannot be brought into compliance with the world safety standards. Works at the OS are performed under multiple-factor occupational hazardous conditions with a dominant radiation factor amplified by general industrial hazardous issues and contamination in the hard-to-get-to workplaces of the destroyed nuclear reactor. Radiation and non-radiation factors form the unique extreme surrounding environment for the staff working at the OS. All the above-mentioned stipulate exceptional requirements to the somatic health and psychophysiological qualities of personnel.

Thus, the performance of works by the staff on transformation of OS is executed under a synergy and radiological and common industrial risks both with high psycho-emotional intensity of work. These radiation and non-radiation factors form a unique extreme environment for staff working at the OS.

The normative-legal documents of medical and sanitary-hygienic legislation in Ukraine require ensuring a reliable providing of the check-in (initial) and check-out (final) medical and biophysical control of personnel, involved in works with open radionuclide sources of ionizing radiation, and also the regular current medical and biophysical control of personnel admitted to works. Providing of all types of such control was and is an obligatory provision to receipt a permission of the Ministry of Health of Ukraine (MHU) and also special concordance provisions of UkrInvestExpertize on conduction of works included in the SIP. Safety of works at the OS involves application of arrangements focused on avoidance or minimization of hazards, early diagnostics of initial health disorders in personnel, well-timed prophylaxis or taking workers out of the hazardous exposure. All mentioned above substantiate extreme requirements to the somatic health and psycho-physiological capabilities of personnel.

According to the recommendations of MHU the SI «NRCRM of NAMS of Ukraine» as a leading medical research institution in Ukraine in the field of radiation hygiene, dosimetry and clinical radiation medicine, that provides scientific research medical survey and dosimetric support and executes basic volume of works for minimization of medical consequences of the Chornobyl catastrophe and during all postaccidental years actively provides monitoring of health status and dosimetric control of the OS, ChNPP and exclusion zone personnel, and also as a Center collaborating with WHO in the international system for urgent reacting at radiation accident (The Radiation Emergency Medical Preparedness and Assistance Network – REMPAN) was assigned to work out and lead the program of medical and biophysical services of works for transformation of the OS into environmentally safe system.

A system of medical and biophysical monitoring of health, working ability and radiation protection personnel performing work on converting the SO to an environmentally safe system was developed based on the unique experience of medical, biological and dosimetric and maintenance work on the impact of extreme radiation and non-radiation risk factors on the health and performance of staff [4–6] with the requirements of the basic normative-legal and regulatory documents [7–13], guidelines [14, 15], existing departmental standards of the MHU, as well as national and international consensus on the diagnosis of diseases that are contraindications to work in extremely dangerous and hazardous conditions – EDHC (ionizing radiation, radioactive substances and sources of ionizing radiation; works at height, general medical contraindications for work in EDHC) [16].

The check-in, periodic (annual), special and final (including emergency) medical and psychophysiological controls, both with additional – individual inspection and routine (before(pre)/after shift) medical control are the principal interrelated elements of comprehensive medical control (Fig. 7.1).

Ensuring of radiation and general-industrial safety is a main objective of medical support for

Medical control of the SIP contractors personnel		
Check-in control	NRCRM Clinic, Kyiv	Medical conclusion (deed) for admission or nonadmission for SIP works
Individual inspection control	NRCRM Clinic, Kyiv	Confirmation Medical conclusion (deed) for admission or non admission for SIP works
Special control	NRCRM Clinic, Kyiv	Confirmation Medical conclusion (deed) for admission or non admission for SIP works
Routine (pre/after shift) control	1430 Change Facility (ChNPP site)	Confirmation Medical conclusion (deed) for admission or non admission for SIP works
Periodic (annual)control	NRCRM Clinic, Kyiv	Confirmation Medical conclusion (deed) for admission or non admission for SIP works
Final (check-out) control	NRCRM Clinic, Kyiv	Medical conclusion about health status after SIP works

Figure 7.1. The scheme of medical monitoring of SIP contractors personnel

the SIP works. It is implemented through the compliance with Ukrainian legislation and the use of best international practices with necessary measures to prevent or reduce adverse factors, primarily radiation, influencing on health and workability of employees, early diagnosis of initial deviations in their health, the timely implementation of measures for preventive withdrawal of personnel from the zone of harmful factors influence on the basis of a comprehensive medical examination and subsequent peer review (medical supervision) the state of health on admission to work in EDHC at OS (ionizing radiation, general occupational hazards, work at height) required number of staff.

The main objectives of medical and biophysical control monitoring program for SIP personnel are the following:

1) minimization of potential admission of personnel to work under extremely hazardous conditions that are not physically or mentally capable of performing the work;

2) avoidance of any industrial accidents and casualties that can make any health deterioration in personnel and/or lead to radiation accidents;

3) control of internal radiation doses ensuring that internal radiation exposure does under works conduction at the OS are meeting the radiation safety requirements;

4) prevention of radionuclide incorporation in personnel through education and adherence to discipline by workers, both with proper choice of individual means of protection; availability of independent assessment of personnel exposure risk by means of available tools is an important point;

5) in the case of detection of internal contamination above a pre-set limit an additional health check-up and biophysical examination should be conducted to assay the dose limits established by the respective regulatory documents in the field of radiation hygiene regulation, and to define the possibility of work continuation at the ChNPP.

Implementation of these provisions also help to avoid possible lawsuits from staff about the loss of health in connection with participation in the work on the SIP. In addition, this approach provides for the ChNPP and contractors saving labor resources required for work on the SIP.

In view of radiation hygiene and general-purpose features of works on OS, a set of comprehensive requirements for health and physiological qualities of candidates for admission to work, the only regulation of medical, physiological and professional selection was established, which was summarized in determining the categories of personnel's health. Medical examination involves assessment of hematopoietic, immune, endocrine, respiratory system, eye, nervous system, mental and physiological adaptation, hearing and balance, circulatory, digestive, urogenital and the musculoskeletal system.

As a part of the program admission and radiation safety works at the OS the applied biophysical control (Fig. 7.2) is a complex of physical and biodosimetric measures aimed to identify the cases of incorporation of radioactive substances in personnel, calculation of the actual individual internal exposure caused by these events, and conformity of radiation-hygienic conditions in the workplace to the sanitary requirements of Ukraine.

In terms of work for the SIP implementation the biophysical monitoring includes a collection of primary dosimetric information on employees and workplace and current radiation-hygienic and biophysical control. Input and output, special, urgent (emergency) biophysical controls are performed in parallel and simultaneously with medical supervision [17].

The check-in (input) biophysical control is a control before starting the work as part of mobilization of personnel. The check-out (output) biophysical control is a final control within a demobilization of personnel.

Biophysical monitoring is an extended control that is performed when an excess of content of transuranic elements is detected in the samples of daily feces. The purpose of this control is to check the fact of radionuclide incorporation and determination of the exact value of the exposure of the worker.

Current (routine) biophysical control is a basic biophysical monitoring performed according to predetermined schedule of the regular measurements. Current biophysical control consists of the following components: biophysical measurement before the shift, biophysical measurement after the shift; examination after the shift; the intra-shift biophysical measurements.

Special biophysical control is an expanded control initiated when pre-defined biophysical sample thresholds are exceeded by transuranium ele-

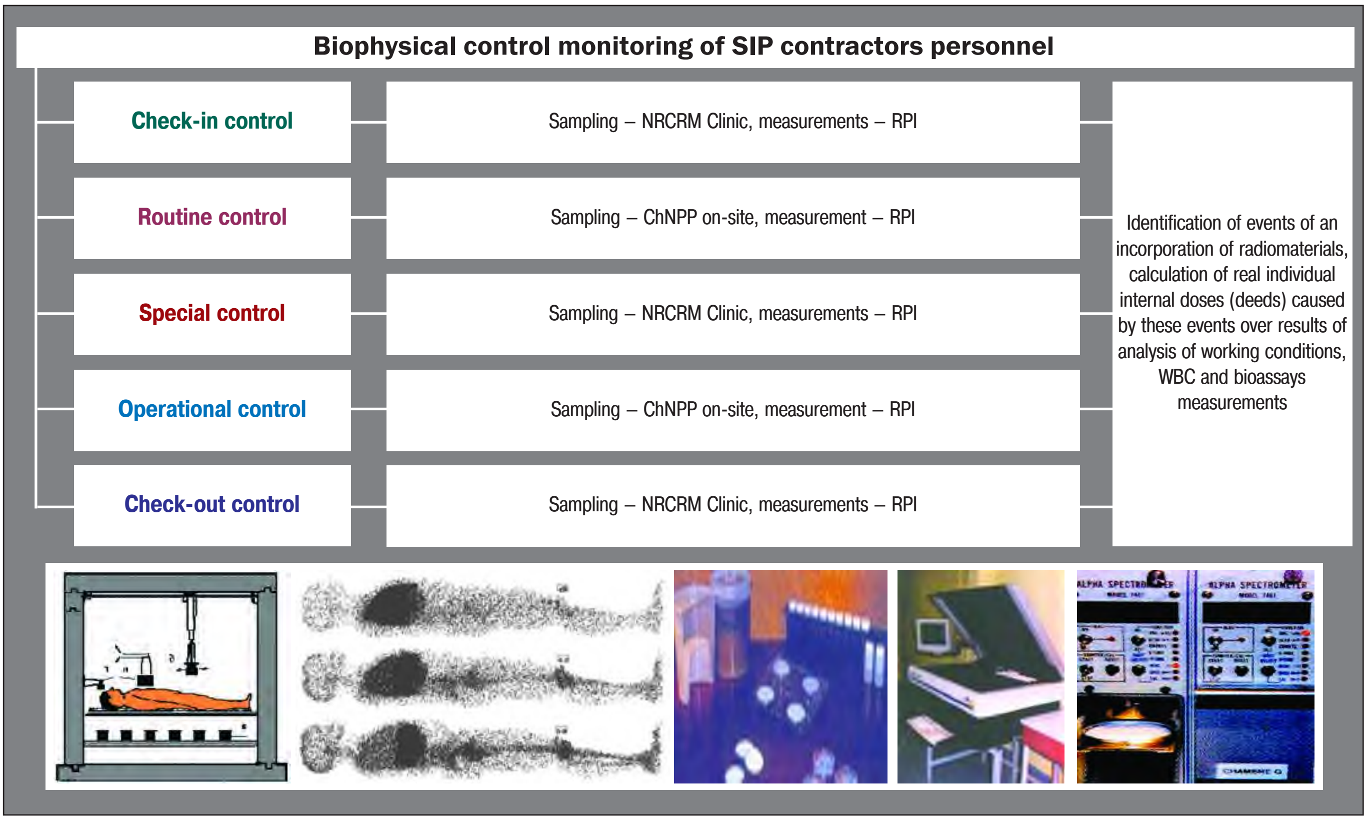

Figure 7.2. Scheme of biophysical monitoring of SIP contractors personnel

ments concentration value in the daily samples of faeces. The purpose of this control is to verify the fact of incorporation and to define an accurate value of individual internal dose exposure of the employee.

Evaluation and analysis of the complex medical and psycho-physiological examination and dosimetric data of external and internal exposure are the basis for decision-making by the expert commission of compliance of health, physiological characteristics and parameters with radiation-hygienic requirements to the personnel at work on the OS (Fig. 7.3).

The basis of the medical control was a complex clinical, instrumental and laboratory examination of the organs and systems of the body (blood and hematopoiesis, immunity, blood circulation, organs of vision, respiratory system, endocrine system, digestive system, urinary system) aimed at expert proof confirmation of the absence of general and specific contraindications (including risks of occupational and oncological diseases) for work in radiation-hazardous conditions and work at height [16] (Fig. 7.3).

During the period since October 12, 2004 till February 28, 2019 for admission to work at the OS the check-in medical and biophysical control were applied to the 16,898 staff employees of 58 contractors involved in the implementation of the SIP.

The staff involved in the SIP included the following groups of workers: 1) clean-up workers, evacuees from the 30 km zone of Chornobyl, residents of contaminated areas; 2) professionals of nuclear energy industry; 3) workers who had not been exposed earlier to ionizing radiation.

According to the results of check-in medical control the 8,721 workers (51.6 %) were allowed to work, 8,1777 (48.4 %) – not allowed (Table 7.1).

The reasons for the non-admission were: chronic diseases of digestive system (52.4 %), eye diseases (15.0 %), endocrine system disorders (14.2 %), circulatory system abnormalities (6.4 %), neoplasms (6.5 %), respiratory system diseases (4.6 %), pulmonary tuberculosis (1.6 %), diseases of the nervous system, mental and behavioral disorders (8.7 %), diseases of mostly immune genesis (1.5 %), diseases of blood and hemopoietic organs (3.3 %), urogenital system diseases (2.1 %), skin diseases (4.0 %), and hearing disorders (2.3 %).

Staff of SIP contractor authorized to work have had 2 to 10 chronic diseases (mainly of the respiratory, cardiovascular, digestive, and nervous system). Stage and course of these diseases were not a con-

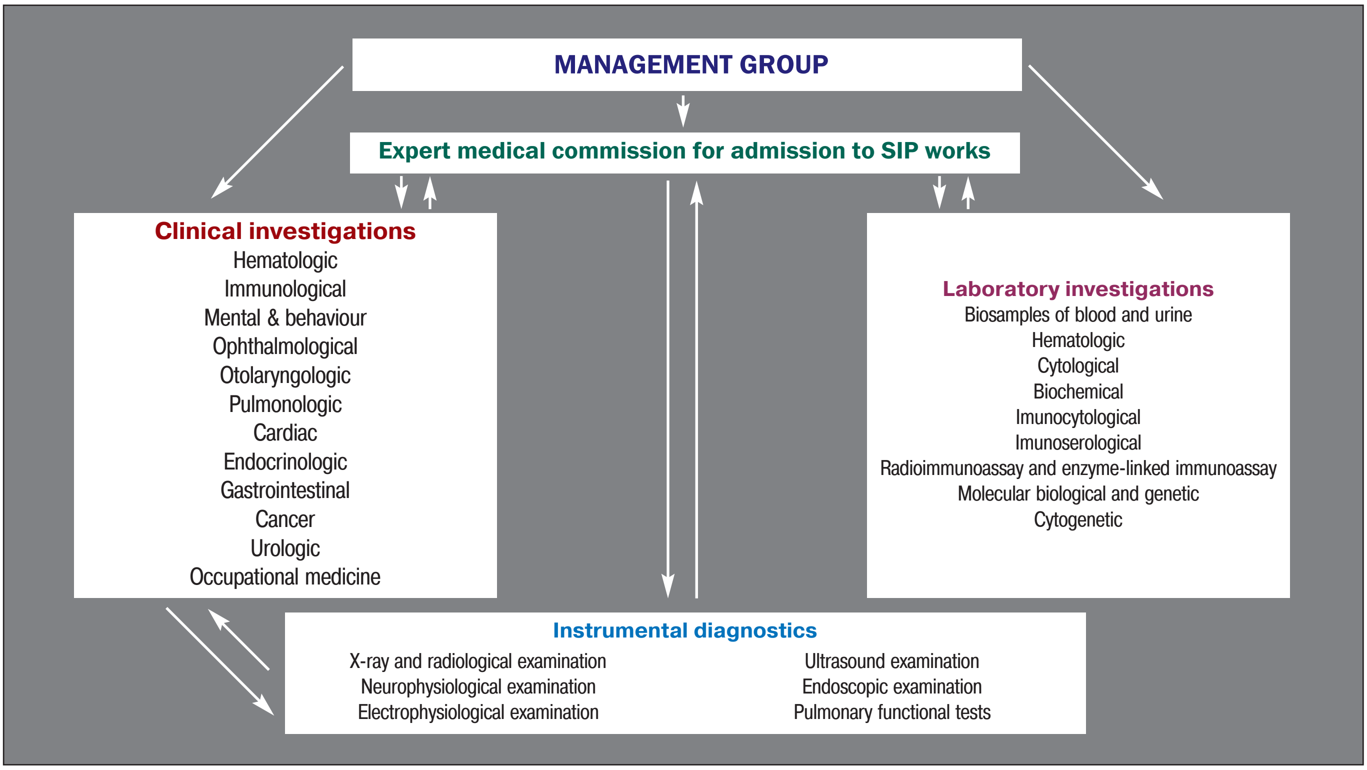

Figure 7.3. **Organization of works to provide the check-in, periodic (annual), individual inspection, special and final (check-out) medical examination**

traindication for admission to work on SIP, but required a complex rehabilitation.

In the periodic (annual) medical control the 9,686 employees (73.9 %) were admitted to radiation-hazardous work, 3,410 (26.1 %) were not dmitted (Table 7.1).

Non-admission to work according to the periodic control monitoring results mainly was due to exacerbation of existing chronic diseases of the digestive system (43.07 %), respiratory system (24.16 %), circulatory system (12.60 %), diseases of the nervous system, mental and behavior disorders (18.69 %), diseases of eye (1.47 %). This suggests, first of all, not for the impact of hazards at the site of OS, but for a lack of work with staff to prevent relapse of these diseases.

Inspectional medical control was carried out according to individual targeted diagnostic programs and made it possible to effectively provided treatment and rehabilitation measures in relation to chronic diseases, exacerbations of which were detected during the initial, periodic or special medical control and were contraindications to work in radiation-hazardous conditions. A total of 5,793 cases of inspection control were conducted: 4,449 (76.8%) persons were admitted to radiation-hazardous work, 1,344 (23.2%) were not admitted.

During the examination under the program of special medical control, no employee was found to have any damage to their health or work capacity due to the influence of ionizing radiation, however, 198 people (8%) subsequently required next inspectional medical control due to exacerbation of chronic diseases.

Biophysical control with the definition of internal exposure doses over the 2004-2015 period was pro-

Table 7.1
Results of medical monitoring of SIP contractors personnel for the period 12.10.2004 – 28.02.2019 (number of people)

Type of control	Allowed	Not allowed	Total
Check-in	8721 (51.6 %)	8177 (48.4 %)	16898
Periodic (annual)	9686 (73.9 %)	3410 (26.1 %)	13078
Individual Inspection	4449 (76.8 %)	1344 (23.2 %)	5793
Special		2,042 – individuals; 2,486 – cases	
Final (check-out)		746	

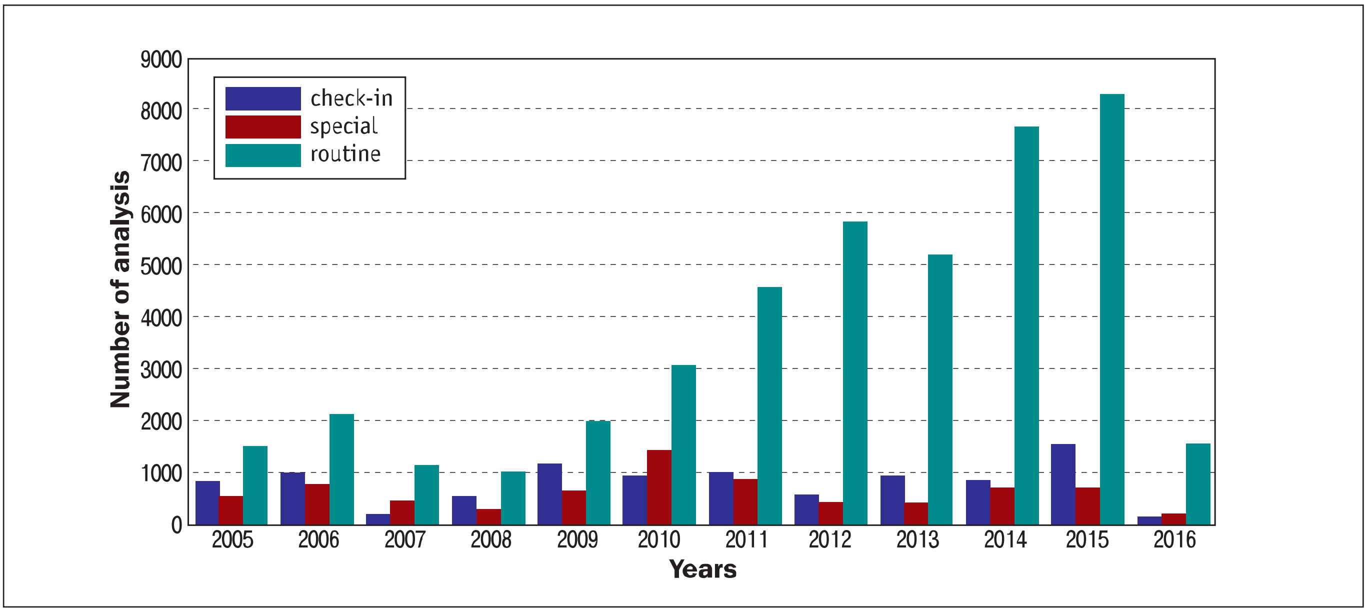

Figure 7.4. **Distribution of radiochemical assays by type of biophysical control for internal dose monitoring in the SIP contractors workers**

moted in general to 10,010 individuals – employees of the SIP contractors. The 63,945 radiochemical assays were done for the control of internal exposure. Analysis of distribution by the type of biophysical control is shown in Fig. 7.4.

Structure of radiochemical assay for monitoring of internal dose was as follows: check-in control was 15 %, routine – 68 %, special – 16 %, final – 1 %.

During the check-in biophysical control of candidates to participate in the SIP works, practically neither radionuclides in the body, nor the radionuclide content in biosamples (feces, urine) were found.

External doses were controlled by the Radiation Safety Department of the SSE Chornobyl NPP. Distribution of the average external exposure of personnel of SIP contractors within 2004–2016 is shown in Fig. 7.5.

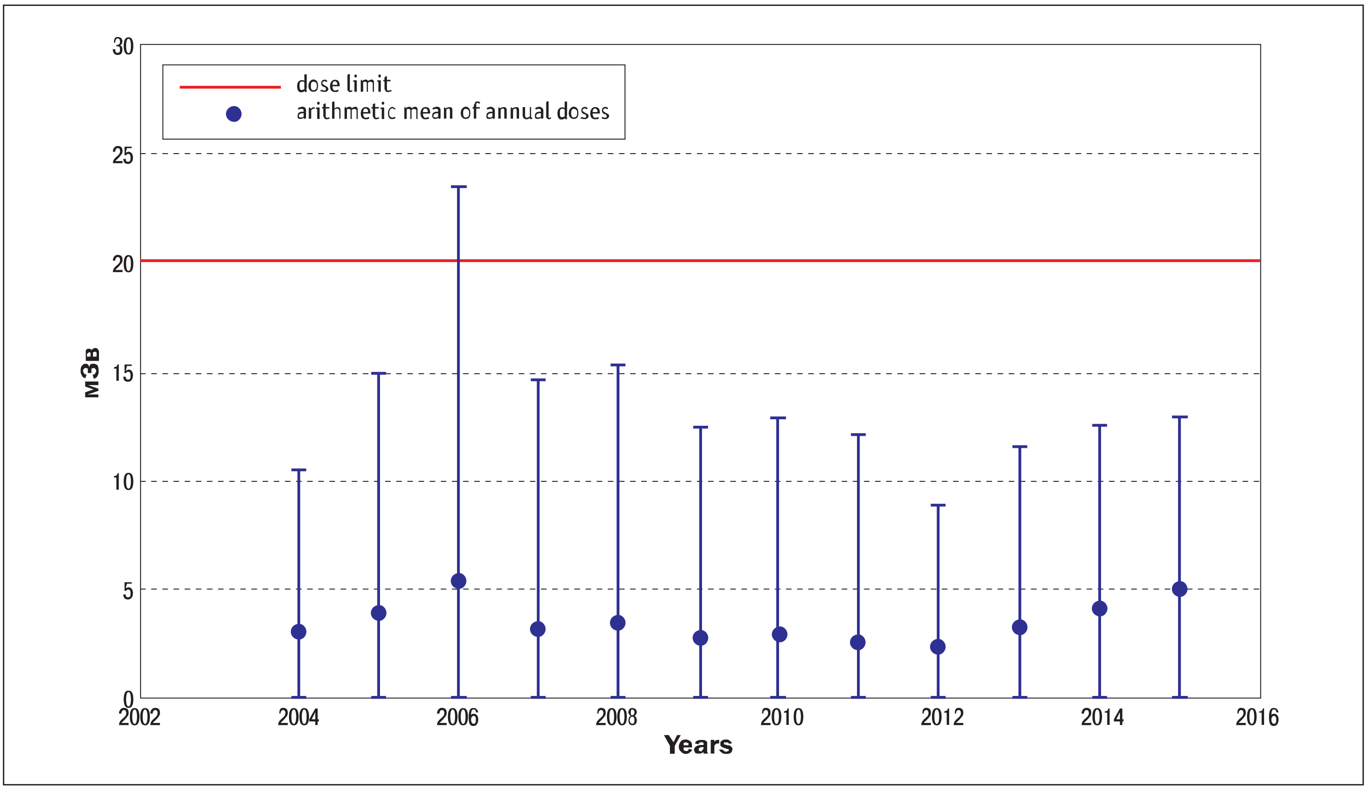

Figure 7.5. **Distribution of yearly average external exposure of SIP contractors personnel within 2004–2016**

Average individual annual effective dose of external exposure of personnel during works is 3.73 mSv (STD = 4.02 mSv). Doses received by the staff due to individual permission of Ministry of Health of Ukraine in 2006 and other years are not included.

Data obtained during the routine (current) biophysical control monitoring of the personnel involved in the work of the OS (Fig. 7.6) indicate that the measured levels of $^{239+240}$Pu in samples of feces were exceeding the level of response and worker was sent to a special control (SC).

The SC is exceptional and is to be done when during the routine (current) biophysical control monitoring in samples of feces $^{239+240}$Pu a content level exceeding the value of 1.5 mBq/test was found and there is a risk of exceeding the individual exposure level of 1 mSv·year^{-1}. This value corresponds to the reference level of annual individual internal exposure at the Chornobyl NPP set for the period of work on the OS. Quantity of workers called to SC serves as an indicator of the radiation safety quality, measures concerning compliance with individual and collective protection of personnel, preventing radionuclides entrance into the body. Overall, in 2005–2015 there were 2,315 cases of initialization procedure of the special medical and biophysical monitoring (some persons were submitted to SC 3 and more times).

The results of radiochemical analysis of biosamples selected under the special biophysical monitoring showed no systematic inflow of $^{239+240}$Pu to the body of workers and enable to conclude that the oral intake was the most likely way of radionuclide incorporation. Total individual doses of internal radiation (Fig. 7.6) calculated within special biophysical monitoring not exceeded 6 mSv and were on average 0.85 mSv (STD = 0.69 mSv).

As the analysis has shown the need to call the workers for a SC at initial stages of work on the SIP was primarily caused by insufficient organization of work and nonconformance of this type of work to radiation-hygienic requirements. However, as it turned out, low sanitary culture of workers is a main cause at the current stage of work.

That is why there is always an intensive verification of ways of radionuclides incorporation and characterization of radioactive aerosols, which are at the working place and recommendations providing on the use of individual respiratory protection tools, as well as avoidance of external contamination when biosampling. A clean room was created and equipped at the ChNPP site to collect biosamples with prevented external contamination. Instructions and guidelines for the control of internal exposure of the SIP personnel were developed and approved by regulators and implemented in practice at the ChNPP.

The above-mentioned results of medical and biophysical monitoring indicate a critical importance of the continued medical and biophysical maintenance of works on the SIP, because the issues of preventing the personnel exposure is a key point in performance of works in these radiation-hygienic conditions.

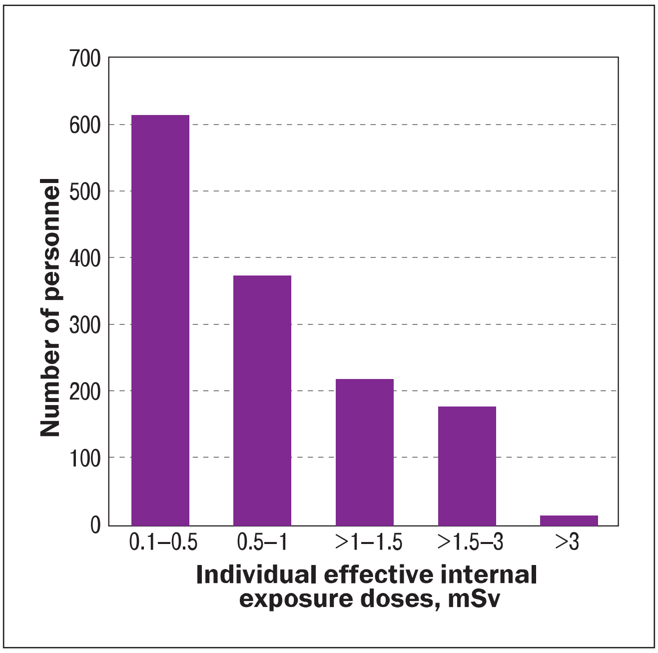

Figure 7.6. **Distribution of internal exposure of personnel who passed the procedure of special biophysical and medical control**

In October-November 2005 after the first year of work on medical and biophysical support of SIP works the ChNPP assessed the program by means of international audit. The audit team consisted of experts from the RTI International (Research Triangle Park, NC, USA), Battelle Memorial Institute (Richland, WA, USA), and Duke University (Durham, NC, USA). According to the conclusion of the international audit, this project deserves appreciation and full support of both the methodology used and organization of work applied with some recommendations on how to optimize its management.

Audit work on the SIP held by the Mouchel Parkman Corporation in February 2007 noted in the final report that the program of medical and biophysical monitoring was extremely successful to achieve its main objective i.e. ensuring medical compliance of the SIP workers and preventing litigation in connection with damage to health from current and former employees involved in the SIP.

The results of medical and biophysical control during SIP project work at the OS became the evidentiary basis for scientific studies of the impact of ionizing radiation in small doses on the human body and the development and implementation of innovative technologies of medical and biophysical control for radiation protection.

In the early period after exposure to professional limits up to 20 mSv, D.A. Bazyka and I.M. Ilyenko [18] first established 1) an increased intensity of apoptosis in a complex with activation reactions at the level of mature cells; 2) the peculiarities of the regulation of the telomere-telomerase complex by *TERT*, *TERF1*, *TERF2* genes in the early period after irradiation are characterized 3) the activation of protective and compensatory processes and the inclusion of pathogenetic pathways of radiation aging of immunocompetent cells due to violations of gene regulation of the telomere-telomerase complex and overexpression of antigens related with antiviral immunity and antitumor surveillance. The study of gene expression in the early period after exposure in the employees of the OS made it possible to propose genetic markers for the evaluation of the action of ionizing radiation during occupational exposure, which opens the way to the creation of new methods of biological dosimetry and the evaluation of the effectiveness of therapeutic and preventive measures for the restoration of immune system after irradiation [19].

Studies of the individual frequency of specific markers of recent exposure – unstable chromosomal exchanges with an accompanying paired fragment in personnel confirmed the probability of excessive exposure of workers during the performance of certain radiation-hazardous work at the OS that received special permits with the permission of the MHU [20]. According to the magnitude and dynamics of the background and bleomycin-induced cytogenetic effects at different periods of lymphocyte cultivation, the examined group of personnel from among the workers of the SIP contracting organizations probably differed from the comparison group in terms of the growth of indicators of chromosomal instability with significant individual fluctuations [21].

The study of the cellular composition of bronchoalveolar lavage was conducted for 218 employees of SIP contractors after participating in the performance of radiation-hazardous work at the OS in 2004–2007. For employees with an annual radiation dose of more than 10 mSv, a correlation between the increase in the number of macrophages with intense staining, a decrease in the number of neutrophil leukocytes and the dose of radiation exposure (average (14.26 ± 0.62) mSv) was found. Probably, in the early stages of the influence of ionizing radiation on the bronchopulmonary system (mainly by inhalation), the activation of the phagocytic link is observed, which is aimed for removing inhaled particles from the body [22], and is accompanied by the development of catarrhal and catarrhal-sclerotic changes in the mucous membrane of the bronchi, which are recorded during bronchofibroscopy.

The clinical and endoscopic features of the course of diseases of upper parts of the gastrointestinal tract were studied in the personnel who performed radiation-hazardous work at the OS, consisting of an increase in reflux (up to 82 %), inflammatory (up to 79 %), erosive-ulcerative (up to12 %) and dysregenerative damages (up to 45 %). It has been proven that tobacco abuse, alcohol use and an unstable psycho-emotional state significantly affect on the frequency of exacerbations of chronic diseases of the gastrointestinal tract. According to the results of the morphological study of biopsies, the peculiarities of the microstructural changes of the gastric and duodenum mucosa were determined, which consist in the presence of Helicobacter pylori (HP)-associated pangastritis, dysregenerative changes in the epithelial cells, which leads to the development of atrophy of the gastric mucosa (non-metaplastic or metaplastic type), damage microcirculatory vessels with trophic disorders and, accordingly, further development of erosive-ulcerative lesions of the upper parts of the gastrointestinal tract [23, 24].

It has been proven that the performance of radiation-hazardous work in the conditions of radiation exposure and open sources of radiation poses for personnel a risk for the development and, in the presence of chronic diseases, to an increase of the recurrence of inflammatory diseases of the esophagus, stomach and duodenum [23, 24].

For the first time, based on the assessment of the odds ratio (OR), the role of the influence of radiation exposure in small doses at the level of professional limits (up to 20 mSv of total and 1 mSv of internal exposure) on the formation, course and development of exacerbations and complications of diseases of the stomach and dudenum in radiation-hazardous conditions was proved [23, 24].

The work on the creation and implementation of an effective system of medical and biophysical control of the state of health and working capacity and radiation protection of personnel who performed work for the transformation of the OS into an environmentally safe system was awarded the by Prize of the Cabinet of Ministers of Ukraine 2017 for the development and implementation of innovative technologies.

Conclusions

1. The program of medical and biophysical services for reconstruction works on the OS proved its necessity and efficiency because it appeared that in unique radiation-hygienical conditions not engineering and technical problems are the most critical ones but how to save the health and workability of people and prevent the overdose of personnel due to an internal irradiation.

2. The health status of workers that undergo the check-in medical control is incompatible with requirements to participating in SIP works more than in 50 % cases, regardless of previous regional medical examinations. Therefore, the check-in and final medical control for access to such radiation hazard works must be conducted only in highly specialized, adequately equipped medical facilities that have practical experience of providing health care and medical control to the persons, who were undergoing radiation exposure and, in particular, the influence of radionuclides incorporation.

3. As a result of realization of the routine biophysical control cases of $^{239+240}$Pu overlevel content in bioassays of faeces were detected. So, it was necessary to conduct the special biophysical and medical control for verification of ways of radionuclides intake to the body and estimations of dose of internal irradiation. Results of biophysical control are also a basis of providing a complex of organizational arrangements on radiation protection and technical safety of personnel of the SIP contractors enterprises and ChNPP, accurate keeping rules and measures that prevent radionuclide incorporation.

4. The worked out and implemented system for control of individual doses of internal irradiation by biophysical methods meets the requirements of sanitary legislation and provides the adequate level of radiation protection of workers from the internal irradiation during participation in the SIP works. Development of the system for control of individual doses of internal irradiation in personnel foresees the integration with radiation safety service of the ChNPP for the control of both internal and external radiation doses that corresponds to the requirements and respective instructional-methodical documents worked out and inculcated in practice of ChNPP.

5. Protection of health and workability of personnel needs providing of complex of health care and rehabilitation arrangements that must be realized within the framework of the special individual programs of treatment on a base of the highly specialized medical establishments.

6. Scientifically based generalizations of the results of medical and biophysical control during SIP project work at the OS became the evidential basis for scientific studies of the impact of ionizing radiation in small doses on the human body and the development and implementation of innovative technologies.

7. Scientifically based generalizations of the results of medical and biophysical control during SIP project work at the OS became the evidential basis for scientific studies of the influence of radiation exposure in small doses on the human body and the development and implementation of innovative technologies.

7.2. Cognitive chronic fatigue syndrome in workers of the «Shelter» Object transformation into an ecologically-safe system

K. Loganovsky (2000) was the first to suggest that Chronic Fatigue Syndrome (CFS) is a characteristic consequence of a radioecological emergency [25]. The National Chronic Fatigue Immune Dysfunction Syndrome Foundation (NCF, USA) has officially announced the link between CFS and low-dose radiation exposure.

A prospective study of personnel working on the transformation of the «Shelter» Object at the Cornobyl NPP into an environmentally safe system showed that the impact of radiological (0–56.7 mSv, M ± SD: (19.9±13.0) mSv) and industrial risk factors can lead to cognitive CFS, characterized by dysfunction of the cortico-limbic system, mainly in the dominant (left) hemisphere with the predominant involvement of the hippocampus [26, 27].

By neurophysiological and neuropsychological studies, the biomarkers of low doses of ionizing radiation exposure have been found. Immediately after irradiation, there were statistically significant changes in the bioelectrical activity of the brain. The organized type of quantitative electroencephalogram (qEEG) has shifted toward the disorganized. An increase in the spectral δ-power in the left anterior temporal region, θ- and α-power in the left temporal region, with a redistribution of α-activity to the front and a decrease in the dominant frequency in the left temporal region were registered. These data indicate hyperactivation of the cortico-limbic system associated with the effects of low doses of radiation, mainly in the dominant (left) hemisphere. Neurocognitive tests revealed the presence of mild cognitive impairment after exposure. Taken together, these disorders can be considered as a cognitive variant of chronic fatigue syndrome as a result of the combined effects of low doses of ionizing radiation, industrial factors, and psycho-emotional stress. Neurophysiological studies can be used as a promising non-invasive diagnostic tool for assessing radiation effects at low doses, especially in the work area with additional psychophysiological requirements. The effect of a «radiation-resistant worker» was found, that is, people who had been previously exposed to radiation («past exposed») without health effects were more resistant to further exposure [26–28].

7.3. State of information support for the population of radioactively contaminated territories and NPP surveillance zones on radiation safety issues

The information strategy in the early and intermediate periods of the Chornobyl accident was distinct with a spontaneous formation of media space. Information supply to population regarding the accident at the Chornobyl Nuclear Power Plant (ChNPP) was unsystematic with significant drawbacks in the information processes. Information of the latter was incomplete, biased, contradictory, which caused a distrust in information sources and in reliability of the latter [29]. In general, the media space of the Chornobyl accident is classified as distorted with subsequent consequences. The latter was due to objective and subjective factors. Legal and all other documents regulating the information process were absent, except for the «classified» ones. According to the latter the scope and semantic features of information were limited. Only in 1990 the available to the public policy documents were issued in Ukraine, Republic of Belarus and Russian Federation. Those documents about time in one way or another defined some principles and procedures for public about the Chornobyl accident consequences, means of protection and damage control and recovery. No generalized world experience of informing the population in case of global man-made disasters was available [30].

Mass media were the main source of information. The press, television and radio communications, which formed media space, were not significantly different in the properties of information. Studies of communicative models of publications show that they were not adequate for public perception. There was a «scissors effect» when the communicator used communicative models not corresponding to the language resources of information consumers. This was especially relevant for the population of rural areas with a lower level of education, when the positive effect of informational influence was not achieved due to a simple misunderstanding of the text content [31].

The information strategy from 1986 to 1990 differed by its cyclical nature in the congestion of media field of mass communication. Structure of qualimetric characteristic of the studied information traffic of printed media for 1986–1990 period was as follows: 1986 – 29.6 %, 1987 – 6.9 %, 1988 – 8.8 %, 1989 – 20.9 %, and 1990 – 34.9 % [32]. The information vacuum of 1987–1988 was created artificially. Information about the protective measures due to the accident took up very little space in documentary stream, namely only 7.5 % of the total. Perception of radiation situation and behavior of population depended on the level of awareness. Subjective risk assessments of population determined their lifestyle, being the most important factor in shaping the human health [33].

Study of the post-Chornobyl information traffic highlighted six information periods that had their own characteristics and affected the psycho-emotional strain of survived population.

1986 – period of ascent of information to the radiation accident, period of understatement of its true scale.

1987–1988 and the first half of 1989 – period of secrecy of information about the scale and consequences of catastrophe, a period of information decline.

The first half of 1989–1991 – period of information peak, various, in particular scientifically unsubstantiated, contradictory information.

1992 – period of information stabilization, which began after the adoption of the Chornobyl laws, which guaranteed some social protection of citizens effected as a result of the Chornobyl disaster.

1993–1994 – second period of information recovery, associated with a reduction in payments of benefits and compensation to survivors.

1995–1999 – period of coverage of health and social consequences, both with the future of ChNPP [34].

In the late period of 2000–2005 there was a decrease in information on the radiation situation and measures of public protection. Cutback of spending on the post-accident clean-up programs was the focus of attention [35].

Period of 2006–2010 was characterized by the lack of complete information on radiation situation at the place of residence. Media remained the main sources of information, but their number was insignificant. Apprehension due to the lack of specific information on radiation situation was 21 %, while concern due to the lack of specific information on health status of population affected by the Chornobyl accident was 37 %. Deformation of media space of the Chornobyl accident has changed the classic features of information perception by a consumer. Population did not trust the means of communication of the authorities. The greatest confidence of population was in the information from international organizations (53 %) and scientists (42 %). The least trust of respondents was to information from the highest officers of state (5 %) [36, 37].

There was no informing the population of radioactively contaminated territories (RCT) in 2011–2015 about the radiation situation and state of their health in the mass media or websites of executive authorities. Only about 15 % of population believed that they had information about the radiation situation at their place of residence. The 84.4 % of managers felt the need to constantly receive a departmental information. Providing the adoption and implementation of managerial decisions on protective measures in the late period of Chornobyl accident, most of them used the departmental information depending on their subordination (Ministry of Health, Ministry of Emergencies, Ministry of Education and Science, etc.) [38]. Specialized collections of documents were in second place among the information sources, referred to by the 23.8 % of professionals. Another 23.8 % of specialists were using the scientific publications. The last position in demand was occupied by proceedings of scientific and practical conferences, which were almost never used by specialists (9.5 %) [39, 40].

Sporadically implemented international information programs were also not very effective. The ICRIN (International Chornobyl Research and Information Network) program was aimed to combine the scientific data with information requests from public. Training seminars for doctors, educators and employees from a number of regions of Ukraine were conducted but did not provide the desired effect. Estimates by the interviewed population of the consequences of work with employees of health care and education institutions a year after the project end were quite low [41].

During 2016–2019 the information system for population of contaminated areas did not function. There was no information on the official websites of state services, in the media on radiation and environmental situation at the places of residence, as well as information on health status of various categories of population at the regional and district levels. On anniversaries of the Chornobyl accident the materials about the event as such and materials on social protection of survived population in accordance with social programs «Social protection of survivors as a result of the Chornobyl accident» appeared in communication media (press, television, radio) and on the official websites of district, city and regional councils. At a runtime of years there were single prints and information in the form of messages and memos in regional and district newspapers of Zhytomyr Oblast, on official websites of local governments of Ovruch, Narodychi, Olevsk, Yemilchyne, Malyn, Korosten districts prepared during the year by civil defense and social service centers. Preparation of population for possible emergencies of man-made, natural and social nature, prevention and clean-up of their consequences was the thematic focus of information prepared by the civil protection sector. This included the threat alerts, evacuation signals, temporary evacuation of civilians from dangerous areas, advice to the public on staying in the simplest protective structures, and laboratory tests of personal respiratory and skin protection tools. This information was useful, but far from the RCT population's demands about the radiation situation. Information from the center of social services concerned certain types of material support, benefits, guarantees and services established by the legislation for adults and underages.

Information letters from the Laboratory of whole-body counters at the National Research Center for Radiation Medicine (NRCRM) were the principal and to a greater or lesser extent periodic materials that provided necessary information to the specialists who worked with population of RCT. Their thematic scope included the key factors in the formation of dose of internal radiation in residents of individual settlements of RCT in Zhytomyr, Rivne and Kyiv Oblasts (content of radionuclides in food, doses of internal radiation) based on the results of comprehensive radiation monitoring. Centers for socio-psychological rehabilitation are working only with the population in its residence and just taking into account the socio-political and socio-economic situation. Their line of effort is more focused on today's issues. Issue of public informing about the safety of living on RCT was risen at the International workshop «Problems of communication and public information in the event of nuclear or radiation emergencies: an example of overcoming the consequences of the Chornobyl accident» (2017) [42].

Considering the fact that population of guaranteed voluntary resettlement zone of RCT belongs to surveillance zone (SZ) of the Rivne NPP (RNPP), the former should be informed about a state of radiation situation in the area. Results of the survey showed that population had no information on radioactive contamination of drinking water, foodstuffs and forest foods. At that no question of the survey form revealed any difference in responses of urban and rural populations of the SZ. Confidence in information from various institutions was close to neutral. In general, the population is very skeptical about a receipt of information from local authorities, as well as from environmental societies and specialists of educational institutions.

Information awareness of the NPP SZ population is determined in everyday life by the activities of information and public relations departments and NPP information centers. Information for population about the radiation situation in satellite cities and SZ is provided on a daily basis through the communication tools. A study conducted at the South-Ukrainian NPP (SUNPP) showed that, according to local government officials, the importance of communication tools in everyday life varies depending on the SZ territory, namely being lower in rural areas, and higher in cities. In general, by information awareness, the official website of «SUNPP» is in the first place throughout the SZ territory, information screens are in the second place, and answering/reporting machines are in the third place. For the city of Voznesensk, located in SUNPP SZ, the telephone hotline is important, while for the rural settlements and city of Yuzhnoukrainsk there are television and a weekly newspaper. Official website of the SUNPP was utmost rated (4.67 on a 5-point scale), answering machines on the level of radiation and the free hotline phone were rated a bit lower (4.33), then followed the TV stories (3.67), reminders (3.33), weekly newspaper (1.33), and thematic brochures (Fig. 7.7).

According to assessments by managers, the information provided to SZ population is quite complete and user-friendly (4 points). Principal thematic

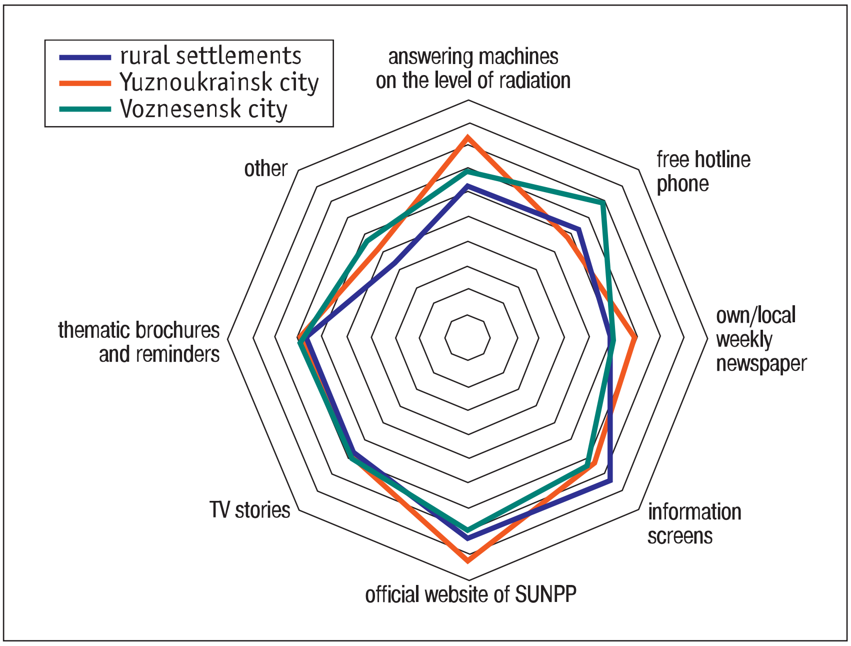

Figure 7.7. **Evaluations of effectiveness of NPP communication tools for providing daily information to SZ population by the local government experts on a 5-point scale**

areas are the radiation monitoring, environmental monitoring, technical condition, modernization and repairs, emergency training, notification, etc. Issues of radiation monitoring and information on a planned training are sufficiently covered for the population of Yuzhnoukrainsk city and rural settlements. The lowest assessment of completeness of information was provided by managers of environmental monitoring data, especially in rural areas (2.8 points).

The Internet sites, followed by quarterly and annual reports are the most informative tools for local government managers. Analytical reports are the third most informative, while press and television are the fourth. Periodically, once a month, the «Press-Fact» bulletin is published with a large amount of information and, in particular, articles on radiation and environmental situation in the SZ, prepared by the SUNPP Environmental Laboratory.

Public opinion on informing about the environmental and radiation situation in SZ differs significantly from the assessments by managers. Interviewing of rural working population of the SUNPP SZ showed low assessments of work of public services, which provide information on the impact of NPP operation on environment. The range of evaluations of all services was from 2.18 points to 2.75 points, i.e., below average (3 points on a 5-point scale). The lowest score was given to environmental companies, as 60.5 % of respondents rated their information as ineffective and 8 % as effective. Estimates of public informing by employees of educational institutions, NPPs, and health care facilities were equivalent (2.54 points). Accordingly, only 21.0 %, 17.8 % and 16.9 % of respondents believed that informing by employees of educational institutions, NPP and health care facilities was effective. Slightly higher scores were received by specialists from the State Emergency Service (2.75 points) and local self-governing bodies (2.71 points). The 27.4 % and 25.8 % of respondents considered the informing by State Emergency Service specialists and local self-government bodies as effective. Information at the place of work was determined to be the most effective, as 40 % of respondents considered it effective. The information channel «neighbors, friends» was essentially meaningful in both the NPP SZ and RCT.

Review of the SZ population survey data on effectiveness of information channels showed that the Internet resource was most effective for rural population (population estimate 3.5 points). The social networks cannel was close to the Internet resource (3.17 points), as in the case of television (3.13 points), and press (2.92 points). However, this score is quite low (3 points score meant a «more or less» effective channel for information providing). Radio, leaflets, memos, lectures were ineffective as channels of information for the majority of rural population, as their scores were 2.34–2.16 points, i.e., «ineffective».

In today's world, the able-bodied rural population of the SZ would like to receive a variety of information related to NPP operation, its impact on environment, including the radiation situation, storage and disposal of radioactive wastes, and socio-economic compensations for the risk of living near NPP. The 73.4 % of rural population of the SZ want to receive information on radiation status of the territory (place) of residence, 63.2 % – data on environmental monitoring and health. More than 50 % of rural working population want to have information on compensations of socio-economic risk of living near the NPP (56.8 %), shipment of radioactive wastes and their storage conditions (53.6 %).

The quality of informing the population of SZ was highlighted by the content analysis of communication media in the RNPP SZ at a runtime of three years. By thematic scope, the largest number of publications was usually occupied by ones of the matter-of-fact style, uninteresting for the general population reports on RNPP operation. Second place in the ranking was a voluminous and multifaceted topic related to the ecology and RNPP operation, namely numerous reports on official environmental inspections, data from the environmental laboratory of automated radiation monitoring system (ARMS), single critical articles and investigations of environmental issues related to the power plant. Articles that cover sponsorship or charitable assistance, along with participation of NPP employees in any positive events, were the third most popular topic in the image-building messages about NPPs. There were almost no publications targeted directly at the average population, which would provide information on what to do in case of emergencies. Most publications were with no stated authorship. In terms of the form of submission, the short messages were in the lead (69.6 %). In terms of informational coloring, the most of articles were neutral. The 94.0 % of selected material were characterized exclusively as informational. The information-analytical and analytical materials took up 6.0 %, but they were the ones better remembered and making a person think. Regional state administrations, being the co-founders of certain media, used no their opportunities to disseminate an information useful for the NPP SZ population and initiated no discussions on either environmental issues or receipt and distribution of subventions.

Based on the above, the government measures and tools aimed at preserving and improving the health of RCT population should be focused on providing the constant information to managers and specialists who implement measures on recovery from the accident at the provincial, regional, and district levels. It is necessary to restore the system of public informing through the healthcare, educational institutions and media. Reforming of the sanitary-epidemiological service led to removal of structure of bodies responsible for sanitary-educational work with population. Therefore, it is necessary to create such a structure on the basis of Ministry of Health and public health centers. System of informing the NPP SZ population in everyday life includes all the necessary components, namely the source of information, modes of information, means of communication, operativeness of information, categories of consumers. There are four key topic areas of information for the population. However when informing the SZ population the socio-psychological component of public status, public inquiries, imperfect feedback between communicator and consumer of information are not taken into account, which requires a respective improvement to deliver and uptake the information content.

7.4. The latest international approaches to the protection of people and the environment in nuclear and radiological emergencies

The basic document in Ukraine in the field of radiological protection is the Radiation Safety Standards of Ukraine (NRBU-97) [43]. NRBU-97 establishes radiation hygiene regulations to control both practical activity and intervention, in particular in case of radiation emergencies. NRBU-97 are based on the principles of radiological protection, which were set out in Publication 60 of the International Commission on Radiological Protection (ICRP) [44]. These ICRP approaches have also been taken as a basis in the documents of the International Atomic Energy Agency (IAEA) and the European Union, in particular in IAEA Publication № 115 [45] and in Council Directive 96/29/Euratom [46]. All the above documents were created more than 20 years ago.

In the time that has elapsed since their preparation and publication, new international approaches to human and environmental protection have been developed, which should also be applied in cases of nuclear and radiation emergencies. The first step in this process was the development of ICRP Publication 103 [47]. Based on it, new international safety standards have been developed [48–50].

For further presentation and analysis of new approaches to radiological protection in emergency exposure situations, it is appropriate to briefly mention the principles and criteria established by the current radiation-hygienic regulations of Ukraine. NRBU-97 [43], in accordance with [44, 45], establish two fundamentally different approaches to ensuring radiation protection:

➢ for all types of practical activities under normal operating conditions of radiation sources; and

➢ during intervention, which is associated with exposure of the population under emergency exposure conditions, as well as during chronic exposure as a result of exposure to technologically enhanced sources of natural origin.

NRBU-97 [43] require that radiological protection in intervention situations should be based on three principles: the principle of justification of countermeasures, the principle of non-exceeding the thresholds of deterministic effects, and the principle of optimisation of the form of intervention, its scale and duration. NRBU-97 [43] define three main levels of countermeasures and their use:

➢ urgent countermeasures to prevent the occurrence of acute clinical radiation manifestations of the effect of radiation on a person;

➢ countermeasures that cannot be delayed and aim to prevent deterministic effects;

➢ long-term countermeasures to prevent radiation doses below the thresholds for any deterministic effects and to reduce the risk of stochastic effects.

NRBU-97 [43] establish specific criteria for the introduction of urgent countermeasures for acute and chronic exposure, the values of which are presented in Table 7.2. In acute exposure conditions, the criteria are specified in terms of the predicted absorbed dose to organs or tissues of the human body, and in cases of chronic exposure, the criteria are specified in terms of the avoided annual equivalent dose.

The criteria for the introduction of countermeasures that cannot be delayed in radiation emergencies are established both in NRBU-97 [43] and in the Law of Ukraine «On the Use of Nuclear Energy and Radiation Safety» [51] (Table 7.3). There is a significant inconsistency between these documents: the numerical values of the intervention levels in both documents are the same, but in [51] they are established for predicted exposure doses, and in [43] they are established for averted exposure doses. At the same time, NRBU-97 [43] consider a countermeasure to be justified if the doses averted in 14 days after the emergency exceed the levels of unconditional justification. If only the lower boundaries of justification are exceeded, then for the justification of the countermeasure, the economic, societal and other factors involved in the optimization procedures must be taken into account. This feature is discussed in [52].

For a long-term countermeasure *relocation*, NRBU-97 [43] also set lower boundaries of justification and levels of unconditional justification. Dose criteria are established for exposure doses averted during the relocation period (200 mSv and 1 Sv, respectively) and in 12 months after the emergency (50 mSv and 500 mSv, respectively).

So, the current criteria for the introduction of countermeasures in Ukraine have been established for predicted absorbed doses, as well as for equivalent and effective doses (predicted and averted). The calculation of such exposure doses is carried out in the System for the operative analysis of the

Table 7.2
Criteria for urgent countermeasures [43]

Organ or tissue	Predicted absorbed dose in an organ or a tissue for 2 days, Gy	Annual averted equivalent dose, $Sv \cdot y^{-1}$
Bone marrow	1.0*	0.4
Lung	6.0	–
Skin	3.0	–
Thyroid	5.0	–
Eye lens	2.0	0.1
Gonads	2.0	0.2
Foetus	0.1	–

Note. *The criterion is usually applied to external exposure

Table 7.3
Criteria for countermeasures that cannot be delayed

Countermeasure	Committed dose for 14 days after an emergency [51]		Dose averted for 14 days after an emergency [43]					
			lower boundaries of justification			levels of unconditional justification		
	effective dose, mSv	committed absorbed dose to thyroid, mGy	to whole body, mSv	to thyroid, mGy	to skin, mGy	to whole body, mSv	to thyroid, mGy	to skin, mGy
Sheltering	5	–	5	50	100	50	300	500
Evacuation	50	–	50	300	500	500	1 000	3 000
Iodine prophylaxis:								
children	–	50	–	50*	–	–	200*	–
adults	–	200	–	200*	–	–	500*	–
Outdoor restriction:								
children	–	–	1	20	50	10	100	300
adults	–	–	2	100	200	20	300	1000

Note. *Committed dose of internal exposure from iodine radioisotopes which intake to the body for 14 days after beginning of an emergency

radiation situation in radiation emergencies, which is used at all nuclear power plants in Ukraine [53–55]. Also, it should be noted that the use of equivalent and effective doses to characterize exposure of people as a result of intake of radionuclides in emergency situations leads to significant uncertainty in assessing the risk of severe deterministic effects and is acceptable only to prevent the occurrence of stochastic effects.

ICRP Publication 103 [47] proposed an updated system of radiological protection, in particular in cases of nuclear and radiation emergencies. The key concept of the updated system is the *exposure situation*, which is defined as one of three situations: *planned exposure situation* is an exposure situation related to the planned operation of a radiation source or other activity within the practice, in particular within the practical activity; *emergency exposure emergency* is an exposure situation in an emergency with a radiation source; and *existing exposure situation* is an exposure situation that already exists when a decision on the need for the control and application of intervention measures has to be taken, and which at the time of such a decision does not have evidences of an emergency exposure situation and does not require immediate protection and safety measures. Requirements to radiological protection differ significantly for each exposure situation.

An emergency exposure situation can arise as a result of any emergency (accident, fire, flood, hurricane, malicious acts, etc.) and requires immediate actions to prevent or reduce adverse effects on people and the environment. The radiological protection system in emergency exposure situations includes preventive measures that reduce the risk of an emergency exposure situation and mitigate its consequences. After an emergency exposure situation occurs, exposure can only be reduced by intervention (protective measures).

In planned exposure situations, preventive measures are provided through safety assessments, analysis of potential exposure, application of preventive design solutions, measures of preparedness and response plans for emergency situations, and conducting emergency response trainings. A forest fire that leads to the carryover of radionuclides from a radioactive waste storage facility is an example of an emergency with a radiation source that was authorized to operate within a planned exposure situation (within the practical activity).

In existing exposure situations, the possibilities of applying preventive design solutions (regarding the occurrence of an emergency exposure situation) are significantly limited. However, adequate remediation measures, assessments of the existing exposure situation and other measures can significantly reduce the impact of an emergency on people. A forest fire on the territory of the Chornobyl exclusion zone is an example of an emergency with a radiation source within the existing exposure situation.

The updated radiological protection system introduces the concept of reference levels used to optimize protection and safety in emergency and existing exposure situations. Reference levels are set or approved by the government or other competent authority and may be specific to particular types of emergency exposure situations. The reference level plays the role of a boundary condition in determining the range of protection options that are considered when optimizing radiological protection. The reference level is the level of dose or risk above which it is not appropriate to allow exposures, and below which optimization of protection and safety is applied. The goal of an optimal protection strategy is to ensure that exposure levels are below the reference level. When an emergency exposure situation occurs, the actual exposure may be higher than the reference level. The reference level is used as a criterion for determining the need for protective measures and, if necessary, for prioritizing their application. Optimization of radiological protection should be applied even if the exposure doses are below the reference level.

The approaches proposed in ICRP Publication 103 [47] formed the basis for new international safety standards [48–50], which propose new criteria for making decisions on protective measures in a nuclear or radiological emergency. The documents [48, 49] establish two classes of general dosimetric quantities and criteria, which are focused on:

➢ prevention or minimization of severe deterministic effects;

➢ reducing the risk of stochastic effects.

Criteria of the 1st class are established for high exposure levels at which protective actions and other response measures must be applied under all circumstances. Criteria of the 2nd class are established for exposure levels when protective actions and other response measures are applied if they can be performed safely and do more benefits than harm.

To prevent severe deterministic effects, criteria are established in terms of the so-called RBE weighted absorbed doses (AD_T) in organs and tissues of the human body. The relative biological effectiveness (RBE) of radiation concerning a given biological effect in an organ or tissue T is an indicator that characterizes the relative ability of radiation to cause this effect. In this case, exposure is characterized by a number of indicators: the type of ionizing radiation (for example, alpha radiation), energy, intensity (dose rate), duration and fractionation. RBE is defined as the inverse ratio of the total absorbed doses of two different radiation types that lead to the same biological effect. Since the RBE of exposure depends significantly on these factors, and the biological effects themselves are also described by a number of indicators (for example, the number of dead cells and the time interval between radiation and the occurrence of the effect), RBE has significant restrictions as a characteristic of exposure. RBE has the advantage of being easy to use.

In modern international safety standards, RBE values ($RBE_{T,R}$) for deterministic effects caused by a type of radiation R in an organ or tissue T are set so that they are representative of the effects that are significant in emergency exposure situations. $RBE_{T,R}$ values are specific to the respective effect, the organ/tissue where the effect occurs, and the radiation type that may cause the effect (Table 7.4).

To prevent severe deterministic effects, [48, 49] establish criteria for AD_T, which can be generated:

➢ by external irradiation in no more than 10 hours;

➢ by internal exposure during the time Δ after the intake of the radionuclide ($AD(\Delta)_T$).

The main value of Δ is 30 days. For exposure of the embryo or foetus, the period of in utero development is used. The use of a time value of 30 days for $AD(\Delta)_T$ formation is a fundamental difference from the use of a much longer time, namely, 50 years for adults or up to 70 years for other ages, when calculating the committed equivalent and effective doses of internal exposure.

RBE weighted absorbed doses, in case of exceeding which response measures should be applied under all circumstances to prevent or minimize severe deterministic effects, are presented in Table 7.5 (for external exposure) and Table 7.6 (for internal exposure).

If the AD_T estimate exceeds the levels from Table 7.5, then, according to [48, 49], modern international safety standards require:

➢ take precautionary urgent protective actions immediately (even under difficult conditions) to keep doses below the generic criteria;

➢ to provide public information and warnings;

➢ to carry out urgent decontamination.

Table 7.4
Values of relative biological effectiveness $RBE_{T,R}$ for severe deterministic effects [48]

Effect	Critical tissue or organ	Exposure*	$RBE_{T,R}$
Haematopoietic syndrome	Red marrow	External and internal γ, internal β Internal α External and internal n	1 2 3
Pneumonitis	Lung (the tissue of the alveolar-interstitial region of the respiratory tract)	External and internal γ, internal β External and internal n Internal α	1 3 7
Gastrointestinal syndrome	Colon	External and internal γ, internal β External and internal n Internal α	1 3 0**
Necrosis	Tissue at a depth of 5 mm below the skin surface over an area of more than 100 cm^2	External β, γ External n	1 3
Moist desquamation	Tissue at a depth of 0.4 mm below the skin surface over an area of more than 100 cm^2	External β, γ External n	1 3
Hypothyroidism	Thyroid	Intake of iodine radionuclides Other radionuclides that accumulate in the thyroid	0.2 1

Notes. *α, β, γ, n mean exposure by α-, β-, γ-particles and neutrons, respectively; external β- and γ-exposure includes exposure due to bremsstrahlung radiation; **For alpha emitters uniformly distributed in the contents of the colon, it is assumed that irradiation of the walls of the intestine is negligible

Table 7.5
Dosimetric criteria for response to avoid or to minimize severe deterministic effects from external exposure

Effect	Criterion	Value
Haematopoietic syndrome, gastrointestinal syndrome, pneumonitis, cataract, hypothyroidism, permanently suppressed ovulation and sperm counts	$AD_{red\ marrow}$ (dose to internal tissues or organs (e.g. red marrow, lung, small intestine, gonads, thyroid) and to the lens of the eye from exposure in a uniform field of strongly penetrating radiation)	1 Gy
Embryo/foetal death, severe mental retardation, malformation, reduction in IQ, growth retardation	AD_{fetus} (embryo or foetus)	0.1 Gy
Necrosis of deep tissues	AD_{tissue} (dose delivered to 100 cm^2 at a depth of 0.5 cm under the surface)	25 Gy
Moist desquamation	AD_{skin} (dose delivered to 100 cm^2 dermis at a depth of 0.4 mm below the surface)	10 Gy

Table 7.6
Dosimetric criteria for response to avoid or to minimize severe deterministic effects from internal exposure

Effect	Criterion	Value
Haematopoietic syndrome	$AD(30)_{red\ marrow}$ (red marrow)	0.2 Gy for actinides, 2 Gy for other radionuclides
Hypothyroidism, acute radiation thyroiditis	$AD(30)_{thyroid}$ (thyroid)	2 Gy
Pneumonitis	$AD(30)_{lung}$ (alveolar–interstitial region of the respiratory tract)	30 Gy
Gastrointestinal syndrome	$AD(30)_{colon}$ (colon)	20 Gy
Embryo/foetal death, malformation, reduction in IQ	$AD(\Delta')_{foetus}$ (embryo or foetus)	0.1 Gy

If the $AD(\Delta)_T$ estimate exceeds the levels indicated in Table 7.6, then modern international safety standards require:

➢ to conduct an immediate medical examination, consultation and recommended medication; introduce long-term medical follow-up;

➢ to carry out special radiological monitoring in order to determine the levels of intake of radionuclides and doses to the injured person;

➢ to take measures of medical intervention in order to remove radionuclides from the human body (so-called «decorporation of radionuclides»), if possible.

Modern international safety standards [48, 49] also define general dosimetric criteria for introducing protective measures aimed at reducing the risk of stochastic effects. Such measures are divided into urgent, early protective and longer term actions. The values of the corresponding dosimetry criteria are given in Table 7.7.

Table 7.7
Dosimetric criteria for response to reduce the risk of stochastic effects

Criterion	Value	Protective actions
Urgent protective actions		
Equivalent dose to thyroid	50 mSv from intake for 7 days	Iodine prophylaxis
Effective dose, the maximum equivalent dose to any organ of the foetus	100 mSv in 7 days	Sheltering; evacuation; prevention of inadvertent ingestion; restrictions on food, milk and drinking water; restrictions on the food chain and water supply; restrictions on commodities other than food; contamination control; decontamination
Early protective actions		
Effective dose	100 mSv in a year	Temporary relocation; prevention of inadvertent ingestion; restrictions on food, milk and drinking water; restrictions on the food chain and water supply; restrictions on commodities other than food; contamination control; decontamination
The maximum equivalent dose to any organ of the foetus	100 mSv for the full period of in utero development	
Longer term medical actions		
Effective dose	100 mSv in a month	Counselling to allow informed decisions to be made in individual circumstances
The maximum equivalent dose to any organ of the foetus	100 mSv for the full period of in utero development	

8. CHORNOBYL – PROTECTION AND REVIVAL STRATEGIES

8.1. General medical consequences

3,259,761 citizens of Ukraine and 2,293 settlements were affected as a result of the accident at the Chornobyl NPP (ChNPP) in 1986 in Ukraine – the largest man-made disaster in the history of mankind. As of January 1, 2021, 1,718,113 people, including 322,876 children, had the status of victims of the Chornobyl disaster in Ukraine.

Among the victims, 105,096 people are persons with a loss of working capacity (persons with disabilities) and an established connection between the disease that led to the disability and the impact of the consequences of the Chornobyl NPP accident (category 1 victims), including 570 disabled «nuclear workers».

The total number of affected adult citizens as of January 1, 2021, compared to 2008, decreased by 441,444 people, or by 24.06 % (from 1,834,536 to 1,393,092 people). During this period, the number of participants in the liquidation of the accident decreased from 276,327 to 181,149, or by 95,178 people (34.44 %), that is, during the last 10 years died almost every third participant in the clean-up works at the Chornobyl NPP. The number of adult victims decreased from 1,558,209 in 2008 to 1,211,943 in 2021, or by 22.22 % (346,266 people). The number of children affected by the accident at the Chornobyl nuclear power plant has decreased from 534,568 in 2008 to 322,876 in 2021, or by 211,692. Regarding the reduction of the number of this category, it is also necessary to take into account the loss of the status of child victims upon reaching the age of majority according to the current legislation.

It is impossible to ignore such a painful and socially important indicator as 41,165 people who have the status of spouses/husbands (widows) of deceased citizens whose death was related to the Chornobyl disaster.

The most important non-neoplastic effects 35 years after the accident are:

- ➢ increase in morbidity and mortality of Chornobyl clean-up works participants from cardiovascular diseases;
- ➢ high frequency of cerebrovascular diseases and cognitive disorders in Chornobyl clean-up works participants;
- ➢ increasing the frequency of radiation cataracts, macular degeneration and vascular pathology of the eye;
- ➢ increase in the incidence of non-neoplastic diseases of the thyroid gland;
- ➢ mental health disorders in children who were irradiated in utero.

The most important tumor effects include:

- ➢ the incidence of all forms of cancer in the participants of clean-up work at the Chornobyl NPP exceeds the national level: SIR = 106.7% (95% CI: 104.9–108.5); significantly exceeding the expected incidence rate of thyroid cancer among Chornobyl clean-up workers – by 4.4 times, evacuees – by 4.0 times, residents of contaminated territories – by 1.3 times;
- ➢ the incidence of leukemia and lymphomas of the Chornobyl clean-up workers is 1.5 times higher than the national level and that of evacuees is 1.4 times higher;
- ➢ the incidence of breast cancer among Chornobyl clean-up workers women is 1.6 times higher than the expected level;
- ➢ a higher level of morbidity was established in the female and male population of the territories of Ukraine that were exposed to greater ^{131}I contamination and, accordingly, had higher average doses of radiation to the thyroid gland (more than 35 mSv) compared to the indicators of the rest of the regions (less than 35 mSv).

8.2. Estimation of radiation doses and radiation-hygienic monitoring in the remote period after the Chornobyl disaster

Radiation-hygienic monitoring of settlements and radiation doses in population of territories that were radiologically contaminated as a result of the Chornobyl disaster

According to the Law of Ukraine «On the Legal Regime of the Territory Contaminated by Radioactive Contamination as a Result of the Chornobyl Accident» and Resolutions of the Cabinet of Ministers of the USSR № 106 from 23.07.1991 2021 settlements (ST) were subject to dosimetric control. In the current version of the Law of 16.10.2012 № 5459-VI (version 07.11.2015) the 4th zone (enhanced radioecological control) was removed. Accordance with the new version of the Law 842 settlements of Ukraine in 3rd zone (zone of guaranteed voluntary resettlement) are subject to radiation and hygienic monitoring.

On the other hand, according to the results of the State Program «General Dosimetric Certification of Settlements of Ukraine», conducted in 2011–2013, 127 ST of Ukraine have «passport doses», which exceed 0.5 mSv · year^{-1} and can be attributed to radioactively contaminated territories (RCT) and are subject to radiation-hygienic monitoring. These are ST of Rivne (64) and Zhytomyr (53), Kyiv (4), Volyn (6) oblasts. Since 2014, dosimetric control of the population of RCT in Ukraine is practically not carried out. The only institution that conducts work on the complex radiation and hygienic monitoring of radiation contaminated territories (RCT) remains the State Institution «National Research Center for Radiation Medicine of the National Academy of Medical Sciences of Ukraine «(NRCRM). The work is carried out in the framework of research work of the National Academy of Medical Sciences of Ukraine.

According to the results of the research, it is established that the annual effective doses of the population from the «Chornobyl component» in surveyed settlements are formed in mainly due to doses of internal radiation. The main part of the dose is internal irradiation of residents of the surveyed ST of Rivne, Zhytomyr oblasts is formed due to the receipt of ^{137}Cs with local household products – milk, and products of natural origin – especially dried mushrooms and berries. ^{90}Sr does not make a significant contribution to the dose of internal radiation, as its content in products is much lower than the permissible level. For residents of the surveyed ST of Kyiv oblast, where the content of radionuclides in milk and potatoes significantly lower than the permissible levels provided by the Hygienic Standard HS 6.6.1.1-130-2006, the main part of the dose of internal radiation is formed due to the consumption of forest products.

It was found that the main factor that forms the dose of internal radiation is the intake of ^{137}Cs in the body of residents with such basic foods as milk and forest products, especially mushrooms, which in the Polissya region traditionally occupy a significant part of the diet. The ^{137}Cs content is predominant part of the samples of milk and mushrooms collected in the surveyed ST of Rivne oblast in 2017 significantly exceeds the permissible levels. The maximum recorded content of ^{137}Cs in the collected milk samples is 384.7 Bq · l^{-1}, which is 4 times higher than permissible levels, in dried mushrooms – 36.9 kBq · kg^{-1} – 15 times higher than permissible levels. 1.6–2.3 times increase in the content of the incorporated ^{137}Cs in the residents of the surveyed ST from May to October against the background of a decrease in the content of this radionuclide in milk in the same period of time, according to that the main dose-forming factor is forest products, which in 2017 due to the rainy summer and autumn gave a «harvest rich « and the population was able to collect them in large quantities. In none of the potato samples did the ^{137}Cs content exceed the permissible level of 60 Bq · kg^{-1}. Contents ^{90}Sr in the vast majority of samples is below the sensitivity of the method (1 Bq · kg^{-1}), and does not make a significant contribution to the formation of the dose of internal radiation.

Due to the fact that RCT products of own economy (milk, potatoes) and natural origin (especially wild mushrooms and berries) are contaminated with radionuclides, and the unstable socio-economic situation contributes to increasing the share of these products in the diet, it is essential to conduct comprehensive radiation monitoring, which makes it possible to determine the main radiation and hygienic factors of formation radiation doses at the current stage of the accident, which, in turn, is the basis for ensuring adequate measures to minimize radiation doses to the population. Thanks to the work carried out over the last 30 years, unique in structure and content databases have been created, which contain quantitative characteristics territorial-temporal distribution and dynamics of changes in a number of important radiological indicators, namely: content of ^{137}Cs and ^{90}Sr in food products (milk and potatoes) of local production (over 500 thousand measurements); more than 1.3 million measurements of the content of radiocaesium in the body of the inhabitants of the radiation contaminated territories of Ukraine; about 100 thousand estimates of radiation doses (separately external and internal) of residents of emergencies located in radioactively contaminated areas.

Analysis of relationship between socio-psychological status and morbidity of the adult population in radiologically contaminated territories

More than 35 years after the Chornobyl accident, the population believes that the environmental situation at the place of residence is determined by the consequences of the Chornobyl accident. About 51.0 % continue to perceive the radiation situation as dangerous to health. 70.6 % are concerned about their own health and the health of children, and 35.3 % are concerned about the lack of information about the health of the population. Health concerns affect mental health state of the population. The Generalized Mental Health Rate (GHQ 28) is higher in the radiation contaminated territories population than in other areas, but in the former it is determined by somatization and anxiety scales, in the latter by somatization and social dysfunction. This is especially pronounced in the age groups 45–49 years, 50–55 and 56–59 years.

Adult morbidity rates are higher on radiation contaminated territories compared to adult morbidity rates in other areas, in particular by class diseases: blood and hematopoietic organs, endocrine system, mental and behavioral disorders, circulatory, digestive, skin and subcutaneous fiber, musculoskeletal and trauma, poisoning and other consequences.

Under such conditions (socio-psychological condition, morbidity of the population) the level of health and safety is quite low, as indicated 52.0 % of the population. Of particular concern to the population are issues of medical and preventive care, provision of medicines and emergency medical care.

8.3. Urgent tasks of overcoming the consequences of the Chornobyl catastrophe

General dosimetric certification of Ukraine settlements

The first general dosimetric certification was started in 1991, its data became the basis for the introduction of certain anti-radiation measures in different territories. As a result of re-certification in 2011–2012, it is shown that in 2011 almost 85 % of those settlements of Kyiv and Zhytomyr oblasts, which were previously referred to the zone of unconditional resettlement, the zone of guaranteed voluntary resettlement or in fact had a «passport» dose of less than 0.5 mSv/year, ie according to the dose criterion have already lost the status of «victims». The same applies to 52 % of all settlements certified in 2012. There is an annual decrease in the number of settlements that according to the dose criterion should be assigned to the 3rd zone (1–5 mSv · year^{-1}).

In 2011 and 2012, only 25 and 26 settlements from Zhytomyr and Rivne oblasts fell into the range of 1–5 mSv · year^{-1} (guaranteed voluntary resettlement zone), respectively. Regarding the zone of unconditional resettlement (dose> 5 mSv), since 2005 there have been no existing settlements corresponding to this zone. There is a need for a new general dosimetric certification, the results of which will be the basis for the correction of anti-radiation measures in different areas. Only the results of dosimetric certification should be the only objective criterion for the suspension of any interventions in the event of achieving a normal (pre-emergency) radiological situation in the areas classified as unconditional and guaranteed voluntary resettlement. It is important to maintain a system of control over the levels of internal exposure of the population with the help of radiation meters the person who is a basis for control of dose loadings of the population.

State Register of Ukraine of Chornobyl victims – problems and prospects for renewal

One of the measures for social protection of the population affected by the Chornobyl accident was medical control their health and health-improving measures in specialized medical institutions (radiation protection dispensaries at the regional level and NSCRM – the leading institution). The NSCRM was involved in monitoring the level of contamination of food produced in the contaminated area, and measuring the doses of radiation to the population, reconstruction of doses in the event of their loss or absence. Examination and treatment of victims of different categories according to special protocols contributed to the development and implementation of recommendations aimed at reducing the content of radionuclides in adults and children, as well as to restore their viability (restoration of efficiency and prolongation of healthy life). A significant achievement was the development of educational work with the population on the observance of personal and occupational hygiene measures that help cleanse the body of radionuclides. Medical and health-improving measures, in addition to the listed methods, include regular medical examination of the population living in the contaminated area, sanatorium treatment and rehabilitation of this population.

This is especially true for children and pregnant women. In addition, as evidenced experience of working with victims, we must not forget about the socio-psychological rehabilitation of the population.

Modern nuclear safety standards adopted by the International Atomic Energy Agency (IAEA) require member countries to establish and the functioning of national medical and dosimetric registers of occupational radiation exposure. Today in many countries there is experience in the development, creation and operation of medical, dosimetric and medico-dosimetric registers.

In Ukraine, after the Chornobyl accident, the State Register of Ukraine of Persons Affected by the Chornobyl Accident (SRU) was established in order to solve the problems of medical and social support of persons affected by the Chornobyl disaster. To him consists of medical, dosimetric and sociological sub-registers, which allows for personal accounting of persons exposed to radiation the Chornobyl disaster, their children and future generations, and assess their health and changes over time. The SRU databases are filled in based on the results of the annual medical examination of victims conducted by territorial health authorities. To solve the problems of state policy in the field of preserving the health of victims of the Chornobyl accident, reduce their mortality and morbidity, find reserves to save financial resources spent on medical and social protection of the affected population, improve SRU funding, strengthen staffing and logistics.

Measures to preserve the health of victims

During the post-Chornobyl period, a system of medical care was provided and streamlined in Ukraine for the population affected by the Chornobyl disaster. It consisted of inpatient care; conducting annual medical examinations (medical examinations); creation and functioning of the SRU; the work of interdepartmental expert commissions to establish the causal link between disease, disability and death from the action of ionizing radiation and other harmful factors as a result of the Chornobyl accident; equipping medical institutions with modern diagnostic and therapeutic medical equipment; provision of medicines and medical supplies; treatment of seriously ill patients; social and psychological rehabilitation; introduction of scientific developments in medical practice.

Special attention needs to be paid to maintaining state support of the network of specialized medical institutions for radiation protection (dispensaries for radiation protection of the population and restoration of medical and sanitary units of nuclear energy complex): Main institution – National Research Center for Radiation Medicine as a center that cooperates with the WHO in the network of medical preparedness and assistance in radiation accidents («REMPAN»). Maintaining the activities of this system at the appropriate level contributed to limiting the growth of disability and mortality, maintaining the ability to work of persons with partial loss, ensuring social and psychological rehabilitation.

Strategic directions of prevention and health protection of the adult population affected by the Chornobyl disaster in the remote period

The strategy of prevention and health protection of the adult population affected by the Chornobyl disaster in the late terms upon accident should be comprehensive and include measures of both primary and secondary prophylaxis. The key directions of prevention are presented in diagram (Fig 8.1).

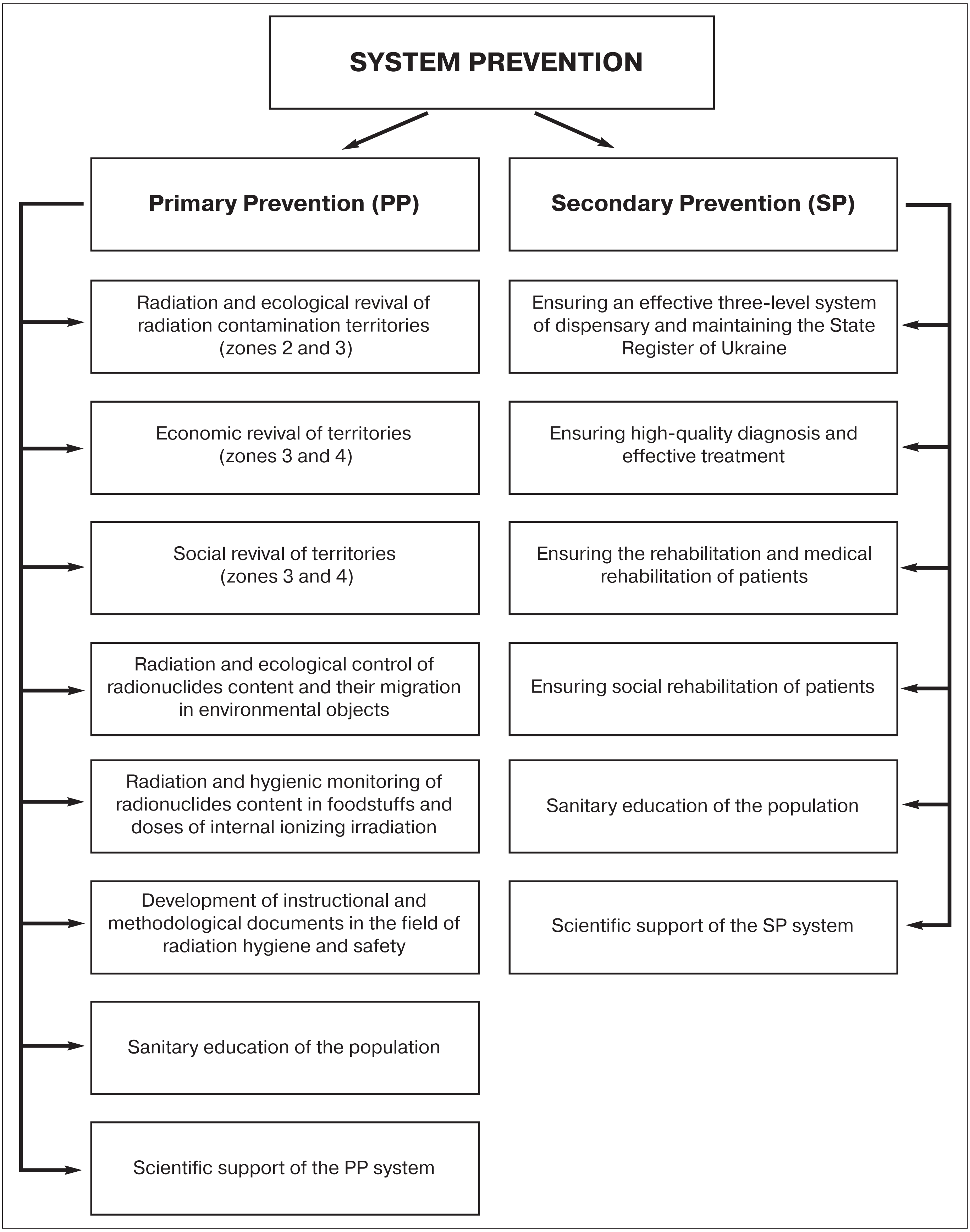

Figure 8.1. Scheme strategic directions of prevention and health protection of the adult population affected by the Chornobyl disaster, in a remote crash period

The following positions are relevant in the primary prevention system:

➢ radiation and hygienic renewal of radiologically contaminated territories with ^{134}Cs and ^{137}Cs soil contamination density of 1 Ci/km^2 and more with an average population dose of chronic ionizing irradiation of 0.5 mSv/year;

➢ economic renewal of radiologically contamination territories featuring the creation of infrastructure of agricultural and industrial enterprises, network of technical and secondary technical occupational education, and job market;

➢ ensuring the social well-being e. g. living conditions, material prosperity, employment perspectives, professional growth (first of all for young people), availability of effective healthcare; cultural and spiritual education deserves a special attention there;

➢ it is still relevant to ensure the long-term radiation and ecological monitoring of ^{134}Cs, ^{137}Cs, ^{90}Sr radionuclide and transranium elements' behavior in environmental objects (soil, plants, reservoirs) and in drinking water (wells);

➢ radiation and hygienic monitoring of radionuclide content in food products produced at private farms and in forest products (mushrooms, berries);

➢ a special package of normative and regulatory documents is required to ensure the radiation-safe living conditions for health and activities of daily living of the radiation-contaminated areas residents;

➢ raising knowledge, first of all, of the radiation-contaminated areas population in the field of radiation hygiene and safety.

When conducting the prophylactic medical examinations of the affected population the diagnostic, therapeutic and preventive care (treatment, health improvement, and rehabilitation) should be focused at the prevention of principal non-neoplastic diseases that are decisive on morbidity, disability and mortality levels.

Of circulatory system diseases the coronary heart disease, cardiomyopathy, acute cerebrovascular disease and their consequences, diseases of arteries, arterioles and capillaries are of top-priority, especially in persons over 40 years of age at the time of examination.

Regarding the list of a required scope of clinical, experimental, and laboratory examinations for early diagnosis of certain non-neoplastic diseases conditioning a high risk of health loss we recommend to follow the Guidelines «Improving of medical control over the health of adult population living on radiologically contaminated territories» issued earlier in 2010.

Of course, the implementation of these strategic directions for the prevention of health loss in population affected by the Chornobyl accident can be carried out only on the basis of comprehensive state targeted programs with sufficient budget funding. In recent years, the public interest in undergoing the prophylactic medical examinations has decreased significantly. According to SRU data the 70.9 % of sufferers were covered in 2017. Lack of financial opportunities for obtaining the high-quality diagnosis, qualified treatment, and rehabilitation is one of the reasons here.

CONCLUSIONS AND BRIEF RECOMMENDATIONS

1. At this stage of the long period after the Chornobyl accident, the main contribution to its medical consequences is made by non-stochastic effects in the form of a wide range of non-neoplastic diseases, as well as stochastic – oncological and oncohematological pathology. In most cases, they are the leading causes of disability and mortality, and are the main source of funds needed for treatment and prevention.

2. According to the results of the research, it is established that the annual effective doses of the population from the «Chornobyl component» in the surveyed settlements are formed mainly due to the doses of internal radiation. The main part of the internal radiation dose of the residents of the surveyed Rivne and Zhytomyr regions is formed due to ^{137}Cs with local household products – milk, and products of natural origin – primarily dried mushrooms and berries. For the residents of the surveyed state of emergency of Kyiv region, the main part of the dose of internal radiation is formed due to the consumption of forest products.

3. There is a need for a new general dosimetric certification, the results of which will be the basis for the correction of anti-radiation measures in different areas. Only the results of dosimetric certification should be the only objective criterion for the suspension of any intervention in the event of achieving a normal (pre-emergency) radiological situation in the areas classified as unconditional and guaranteed voluntary resettlement.

4. It is important to maintain a system of monitoring the levels of internal exposure of the population

with the help of human radiation meters, which is the basis for monitoring the dose of the population.
5. The health of the adult population affected by the Chornobyl disaster in the remote post-accident period should be assessed as «extremely unsatisfactory». Non-neoplastic somatic diseases are a major contributor to ill health. At present, 95 % of Chornobyl clean-up workers at the 1986–1987 Chornobyl nuclear power plant and 70 % of evacuees have the third health group, ie chronic somatic pathology. In the structure of the causes of non-neoplastic diseases in the liquidators, evacuees, residents of radioactively contaminated territories in the most remote period of the accident (2013–2016), the main shares are diseases of the circulatory system, digestive, respiratory, musculoskeletal and nervous systems. These diseases account for up to 90 % of all non-neoplastic cases.
6. During the post-accident period, the level of disability of the studied contingents from non-neoplastic diseases significantly increased. In the structure of the causes of disability of liquidators, evacuees, residents of radiation-contaminated areas the main shares are diseases of the circulatory system, digestive, respiratory, nervous, endocrine systems. The highest level of disability was found among people whose age at the date of the Chornobyl accident was 40–60 years.
7. In the remote period of the accident, the death rate of liquidators, evacuees, and radiation-contaminated areas residents from common somatic diseases increased significantly. The most significant mortality rates were established in 1998–2012 (12–26 years after the accident). In the last observation period (2013–2016) there was a certain tendency to reduce the mortality rate of the studied contingents of the population, mainly due to the elderly, ie 40–60 years on the date of the accident, due to the impact of «extinction» and with the manifestation of natural selection. In the structure of the main causes of mortality of the affected contingents of the adult population, the determinants are diseases of the circulatory system (from 71 to 94 %), diseases of the digestive system (from 8 to 12 %, mostly in younger age groups), respiratory organs (from 1 to 7 % age). The contribution to the structure of mortality of diseases of the nervous system is about 2 %.
8. Among the stochastic consequences is the implementation of thyroid cancer in children and affected adults of all categories, increased incidence of other solid tumors, increased incidence of Chornobyl clean-up workers leukemia and breast cancer in women involved in Chornobyl clean-up works, increased instability of the irradiated genome persons and their descendants.
9. About 51.0 % of the radioactively contaminated territories population continues to perceive the radiation situation as dangerous to health. 70.6 % are concerned about their own health and the health of children, and 35.3 % are concerned about the lack of information about the health of the population. Health concerns affect the mental state of the population. 10. Effective medical protection of victims for the coming years and decades requires the restoration and concrete filling of the National Program for Overcoming the Consequences of the Chornobyl accident and the restoration of the State Budget Program «Comprehensive Health Care and Treatment of Oncological Diseases».
11. The Government of Ukraine should continue to improve the system of health care and social protection of the population affected by the Chornobyl accident, paying special attention to the contingents of priority medical surveillance.
12. It is necessary to continue monitoring the medical and demographic consequences, the peculiarities of the biological aging of the affected population, given the expected persistence of increasing trends in many classes of diseases that cause high levels of disability and mortality. The results of the monitoring should fill the State Register of Ukraine of Chornobyl Victims, which needs radical changes to transform the bank's passive one-way data collection into a tool for operational analysis of verified information needed for strategic and tactical management decisions. Such changes are possible under conditions of stable and sufficient funding, updating the technical base of the register and staffing at all levels of its operation, scientific and methodological, dosimetric and information and analytical support.
13. Since certain types of solid tumors after radiation exposure have different latent periods of occurrence (from 10 to 45 years), there is a need for further monitoring of this pathology with special attention to diseases such as breast, esophageal, gastric, lung, colon, kidneys, bladder. Particular attention should be paid to those groups of the population who were 0–9, 10–19 years old at the time of the Chornobyl accident.
14. In order to prevent thyroid cancer in the irradiated population and Chornobyl clean-up workers, it is necessary to take scientifically sound measures

aimed at timely detection and treatment of precancerous pathology.

15. Special attention needs to be paid to the study of the peculiarities of cataractogenesis, development of retinal and vascular eye pathology in Chornobyl accident clean-up workers with external radiation doses over 0.25 Gy. Also, the improvement of methods of treatment of macular pathology in radiation-exposed persons is becoming increasingly important.

16. It is expected that the population of the cohort born in 1968–1986, living on radioactively contaminated territories, will have reduced, viability in the range of middle and old age. Therefore, preventive, treatment-diagnostic and rehabilitation measures for radioactively contaminated territories should be aimed at maintaining the health of young and middle-aged people.

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Chapter 3

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Chapter 7

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