

**GOMEL STATE MEDICAL INSTITUTE**

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**PATHOPHYSIOLOGY  
OF INCORPORATED  
RADIOACTIVE EMISSION**

**Gomel, 1998**

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The publication deals with the effect of incorporated radioisotopes upon the condition of vital systems of the organism. The author has employed the clinical and experimental approach to analyze the relationship between the origination of a variety of pathological conditions and the quantity of radioisotopes incorporated by the organism, primarily <sup>137</sup>Cs, considering its extensive propagation in the environment after the disaster at the Chernobyl nuclear power plant.

The publication is intended for practitioners, researchers investigating the problems of radiation effect upon the human organism. It can also serve as a

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## FOREWORD

The Chernobyl disaster has brought about a lot of grief and suffering to the people of Belarus, Ukraine, Russia. Partially it has been due to the lack of awareness about valid information how the factors of radioactive fall-out affect the human organism.

Release of a huge quantity of radioisotopes into the environment has placed the lives of many thousands and millions of people of the living and future generations under constant threat.

In order to reduce the negative effect of radiation agents upon the human organism to the minimum, profound medical research is required using the results of fundamental studies. The present publication evaluates the results achieved by the author and researchers of the Gomel Medical Institute in numerous research projects aimed at assessing the effect upon the human organism of the Chernobyl radioisotopes which contaminated the environment. The accomplished research has been based on the following methodological approaches:

1. Assessment of the medical and biological effects with the consideration of the dose of radioisotopes incorporated by the organism.
2. Investigation of pathological processes clinically and by experimental simulation among laboratory animals (the clinical and experimental approach).
3. Investigation of structural, functional and metabolic modifications evolving in the organism, its individual organs and systems (the morphofunctional approach).
4. Assessment of the severity of pathological conditions, such as disorders of the integrating processes in the organism in order to combine together the pathological modifications evolving in different organs.

The author hopes that the treated problems will attract the medical and scientific community and will welcome with appreciation all comments and suggestions.

## Chapter I

### 1. RESPONSES OF HUMAN AND ANIMAL ORGANISMS TO RADIOISOTOPES RELEASED BY THE CHERNOBYL DISASTER. FEATURES OF INCORPORATION OF $^{137}\text{Cs}$ AND $^{90}\text{Sr}$ BY THE ORGANISM AND THE GOVERNING FACTORS

The disaster at the Chernobyl Nuclear Power Plant in 1986 led to a release of at least 180 million Curies of radioactive substances (letting alone the radioactive fallout of several tons of nuclear fuel around the station (V.B. Nesterenko, 1992). Among all the radioisotopes released into the atmosphere the major contributors into the dose rate are Iodine-131, Cesium 137 and 134, Strontium-90.

Iodine-131 has the half-life 8.05 days, Cesium-134 — 2.06 years, Cesium-137 — 30 years, Strontium-90 — 29.12 years, meanwhile Plutonium-239 — 24,390 years (V.B. Nesterenko, 1992).

While the short-living isotopes (iodine-131, strontium-90), inert gases (krypton, xenon, etc.) were the main contributors into the dose rate, Cesium 137 and 134 became the governing contributors in the second period. Also the effect of strontium-90 and transuranium radioisotopes (Plutonium) included into the composition of "hot" particles should be taken into consideration. These radioactive elements are incorporated by the organism with food, water and air, in addition to creating the external gamma-background.

Iodine-131 has the half-life 8.05 days and the main paths of its incorporation are gastric, inhalation (absorption through outer skin makes up 1-2%) (V.A. Bazhenov et al., 1990).

Significant sources of penetration of radioactive iodine into the human organism are foodstuffs of plant and animal origin, specifically milk, fresh milk products, leaf vegetables. Iodine-131 concentration in the organisms of goats and sheep exceeds that in cows several times. Meat basically does not contain this radioisotope, yet its significant quantities are contained in bird eggs.

Iodine-131 is rapidly absorbed by blood and lymph. The quantity and rate of absorption, accumulation of this radioisotope in organs and tissues, the rate of its excretion from the organism depend upon age, sex, concentration of stable iodine in food (V.B. Bazhenov et al., 1990). The thyroid gland manifests its maximum concentration. Already two hours after introduction of the isotope its concentration in the thyroid amounts to 5-10%, and after 24 hours 25-30% of the total amount (V.A. Bazhenov et al.).

Other organs (kidneys, liver, muscle and bone tissues) accumulate this radioactive isotope in much smaller quantities.

It has been revealed that iodine-131 crosses the placental barrier and penetrates from the mother's organism into the fetus predominantly accumulating in the thyroid (V.A. Bazhenov et al, 1990).

Primarily kidneys excrete the radioactive iodine from the organism. Iodine-131 effects upon the human organism during the first days after the disaster are injuries of the thyroid. The dose burden upon this organ due to the incorporation of radioactive iodine by humans is produced within a relatively short period of time 2.5-3 months after the disaster because of the short half-life of this element.

It has been revealed that the thyroids of children (aged 0-17 years) living in the Khojniki district received the highest doses of radiation (242-527 cGr). The thyroid doses in Gomel amount to 15-60 cGr, in Minsk - from 2.4 to 9.2 cGr.

Cesium has 23 known radioactive isotopes, yet at present the current situation is primarily determined by  $^{137}\text{Cs}$  and  $^{134}\text{Cs}$  isotopes.

mushrooms 9,787 Bq/kg (V.B. Nesterenko, 1986). Small quantities are incorporated through respiratory tracts (0.5%). After peroral incorporation and absorption by blood significant quantities of Cesium-137 are secreted into the intestinal lumen and reabsorbed by the colon. Such natural incorporation of the radioisotope together with food (grain crops grown in the areas contaminated with radioisotopes) leads to its different accumulation in tissues and organs.

Feeding female and male common breed albino rats and Vistar line rats with oats containing about 400 Bq/kg of  $^{137}\text{Cs}$  would result in its significant accumulation in the organism after several weeks.

The maximum  $^{137}\text{Cs}$  concentration has been registered in the tissue of the myocardium (Fig. 1), while its concentration in bone and muscle tissues is much less (Yu.I. Bandazhevsky, G.S. Bandazhevskaya, 1995). Radiometric measurements of the autopsied material have revealed the maximum quantities of this radioisotope in the thyroid gland per unit of the organ weight, somewhat less in the heart, liver, skeleton muscle (Yu.I. Bandazhevsky, A.M. Perepletchikov, 1996). These results are confirmed by the studies of E.F. Lushnikov et al. (1996) who have demonstrated that the maximum quantities of  $^{137}\text{Cs}$  are registered in the internal organs among the residents of the Bryansk and Kaluga Region.

Pronounced differences in the accumulation of  $^{137}\text{Cs}$  by males and females should be emphasized. When the radioisotope is incorporated enterally male organisms accumulate it more intensively than females. It is confirmed by the results of numerous experimental studies of laboratory animals (Yu.I. Bandazhevsky, N.E. Fomchenko et al., 1995) and by radiometric measurements among the residents of the Gomel Region (Yu.I. Bandazhevsky et al., 1996).

A comparative analysis of accumulation of  $^{137}\text{Cs}$  by children has manifested that its concentration increases as a function of age (Fig. 2). In particular, children born in 1978-1981 had the  $^{137}\text{Cs}$  concentration about 120 Bq/kg, meanwhile the children born in 1989-1996 had it equal to 60 Bq/kg.

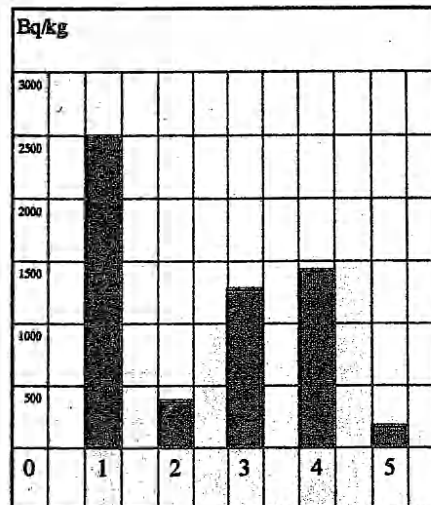


Fig. 1. Accumulation of  $^{137}\text{Cs}$  by organs and bodies of experimental animals: 1 - heart; 2 - liver - 3 - spleen; 4 - kidneys; 5 - body

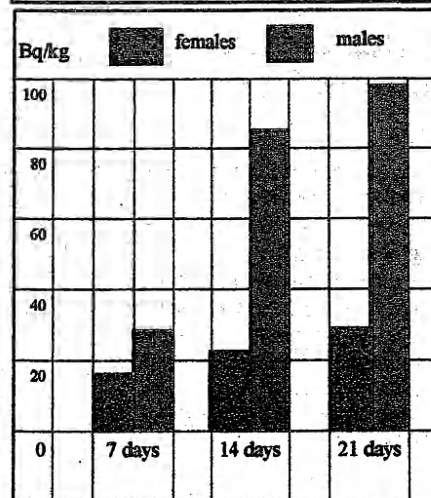
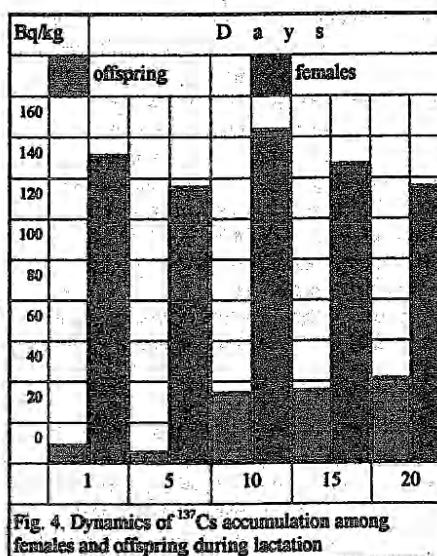
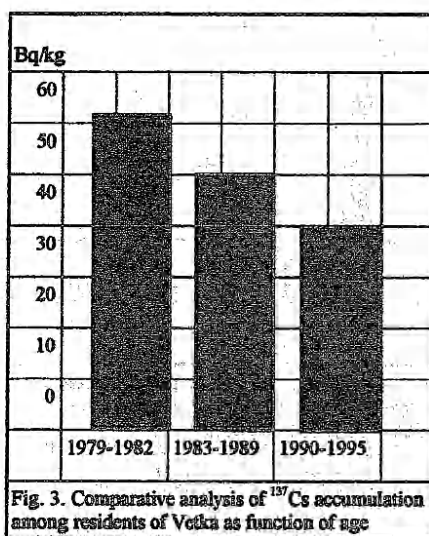


Fig. 2. Accumulation of  $^{137}\text{Cs}$  in organisms of experimental males and females

Laboratory newly-born animals manifest the least  $^{137}\text{Cs}$  concentration in experiments (Fig. 3) (Yu.I. Bandazhevsky, T.S. Ugolnik, 1995). It is confirmed by the results of radiometric studies of the autopsied material of the children of the first year of life (Yu.I. Bandazhevsky, A.M. Perepletchikov, 1996; E.F. Lushnikov et al, 1996). Meanwhile, the concentration of gamma-sources ( $^{137}\text{Cs}$  and  $^{134}\text{Cs}$ ) increases strongly in the mother's organism during pregnancy (Yu.I. Bandazhevsky, T.S. Ugolnik, 1995) exceeding the accumulation by non-pregnants (Fig. 3).

Analysis of accumulation of radioisotopes in the organisms of the offspring manifests its rise in the areas with heavier  $^{137}\text{Cs}$  contamination (Yu.I. Bandazhevsky et al., 1996).

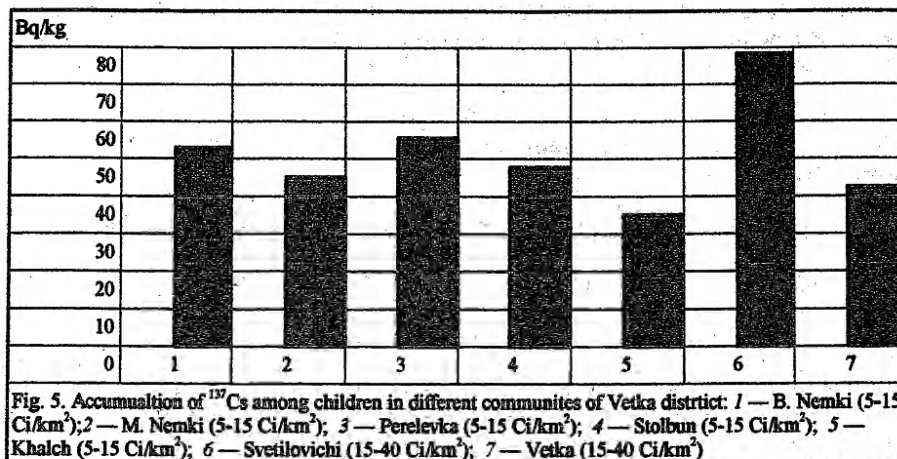
In particular, the average  $^{137}\text{Cs}$  concentration in the organisms of Gomel children per unit of body weight amounts to 30.0 Bq/kg (at a contamination level with this element 1-5 Ci/km<sup>2</sup>), meanwhile its accumulation is much larger in the areas with a much higher contamination level (Fig. 4).



In particular, the average  $^{137}\text{Cs}$  concentration per body weight in the organism of Gomel children in 1994 amounted to 30.0 Bq/kg (with the soil contamination 1-5 Ci/km<sup>2</sup>), meanwhile in the areas with a higher level of contamination, its accumulation is significantly higher (Fig. 5).

A high probability of incorporation of radioisotopes with mushrooms and berries in the radiation contaminated areas should be taken into consideration.

Mainly kidneys are responsible for the excretion of  $^{137}\text{Cs}$  from the organism when up to 80% of  $^{137}\text{Cs}$  introduced within a single time is excreted within a month. The period of half-excretion of  $^{137}\text{Cs}$  from human organism is 70 days, from mice 3 days, from rats 18 days, from guinea pigs 19-25 days, from rabbits 19 days (N.V. Zhuravlev, 1990).



There is a number of reagents influencing the process of incorporation of radioactive cesium by human and animals organisms, enterosorbents, in the first place, which combine radioactive elements, microelements, bacterial preparations, chemical compounds in the lumen of the gastrointestinal tract which excrete them.

A variety of different groups of such compounds have been proposed. Yet, not all of them satisfy the requirements: (1) to reduce the accumulation of radioisotopes in the organism; and (2) to restore the processes of metabolism.

A number of enterosorbents have been tested at the Gomel Medical Institute in experiments with laboratory animals to assess their effectiveness in respect to  $^{137}\text{Cs}$ . The sorbent containing 60% of modified clay and 40% dextrin has been rated as the most promising enterosorbent which never aggravates the effect of radioisotopes upon the liver and kidney tissues, unlike other sorbents, such as organic silica or charcoal (N.E. Fomchenko, 1997).

Experiments with sorbents containing pectins, have manifested their high effectiveness in excreting radioisotopes from the organism. Pectopal belongs to this group of effective compounds (Yu.I. Bandazhevsky, I.K. Lyakhova, 1997).

Strontium ( $^{90}\text{Sr}$ ) is a radiation source having half-life 28.5 years (V.F. Zhuravlev, 1982). Strontium is a stable microelement actively involved in the metabolism of plants, it is constantly present in the tissues and organs of man and animals. Being analogous to calcium, upon incorporation it gets involved in the mineral metabolism.

It penetrates into the organism through the intestinal gastric tract, lungs and skin (V.S. Kalistratova, 1990). The greatest risk is produced when irradiation is due to the penetration of  $^{90}\text{Sr}$  through the nutrition tract (V.I. Ternov, 1988) when the levels of absorption of strontium vary from 5 to 100% (V.S. Kalistratova, 1990).

This process is influenced by a number of physiological factors (age, pregnancy, lactation, condition of vital systems of the organism). Irrespective of the way and rate of incorporation, soluble  $^{90}\text{Sr}$  compounds are accumulated by the bone tissue.

Concentration of this isotope in the bones of rat is 40-60 times higher already after 24 hours than in kidneys, spleen and muscles (V.S. Kalistratova, 1990) with skeletons of male rats accumulating more than the skeleton of female rats. Introduction of  $^{90}\text{Sr}$  into the organism of pregnant animals leads to its accumulation in the bone tissue of the offspring (V.S. Kalistratova, 1990).



The rate of strontium metabolism in the bone tissue of man is directly proportional to age: it is 100% among infants (up to one year of age), 40% among children and adolescents, 20% among adults (V.I. Ternov, 1988).

Thus, continuous incorporation of  $^{90}\text{Sr}$  leads to its maximum accumulation in childhood. Paroxysmal incorporation of this radioisotope leads to its greater concentrations among senior age adults.

## 2. BIOPHYSICAL EFFECTS OF INCORPORATED RADIONUCLIDES

Considering that the main spectrum of the radioactive elements in the Chernobyl atmospheric fallout are the isotopes with gamma- and partially beta-emission, their effect upon the biophysical processes in the cell and its ultrastructures will be considered in the first place.

Nuclear emission breaks off electrons from atoms in the cells producing ions and excited atoms and causing the appearance of radicals which induce various reactions in the organism (V.F. Zhuravlev, 1990).

One of the primary reactions induced by the ionizing radiation is the evolution of free radical processes of peroxide oxidation of lipids yielding toxic substances as final products. They affect the components of the cellular membrane, numerous enzymes and the genetic apparatus causing evolution of radiation injury (I.N. Verkhoglyad et al., 1991).

The organism possesses a chemophysical system of controlling the cellular metabolism with membranes. The main components of the system are the generation of peroxide radicals of lipids, antioxidants, composition of lipids, fluidity of the lipid component of membranes, membrane-bound proteins-receptors, enzymes, passage forming proteins. In the normal condition all these parameters are interrelated structurally and functionally, in case one is modified the remaining are modified also.

Even many years after exposure to ionizing radiation of any rate individuals retain modifications in the system controlling peroxide oxidation of lipids (E.V. Berulakova et al, 1996).

Thus, nucleoproteids and biolipids are the main substrates of the primary oxidation reactions.

The nuclear DNA in eukaryotic cells is the main target damaged by radioactive emission (G.M. Oburatov, 1996). Various primary damages of DNA result from intranuclear ionization. Only double-thread ruptures of DNA can cause genetic and lethal effects.

The method based on the analysis of the frequency of chromosomal aberrations or the number of dicentric and circular chromosomes is the most perfected and objective method of evaluating the effect of radioactive emission upon the cell's genetic apparatus (N.P. Bochkov, 1993). This method has allowed to detect chromosomal damage of human lymphocytes induced by small radiation doses (Lloyd, Edwards, 1993), specifically by radioisotopes in Gomel, the Gomel region, in a number of areas of the Ukraine (M.A. Pilinskaya et al., 1992), (M.A. Pilinskaya, S.S. Dybskiy, 1992), (E.V. Domracheva et al, 1992), (V.G. Zajnullin et al., 1992).

The data about the doses of irradiation of residents of two districts of the Gomel Region and the city of Gomel indicate that over 15% of the population have received over 20 cGr, about 3% over 60 cGr (E.V. Domracheva et al., 1991).

Thus, the cytogenetic method can be useful for reconstructing radiation doses received by population (A.V. Sevankaev et al, 1992; N.P. Bochkov, 1993a).

The genom instability after chronic irradiation of cells *in vitro* and *in vivo* is manifested by a higher incidence of lymphocytes with micronuclei which result from terminal divisions or the appearance of dicentrics and rings (I.I. Pelevina et al., 1996).

Experiments with laboratory mice using the food produced in the areas contaminated with radiation have manifested that significant accumulation of  $^{137}\text{Cs}$  and concurrent external irradiation of the animals' organisms cause various types of cytogenetic injuries: structural (primarily reciprocal translocations) and genomic (tetra-, hexo-, octo- and higher level ploids). While the frequency of chromosomal aberrations in somatic cells increases together with the dose burden, this relationship is absent in sexual cells. Males have manifested the most pronounced cytogenetic effects (R.I. Goncharova, N.I. Ryabokon, 1995). It is believed that the difference in the pattern of dose-effect curves based on the frequency of chromosomal aberrations in somatic and immature sexual cells can be explained by a number of causes, including dose differences in the induction of reparative systems of sexual and somatic cells.

The effect of small doses of ionizing radiation upon the organism is explained by a number of researchers (A.H. Ejdus, 1996) from the point of view of the theory of non-specific responses of cells to the damaging effect. The theory is based on the principles of non-specific regulation of the activity of enzymes by low-molecular substances and compartmentalization of low-molecular substances in the cells. The result is that each portion of the cells maintains a low enough concentration of those substances which would strongly inhibit the evolving reactions of fermentation, while elevated concentrations in other compartments are adapted to the enzymes localized in them due to the differences in the concentration of effective control of various enzyme-ligand couples within the above range of non-specific regulation. According to this mechanism, it is enough to reduce the concentration of low-molecular components by reducing a portion of them using an external agent to destroy the integrity or permeability of the plasmatic membrane in order to stimulate the activity of some enzymes.

Small doses of radiation (1 cGr) increase the adaptation response of the organism and only significantly higher doses intensify the inhibiting effect of reverse compartmentalization of cellular substrates due to the damage of the function of intracellular membranes.

V.A. Vetukh and V.N. Malakhovsky (1991) assume that dose dependencies in the appearance of a number of genetic disorders admit a linear threshold-free dependence. The effect of ionizing radiation upon the phospholipid layers of the membranes of erythrocytes lead to structural and conformation modifications of the latter due to intensified mobility and reduced degree of ordering (V.I. Dreval, 1993).

The surface charge of membranes changes, the viscosity of lipids reduces without any substantial modification of the structure of membrane proteins (V.I. Dreval, 1993).

Variations of the concentration of phospholipids in the membranes of mitochondria of the fetus' and mother's liver have been registered after a single-time exposure to one and two Gy doses of ionizing radiation (I.A. Shirinova et al., 1992).

The above modifications of lipid-protein interactions persists until the 50th-100th day after exposure (G.G. Egutkin et al, 1993), meanwhile pronounced modifications of membrane lipids are observed during the initial 50 days after exposure, the level of cholesterol increases, the relative concentrations of linoleic, arachidonic and other non-saturated fatty acids, the concentration of phospholipids reduce (G.G. Egutkin et al, 1993).

The damage of membranes, specifically inhibition of membrane enzymes  $\text{Na}^{+}$ -,  $\text{K}^{+}$ - ATP-ase,  $\text{Mg}^{2+}$ -ATP-ase may be induced by irradiated solutions of sugars (I.P. Edimecheva et al., 1992).

Damage of the brain tissues is attributed to the toxic effect of a highly reactive nitrogen oxide (NO) appearing already during the first minutes after irradiation (V.L. Sharygin et al., 1994).

## Chapter II

### MORPHOFUNCTIONAL MODIFICATIONS IN THE ORGANISM IN RESPONSE TO DIFFERENT DEGREES OF INCORPORATION OF RADIOISOTOPES

#### 1. CARDIOVASCULAR SYSTEM

The problem of the effect of radiation upon the cardiac functions of man and animals has been reflected in local and foreign publications. In the majority of cases the cardiac functions have been rated with the consideration of external irradiation of the whole body or in the region of the heart primarily in experimental conditions. In particular, single time exposure of experimental animals (dogs, rabbits, rats) to a dose of 15 Gy and more produces degenerative and necrotic modifications of the myocardium (A.P. Amvrosjev et al., 1989) accompanied by the evolution of exudative pericarditis (Schultz-Hector, 1992) leading to hemodynamic disorders in the form of minute and impact volume reduction, expansion of the diastolic volume of the left ventricle (Schultz-Hector et al., 1992). It has been observed that the functioning of the cardiovascular system is upset by general irradiation with  $^{60}\text{Co}$  gamma quanta of rats due to the exhaustion of the activating effect of the median brain blue spot (V.A. Fedorovich, 1991) and suppression of the modulating effect of the rear nuclei of the brain seam (V.A. Sjusukin, A.I. Ledeneva, 1991).

The detected restructuring of the neurohormonal control governs the suppression of adaptation capabilities of the blood circulation system and may stimulate the evolution of prepathological conditions (L.M. Lobanok, 1991).

External exposure of the organism, including the heart, causes suppression of the contractile activity of myofibrils, reduction of the volume rate of coronary circulation (M.A. Tatarinchik, A.E. Kirienkov, 1991).

Functional modifications of the cardiovascular system can possibly be attributed to the damage of blood vessels, specifically arterioles (A.G. Zakharov et al., 1992), or capillaries (Darcourt et al., 1992), variation of the volume of catecholamines and electrolytes in vessel walls (S.A. Litvinov, 1992).

Using isolated rat heart preparations it has been demonstrated that external gamma irradiation with a dose 6 Gy suppresses the contractility of the myocardium and alters the chronotropic relations: the relationship between the frequency-force and the potentiating effect in the atria at the interval of rest increases, while the potentiating effect in the ventricles reduces. Modification of the chronotropic relationships may be due to the alteration of the calcium transport in the heart cells (V.V. Shilov, L.M. Lobanok, 1991).

After a single exposure to X-ray and neutron irradiation in doses 0.4 and 1.0 Gy the rabbits would not manifest any significant disorder of the functional condition of the cardiovascular system, yet pronounced responses to pharmacological preparations have been registered (G.P. Katsnelson, 1991). It is possibly due to the modification of the structural and functional density, the affinity to the "beta" agonist and sensitivity to the sulfhydryl reagent (N.V. Gerasimovich, 1991).

The results of the experimental research accomplished by E.F. Konoplya et al. (1996) allow to conclude that acute gamma-irradiation with doses 0.25; 0.5 and 1.0 Gy upsets the calcium transport system of the sarcoplasmic reticulum of the muscular tissue. The activity of  $\text{Ca}^{2+}$ -ATP at doses 0.25 and 0.5 Gy increases, while it is strongly suppressed at a dose 1.0 Gy.

It is assumed that the appearance of peroxide groupings in fatty acidic chains of phospholipids under the effect of ionizing radiation alters the structure of the



membranes of the sarcoplasmic reticulum, their penetrability by various substances and the activity of membrane-bound enzymes, specifically  $\text{Ca}^{2+}$ -ATP.

These results are corroborated by the data obtained while screening the population affected by the Chernobyl radiation. In particular, 95.5% of the children and adolescents have manifested disorders of the functional condition of blood circulation in the form of upset rhythm of the cardiac activity, conduction, metabolic and restorative processes in the myocardium, suppressed tolerance of physical exercise, elevated arterial pressure.

These disorders of the functional condition of the cardiovascular system are most pronounced among the children aged between 6 and 10 years assumed healthy before (V.N. Novikova, 1991).

I.S. Tsybul'skaya et al. [143] indicate also that 74.4% of the children during their first year of life in the areas where the soil is contaminated with radiation within  $5\text{--}20 \text{ Ci/km}^2$  manifest pronounced electrocardiographic modifications: intricate rhythm disorders, alteration of the teeth of the ventricular repolarization.

Domination of the syndrome of premature repolarization of ventricles and elevated arterial pressure are typical for these groups of children (A.N. Arinchik, G.L. Nalivajko, 1991).

Vagotonia with asympathycotonic reactivity has been revealed among 36 out of 102 examined children aged 11-15 years living in the area with the  $^{134}\text{Cs}$ ,  $^{137}\text{Cs}$  soil contamination  $0.4\text{--}10 \text{ Ci/km}^2$ . The children in this group have manifested disorders of the lipid metabolism in the form of hypocholesterinemia, hypolipidemia, hypophosphatemia (L.V. Kvashnina et al., 1992). V.V. Nedvestkaya and S.A. Ljalikov (1994) also indicate modifications of the vegetative regulation evolving among the children aged 6-17 years in the contaminated areas of Belarus which are more pronounced among girls than among boys. These modifications are characterized by the suppression of the tone of the sympathetic compartment of the nervous system, a tendency towards hyporeactivity and stress of the compensatory mechanisms of the parasympathetic compartment. Correlation analysis has revealed a close relationship between vegetovascular dystonia appearing among the children evacuated from the heavily contaminated areas, and thyroid hyperplasia, psychic disorders, disorders of digestive organs (A.U. Lagutin, V.M. Sidelnikov, 1992).

Children from the affected areas manifest modifications of the responses of the cardiovascular system to catecholamines (L.S. Valeva et al., 1993).

Arterial hypotonia detected among 34.3% of boys and 30.2% of girls in the Gomel and Moguilev regions reflects disorders of the vegetative regulation of cardiac functions (A.V. Sikorenskii, G.E. Vagel, 1992). Modifications of cardiac functions are registered among adults exposed to external irradiation, in addition to children.

It has been demonstrated that men aged 20-40 years who were involved in the cleaning-up operations in 1986-1988 after the disaster manifest disorders of neurohumoral regulation of the cardiac tone and myocardium contractility (S.S. Korytko, 1991). The incidence of cardiac ischemias and arterial hypertension among liquidators of the Chernobyl aftermath is validly higher than among individuals in the control group in Moscow (V.M. Shamarin, et al., 1996). Disabled individuals with cardiac ischemias living in the contaminated areas have more frequent and stable cardiac rhythm disorders than individuals with similar pathologies living in "clean" areas (N.T. Arinchina, V.K. Milkamanovich, 1992).

Dysfunction of the vegetative nervous system in the form of secondary domination of the stray nerve tone as bradycardias and ectopic precardiac rhythm has been observed among male liquidators and evacuated individuals (G.P. Karaseva, 1991).

Evolution of arterial hypertension is one of the manifestations of the above condition (N.S. Zanozdra, E.G. Kuchinskaja, 1991). In particular, borderline hypertension has been detected among individuals in the contaminated areas 1.5 times more frequently than in the "clean" areas (I.I. Goncharik, 1992).

Thus, stable neurovegetative disorders in the form of the neurocirculatory dystonic syndrome among the individuals affected by radioisotopes indicate the involvement of hormonal and humoral mechanisms in the induction of functional pathology, including that of the cardiovascular system (A.M. Kovalenko, 1991). Yet, for evaluating the consequences of the Chernobyl disaster it is more essential to determine the effect of internal irradiation from incorporated radioisotopes upon the condition of vital systems, including the cardiovascular system.

In particular, when incorporated  $^{131}\text{I}$  creates absorbed doses in the thyroid after 1-12 months at a level 94.6-94.7 Gy, the responses of the myocardium to the stimulation of alpha-adrenergic receptors is attenuated, while the responses of the coronary passage to such stimulation are intensified (A.E. Kirienko et al., 1992). Incorporation of  $^{131}\text{I}$  and  $^{137}\text{Cs}$  by rats induces modifications of the heart pace-maker activity, the functional condition of the coronary vascular passage, electric and contractile activity of cardiomyocytes and flat muscle vascular cells (A.E. Kirienko et al., 1990).

Examinations of the children living in the contaminated areas (Gomel — 1-5 Ci/km<sup>2</sup>) have revealed high frequency of disorders of cardiac activity - 72.3%, primarily due to the disorders of conduction of the cardiac impulse in the form of incomplete blockades of the His right stem bundle, upset redox processes and vegetovascular dystonias, together with a close relation between the doses of endogenously incorporated radioisotopes and electrocardiographic disorders. Though the average accumulated dose in the organisms of children in these two groups did not have any valid difference and amounted to  $30.32 \pm 0.66$  Bq/kg in the test and  $29.74 \pm 0.67$  in the control ( $p > 0.1$ ), the Gomel children have manifested a more pronounced and statistically valid direct proportionality between the accumulated dose and ECG modifications, valid differences between the subgroups of 11-25.9 Bq/kg and 37.0-74.0 Bq/kg (Fig. 6).

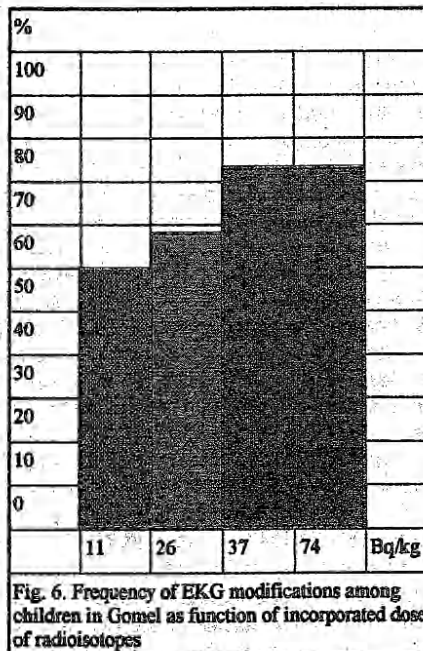


Fig. 6. Frequency of EKG modifications among children in Gomel as function of incorporated dose of radioisotopes

The children with the above accumulated doses but living in Grodno did not manifest any valid differences in the frequency of registered ECG modifications.

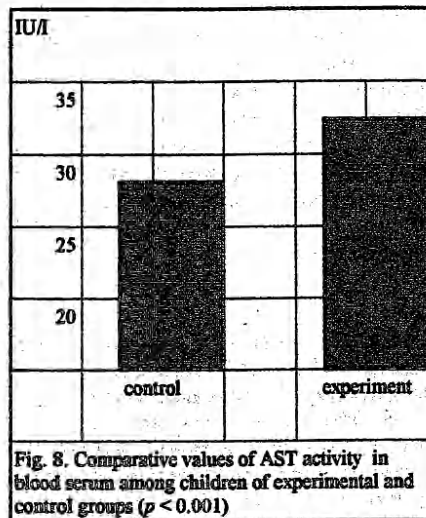
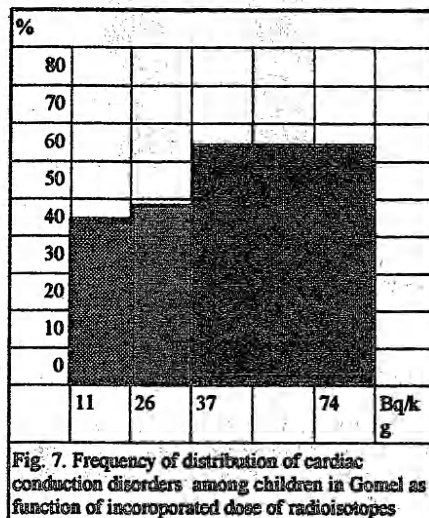
This fact in the main group is basically due to the disorders of intraventricular conduction in the form of incomplete blockades of the His right stem bundle (Fig. 7).

When children accumulate significantly higher doses of radioisotopes  $89.93 \pm 3.65$  Bq/kg on the average (Vetka) the ECG-registerable effects have been detected among 86.8% with the disorders of the intracardiac conduction amounting to 53.95% (G.S. Bandazhevskaya, 1996).

Examinations of the students of the Gomel Medical Institute have yielded similar results (Yu.I. Bandazhevsky, et al., 1996).

Thus, investigation of the electrophysiological processes in the cardiac muscle among children in the areas with higher levels of radioactive contamination has revealed a number of modifications of electrocardiographic activity with the frequency being a function of the internally accumulated dose.

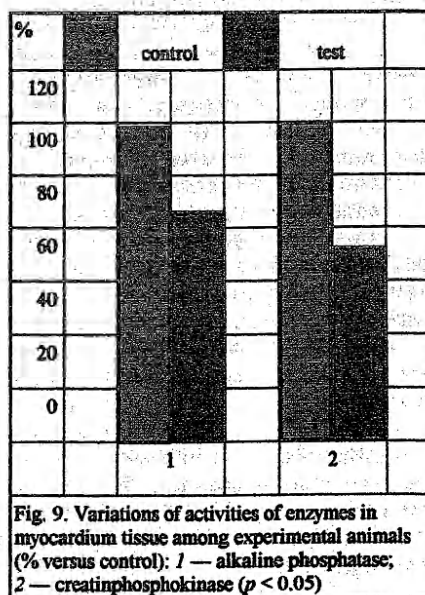
Damage of the myocardium structure is accompanied by the intensified activity of AST in the blood serum (Fig. 8).



Experimental studies of laboratory animals (the Vistar line rats) evidence the effect of endogenously incorporated radioisotopes upon the myocardium.

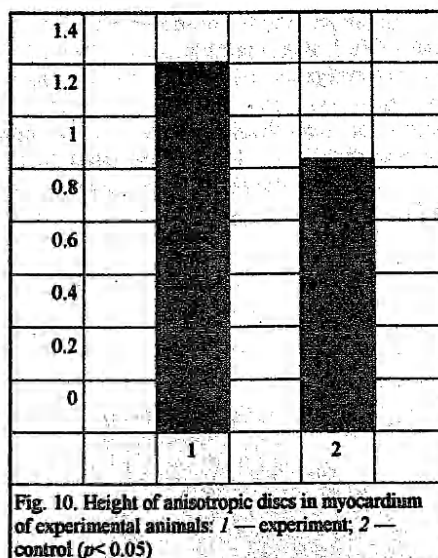
The experimental animals were kept during ten days on a diet of oats containing radioactive elements in the concentration exceeding the control level 10 times ( $^{137}\text{Cs}$  concentration was 445.7 Bq/kg,  $^{90}\text{Sr}$  - 15.5 Bq/kg). This diet would bring the  $^{137}\text{Cs}$  concentration in the organisms of the animals in the test group to  $63.35 \pm 3.58$  Bq/kg versus  $5.43 \pm 0.87$  Bq/kg in the control group ( $p < 0.001$ ).

In this way the animals would accumulate radioisotopes within a relatively short period of time,  $^{137}\text{Cs}$  in particular. A direct proportionality between the accumulated  $^{137}\text{Cs}$  dose and the concentration of this element in the



Analysis of the results has indicated that the myocardium tissue acquires the maximum concentration of this radioactive element.

Significant concentrations of  $^{137}\text{Cs}$  have been registered among the residents of Gomel and the Gomel Region (Yu.I. Bandazhevsky, A.M. Perepletchikov, 1996). It is manifested by the suppressed activity of the most essential enzymes, such as alkaline phosphatase and creatin phosphokinase (Fig. 9). Considering that creatin phosphokinase is a key enzyme of the energy metabolism in the cardiac muscle governing reactions between macroergic phosphate and creatinin, its suppressed activity leads to substantial disorders of the functions of cardiomyocytes.



Disorders of energy processes in the heart modify its contractile apparatus, vis. myofibrils in the form of contractions or their declustering and lysis in various degrees of expression (L.M. Nepomnjashchikh, 1966).

Modification of the polarization behavior of cardiomyocytes in the form of expanding A-discs is a morphological criterion of this pathology (Fig. 9-10). The obtained data explain origination of disorders of cardiac conduction, including the cardiac rhythm, induced by incorporated radioisotopes.

Examinations of the biopsied material have manifested that contracted cardiomyocytes with ultrastructural modifications and disorders of the structures of insert discs and atrophic cardiomyocytes and cells with signs of apoptotic degeneration typical for this condition prevail in the arrhythmogenic portions of the heart, unlike the non-arrhythmogenic zones (Bakerija, et al., 1995).

Thus, it has been experimentally demonstrated that incorporation of radioisotopes by laboratory animals with food (primarily  $^{137}\text{Cs}$ ) damages the myocardium cells producing relevant structural and functional modifications. Clinical and experimental studies have revealed a significant sensitivity of the myocardium cells of a growing organism to incorporated radioisotopes. A whole combination of modifications evolves evidencing a direct injury of the cardiac muscle, organs and systems controlling its functions. The role of pathological processes evolving in the cardiac nervous apparatus should be taken into consideration by all means.

Hence, the problem of reducing doses of internal accumulation of radioisotopes comes into foreground, including application of sorption preparations (Yu.I. Bandazhevsky et al., 1994), requiring to project treatment actions for improving metabolic processes in the myocardium.

Analysis of the arterial pressure among children with different incorporated doses has revealed a dose-dependent effect. As the dose increases the number children with hypertension goes up. Totally 41.6% of the children in the areas contaminated with  $^{137}\text{Cs}$  in excess of  $15 \text{ Ci/km}^2$  manifested arterial hypertension (A.I. Kienja, N.M. Ermolitskii, 1997).



## 2. NERVOUS SYSTEM

The nervous system is one of the first to respond to radiation effects, both local and general, affecting the entire organism (U.I. Moskaley, 1991).

Penetration of long-living radioactive elements ( $^{137}\text{Cs}$ ,  $^{90}\text{Sr}$ ) into the organism causes a pronounced loss of equilibrium of neuroactive amino acids and biogenic monoamines in various compartments of the central nervous system, specifically the exciting transmitter, such as aspartate and glutamate, and decelerating agents, such as gamma amino oleic acid (GAOA), glycine. The degree of expression of the process is determined by the duration of incorporation of radioisotopes by the organism.

A more intricate pattern of variations of the bank of biogenic amines and neuroactive amino acids under the effect of incorporated radioisotopes is noteworthy, compared with external irradiation, still a number of reconstructed effects (inhibition of the serotonin system, early activation of the GAOA-system) is comparable with the effect of moderate lethal and superlethal doses for experimental animals (V.V. Lelevich, E.M. Doroshenko, 1995).

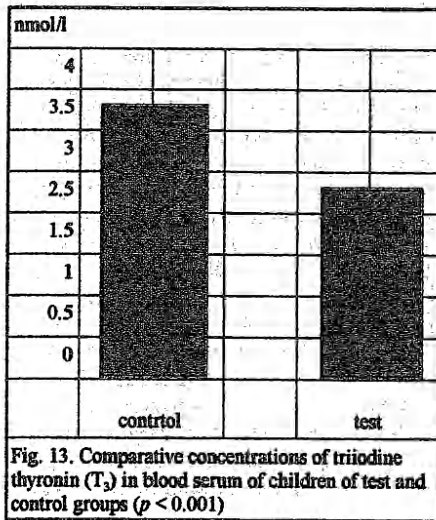
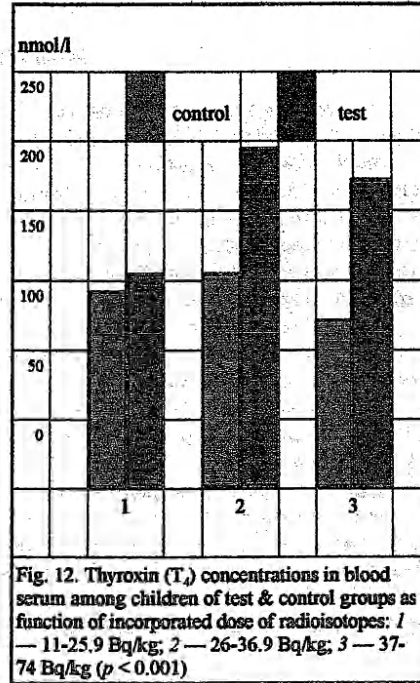
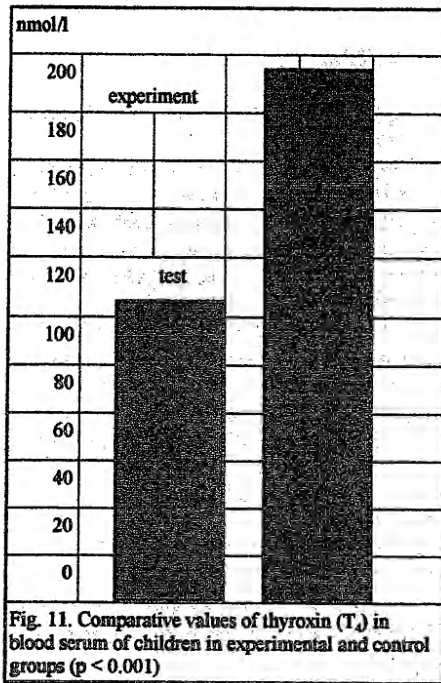
Injury of the brain tissues can be due to the toxic effect of the highly reactive nitrogen oxide they contain (V.L. Sharygin, et al., 1994).

Incorporation of  $^{137}\text{Cs}$  causes dysfunction of the vegetative nervous system, with the incidence of the elevated tone of the sympathetic nervous system being directly proportional to the quantities of the incorporated radioisotope. When its concentrations in the organisms of children exceed 100 Bq/kg the numbers of

## 3. THYROID GLAND

The thyroid gland is the most vulnerable organ in respect to radiation and has suffered most from the Chernobyl disaster. The gland has manifested pathological effects specifically clearly after a significant period. In particular, the diseases of the thyroid gland in 1990 in the Gomel region amounted to 126.1 cases per 100,000 with the rise in 1995 to 1,154.5 cases, meanwhile among children these cases numbered 3106.1 per 100,000. These figures are still higher in the areas proportionally denser radioactive levels amounting to 4,056.9 generally in the Braguin district and to 1,9072.6 among the children. The leading factor of internal irradiation has been  $^{131}\text{I}$  with the collective dose for the thyroid gland amounting to 22,000 (R.I. Halitov, et al., 1993). Exactly this radioisotope has led to substantial disorders in the areas adjacent to Chernobyl. In particular, examinations of the individuals after their involvement in the cleaning-up operations have demonstrated the compensated condition of the thyroid system just among 35.6%, hyperthyreosis among 39.7%, hypothyreosis among 24.7% (V.N. Petrov, N.M. Petrov, 1991). Dr. O.V. Kopylova and her co-researchers have obtained similar results showing the condition of hyperthyrexinemia among 40.0% of the children in the areas of radiation risk, other medical researchers (N.B. Pashinskaja et al., 1991) also report a suppressed function of the thyroid gland among 37.9% of the children.

G.S. Bandazhevskaya (1966) registered a higher concentration of thyroxin in the blood among children aged 3-7 years old in 1995 in Gomel (1-5 Ci per  $\text{km}^2$  of  $^{137}\text{Cs}$ ) compared with the control having a directly proportional relation with the concentration of incorporated radioisotopes (Fig. 11, 12). Meanwhile the concentration of triiodine thyronin is much below the control level (Fig. 13). E.L. Strukov et al. (1994) believe that this condition accompanies a complicated evolution of diseases of the cardiovascular and digestive systems.



It should be remarked that the above hyperthyrexinemia commonly evolves without any pronounced clinical manifestations (E.V. Epshtein et al., 1993). A somewhat higher level of triiodine thyronin in the blood with a simultaneous reduction of the secretion of thyretotropin was observed among the children and adolescents during the first three years after Chernobyl indicating a functional activation of the thyroid system (A.F. Tsyb et al., 1991). The intricate metabolism of thyroid hormones should be taken into consideration. The basic hormone of the thyroid gland of a normal man is T<sub>4</sub>. Less than 20% of the total zero of T<sub>3</sub> is produced directly by the thyroid gland, 80-90% result from the

monodeiodinizing of T<sub>4</sub> in peripheral tissues. The liver and kidneys are the main transformers of T<sub>4</sub> into T<sub>3</sub> (I.I. Dedov et al., 1992). The basic effects of the thyroid hormones are determined by T<sub>3</sub>. Small doses of radiation lead to suppressed secretion of the thyroxin binding globulin, a higher total concentration of thyroxin in the blood would occur versus the reduced concentration of progesterone and prolactin among

pregnant women (weeks 12-32 of pregnancy) (N.S. Akulich et al., 1990). Individuals with a dose burden 400 Gy upon the thyroid gland become predisposed to hypothyreosis (L.N. Astakhova et al., 1993).

In addition to the altered hormonal secretion by the thyroid gland, structural modifications have been detected proving the evolution of the gland's pronounced pathology. The ultrasound screening of girls aged 6-18 years who stayed within the 30 km zone during the explosion revealed changes in their thyroid glands typical for hypoplasia and moderate thyreofibrosis (I.V. Vovk et al., 1992).

Pathoanatomical investigations of the thyroid glands of fetuses and children in the Gomel region who died of various diseases, have revealed morphological manifestations of a stronger functional activity of the gland, such as noticeable stimulation of the processes of desquamation of thyrocytes, reduction of the relative volume of the thyroid epithelium in the gland due to cytolysis, valid reduction of the sizes of follicles followed by their collapse and substitution with the connective tissue stroma (E.D. Cherstvoj et al., 1993).

Experimental studies corroborate the results of clinical observations. In particular, intra-abdominal administration of 500 kBq of  $^{131}\text{I}$  would alter the calcium-phosphorus metabolism and its hormonal regulation among rats and cause a shift in the production of thyroid hormones (I.M. Bagel et al., 1990). In addition to  $^{131}\text{I}$ , significant changes in the thyroid gland can be induced by repeated external gamma irradiation (1 Gy) leading to stable structural and functional disorders among laboratory animals. In the long term these disorders result in the appearance of hypothyreosis demonstrated by the reduced concentration of thyroxin in the blood, stimulation of the thyretropic function of the hypophysis, inhibited activity of -glycerophosphate dehydrogenase as a thyroxin dependent enzyme in the liver (J.H. Turakulov et al., 1992).

The incidence of the thyroid nodular pathology among the children in the Gomel Region exceeds 15%, including 2.54% thyroid cancers ((L.N. Astakhova et al., 1993). The Kaluga Region manifests similar results where nodular goiters have been increasing since 1994, together with thyroid cancers (follicular and papillary forms). The dose of radioactive iodine absorbed by the thyroid gland varied from 25.6 to 169 cGy (E.G. Matvienko et al., 1996).

Nevertheless, the children in the Khojniki district (aged 0-17 years) show the highest doses of irradiation of the thyroid gland (242-527 cGy) versus 15 to 60 cGy in Gomel, 2.4 to 9.2 cGy in Minsk. The children which were aged under five years at the moment of the disaster received the maximum doses (I.I. Dedov et al., 1992).

This effect of radioactive iodine resulted in more frequent thyroid disorders, specifically thyroid cancers, nodular goiters, autoimmune thyreoditis. A sharp rise in the number of thyroid cancers occurred in the Republic of Belarus on the fifth year after Chernobyl. During the last decade 422 cases have been registered among children and 3,492 among adults and adolescents (I.M. Drobyshevskaja et al., 1996). Thyroid cancers are most frequent among adolescents in the Khojniki district.

The clinical and morphological analysis of thyroid cancers among the children in Belarus has revealed several features of the diseases:

1. A relatively short latent period between the probable cause factor and the clinical manifestation of tumors.
2. Domination of capillary carcinomas with manifestations of reduced histological differentiation having a pronounced localization and a high frequency of metastasizing (A.V. Furmanchuk et al., 1992; L.S. Baleva, E.E. Karneeva, 1996).

The pathogenesis of the above pathological conditions is primarily due to the initial effect of  $^{131}\text{I}$ . It has been noted that the disaster led to the release of 20 to 30% into the atmosphere from 60-70 million Curies of  $^{131}\text{I}$  contained in the reactor (G.A. Gerasimov, 1991). The "iodine impact" severely injured the structural components of the thyroid tissue. Taking into consideration the short life of  $^{131}\text{I}$  a period of repair - restoration followed, when the immunity system would play a paramount role of controlling the processes of proliferation and differentiation of the follicular epithelium and the neighboring cells.

Apart from  $^{131}\text{I}$ , the radioactive releases created conditions when other long living radioisotopes would affect continuously the human organism, specifically  $^{137}\text{Cs}$  and  $^{90}\text{Sr}$ . They would modify the functions of many vital systems and tissues of the organism, including the immunity system and the thyroid cells which would accumulate them intensively (Yu.I. Bandazhevsky, A.M. Perepletchikov, 1996). It would lead to the damage of the most essential ultrastructures of the cells, modification of the antigen determinants on the surfaces of the cytoplasm membrane.

The result is that the structural components of thyroid cells become antigens for the immunity system. An immunological response appears when the cellular structures of the thyroid gland are damaged by the autoantibodies and immunocompetent cells, finally leading to the appearance of autoimmune thyroiditis and, after that, in a number of cases, to thyroid cancers. A relationship has been established between the radiation burden upon the thyroid gland, the populations of antigens and the microsomal fractions of the thyroid gland (A.M. Poverennyi et al., 1996).

The reactions between immunoglobulins and thyroid hormones, such as thyroxin, should be taken into consideration in the pathogenesis of thyroid diseases. It has been established that immunoglobulins of different classes (J, A, M) are capable to bind thyroxin, triiodine thyronin (O.V. Sviridov et al., 1992). The children in Gomel have manifested correlation between the concentration of Ig and the level of T4, while the children in the control areas have manifested none.

When the hormones are bound by immunoglobulins, they are eliminated from the metabolic chain and naturally the functions of the hypophysis - thyroid system become upset.

The processes lead to the liberation of significant quantities of thyreotropic hormone enhancing the pressure upon the thyroid gland and boosting proliferation of the follicular epithelium creating conditions for neoplastic transformations.

#### 4. IMMUNITY SYSTEM

Radioactive elements produce a pronounced effect upon the immunity system. Similarly like it is done for other vital systems, pathological effects should be discriminated based on the external irradiation and internal irradiation of the organism from incorporated radioisotopes.

In the first case adults manifest an acute radiation disease with a strong drop of the total quantity of leukocytes and lymphocytes with variations of the concentration of immunoglobulins and C-reactive protein in the peripheral blood as a function of the stage of the disease (A.A. Ivanov et al., 1991).

The thymus-dependent  $\text{CD}^{4+}$  and the lymphocytes belong to the group of T-helpers in the peripheral blood and make up the most vulnerable lymphocyte population (A.A. Chumak et al., 1991).

Variations in the system of proteins of the acute phase, vis. a reduction of the concentration of complements and a rise of the C-reactive protein concentration are typical for the primary response during the initial period. The peak period of the



radiation disease is characterized by pronounced modifications of the cellular and humoral immunity and the factors of non-specific protection, viz. a reduction of the lymphocyte count and concentration of properdin, lysosim, immunoglobulins in the blood and a rise of the concentration of the C-reactive protein and the complement. Hyperleucocytosis with the leftward shift of the blood formula towards myelocytes and singular myeloblasts are registered among the majority of the children with radiation injuries during the first days (V.N. Bebesko et al., 1991).

Both a temporary rise and decline of the leukocyte count together with the disorders of concentrations of T- and B-lymphocytes and a distorted ratio between helpers and suppressors can occur in the remote period of the disease (A.A. Ivanov et al., 1991; A.A. Ivanov et al., 1993).

Fitters, erectors and designers after involvement in the elimination of the Chernobyl aftermath demonstrated four years later lack of equilibrium and a dysfunction of the immunity homeostasis, irrespective of the dose of ionizing irradiation (N.P. Savina, et al., 1995).

Loss of equilibrium of the subpopulation composition of T-lymphocytes, periodical reduction of the concentration of B-lymphocytes, major classes of immunoglobulins in the blood serum, reduction of the parameters of the index of immunoregulation have been registered among individuals after involvement in the cleaning-up operations (T.V. Vorontsova et al., 1990, R.J. Bruveret, 1991; V.G. Komissarenko et al., 1991; T.V. Kozyreva et al., 1991; I.V. Radovskaja, 1992), as well as among children from the Chernobyl orphanage which manifested reduction of the concentration of immunoglobulins M, G and A, suppressed phagocytary activity of neutrophil granulocytes at normal hematological parameters (Z.G. Isaeva et al., 1991).

Liquidators basically healthy at the moment of examination manifested reduction of the subpopulation of T-active lymphocytes and concentration of rosette-forming neutrophils alongside with the rise of the number of autorosettes (N.M. Galitskaja et al., 1991).

Microcytosis of lymphocytes is 6-7 times more frequent among the children in the contaminated areas compared with the control is a typical feature of the cells of the lymphoid series (I.P. Danilov, L.Ja. Krylova, 1991).

A large dense nucleus and a meager cytoplasm are typical for the lymphocytes of the peripheral blood (Ju.K. Novoderchinina et al., 1995).

The population of natural killers, their cytotoxic activity, the concentration of immunoregulatory cells and B-lymphocytes most frequently deviate from the norm among the individuals living in the area with  $^{137}\text{Cs}$  contamination 15-47 Ci/km<sup>2</sup> (E.G. Kuzmina et al., 1993; N.I. Ljsjanyi et al., 1991).

A similar situation is observed among the liquidators involved during 1986-1987 in the Chernobyl area 5-6 years after the disaster (T.V. Mikheenko et al., 1996).

The immunity status of the examined persons typically manifests lymphopenia, reduction of the percentage of general rosette-forming lymphocytes and the population of NK-cells, T-suppressors-killers, deficiency of B-cells, inhibited activity of neutrophils (I.V. Oradovskaja, 1993) and monocytes (I.V. Volchek et al., 1991).

Disorders of the composition of subpopulations of lymphocytes feature reduction of the concentration of CD<sup>43</sup>, HLA-DR- cells (A.A. Chumak et al., 1992).

So, the examined individuals have shown modifications primarily of the T-cellular immunity with a significant rise of Ig, A and M (T.V. Kozyrev et al., 1991; V.I. Telkov et al., 1993). Still, reduction of the concentration of all immunoglobulins (V.G. Komissarchenko et al., 1991) rise of Ig, M A.A. Ivanov, 1991; A.A. Akleev et al., 1991) and Ig G, and drop of the concentration of Ig A (V.G. Koledenko et al., 1991; N.N. Salitskaya et al., 1990), have been registered. Reduction of the secretory Ig A in the saliva (O.F. Melnikov et al., 1991) were observed during two post-disaster years.

The detected modifications reflect the condition of B-lymphocytes under the effect of radioisotopes (T.V. Miheenko et al., 1991).

Like the adults, the children in the contaminated areas have manifested a valid reduction of the concentrations of T- and B-lymphocytes, major classes of immunoglobulins (G.I. Vinogradov, V.K. Vinarskaja, 1991; N.N. Galitskaja, A.V. Elinov, 1992), suppressed proliferative activity of T-cells during stimulation of PGA (O.E. Vatin et al., 1991).

The children in the areas contaminated with  $^{137}\text{Cs}$  to the tune of 1-5 Ci/km<sup>2</sup> have manifested inhibition of the phagocytary activity of neutrophil leukocytes against the rise of the concentration of IgM and drop of the concentration of IgA in the blood compared with the control (Ju.I. Bandazhevsky et al., 1995). Meanwhile a possibility to stimulate effectively the cytotoxic activity of natural killers with immunomodulators having different mechanisms of actions allows to assume that the suppression of the activity is of functional nature and is reversible (O.F. Melnikov et al., 1991). Domination of the helper population of T-lymphocytes is a typical feature (G.I. Kovalev et al, 1990; A.K. Cheban et al., 1991).

Exclusively high radiosensitivity of the population of T-suppressors and their precursors is noteworthy among all the cells of the lymphoid series (V.T. Komissarenko et al., 1993). Predominant inhibition of the suppressor link of the immunity system among the children in the areas affected by radioisotopes (O.S. Dehtjareva et al., 1991) is accompanied by the rising concentration of IgM, G and circulating immunity complexes in the blood (S.K. Evtushenko et al., 1992).

A higher concentration of interferon among the children in the heavily contaminated areas can be assumed as the organism's response to radiation (I.V. Korobko, L.P. Titov, 1991).

Some of the examined liquidators manifest a higher concentration of circulating interferon in the blood and all the examined individuals manifest inhibition of the synthesis of gamma-interferon evidenced by the suppressed functions of the interferon system (I.V. Korobko et al., 1996). This protein has an exceptional significance for the immunity system.

Basically healthy young individuals in Kiev have manifested five years after the disaster a reduced humoral and T-cell immunity and a noticeable inversion of the theophyllin effect evidencing functional modifications of the T-cell immunity system (V.G. Komissarenko et al., 1993).

The results of the immunological screening of the population affected by radioisotopes are corroborated by the experimental studies of laboratory animals. During 1989-1990 the laboratory animals (rats, mice) kept in Chernobyl manifested strong modifications of the immunity system evidenced by the reduction of the absolute concentration of immunocompetent cells, specifically T-lymphocytes, stable and prolonged suppression of the activity of natural cytotoxic cells and antibody-dependent killer-cells (O.F. Melnikov et al., 1991). Meanwhile the population of B-lymphocytes in the experimental animals remains basically unchanged (Z.D. Savtsova et al., 1991).

The sheep in the Belorussian Lowlands with the density of radioactive contamination 40-100 Ci/km<sup>2</sup> manifest suppressed activity of neutrophils, reduced concentrations of T and B-lymphocytes (V.A. Budarkov et al., 1991).

The animals of the first and second generations have manifested the strongest immunity deficit modifications (O.F. Melnikov et al., 1991). Gamma-irradiation of the Vistar line rats has reduced the population of lymphocytes in the thymus, spleen and bone marrow and caused structural and functional damage of these cells (L.G. Bortkevich et al., 1989).

A significant suppression of the spontaneous cytotoxic behavior of NK-lymphocytes has been observed among the rats kept on a diet to achieve a dose of  $^{90}\text{Sr}$  equal to 200 Bq/animal and  $^{137}\text{Cs}$  equal to 250 Bq/animal after 30 days (N.N. Volkova, V.N. Korzun, 1991).

Disorders of the immunity response to the thymus-dependent antigen (ram's erythrocytes) persisted among the mice of the "clean" lines after injections of  $^{125}\text{I}$  and  $^{131}\text{I}$  (U.N. Anohin, N.V. Belorukova, 1992).

The above modifications of the immunity status of the individuals in the areas contaminated with radiation are due to a high radiosensitivity of immunocompetent cells. Different doses of radiation damage different cell populations. The doses 1.2-1.8 Gy produce pathologic effects in B-lymphocytes, the doses 2.0-2.5 Gy and up produce such effects in T-cells (A.A. Jarilin, 1988), among them T-suppressors are most vulnerable (I. Wasserman et al., 1979). It should be noted that thymocytes at the final stages of differentiation are more than twice sensitive to radiation than the thymocytes at the initial stage (V.M. Graevskaja, N.N. Zolotareva, 1991). Modifications of the functional activity of macrophages in the organism after exposure to radiation are due to a stronger permeability of cellular membranes (M.A. Tumanjan et al., 1992).

It is noteworthy that the intrauterine irradiation causes more pronounced modifications of immunity than irradiation during the first years of life (A.V. Akleev, M.M. Kosenko, 1991).

Dysfunctions of the macrophage system are due to the suppression of the antioxidant system (E.A. Lunina, et al., 1995).

Thus, radioisotopes produce strong modifications in the immunity system of man evidenced by a higher incidence of lymphadenopathies and secondary immunity deficits, basically due to the suppression of the T-system of lymphocytes (general and T-cell deficiency, deficit of T-helpers). The degree of clinical manifestations of immunity deficit stays below critical which is typical for primary immunological deficiency (L.S. Baleva, E.E. Korneeva, 1996).

Therefore, the immunity system should be considered as a critical organ affected by all types of radiation.

Damage of the immunity system links causes evolution of the immunological processes, specifically such as allergies and autoimmune conditions. Among the latter the most noticeable is autoimmune thyroiditis or Hashimoto goiter. Its spread among children has been registered in the areas with  $^{137}\text{Cs}$  contamination above 1 Ci/km<sup>2</sup> five and six years after the disaster.

Rising numbers of autoimmune processes when antibodies to the antigens of the thyroid tissue appear positively correlates with the doses incorporated by the thyroid (I.M. Hmara, L.N. Astahova, 1996).

Allergies become more frequent among the children in the contaminated areas in response to quite common antigens, such as cow milk protein. The children in the areas with higher  $^{90}\text{Sr}$  concentrations the tendency to allergies has been registered using the reaction of degranulation of obese cells in 36.8% of cases (versus 15% in the control). Cortisone concentration in the blood of the children is validly lower in a number of cases (Yu.I. Bandazhevsky et al., 1995).

Positive and strongly positive allergic reactions to the cow milk protein, allergens in oranges have been manifested in 1997 by 50% of the students of the Gomei Medical Institute and schoolchildren in the community of Svetilovichi (Yu.I. Bandazhevsky, I.A. Verner, 1997).



## 5. HAEMOPOIETIC SYSTEM

Radioactive emission is capable to produce corresponding modifications in the haemopoietic systems of man and animals as a function of radiation intensity and duration.

When man is exposed to a dose from 1 to 10 Gy an acute radiation disease appears. The hematological syndrome emerges on the 3rd or 4th week in the form of granulocytopenia, thrombocytopenia and anemia and plays an important role in the pathogenesis of the diseases (A.E. Ivanov, 1991).

Stable modifications of quantitative and qualitative parameters of the peripheral blood and bone marrow, strong modifications of the system of metal proteids of the blood plasma, reduced concentrations of Fe-transferin and Cu<sup>2+</sup>-ceruloplasmin occur during reconvalescence after acute radiation disease and among patients with the initial stages of depression of haemopoiesis after doses 0.3-1.0 Gy.

Scrutiny of cultures shows that the haemopoietic function at the level of closest offsprings of stem cells is retained by the majority of these individuals (V.G. Bebeshko et al., 1996).

During the initial fortnight in the Chernobyl zone the liquidators had transient leucocytosis, reticulosis, eosinophilia (U.N. Shishmarev et al., 1992), a greater number of stem nuclear neutrophil leucocytes (L.N. Ljubchenko et al., 1991; N.M. Oganessian et al., 1991) and basophils (L.N. Ljubchenko et al., 1991). The nuclei of mononuclears would increase in dimensions and become less optically dense.

Zverkova et al. (1991) indicate that after involvement in the elimination of the Chernobyl consequences a number of individuals would manifest neutrophilopenia, a leftward shift of the leucocytary formula, a greater concentration of monocytes.

During the next 30-50 days in the Chernobyl zone the count of thrombocytes, erythrocytes and reticulocytes would reduce (U.N. Shishmarev et al., 1992).

Four or five years later these individuals would manifest absolute lymphocytosis and monocytosis, reduced index of segmentation of cell nuclei, reduced concentration of myeloperoxidase in leucocytes (I.E. Danilov et al., 1992).

Five or six years later quantitative and qualitative modifications of the leucocytary link are observed in the form of moderate relative and absolute lymphocytosis, eosinophilia and neutropenia. Larger radiation doses would produce lymphocytes and neutrophil leucocytes with a jagged nuclear shape, would cause appearance of additional nuclei. The number of chromatin outgrowth in neutrophils would increase (K.P. Zak et al., 1995).

Moreover, the liquidators showed four years later manifestations of the functional loss of organization in the hemostasis system: activation of hemocoagulation and aggregation of thrombocytes against the suppressed activity of fibrolysis and antithrombogenic features of vascular walls (S.I. Chekalina et al., 1995).

Like among adults, the children in the radiation-affected area manifest modifications of the haemopoietic system. The children in the areas with heavy contamination have the average concentrations of erythrocytes, hemoglobin validly less compared with the norm (T.I. Kozorezova et al., 1993). Basically healthy children evacuated from the city of Pripyat 36-40 hours after the disaster have manifested a moderate leucocytosis and a higher relative and absolute concentration of the cells of the granulocytary series (the stem nuclear and segment nuclear neutrophils, eosinophils).

The leucograms of these children typically show granular lymphocytes (V.G. Bebeshko, 1991) and enlarged neutrophil leucocytes with a toxigen and immature granularity (U.V. Stepanov et al., 1992). Hexagrams of these children did not manifest



any significant modifications 1-4 years after the disaster. Also, the children after exposure to small doses of radiation manifest modifications of the morphological composition of the peripheral blood which have no pathological nature, such as leucopenia, lymphocytopenia (D.A. Torubarova, G.I. Kovalev, 1991). Suppressed activity of alkaline phosphatase in neutrophil granulocytes has been revealed among a number of children, together with a significant rise of the concentration of eosinophil granulocytes (K.P. Zak et al., 1991).

Analysis of an extensive bank of data of laboratory hematological examinations of children and adolescents living in the contaminated areas has revealed disorders in hexagrams, such as reduction of the number of erythrocytes accompanied by macrocytosis, leuco- and lymphopenias in a number of cases (A.F. Tsyb et al., 1996).

Thus, the peripheral blood of the children, after protracted exposure to small doses of radiation, manifests both qualitative and quantitative modifications in the erythroid series, neutrophil leucocytes, eosinophils, B-lymphocytes, the pattern and the tendencies of these modifications being dependent upon the age of the children and the level of general radiation (L.V. Evets et al., 1992).

No pronounced rise of the incidence of leukemias or any other diseases of the myelocytary function has been registered in the affected areas during the period since the Chernobyl disaster (I.V. Osechinskii et al., 1994).

Yet, a statistically valid rise of the frequency of chronic lympholeucosis, paraproteinemic hemoblastosis, non-Hodgkin's lymphomas is noteworthy. Moreover, since 1988 a statistically valid rise of acute non-lymphoblastose leukemias, chronic myeloleucoses has been registered (I.V. Osechinskii et al., 1991).

The hemoblastosis incidence is somewhat higher in the areas with mild radioactive contamination basically due to the number of acute lymphoblastose leukemias, chronic lympholeucoses and lymphogranulomatoses (I.V. Osechinskii et al., 1996).

Hence, the population affected by the Chernobyl disaster has been manifesting substantial modifications of the haemopoietic system for a number of years. They are typically related to the quantities of radioisotopes incorporated by the organism. It is evidenced by the results of evaluation of hematological examinations of children from the communities with different levels of soil contamination and different levels of radiation accumulation in the organism.

A reverse proportionality exists between the concentration of erythrocytes in the blood and the quantities of incorporated radioisotopes (Fig. 14)).

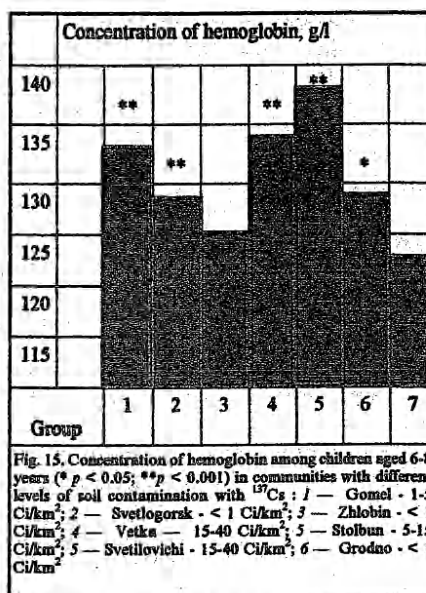
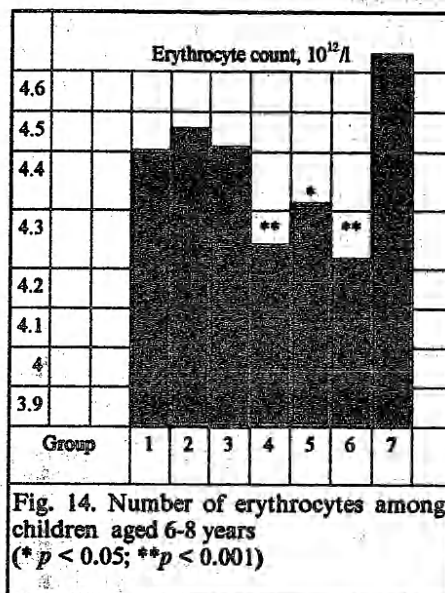
The children from the community of Svetilovichi (15-40 Ci/km<sup>2</sup> of <sup>137</sup>Cs) manifest the most pronounced reduction of the erythrocyte count. Yet, the concentration of hemoglobin among these children is much higher than the control level (Fig. 15). Other groups demonstrate a similar dependence. The results of clinical examinations and laboratory tests are corroborated by experimental studies of laboratory animals.

Rats born during the first months after the disaster would manifest throughout their life significant modifications of the peripheral blood and the bone marrow haemopoietic system, such as eosinophilia, lymphopenia, hypersegmentosis and fragmentation of the nuclei of neutrophils, their giant dimensions, double and more nuclear lymphocytes, inclusions of the nuclear matter in the cytoplasm of lymphocytes and erythrocytes, giant shapes of thrombocytes, porosity of the cytoplasm of eosinophils (V.G. Pinchuk et al., 1991).

Ultrasound investigation of the bone marrow cells among male rats kept within the 30-km zone around Chernobyl has revealed significant submicroscopic modifications of the cells at various stages of maturity, including non-differentiated

regions and mature forms of the cells of the neutrophil, eosinophil, monocytary and erythrocytary series of haemopoiesis and similar modifications in the stroma elements of the microenvironment, megakariots and endothelium (V.V. Afanasjeva et al., 1991).

Feeding Vistar line rats with oats containing  $^{137}\text{Cs}$  in a concentration 445.7 Bq/kg during 20 days would reduce the concentration of erythrocytes in the blood compared with the control group fed with the grain containing  $^{137}\text{Cs}$  in a concentration 44.2 Bq/kg (I.V. Vuevskaja, 1997). The concentration of  $^{137}\text{Cs}$  in the organisms of the rats in the experimental group amounted to 62.76 3.84 Bq/kg compared with 9.76 1.77 Bq/kg in the control group ( $p < 0.05$ ).



So, individuals after exposure to elevated doses of external and internal radiation manifest suppressed proliferative activity of the haemopoietic function.

Meanwhile the process of saturation of the organism with iron suffers no changes. Yet, there is a number of reports of iron-deficit anemias in several regions which have gone up several times recently (V.I. Ponomarenko et al., 1993).

In a number of cases evolution of anemias among the children in the areas contaminated with radiation can be attributed to the disorders of lysis of transferrin as one of the major glycoproteids of the blood plasma. Disorders of this process have been registered among experimental animals long time after exposure which unfavorably affects the iron transport in the organism (N.M. Shilina et al., 1997).

Liver damage induced by the incorporated  $^{137}\text{Cs}$  is one of the causes of this pathological process (Ju.I. Bandazhevsky, N.E. Fomchenko, 1996) (Fig. 14).

## 7. LIVER AND METABOLISM CONDITION

Radioactive elements induce a combination of integrated structural and metabolic changes in internal organs and tissues under different conditions of their effect upon the organism.

The liver is one of the key organs governing the level of metabolic and exchange processes in the organism. Studies of the condition of the liver among wild rodents in the areas affected by radioactive elements and among albino rats, kept for long periods in the real Chernobyl conditions, have revealed a multiplicity of the types of liver damage, among them the most frequent are fat and vacuole dystrophies, coagulating necrosis of hepatocytes (V.G. Pinchuk et al., 1991; L.N. Shishkina et al., 1992).

Microscopic studies of liver tissues of experimental male and female animals after 45 days of dieting on oats containing radioisotopes  $^{137}\text{Cs}$  in a concentration 373 Bq/kg have shown granular and vacuole dystrophies of hepatocytes, expansion of the Disse space. Moderately pronounced disorders of blood circulation in the form of abundant blood in the intralobular veins are observed.

Intensified processes of peroxidation of lipids, alteration of the phospholipid composition of cytoplasmic membranes are typical features of the radiation effect upon the human organism. They may occur in any tissue, including the intestinal mucosa (J.V. Stepanov et al., 1992), in thymocytes (V.I. Dreval, 1993; Ahlers et al., 1992), fat tissue (G.G. Egutkin et al., 1993), lung tissues (E.A. Galitskii et al., 1992), muscular tissue (E.A. Galitskii, M.I. Selevich, 1992).

A single gamma irradiation of pregnant rats *in vivo* in doses 1 and 2 Grays would cause accumulation of the products of peroxidation of lipids and suppression of the activity of cytochrome-c-oxidase, NADN cytochrome-c-reductase, ATP-ase and PNA-ase in the nuclei of liver cells of these animals and their embryos (A.K. Mirahmedov et al., 1992).

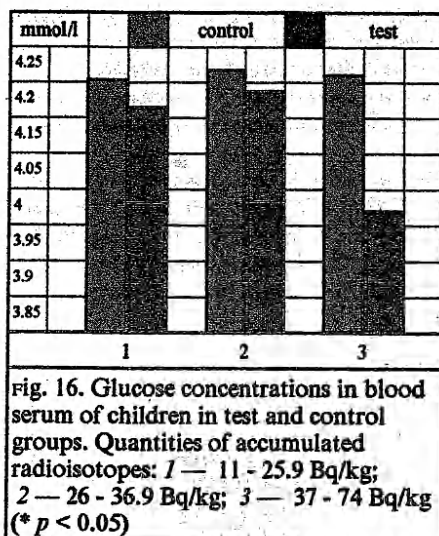
Lipid peroxidation is assumed to be the main cause of damage and structural modification of cytoplasmic and mitochondrial membranes (A.A. Miljutin et al., 1993; Xiong Ve, Chen Zongrong, 1993).

Thus, alterations in the functional condition of the lipid peroxidation system have been established in the organisms of humans and animals in the areas contaminated with radiation (G.R. Gatsko et al., 1992), its inhibition (V.K. Kuhta et al., 1993). Still, it should be remarked that a new dynamic equilibrium between the lipid peroxidation system and the antioxidant protection is rapidly restored making it a mechanism of fast adaptation (A.V. Paranich et al., 1992).

Deficit of carotenes and vitamins acting as antioxidants is one of the factors impairing the antioxidant protection (T.S. Morozkina et al., 1993).

The organism's integral response to irradiation is reflected in the dynamics of reactions in the processes of transformation of hydrocarbons. The first phase (first hours after irradiation) is characterized by accelerated production of glycogens and delayed glycogenolysis; the second phase (3-16 days) is characterized by the retarded synthesis and intensified disintegration of glycogen in the liver tissue; the third phase (the end of the third and the beginning of the fourth weeks after irradiation) is characterized by the restoration of the liver's glycogenolytic and glycogen producing functions (B.M. Graevskaja, N.N. Zolotareva, 1991). A stimulating effect of radioisotopes upon the beta cells of the pancreas until a definite level of their accumulation should be taken into account when assessing how transformations of hydrocarbons change (L.V. Evets, et al., 1992). It is confirmed by the reduction of glucose concentration in the blood of the children aged 3-7 years when the concentration of  $^{137}\text{Cs}$  in the organism exceeds 37 Bq/kg (Fig. 16).

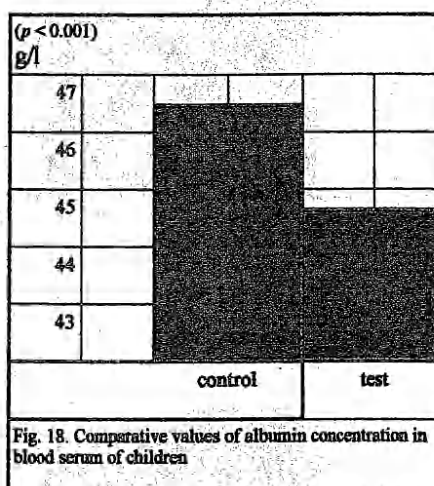
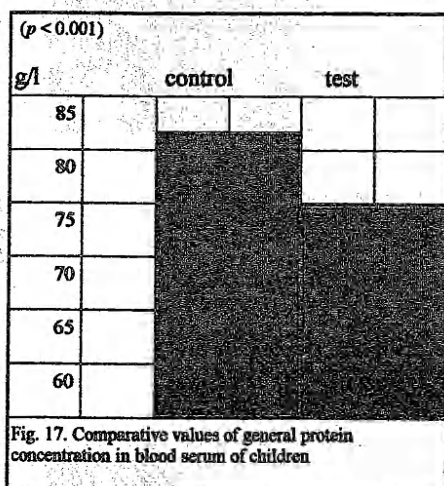




Glucose-6-phosphate dehydrogenase is one of the enzymes involved in the transformation of hydrocarbons, its suppressed reactivity has been observed among preschool children exposed to radioisotopes, primarily to  $^{137}\text{Cs}$  (R.V. Trebukhina et al., 1993).

Radiation induces modifications of the protein metabolism in the organism. One of the earliest responses of the organism to radiation is protein synthesis acceleration and protein accumulation in the blood plasma (Martin et al., 1992; Racek et al., 1992). Also, males who were involved in the elimination of the Chernobyl aftermath, and children aged between 3 and 7 years exposed to radiation in the contaminated areas

have manifested cases of hypoproteinemia and hypoalbuminemia (Fig. 17, 18).



It is possibly due to changes in the DNA concentration in the cells (L.G. Orlova et al., 1991) or to the activity of the mitochondrial and cytoplasmic enzymes. Gamma irradiation of rats with doses 4 Grays boosts specifically the activity of 5-nucleotidase and suppresses the activity of protein kinase (J.V. Bezrodnyi, O.V. Bozhen, 1992; S.M. Jakubovskii, 1993). Single external irradiation of rats with one Gray doses induces oppositely directed changes in the ratio between isoenzymes of lactate dehydrogenase, malate dehydrogenase, esterase and sour phosphatase in the cytoplasm of brain cells during earlier terms (P.P. Chajalo, A.F. Protas, 1992). Suppressed activity of piruvate kinase and lactate dehydrogenase occurs in the early term of radiation disease (1-3 days) and during incorporation of radioisotopes (19) followed by their growing activity in later terms (5-10 days) (V.F. Sukhomlinov et al., 1993).



The activity of enzymic systems relates to the changes in concentrations of regulating substances, such as cyclic adenosine monophosphate and guanine monophosphate (c-AMP and c-GMP). A higher ratio between c-AMP and c-GMP in the blood plasma of rats at later stages after irradiation (the total gamma - dose amounted to 10-20 Gy) evidences a predictably negative domination of adrenergic homeostatic mechanisms (E.I. Kiselgof, V.B. Shorokhova, 1992). It is confirmed by the studies accomplished by A.I. Dvoretckii, I.A. Kulikova (1993) who demonstrated that whole-body X-irradiation of the organism with doses 0.155 and 0.310 Ci/kg modifies the activating effects of noradrenalin and serotonin as well as the biphasic effect of dophamin upon Na, K-pump of the membranes of neurons. Single-phase changes in the activity of adenylate cyclase should also be taken into consideration (L.V. Slozhenikina et al., 1992).

It has also been observed that the children in the area with the density of contamination 15-45 Ci/km<sup>2</sup> demonstrate a higher concentration of adrenalin in the blood (L.S. Baleva et al., 1992). Yet, S.V. Petrenko and V.A. Zajtsev (1997). Thus the children in the areas contaminated with radioisotopes manifest reduction of catecholamines as well as hyporeactivity of the hormonal response of adrenals to the stimulating effect of the endogenous adrenocorticotrophic hormone (ACTH). V.A. Zajtsev also outlines these effects (1992). The individuals who participated in the elimination of the Chernobyl aftermath manifest a significant rise of histamine concentration, a stronger monoamine oxidant activity and a 4.5 time rise of serotonin in the blood (N.F. Ivanitskaja et al., 1991).

Disorders of the functions of adrenals are one of the key links in the pathology of metabolism under the effect of radiation. The children exposed to protracted small doses of radiation have manifested suppressed functional activity of adrenals, upset equilibrium between the concentrations of cortisone and ACTH in the blood plasma (S.V. Petrenko, V.A. Zajtsev, 1993). The children aged 3-7 years in the areas with the levels of <sup>137</sup>Cs concentration 1-5 Ci/km<sup>2</sup> have manifested a valid reduction of cortisone concentration in the blood compared with the control (Fig. 23). Suppressed capability of the liver to utilize cortisone is significant in the metabolic pathology leading to accumulation of metabolites in the organism (L.A. Litskevich, 1991).

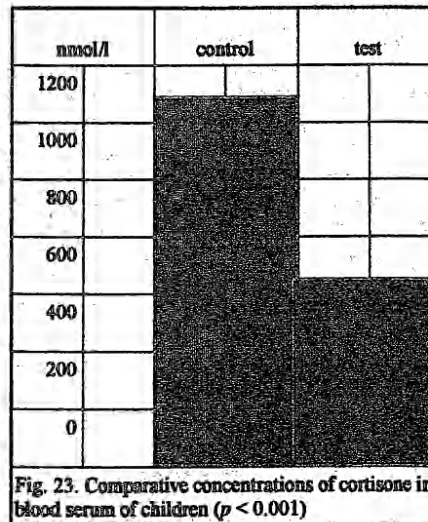


Fig. 23. Comparative concentrations of cortisone in blood serum of children ( $p < 0.001$ )

It should be noted that X-irradiation reduces the concentration of sex hormones, lutropin and testosterone specifically (S.V. Vjarga, 1993) which play a significant role in metabolism.

### 8. GASTROINTESTINAL TRACT

Gastrointestinal tract is one of the major paths of incorporation and excretion of radioisotopes. Strong  $^{137}\text{Cs}$  doses, causing the appearance of acute radiation disease among experimental animals, induce the development of gastroenterocolitis with a pronounced disorder of blood circulation in all layers of the intestinal tube (J.I. Moskalev, 1995) and the edema of the mucosa (M.I. Jakubovskii, et al., 1997).

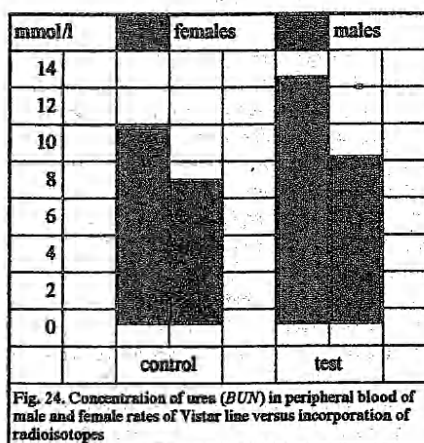
Incorporation of relatively slight amounts of  $^{137}\text{Cs}$  by the organisms of children with food leads to chronic stomach inflammations. Over 80% of the children in the contaminated areas suffer from chronic gastritis and gastroduodenitis. Specifically strong contamination of the stomach mucosa with bacteria is noteworthy. Typical manifestations are the atrophied stomach mucosa and its intestinal metaplasia (Chernobyl, 1996).

The liquidators manifest more frequent erosive gastroduodenitis which typically evolves without symptoms, tends to relapse and combine with latent immunity deficit (O.J. Dementjeva, et al., 1997).

It can be due to the effect of internal irradiation of intestines with incorporated radioisotopes upsetting the final stage of the biogenesis of intestinal enzymes and their combination with the enterocytal plasmatic membrane (V.V. Lelevich, et al., 1995).

### 9. KIDNEYS

Kidneys are actively involved in metabolism. Incorporation of radioisotopes ( $^{137}\text{Cs}$ ) by the organisms of experimental animals in the quantities over 100 Bq/kg and up produces pronounced changes in the glomerules in the form of proliferation of mesangial cells, infiltration of lymphoid histiocyte elements into the loops, fragmentation and death of glomerules (Yu.I. Bandazhevsky, N.E. Fomchenko, 1996). It results in the accumulation of urea and products of protein metabolism in the blood serum (Fig. 24).

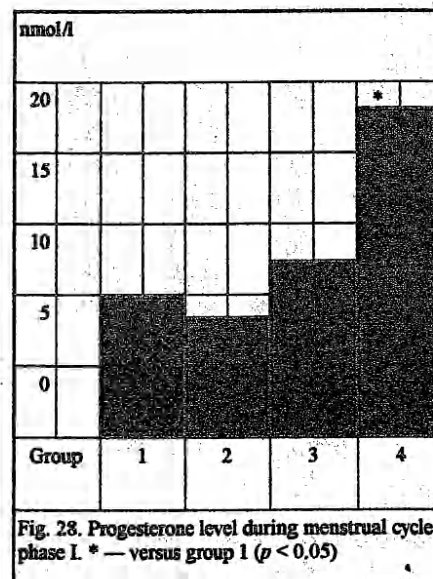
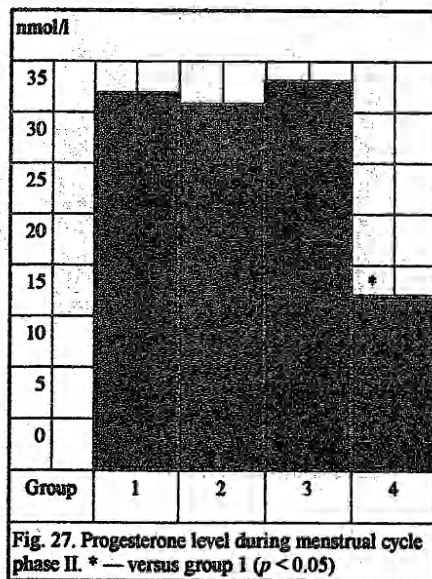
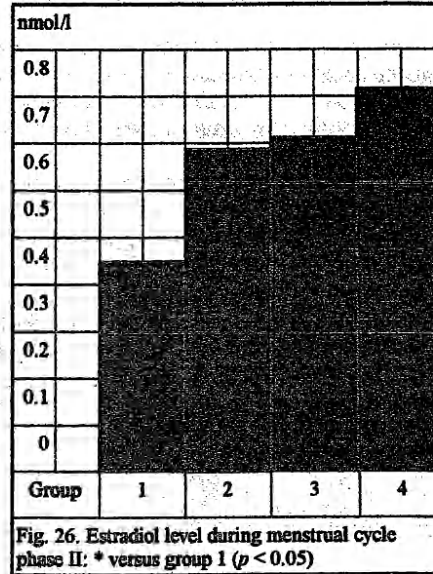
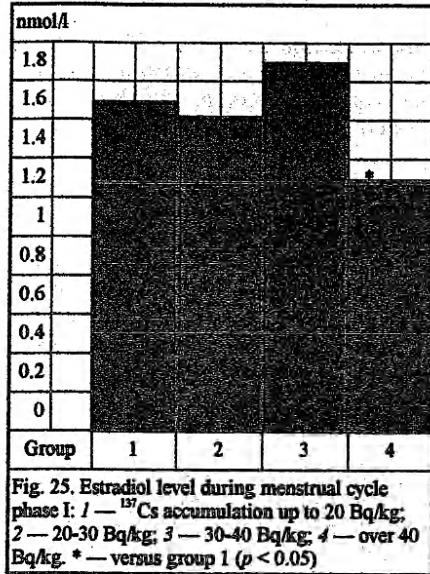


### 10. FEMALE REPRODUCTIVE SYSTEM

The female reproductive system is sensitive to ionizing radiation. Disorders of its functions are induced by different types of radiation and they are registered both clinically and experimentally.

Hormonal modifications occur typically in the hypophysis-ovary-uterus system leading to the disorders of ovulatory and menstrual functions.

Incorporation of radioactive elements by female organisms in the areas affected by the Chernobyl disaster leads to the inversion of the hormonal background resulting in the upset menstrual cycle. When accumulation of  $^{137}\text{Cs}$  exceeds 30 Bq/kg, a valid reduction of estradiol and rise of progesterone concentration occur during the first phase of the cycle and vice versa during the second phase (Fig. 25-28).



A similar relationship has been revealed in experiments with laboratory animals when the reduction of progesterone has been registered in the estrus cycle resulting in the thinning of the uterine mucus (Yu.I. Bandazhevsky, Yu.V. Antonova, 1995).

It should be remarked that accumulation of radioisotopes in the organisms of fertile age females intensifies generation of testosterone governing the appearance of masculine attributes (D.V. Vvedensky, I. Yagovdik).

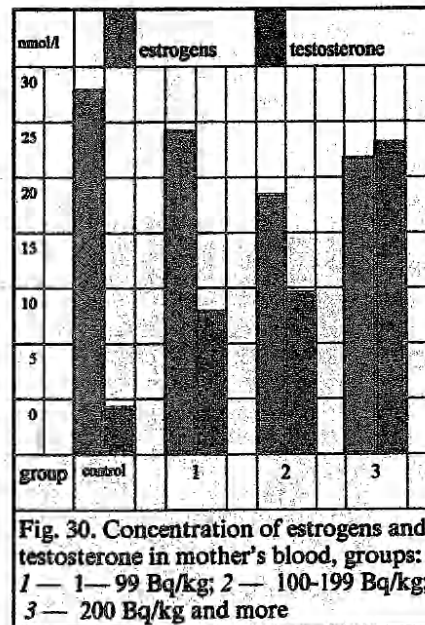
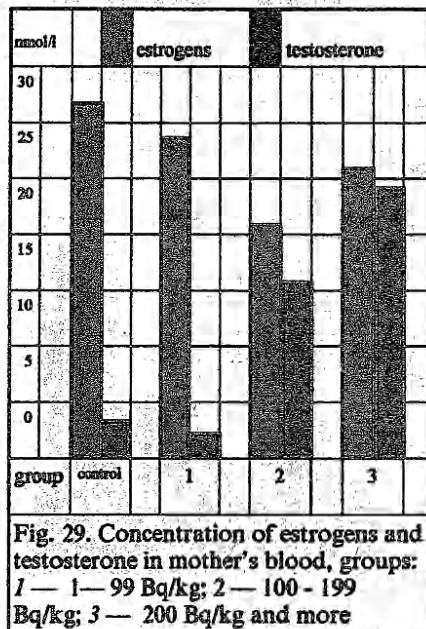


## 11. EVOLUTION OF PREGNANCY AND FETUS DEVELOPMENT

Pregnancy is accompanied by a pronounced accumulation of  $^{137}\text{Cs}$  in the mother's organism. Feeding laboratory animals with oats containing this radioisotope in the amount 445 Bq/kg has manifested that its concentration by the end of pregnancy (the 21st day) exceeds 120 Bq/kg (Yu.I. Bandazhevsky, T.S. Ugolnik, 1995).

This radioisotope accumulates primarily in the placenta where its concentration can reach 200 Bq/kg and up in humans (Yu.I. Bandazhevsky et al, 1997).

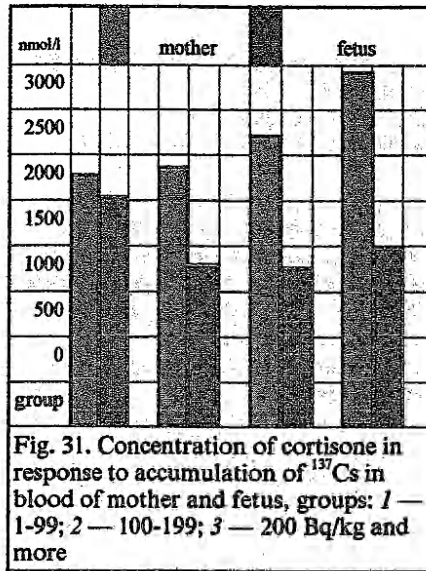
Meanwhile,  $^{137}\text{Cs}$  does not penetrate basically into the fetus organism (Yu.I. Bandazhevsky, T.S. Ugolnik, 1995). Since the functions of the placenta belong to the most essential among provisory organs, accumulation of radioisotopes definitely affects the functions of the fetoplacental complex. Primarily it relates to the hormonal condition. In particular, the concentration of estradiol in the mother's and fetus' blood reduces by the end of pregnancy, while the concentration of testosterone increases compared with the control group (Fig. 29-30). Concentration of



Meanwhile progesterone increases insignificantly in the fetus, thyroxin and triiodine thyronin are absent, the concentration of cortisone reduces progressively as the concentration of  $^{137}\text{Cs}$  in the placenta increases (Fig. 31).

Intricate metabolic modifications are accompanied by structural changes of the placental villus apparatus when the number of intermediate villi increases and that of terminal villi reduces.

The surfaces of the villi manifest a significant number of trophoblastic cells evidencing their metabolic activity. Rise in the number of the syncytial buds, angiomatosis of terminal villi, cytotrophoblast evolution prove that the compensatory processes and the hormone producing function of the placenta are activated.



Metabolic modifications in the mother-fetus system affect the fetus development, increase chances of failed preimplantation, the process of bone system development, such as osteogenesis of tubular bones, is inhibited.

The count of leukocytes and lymphocytes in the blood reduces, while that of eosinophil leukocytes increases (T.S. Ugolnik, 1996).

A larger incidence of congenital defects in the radiation contaminated areas is noteworthy. (*Chernobyl: Consequences for the Environment, Health and Human Rights*, Vienna, Austria, pp. 155, April 12 - 25, 1996.

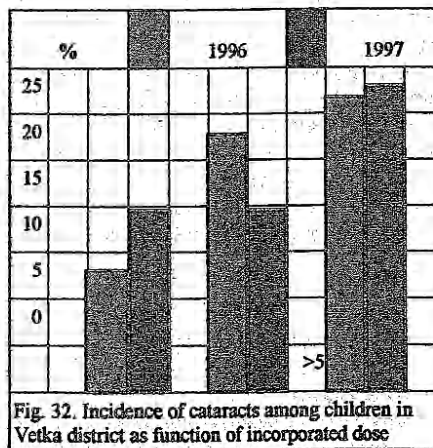
## 12. THE ORGAN OF VISION

The organ of vision is highly sensitive to radioactive emission. External irradiation with 3-5 Gy damages the lens and induces cataracts.

Similar results are registered among humans after exposure to an external source of radioactive emission (Yu.I. Moskalev, 1991).

Incorporation of radioisotopes by the organism also leads to significant structural modifications, specifically of the lens. A direct proportionality is clearly observed between the quantity of accumulated radioisotopes ( $^{137}\text{Cs}$  primarily) and the incidence of cataracts (Fig. 32). It is manifested by the individuals living in the areas with significant radiocesium contamination (over  $15 \text{ Ci/km}^2$ ).

In addition to cataracts other morphofunctional disorders of the vision apparatus are registered, such as destruction of the vitreous body, cyclastenias, abnormal refraction.



Reduction of the quantity of radioisotopes in the organism eliminates the above pathological conditions as it is evidenced by the results of population screening in the Vetka district (Yu.I. Bandazhevsky, A.N. Kurilenko, 1997).

Experiments with laboratory animals (albino rats) have manifested that radioactive cesium causes disorders in the development of the cornea when it loses fibers and becomes vascularized (Yu.I. Bandazhevsky, A.N. Kurilenko, 1997).







### Chapter III

#### PATHOGENETIC LINKS BETWEEN BASIC PATHOLOGICAL PROCESSES IN THE ORGANISM IN RESPONSE TO THE INCORPORATION OF RADIOACTIVE ELEMENTS. THE SYNDROME OF INCORPORATED LONG-LIVING RADIOISOTOPES

The ecological situation in the center of Europe after the Chernobyl disaster is determined by the release of a huge quantity of radioactive elements into the environment which have different half-lives. Depending upon the duration of their existence and the features of reactions with biological structures, these agents differently affect the organisms of humans and animals. Hence, the periods of effects of short-living  $^{131}\text{I}$  and  $^{89}\text{Sr}$  and long-living  $^{137}\text{Cs}$  and  $^{90}\text{Sr}$  isotopes are discriminated.

Radioactive  $^{131}\text{I}$  penetrates into the human organism via the gastrointestinal and respiratory organs, through skin, wounds and burns. Digestion and inhalation paths are most essential for practical purposes. After penetration into the organism, iodine is rapidly absorbed by the blood and lymph, it accumulates in the thyroid, liver, muscles, bones. The extent of its accumulation by the thyroid depends upon its condition. Iodine accumulates quicker in the case of hyperthyreosis and slower in the case of hypothyreosis. About 20% of iodine is combined by proteins in a normally functioning thyroid gland.

Acute and severe radiation injuries occur leading to lethal outcomes when  $^{131}\text{I}$  concentration amounts to 55 mBq/kg in humans and 1850 mBq/kg in rats. Smaller iodine quantities cause pathological modifications in the thyroid, in the blood, in the immunity system and in a number of metabolic links.

Radioactive iodine causes malignant pathologies in the thyroid, primarily cancers, the latter are due to strong changes in the immunity system.

There are grounds to believe that  $^{137}\text{Cs}$  and  $^{134}\text{Cs}$  play their role in the induction of thyroid cancers, in addition to  $^{131}\text{I}$ . Cesium isotopes negatively affect the immunity system which acts as a controller of thyroid cells, it annihilates those cells which get out of control.

In addition to the blastomogenous effects of iodine it induces hypo- and hyperfunctions of the thyroid and autoimmune disorders.

Yet, the population in the radiation contaminated areas is primarily affected by long-living radioisotopes,  $^{137}\text{Cs}$ ,  $^{134}\text{Cs}$ ,  $^{90}\text{Sr}$ , in the first place, which are incorporated with food ingredients. The degree of accumulation of these elements in tissues and organs is a function of a number of factors:

- (1) concentration in consumed food;
- (2) age;
- (3) sex;
- (4) blood group and rhesus factor;
- (5) physiological condition;
- (6) agents governing the incorporation of radiation in the gastrointestinal tract or its excretion.

The largest concentrations of gamma-sources ( $^{137}\text{Cs}$ ) have been registered in the communities which have mushrooms and forest berries in their diets and which are collected in the areas with the heaviest contamination. These radioisotopes are major contributors into the dose of irradiation. A direct proportionality has been revealed

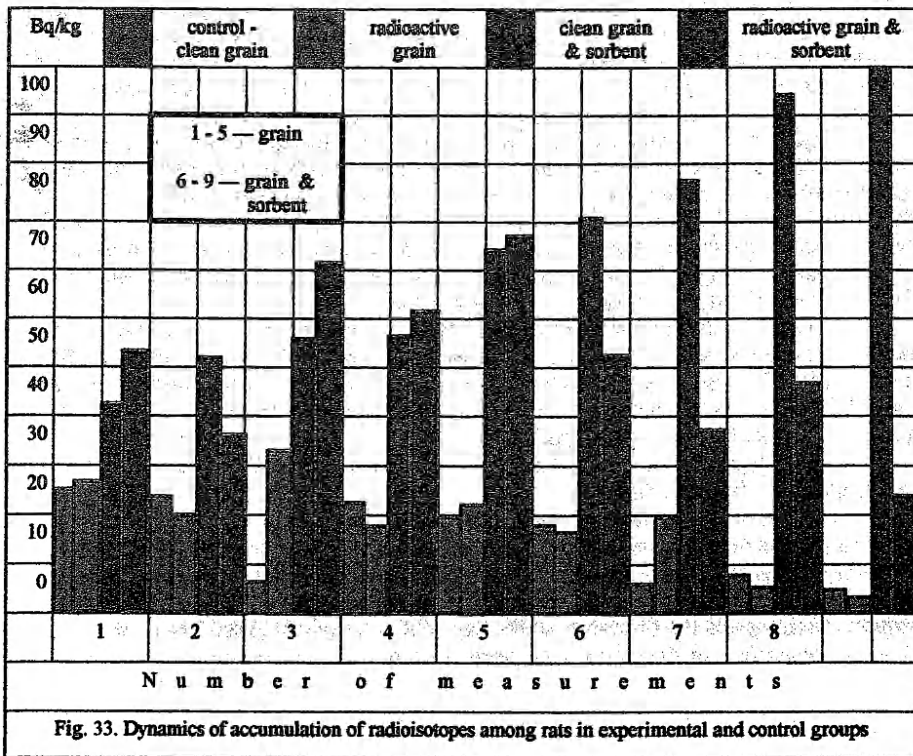
between age and the amount of accumulated radioisotopes, with senior children having manifestly larger accumulated doses.

Experimental and clinical studies have revealed that females accumulate radioisotopes much less than males under the same conditions. A relationship has been revealed between the degree of expression of <sup>137</sup>Cs incorporation and the group (Rh) identification. Individuals with Rh<sup>-</sup> accumulate smaller doses of radioisotopes (Yu.I. Bandazhevsky et al., 1997).

Yet, accumulation of radioisotopes strongly increases in pregnancy going up multifold primarily in the placenta and leading to a pronounced disorder of the hormonal equilibrium both in the organisms of the mother and the fetus, with doubtless effect upon the fetus further development. Meanwhile, penetration of <sup>137</sup>Cs into the organism of the fetus reduces to the minimum among mammals and man with the hemochorial placental structure when the placenta as a provisory organ creates a barrier effect. Any injury of the placenta barrier kills the fetus.

Accumulation of radioisotopes depends in many respects upon the environmental factors to which the organism is exposed, specifically when the gastrointestinal tract, among them the agents capable to sorb radioisotopes and boost their excretion from the organism and these agents occupy a specific place.

There are preparations, or enterosorbents, which possess various chemical structures and different sorption effectiveness in respect to <sup>137</sup>Cs. The results obtained at the Gomel Medical Institute manifest that clayey pectin compounds, pectopal specifically, are the most promising preparations, being capable to obstruct the enteral penetration of radiation (Fig. 33).



Radioisotopes,  $^{137}\text{Cs}$  primarily, differently accumulate in the tissues and organs when they penetrate with food.

Based on the examinations of sections and experimental material the largest accumulated doses have been registered in the parenchimatose organs, the heart and the thyroid gland, in the first place.

Incorporation of radiocesium causes structural and metabolic changes in the organs and tissues, the severity of these changes is directly proportional to the quantities of accumulated radioisotopes.

Clinical, experimental material and sections have manifested pathological effects in the heart, liver, kidneys, central and vegetative nervous, endocrine, immunity, reproductive systems, among other organs and systems.

The cardiovascular system in particular manifests disorders of the electric impulse conduction in the form of different blockades, as well as structural and metabolic modifications of the myocardium tissue leading to pathological modifications of the actin-myosin complex. The children in the radiation contaminated areas show various frequencies of the His stem bundle blockades which are directly proportional to the quantities of incorporated radioisotopes.

Injuries of the myocardium can be aggravated by the depleted concentration of thyroid hormones, upset functions of the vegetative nervous system.

Accumulation of radioisotopes in the internal organs, first of all in the liver, kidneys, endocrine glands, upsets the metabolic processes in the organism with relevant manifestations in the blood biochemical parameters.

Injuries of kidney tissues should be emphasized, specifically affecting the globular and duct apparatus, alongside with the injury of the liver tissue leading to the accumulation of protein metabolism products in the organism.

The pathology of the immune system manifests itself in the inhibition of the functional activity of the immunity competent cells leading to the growing incidence of a number of infectious and parasitic diseases, tuberculosis, in the first place. A real manifestation of this phenomenon is the inhibition of the phagocytary activity of neutrophil leukocytes and reduction of IgJA concentration in the blood.

The injury of the haemopoietic function should be outlined specifically. A valid reduction of the erythrocyte number at the normal hemoglobin concentration has been registered among the children in the areas with more severe contamination (above 40 Ci/km<sup>2</sup>) with significant accumulation of  $^{137}\text{Cs}$  in the organism (500 Bq/kg and up). Accumulation of the same radioisotope under 50 Bq/kg in the organisms of the children in the areas with the  $^{137}\text{Cs}$  contamination between 1 and 5 Ci/km<sup>2</sup> creates no pronounced modifications of the haemopoietic system.

The damage of the endocrine system, primarily the thyroid gland, is due to the exposure to radioactive iodine during the initial days after the Chernobyl disaster. Still, the effect of  $^{137}\text{Cs}$  should not be excluded when it is intensively accumulated by this organ. A relationship has been revealed between the concentrations of T<sub>3</sub> and T<sub>4</sub> and the concentration of  $^{137}\text{Cs}$  in the organism.

A similar relationship has been traced in respect to cortisone as one of the hormones of the adrenal cortex.

Modifications of the immunity system induced by  $^{137}\text{Cs}$  play a significant role in the injuries of the thyroid gland with a noticeable correlation between IgJ and the thyroid hormones among the children in the contaminated areas, based on their ability to enter into reactions. It can be assumed that elimination of these hormones from the metabolic chain upsets the functions of the hypophysis - thyroid gland system with a significant generation of the thyrotropic hormone which stimulates the thyroid gland c

causing intensified proliferation of the follicular epithelium which creates conditions for neoplastic transformations.

Therefore, in our view, the effect of incorporated radioisotopes,  $^{137}\text{Cs}$  primarily, upon the endocrine system should be considered due to the disorders of the immunity regulation upsetting the functioning of tissues and organs, the proliferation and differentiation of their cellular elements should be taken into consideration in this case. Under the existing conditions the repair and restoration of the thyroid gland after a short-time exposure to  $^{131}\text{I}$  evolve under a protracted effect of  $^{137}\text{Cs}$  and  $^{90}\text{Sr}$  both upon the tissues of the organ proper and upon the immunity system controlling the processes of proliferation and differentiation of the follicular epithelium and the adjacent cells. This effect transforms the structural components of the thyroid cells into antigens for the immunity system. An immunological response appears when the structural thyroid components are damaged by autoantibodies and immunocompetent cells result from the evolution of autoimmune thyroiditis, accompanied by thyroid cancers in a number of cases.

Functions of the central nervous system during incorporation of radioisotopes manifest various vegetative disorders based on the loss of equilibrium between biogenic monoamines and neuroactive amino acids.

The organs of senses are also affected by incorporated radioisotopes.

High incidence of pathologies of the organs of vision among children, specifically cataractous modifications of the lens, prevails in the areas with heavier contamination (the Vetka district with  $^{137}\text{Cs}$  contamination over  $15\text{ Ci/km}^2$ ).

Pathologies of the female reproductive system directly relate to the disorders of endocrine functions. A definite loss of the balance between progesterone and estrogens has been established among the fertile age females with the degree of expression dependent upon the concentration of incorporated radioisotopes. In case of some pronounced accumulation of  $^{137}\text{Cs}$  in the placenta in pregnancy the hormonal disorders are registered both in the organisms of the mother and the fetus. In particular, the concentration of testosterone goes up following the growing concentration of radioisotopes. In addition to it mother demonstrates also a rise in thyroid hormones and cortisone in the blood.

Modifications of the hormonal condition of the mother-fetus system extend the duration of pregnancy, cause complications in labors and postnatal development.

Thus, natural incorporation of radioisotopes leads to disorders of metabolic processes in vital organs and tissues in which the physiological conditions do not favor or exclude sufficient proliferation of cells (the myocardium). They would continuously accumulate  $^{137}\text{Cs}$  which can produce negative influence, primarily due to the toxic effect of the radioisotopes when they intrude into metabolic processes and damage membrane structures of cells. Considering the affinity between  $^{137}\text{Cs}$  and  $\text{K}^+$ , it can be assumed that the radioisotope gets involved in to the K-dependent processes, the electrolytic exchange in particular.

It results in structural and functional disorders of numerous vital systems, primarily the cardiovascular system. No pronounced damage of cells is induced by  $^{137}\text{Cs}$  in the tissues with active proliferation. It is due, in our view, to its long half-life, hence its ionizing effect is not so much manifest at present.

In this connection, it should be admitted that disorders of metabolic processes in the organism are basically caused at present by the toxic effect of cesium and other radioactive elements with long half-life periods which were released in huge amounts into the environment during the disaster.

The ionizing effects of the long-living radioisotopes will become manifest after a significant period of time, hence the top-priority task of medical science and practice is to create conditions for decorporating these agents from the organism.

Thus, small doses of  $^{137}\text{Cs}$  with a little ionizing effect produce a noticeable effect when their toxic effect upon the vital organs and systems is taken into consideration. The pathological modifications they induce in the organisms of humans and mammals can be integrated into the syndrome of incorporated long-living radioisotopes (SILR).

The syndrome appears among the individuals after incorporation of the long-living radioisotopes ( $^{137}\text{Cs}$ ,  $^{90}\text{Sr}$ ). It is characterized by the pathology of metabolism determined by the structural and functional modifications of the cardiovascular, nervous, endocrine, immunity, reproductive, gastrointestinal, hepatobiliary and urine excreting systems.

The quantities of the radioisotopes sufficient to induce the syndrome may be different depending upon the age, sex, physiological condition of the organism. Children particularly manifest pathological conditions of the organs and systems when accumulation of  $^{137}\text{Cs}$  exceeds 50 Bq/kg.

The main actions to avoid evolution of the syndrome are to prevent incorporation of the radioisotopes by the organism, therefore radiological monitoring of the population and food is compulsory in the areas affected by the Chernobyl radiation (Fig. 34) or their excretion from the organism using sorption agents.

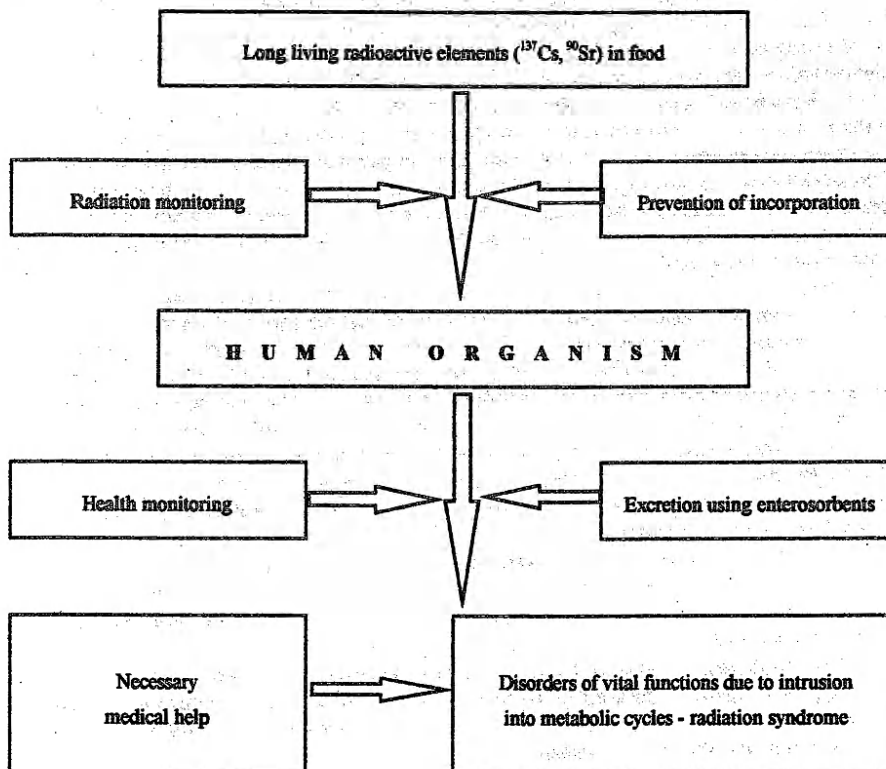


Fig. 34. Diagram of interactions between human organism and radioisotopes



**LIST OF ABBREVIATIONS**

<b>ATP-ase</b>	<b>adenosintriphosphatase</b>
<b>AST</b>	<b>asparate aminotransferase</b>
<b>ALT</b>	<b>alanin amino transferase</b>
<b>T<sub>3</sub></b>	<b>triiodine thyronin</b>
<b>T<sub>4</sub></b>	<b>thyroxin</b>
<b>GAMC</b>	<b>gamma-amino oleic acid</b>
<b>GGTP</b>	<b>gamma-glutamit transpeptidase</b>
<b>LDH</b>	<b>lactate dehydrogenase</b>

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