

Human Health and Incorporated Radionuclides.

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The population of the Republic of Belarus, Ukraine and the Russian Federation living in areas affected by the accident at the Chernobyl nuclear power plant has been exposed to adverse effects of long-living radionuclides for 28 years, and primarily of ^{137}Cs (radiocesium), given the amount released into the biosphere in 1986 [1]. Immediately following the accident, radiocesium had been on the surface of the soil, and naturally could not have been available to the root system of plants, unless the upper layers of the soil were inverted while ploughing. For the same reason, the mushrooms just after the Chernobyl accident could not have contained Chernobyl cesium in high concentrations. It takes several years for them to accumulate significant quantities of radionuclides. However, the mushrooms that grew in the affected area in 1986, had contained high concentrations of radiocesium. This situation may be explained by the findings of the studies carried out by the Institute of Biophysics of the Ministry of Health in the Russian Soviet Federated Socialistic Republic, which prove that a large part of the Republic of Belarus had been contaminated with radiocesium in the 60s of the last century, for which reason this radionuclide had been detected in meat and dairy products in high concentrations [2]. Radiocesium contamination maps for the Belarussian-Ukrainian territory Polesye before and after the Chernobyl accident are practically identical [3].

So what did the specialists that carried out radiometric measurements in areas affected by the Chernobyl accident in 1986 find?

This raises the question relating to the calculation of radiation doses absorbed by the population living in these areas. At the official level, it was decided to calculate doses received by the population from affected territories starting from April 26, 1986 - the date of the Chernobyl accident. The health of the population has been assessed and continue to be assessed also beginning from this date. But what about radiation doses received by the same population over a 20-year period prior to the Chernobyl accident?

Based on the above, we can conclude that the results of Belarus's population health assessment do not conform to radiation doses that have been officially presented, including data related to such radionuclides as ^{137}Cs .

Research institutions in the USSR and CIS countries have for many decades studied and continue to study effects on the living organism mainly caused by external radiation, while in reality the population receives 80% of the radiation load due to internal irradiation.

The absence of full data on the impact of incorporated radionuclides on the human body did not allow to carry out an effective policy of protection of health of the population affected by the Chernobyl accident at the state level, which led to serious medical and demographic consequences [3].

The radiation load of no more than 1 mSv per year corresponding to the specific activity of radionuclides in the organism of 400 Bq/kg is currently accepted to be safe for the human health in the Republic of Belarus, Ukraine and the Russian Federation. However, the studies conducted by Gomel State Medical University in 1991-1999 had shown that the incorporation of even smaller amounts of ^{137}Cs negatively affect the human health (see below).

Most radionuclides are transferred from soil to the human body mainly through the food chain, thus regular radiological monitoring of foodstuffs is required to protect the health of the population. The institutions that carry out monitoring have been and are still guided by the food radiation standards, the so-called permissible radiation limit values, established by the government.

In determining permissible radiation limit values for food, the government applied the principle of economic viability and therefore it was allowed to produce agricultural products in vast areas affected by the Chernobyl nuclear power plant accident. In addition, the threshold limit values for radionuclides in food for the population were calculated not on the basis of the danger that may be posed to the organism by specific amounts of radionuclides, but based on the level of contamination of major farm products by these agents. Once the level of contamination of the major part of products of vegetable and animal origin has fallen, the maximum permissible levels can be toughened, i.e. the permissible limit values can be lowered.

According to applicable radiation limit values, the population living in territories affected and not affected by the Chernobyl accident may regularly consume food products containing high concentrations of ^{137}Cs and ^{90}Sr [4]. As a result of consumption of these products, radionuclides are accumulated in the bodies of children and adults.

The effects of incorporated ^{137}Cs as the most widespread radioactive element in the environment on vital organs and systems of the human body were studied by Gomel State Medical University in 1991-1999. The study took into account the real life situation in which millions of people permanently residing in areas affected by the Chernobyl accident had been. Clinical observations and pathomorphological analysis of deceased individuals were performed along with experiments on laboratory animals. The obligatory part of these studies was the determination of ^{137}Cs levels in human and animal bodies, internal organs, food products used for feeding laboratory animals.

It was concluded that the degree of the ^{137}Cs accumulation in the body depends on a number of factors:

1. Concentrations in food. The highest levels of radionuclides were found in the body of people resided in areas with the highest rate of contamination with radionuclides and consumed mushrooms and berries [3,5,7].

2. Sex. Females accumulate ^{137}Cs in their body in considerably lower concentrations than males, living in the same conditions [6,7,8].

3. Age. ^{137}Cs concentrations in children's organs significantly exceed the ones

in adults [8,9].

4. Rhesus blood group. Individuals with rhesus negative blood accumulate ^{137}Cs in lower concentrations in comparison with individuals who have rhesus positive blood [7,10].

5. Physiological condition of the body. The ^{137}Cs accumulation by the female body is sharply increasing during pregnancy [6,11].

6. Action of agents affecting incorporation of radionuclides in the digestive tract or their elimination. Enterosorbents including organic and nonorganic components can bind and remove radionuclides from the body. Clay and pectin compounds are the most promising in this regard [6,7].

However, the question on the long-term use of enterosorbents to reduce incorporation of radioactive elements in the organism now remains open. It is due to the fact that during enterosorption, not only ^{137}Cs radionuclides but other essential micro-nutrients can be eliminated from the body.

7. Structural and functional peculiarities of organs and tissues.

For many years research papers devoted to incorporation of ^{137}Cs into the human and animal body stated that the above radionuclide is accumulated mainly by the muscular system [12].

Radiometric measurements performed by Gomel State Medical University in 1996-1997 during autopsies of inhabitants of areas contaminated with radioactive elements found high levels of ^{137}Cs in the heart, thyroid, adrenal and pancreatic glands, small and large intestine, stomach, kidneys, spleen, brain, lung and skeletal muscles [8,9]. The obtained data was proved by results of experimental studies where ^{137}Cs was introduced into the body of laboratory animals. In 10 days after introduction of radiocesium into the body, its highest concentrations were registered in the heart, kidneys, spleen and liver [6]. Only after intragastric introduction of large quantities of this isotope as a part of aqueous solutions, its high concentrations were observed in skeletal muscles [10].

Thus, ^{137}Cs radionuclides simultaneously enter vital organs. This should be taken into account to understand what pathological changes may occur in the body due to this.

The results of post mortem studies and experiments with laboratory animals enabled to establish a relation between ^{137}Cs concentration and pathological changes arising in organs and systems [3,10]. These findings are in line with results of clinical observations and laboratory examination of children of different ages. The complex approach to the study of effects of incorporated ^{137}Cs radionuclides on the human body allowed to determine key phases in the initiation of pathological processes.

With incorporation of ^{137}Cs into the body, cell structures are exposed to:

1. Gamma and beta radiation occurring as a result of the decay of ^{137}Cs incorporated into the body.
2. Undecayed ^{137}Cs radionuclides [13].
3. Barium (Ba) resulted from the ^{137}Cs decay in the body [14-16].

Radiocesium incorporation leads to the disruption of energy and constructive metabolism in highly differentiated cells, causing the development of dystrophic and necrobiotic processes. Radiocesium interferes with metabolic processes affecting membrane cell structures and so an effect of metabolic dysfunction occurs [8,10]. The degree of disruption depends upon the concentration of incorporated radiocesium. The more intense the process of incorporation, the higher the degree of disruption can be stated. The multi-organ nature of the action should be particularly emphasised.

Depending on ^{137}Cs concentration incorporated into the body, the following groups of pathological conditions may be determined:

Group 1. ^{137}Cs incorporation of up to 20 Bq/kg – Multifactorial congenital defects; metabolic, electrophysiological and functional changes in organs and tissues if there is a genetic predisposition (based on insufficient gene activity);

Group 2. ^{137}Cs incorporation of 20-50 Bq/kg - Conditions peculiar to those of Group 1, as well as dystrophic changes in cells, tissues and organs leading to their failure;

Group 3. ^{137}Cs incorporation of more than 50 Bq/kg – Conditions specific to those of Groups 1 and 2, as well as dystrophic, necrobiotic and sclerotic changes in vitally important organs substantially disrupting their function and leading, in some cases, to death of the organism or its disability.

In cases of combined action of radiocesium and toxic agents of different origin having a negative effect on metabolic processes, irreversible pathological changes may occur in vital organs and systems even with a low content of radiocesium in the body.

In our opinion, one of the main reasons for the increase in cardiovascular diseases in the European part of the former USSR over past decades [17] is incorporated radioactive elements, primarily ^{137}Cs . The directly proportional correlation between ^{137}Cs concentration in the child's body and the cardiac abnormality rate was established. Moreover, cardiac arrhythmias were registered in a large number of children with a relatively low specific activity of radiocesium in their body (up to 20 Bq/kg) [18-21].

The occurrence of arrhythmias is associated, in our opinion, with radiocesium involvement in the phenotypic implementation of genetic defects of the system of proteins participating in processes of ion permeability of the cytoplasmic membrane leading to impaired electrical impulse conduction through the heart's conduction system.

The evidence of this hypothesis were results of the studies carried out by IRSN that had revealed the ^{137}Cs ability to change gene expression in heart cells of experimental animals [22].

With increasing specific activity of ^{137}Cs in the child's body, disturbances of metabolic processes in the myocardium based on its radiotoxic effects may occur.

These disturbances are mostly expressed in neonates and children aged up to 1 year [23,24].

The energetic system of the cardiomyocytes is disrupted, and, in particular, of mitochondria where deep structural and metabolic changes occur, including creatine phosphokinase activity suppression [6].

With ^{137}Cs specific activity in the body of over 50 Bq/kg, cell structures of the heart and other vital organs undergo necrobiotic changes. The effect of such widespread external factors as alcohol and nicotine worsens the situation sharply.

According to results of medicolegal autopsies, myocardial injury was registered in 99% of all deaths of inhabitants of areas contaminated with radiation. In addition, diffuse cardiac muscle cell injury, manifesting itself as contractures or overcontractions of muscle fibers, primary cluster disintegration of myofibrils, dystrophic processes with varying degrees of severity and necrosis was found in all cases [8]. The detection of ^{137}Cs in the heart proves its participation in the occurrence of this pathology. The negative role of ^{137}Cs in damaging the cardiovascular system was confirmed by experiments on laboratory animals, to whom radiocesium was given as a part of food or in the aqueous solution [10,25].

The revealed myocardium pathology can be classified as ^{137}Cs related cardiomyopathy [20] that completely corresponds to the definition given by the WHO Experts Committee that recommends to define cardiomyopathy as a myocardium disease of various origin, but not an inflammatory one according to morphology and a coronary one according to origin [26].

^{137}Cs induced cardiomyopathy can be a direct cause of death of people, as well as complicate the course of other diseases and promote to death. It should be considered in undertaking treatment and prevention measures for the population living in areas contaminated with radioactive elements.

Arterial hypertension was observed in 41,6% of children of school age lived in the territory with ^{137}Cs contamination above 15 Ci/km² [7].

In our opinion, the root cause of the disease is related to direct or indirect effects of incorporated radionuclides on muscle elements of the blood vessel wall resulting in their overcontractions and spasm. The spasm of muscle elements of arterial vessels induced by radiocesium may be the reason for the development of classical myocardial infarctions. At the same time, the reduction of antithrombogenic activity of vessel walls and activation of the platelet, coagulation and fibrinolysis phases of hemostasis occur showing that intravascular blood clotting takes place [27].

Pathological changes in the vascular system along with the direct toxic action of radiocesium lead to damaging the cell structures of kidneys, heart, brain and other organs.

The kidneys excrete radiocesium from the body [12]. Because of that, the vascular system of the nephron becomes damaged, resulting in the death of structural and functional elements of the latter, and primarily of glomeruli, with the presence of a

specific histologic pattern called a “melting icicle” phenomenon [8].

Renal damage is one of the main reasons for the accumulation of radiocesium and metabolic waste products in the body and their toxic effects on vital organs, including the heart, and development of arterial hypertension. Significant pathomorphological changes in the kidneys were registered in 89% of cases of sudden death, and in individuals died in inpatient hospitals in Gomel [8]. The above state was not diagnosed during their life time in most cases.

The clinical presentation of the radiation-induced renal pathology has its own specific features. The disease is seldom accompanied with a nephrotic syndrome, but is more quicker and severe in character. It is characterised by a frequent and early development of arterial hypertension becoming a malignant one. Due to this, already after a couple of years chronic renal failure may occur with the development of hyperazotemia, cerebral and cardiac complications.

Serious pathological changes in the liver are also observed with ^{137}Cs incorporation. It is characterised by the development of toxic dystrophy with prevailing destruction of the cellular protein and metabolism transformation resulting in formation of fat-like substances, fatty hepatosis and cirrhosis. In addition, disturbances occur in all phases of metabolism.

The liver is involved in all vitally important processes of the human body, and is closely connected with vital organs and systems. In particular, direct concurrent effects of radionuclides on liver cells and immune system should be examined. Damage to the latter may be manifested by the disruption of protective and integrative functions of the organism directly affecting the liver.

In the protective function analysis schedule, it should be noted that a reduction in phagocytic activity of neutrophilic leukocytes of peripheral blood [7] was observed in children living in the area with high level of ^{137}Cs contamination, testifying that the disruption of the protective function of the immune system facilitating the occurrence of such infectious diseases as tuberculosis and viral hepatitis occurred. An increased prevalence of chronic hepatitis C contributes to the increase in the number of hepatic failure and tumorous diseases of the liver.

In the integrative function analysis schedule, correlations between a series of metabolism indices directly associated with the liver and indices of humoral immunity in children from areas affected by the Chernobyl nuclear accident were determined. Correlations are changed depending on specific activity of ^{137}Cs in the body. It was established that in children lived in the middle of 90 - ies of the last century in the territory contaminated by radiocesium with a level of $1-5 \text{ Ci/km}^2$, unlike in children from radiation-free areas, negative correlations between IgG and most metabolic indices of the blood serum associated with the liver, including with triiodothyronine were lost. At the same time, there were positive correlations between the content of IgG and IgM and thyroid hormones [29,30].

Taking into account the ability of immunoglobulins of different types to bind thyroid hormones [31], we may say about the disruption of immune-endocrine relations under the influence of ^{137}Cs .

The removal of thyroid hormones from the metabolism chain, in particular of triiodothyronine, leads to disruption of the pituitary – thyroid gland system and overproduction of thyroid-stimulating hormone that has stimulating effects upon the thyroid gland causing increased proliferation of the follicular epithelium that contributes to neoplastic transformations. The disruption of triiodothyronine formation may also occur when the processes of thyroxine deiodination both in the thyroid gland and other organs are weakened.

There is every reason to believe that ^{137}Cs takes an active part in neoplastic processes in the thyroid gland in view of its ability to incorporate radiocesium [8,9].

Radiocesium incorporated by the thyroid gland induces in its cells the energy shortage that does not allow reparative processes to occur properly, disturbs cell differentiation and allows that cell structural components become antigens to the immune system [8,10].

The immunological reaction appears, then the thyroid gland becomes damaged by autoantibodies and immunocompetent cells resulting in the development of autoimmune thyroiditis and thyroid cancer against its background. In this connection, we think that the action of radiocesium on the thyroid gland may be regarded from the position of disruption of immune regulation of organ and tissue activities, as well as considering the nature of cellular element injury.

The correlation between the thyroid cancer rate and area radiocesium contamination density was found [32,33].

Adrenal glands incorporate radiocesium intensively [8,9], changing their hormone-producing function. In children lived in Gomel region of the Republic of Belarus in 1992-1993, the blood level of cortisol was decreasing as specific activity of ^{137}Cs in the body was increased [19]. In neonates, whose placentas contained considerable quantities of radiocesium, cortisol production was also modified [7].

The effect of incorporated ^{137}Cs leads to serious disturbances of hormonogenesis in the female organism.

In women of reproductive age lived in the area contaminated by radioactive substances, the inversion of the endocrine profile during the different phases of the menstrual cycle was observed with specific activity of ^{137}Cs in the body over 40 Bq/kg. In addition, during the first phase of the cycle there was an increase in progesterone levels and decrease in estradiol levels, during the second phase there was recorded a decrease in progesterone levels and increase in estradiol levels [6]. The revealed imbalance of the progesterone to estrogen ratio is one of the main reasons for disruption of the reproductive function in women.

In young women with ^{137}Cs concentration in the organism over 50 Bq/kg, increased blood levels of testosterone were registered. Every sixth woman among them had no ovulation [34]. In girls from areas with ^{137}Cs contamination of 15-40 Ci/km², a delay in development of internal genital organs and retarded development of secondary sexual characteristics were observed in 37% of cases, disruption of the menstrual cycle was recorded in 81% of cases. Disruption of the

gonadotropic function of the pituitary gland was found in 39% of examined girls, along with the disruption of biosynthesis of glucocorticoid hormones in 31,5% of cases [35].

Radiocesium may cause negative effects on the prenatal development of the embryo.

Radiometric measurements of human fetuses with congenital defects and their placentas with a gestation period of 15 to 25 weeks aborted due to medical indications in patient care institutions in Gomel region in 1995-1998 detected a high specific activity of ^{137}Cs in them. Furthermore, this value was higher in placentas compared with fetuses amounting to $61,50 \pm 13,50$ Bq/kg and $25,40 \pm 3,20$ Bq/kg respectively. In embryos with congenital defects of the central nervous system the level of radiocesium in placentas was even higher $85,40 \pm 32,70$ Bq/kg [36]. High specific activity of ^{137}Cs was observed in internal organs of the neonates from Gomel region died in the first few days after the birth [8,9]. The presence of radiocesium was registered in the tissue of dysplastic lungs of fetuses from mothers lived in the radiation contaminated territory [37].

Thus, the placenta limits the penetration of ^{137}Cs into embryonic structures. In addition, significant structural and functional changes occur in the placenta that are of compensatory and adaptive nature. In particular, with ^{137}Cs content of over 100 Bq/kg in the above provisional organ the number of intermediate villi increases, and the number of terminal villi decreases having considerable aggregation of cytotrophoblast cells on their surfaces [38].

With increasing concentrations of ^{137}Cs in placenta, there is an increase in the thyroid hormone and cortisol content in the mother's blood, while cortisol concentration is decreased and testosterone concentration is increased in the fetus's blood [38]. Changes of the endocrine status in the developing organism occurring with ^{137}Cs incorporation can be one of the main reasons for disorders of sexual maturation, adaptation to environmental conditions after the birth, and are the root causes of many diseases of the mature organism. After the childbirth, during breast-feeding radiocesium can be transferred from mother to child having an adverse effect on developing organs and systems of the latter.

The determination of ^{137}Cs role in human and animal teratogenesis is of great scientific and practical importance.

Among children born in 1987-1998 in areas with the level of ^{137}Cs contamination of 15 Ci/km^2 , an excess of frequency of isolated and multiple congenital defects was registered in comparison with the control area. Across Belarus, there was a rise in the number of birth defects, to a greater extent, associated with increased incidence of multiple developmental abnormalities, limb reduction defects and polydactyly, i.e. developmental defects with a major contribution of de novo dominant mutations [39,40]. Attention should be drawn to the increased number of children with congenital defects of the central nervous system, facial skull, cardiovascular system, i.e. defects belonging to multifactorial congenital anomalies [36,41,42]. These abnormalities can occur in the presence of certain genetic defects

and due to the action of provoking environmental factors [43].

Experiments on Syrian hamsters showed that ^{137}Cs can induce multifactorial congenital anomalies with its intake during pregnancy [44]. These laboratory animals unlike albino rats have a genetic predisposition to above congenital abnormalities. In embryos and newborns of albino rats under the influence of incorporated ^{137}Cs , hypoplasia of ossification anlagen of the majority of skeletal bones, dystrophic and necrobiotic changes in cells of internal organs were observed [11]. A constant increase in the ^{137}Cs content in the maternal body leads to progressive deterioration of synthetic processes in embryonic tissues, at the same time anlagen of hind limb bones forming in the late embryogenesis stage suffer more than anlagen of fore limb bones that are formed earlier. This effect is similar to that observed in vitamin B1 deficiency modeling using an antimetabolite – oxythiamine [45].

Thus, ^{137}Cs can contribute to congenital defects if there is a genetic predisposition, acting as a provoking environmental factor.

Radiocesium in considerable concentrations may have an embryotoxic effect.

The haematopoietic system is generally considered to be a marker for the effect of radiation upon the human body. In real-world conditions of the post-Chernobyl period, a significant decline in the number of erythrocytes in children from areas of strict control (15-40 Ci/km²) with considerable accumulation of ^{137}Cs in their bodies (70 Bq/kg and more) was registered [28]. It is in line with results of experiments on laboratory animals fed by oats grown 5 years after the Chernobyl accident and contained significant amounts of ^{137}Cs and ^{90}Sr radionuclides [6].

The nervous system can also be exposed to effects of incorporated radionuclides. This is because ^{137}Cs radionuclides can enter the brain. During autopsies, significant amounts of radiocesium were registered in the brain of adults and children lived in areas affected by the Chernobyl nuclear accident [8,9]. In cells of the large cerebral hemispheres of experimental animal brains with radiocesium concentration of 40-60 Bq/kg in the body, major changes in the neurotransmitter metabolism compared with a control group expressed by the increased glutamate content and reduced glycine concentration were observed, which is comparable with the effect of average lethal and supralethal external radiation doses [6]. It can be assumed that such effects may be manifested by various neurological and autonomic disturbances in humans. However, no one compared values of specific activity of ^{137}Cs in the body and the state of the central and peripheral nervous system. Research studies were mainly devoted to nervous system disorders in liquidators of the Chernobyl accident exposed to external radiation.

Ocular pathology reflects adverse effects of incorporated ^{137}Cs on highly specialized cells of the central nervous system.

After ophthalmologic examination cataract was found in children of school age continuously resided in 1996 – 1997 in Vetka district of Gomel region in the Republic of Belarus with soil ^{137}Cs contamination of 5 to 40 Ci/km². The incidence of this pathology was directly proportional to the amount of radioactive elements

in the body. In children with specific activity of ^{137}Cs above 50 Bq/kg cataract was registered in 22% of cases [7]. In most cases, it was combined with cardiovascular, hematopoietic and endocrine system disorders.

Thus, we can talk about a complex change in clinical and laboratory indices in the child's body under chronic exposure to incorporated radioactive elements in areas affected by the Chernobyl accident. Long-living radionuclides of ^{137}Cs when entered the body have a simultaneous adverse effect on its vital organs and systems, causing damage to cell structures, primarily due to the destruction of energy mechanisms accompanied by the degradation of protein structures and necrobiotic changes.

The pathological changes in the human and animal body caused by ^{137}Cs may be joined together into a **syndrome of long-living incorporated radioisotopes (SLIR)** [46]. The syndrome appears in the cases of long-term radiocesium incorporation in the organism and is characterised by the combined metabolic pathology caused by the structural and functional changes in all vital organs and systems. The quantity of radiocesium inducing SLIR may vary depending on age, sex and the functional condition of the organism.

Serious pathological changes in organs and systems are registered in children with radiocesium incorporation over 50 Bq/kg. However, metabolic discomfort in the individual organs and systems, primarily in the myocardium, is observed with an incorporation level of over 20 Bq/kg.

Even with relatively low specific activity in the body, ^{137}Cs promotes to phenotypic implementation of genetic pathological conditions which include disturbances of the electrical impulse conduction in the heart muscle and occurrence of congenital abnormalities belonging to the group of multifactorial congenital defects. Taking into account the on-going decay of ^{137}Cs , it is worth to note that radiocesium may affect the genetic apparatus of somatic and germ cells and act as a mutation inductor.

In some cases, the negative impact of ^{137}Cs can be worsened by the action of other radioactive elements, metals, chemical and bacterial agents, alcohol, nicotine and drugs.

In view of the wide-spread occurrence of ^{137}Cs and other radionuclides in the environment, a system of measures for the protection of health of the population continuously living in areas affected by the Chernobyl nuclear accident, should include, in our opinion, the following provisions:

1. Revision at the state level of existing radiation permissible limit values to tighten requirements as to radioactive agent contents in foodstuffs.
2. Strict radiological monitoring of food, water and air, thus preventing radioactive elements from entering the human body.
3. Development and introduction of medications and methods facilitating the elimination of radionuclides from the body with the help of harmless compounds (based on natural constituents) through the gastrointestinal tract.

4. Use of physical and therapeutic methods for the removal of metabolic toxic waste products from the body formed as a result of action of radionuclides.

5. Regular radiometric control of the population, identification of groups with high specific activity of radiocesium in the body and further clinical and laboratory examination of those individuals.

6. Constant monitoring of health of the child and adult population with obligatory registration of indices of vital organ functions, overall assessment of the body condition and identification of at-risk groups.

7. Regular correction of metabolism and the function of vital systems of adults and children through preventive and therapeutic medicated measures.

8. Development of diets for different groups of population chronically exposed to radioactive elements.

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