

Radioactive Cesium and the Heart:

Pathophysiological Aspects

by Professor Yuri I. Bandazhevsky, M.D.

Original study, Minsk, 2001
New Russian-to-English translation, 2013

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This book is one of a series of the author's publications on the effects of radioactive elements on the human body. The author analyzes the results of his clinical-laboratory studies on the impact of radioactive cesium [primarily ^{137}Cs] upon cardiac function. The book is intended for a wide range of readers, physicians and scientists who are interested in problems of the influence of incorporated radionuclides on the human body.

Original reviewers (2001):

Fernex, Michel- Emeritus Professor, Department of Medicine, University of Basel (Switzerland); Vassily B. Nesterenko - Doctor of Technical Sciences, professor, corresponding member of the National Academy of Sciences of Belarus, Director of the Institute "Belrad".

English translation reviewers (2012-2013):

New Russian-to-English translation was done by Valery Yarynich and Sergei Bershakov. Dr. Yuri Hiranuma provided a great deal of assistance with medical terminology and interpretation, especially in Chapter 4. General editing of the new translation was done by Steven Starr. Financial assistance, which made the translation possible, was generously provided by Physicians for Global Survival (Canada).

Preface

Dr. Bandazhevsky's groundbreaking research on the effects of radioactive cesium upon the children and people of Belarus is not well known in the United States. This is in large part because the government of Belarus chose to persecute him and suppress his work, which threatened to disrupt their plans to repopulate lands grossly contaminated with radioactive cesium. Bandazhevsky was forced to write this study while under house arrest, awaiting many years of subsequent imprisonment and torture. Government agents had already destroyed many of the archived samples, slides and materials that he and his colleagues and students had accumulated during the nine years he was Rector of the Gomel State Medical Institute of Belarus. However, Bandazhevsky had already published much of the statistical data he had obtained in 4 books: *Clinical and experimental aspects of the effects of incorporated radionuclides in the body* [Russian and English]. Gomel 1995; *Pathophysiology of incorporated radioactivity*. Gomel, 1997; *Structural and functional effects of radionuclides incorporated into the body*, Gomel, 1997. *Pathology of incorporated radioactivity*, Minsk, 1999, as well as numerous articles in the collection of scientific works of the Gomel State Medical Institute. He used much of this previously published information in conjunction with the slides that he had preserved at his residence, in order to write this study. For purposes of clarity, I have added a section, at the bottom of page 6, which provides more details on the methodology used by Dr. Bandazhevsky to obtain Whole Body Counts and the specific activity of ^{137}Cs (cesium-137). This section on methodology is taken from "Chronic Cs-137 Incorporation in Children's Organs," published in *Swiss Med Wkly* 2003; 133:488-490. Dr. Bandazhevsky was the author, but note that he was in prison at the time, and the 2003 study was compiled by his European colleagues using data that they had obtained from Dr. Bandazhevsky during their visits to the Gomel State Medical Institute during the period 1997-1999. Dr. Bandazhevsky has recently confirmed to me that that the methodology described in the 2003 study did in fact describe the methodology used during his nine year research recorded in this study.

Steven Starr, March, 2013

Introduction

CARDIOVASCULAR PATHOLGY AS A RESULT OF ENVIRONMENTAL FACTORS

The cardiovascular system plays a leading role in the body and is extremely sensitive to the effects of various environmental factors. Its great capacity to adapt allows it to continue to function even under extremely adverse conditions. In such cases, complex pathological processes are formed that affect structures throughout the body. It is often difficult to identify all such pathways, thus the root cause of many pathologies cannot be defined. In such circumstances, therapeutic measures are mainly related to easing the course of disease, rather than with its complete elimination. The multi-factorial nature of the origin of many heart diseases is exposed without a doubt. However, treating only symptoms often interferes with the identification of the primary cause of disease. Thus the appointed treatment is not etiopathogenic, and it acts only on some links or aspects of pathogenesis.

The pathophysiology of disorders of cardiac activity can be based upon the establishment of general mechanisms of pathological processes that are formed as a result of the disruption of the integrative systems, i.e. the nervous and endocrine systems. The nervism concept [Editor's note: the nervism hypothesis holds that all functions of the body are controlled by the nervous system] provides the basis for the idea that a variety of environmental factors contribute to a given force of impact, which causes a stressful situation that leads to disruption of the cardiovascular activity. The impact of a combination of many factors can lead to similar or almost similar effects: cardiac arrhythmia, spasm of the arterioles with the development of arterial hypertension, disruption of the systemic blood circulation, ischemia or hypoxia of cells and tissues.

The basic principle of prevention of cardiac complications centers upon improving the adaptive response of the cardiovascular system, and other systems, to adverse conditions. In this case, the adaptive capacities of each person are unique to that individual, and they depend upon many factors. These characteristics are not unlimited, and very often cannot prevent death. Merely treating symptoms, however, does not lead to successful cardiology. Without knowledge of the specificity of the damaging agent, it is impossible to prevent cardiovascular diseases. Effective prevention requires the elimination of the impact of the damaging factor. For this it is necessary to at least have information about the etiopathogenesis of widespread diseases of the heart and blood vessels. Alas, modern medicine does not have all the answers.

And despite the rapid development of drug industry and cardiac surgery, death from cardiovascular disease in many countries continues to grow steadily from year to year. However, there are examples of another kind. In particular, in Sweden the prevalence of cardiovascular disease, as well as cancer, is significantly lower than in other countries. [7, 18, 37]. Why is that? One primary reason is due to the environment which surrounds the Swedish population. In this case, all possible measures have been taken to protect the population from the effects of man-made radionuclides.

Among such radioactive agents that are in human environment, the long-lived elements which are most widespread are ^{137}Cs (cesium-137), ^{90}Sr (strontium-90), ^{239}Pu (plutonium-239), and ^{241}Am (americium-241). This is due both to the testing of nuclear weapons and catastrophic

accidents which have occurred at nuclear power plants, the largest [Editor's note: as of 2001, the time of the writing of this article] being the accident at Chernobyl Nuclear Power Plant in 1986 [33]. In this regard, we should note the exposure of the population of Europe and the former Soviet Union to these radionuclides, and to a greater extent with ^{137}Cs , for nearly four decades, as evidenced by relevant literature [26]. Exposure to these agents occurs not only externally, but also internally, as these radionuclides enter into the human body and its individual organs (and as such become more dangerous than via external exposure).

The natural question is: how does this affect people's health? The official statistics of the [Belarussian] Ministry of Health provide evidence of the general deterioration of the health of the populace. Attention is immediately drawn to the steady increase in the rates of cardiovascular disease and cancer, which are the main cause of death in *young people* [18, 37]. However, the influence of radionuclides, which are incorporated into the body, are not examined in the official data.

On one hand, the lack of such consideration is due to the unwillingness or inability, for any reason, to implement such an examination. On the other hand, this is the result of the lack of an appropriate methodical approach to such considerations. Perhaps both factors have caused this situation. There also are publications in which authors argue that incorporated radionuclides, in particular ^{137}Cs , are harmless to the human body [26].

Most studies in the area of radiobiology and radiation medicine are devoted to the effects of external radiation upon humans and animals. We have noted this in previous publications [5, 6]. At the same time, there are no scientific papers analyzing the state of the human body and its individual systems at different ages for different degrees of incorporation of radionuclides.

Long-term (often lifelong) studies of human health in conditions of continuous incorporation of radionuclides, numerous experiments on laboratory animals, the pathomorphological study of autopsy material from persons living in territories contaminated by these agents; all of these observations have allowed us to develop a number of methodological approaches that are applicable to the problem:

- (1) Assessment of medical-biological effects, taking into account the amount of ^{137}Cs , incorporated into the body.
- (2) Study and modeling of the clinical pathological process induced by ^{137}Cs , in experiments upon laboratory animals (a clinical and experimental approach).
- (3) Simultaneous study of structural, functional and metabolic changes, evolving throughout the body, in some organs and organ systems.
- (4) Assessment of the severity, degree and nature of pathological conditions, identified from the disorders of the integrative processes in the body; this allows the linking together of the pathological changes that occur in various organs.

Using these approaches, we can estimate the condition of the body and a number of its vitally important organs and organ systems, as a result of their incorporation of radionuclides. This is especially true for the cardiovascular system, the most striking vital system, and ^{137}Cs , which is the most widespread long-lived radionuclide in the biosphere. In this regard, we undertook clinical and laboratory tests of children of different age groups, as well as experiments on laboratory animals, in order to study the influence of incorporated ^{137}Cs on the cardiac condition and activity.

Chapter 1

CHANGES IN THE CARDIOVASCULAR SYSTEM OF CHILDREN LIVING IN TERRITORIES CONTAMINATED WITH RADIONUCLIDES

Clinical studies included the following groups:

1. Children ages 3-7 years (227 people), living in the city of Gomel (^{137}Cs soil contamination in the city of Gomel equal to 1-5 Ci/km²).
2. Children ages 6-8 years (76 people) in the city of Vetka (^{137}Cs soil contamination equal to 15-40 Ci/km²).
3. Children ages 7-16 years (55 people) in the village of Svetilovichi (^{137}Cs soil contamination equal to 15-40 Ci/km²).
4. Children ages 3-7 years (104 people) in the city of Grodno (^{137}Cs soil contamination less than 1 Ci/km²).
5. Children ages 10-15 years (50 people) in the city of Minsk (^{137}Cs soil contamination less than 1 Ci/km²).
6. Children ages 3-7 years (118 people) in the city of Zhlobin (^{137}Cs contamination less than 1 Ci/km²).
7. Children from the ages of 14 days to 14 months (155 people) and their mothers, continuously residing in the city of Gomel and in settlements of the Gomel region, and receiving treatment in the Gomel Regional Children Clinical Hospital.
8. Children ages 8-15 years (211 people) with chronic disorders of the gastrointestinal tract, constantly residing in territories with levels of ^{137}Cs soil contamination from 1 to 15 Ci/km² and treated in the Gomel Regional Children Clinical Hospital.
9. Students of the Gomel Medical Institute, ages 18-20 years (197 people).

The state of the cardiovascular system of all the children of these groups was assessed using the 12-lead standard electrocardiographic (ECG) method. In some cases, there was analysis of blood chemistry including metabolic indicators and enzymes. The ^{137}Cs concentration in children was determined using health-radiological monitoring (HRM) via a Whole Body Counter.¹ The results of the studies were subjected to statistical analysis. These studies showed a high frequency of ECG changes in all groups, depending on the whole body ^{137}Cs concentration in children, which tended to correspond to the level of the ^{137}Cs contamination in the area where they lived (Table 1).

[Editor's note: The children in Grodno averaged 29.74±0.67 Bq per kilogram of body weight, despite having soil contamination of less than 1 Ci/km² of ^{137}Cs . This is probably an indication of how widespread the contamination of foodstuffs became within Belarus.]

¹ [Editor's note: A Whole Body Counter is a commonly used device that permits a rapid, non-invasive measurement of the gamma radiation being emitted from within a radiologically contaminated person. In this study, the gamma radiation was counted in units of Becquerels per kilogram (Bq/kg) of body weight, where one Becquerel equals one atomic disintegration per second. **Whole Body Counts** (WBCs) were done only on living patients, not on autopsied patients. WBCs were performed on the experimental group of rats before they were euthanized and dissected, in order to examine their internal levels of radiation, see Figs 9 and 10. The instruments used to perform the Whole Body Counts were monitored by the Belrad Institute of Belarus, and are described in the Methodology section at the bottom of page 6. (The Belrad Institute did not participate in the research itself.)]

Table 1
Frequency of ECG changes in children of different groups in relation to their internal ^{137}Cs concentration

[Editor's note, as measured by Whole Body Counts of gamma radiation, and expressed in Becquerels per kilogram of total body weight.]

Observed group	Whole body ^{137}Cs (Bq/kg)	Frequency of ECG changes, %
1. Gomel [$^{137}\text{Cs} = 1\text{-}5 \text{ Ci/km}^2$]; Children ages 3-7 years (n=227)	30.32±0.66	72.3%
2. Vetka [$^{137}\text{Cs} = 15\text{-}40 \text{ Ci/km}^2$]; Children ages 6-8 years (n=76)	82.50±7.32	86.8%
3. Svetilovichi [$^{137}\text{Cs} = 15\text{-}40 \text{ Ci/km}^2$]; Children ages 7-16 years (n=55)	91.20±7.68	94.4%
4. Grodno [$^{137}\text{Cs} < 1 \text{ Ci/km}^2$]; Children ages 3-7 years (n=104)	29.74±0.67	66.3%
5. Minsk [$^{137}\text{Cs} < 1 \text{ Ci/km}^2$] total Minsk-group 1 (n=16) Minsk -group 2 (n=34)	14.00±1.46 0 20.50±0.75	64.0% 18.8% 85.0%
6. Zhlobin [$^{137}\text{Cs} < 1 \text{ Ci/km}^2$]; Children age 3-7 years (n=118)	not determined	55.9%
7. Children, ages 14 days -14 months; (n=155 pairs) their mothers	34.93±3.30 27.10±2.80	88.1% 80.3%
8. Children with disorders of the digestive and gastrointestinal tract (n=211)	19.70±0.90	84.9%
9. Students of the Gomel Medical Institute, ages 18-20 years (n=197)	25.98±2.04	48.7%

Methods

Methods used at Gomel Institute of Pathology

Caesium is both a gamma and a beta emitter. Since beta rays are more radiotoxic for the genome and cell structures than gamma rays, the latter are used to measure the specific activity of caesium in humans. For either whole body measurement or during autopsies we used different equipment to measure the level of Cs-137 accumulated in various organs.

The accuracy of measurements by the mobile teams of the Belrad Institute, the independent radioprotection agency, is guaranteed by compulsory annual state inspection of the equipment. Furthermore, as part of a joint German-Belarusian project it was possible by intercalibrations to verify the different items of equipment (the

7 whole-BC "Screener-3M" of Ukrainian origin from the Belrad Institute, and the 2 mobile whole-BC laboratories of Juelich Research Centre ["Canberra Fastscan Whole BC", Germany]). While initially the error limit was as high as 11%, later it did not exceed 7%. Below 5 Bq/kg body-weight measurements become less accurate.

For laboratory measurement of specific activity in samples, such as organs examined during autopsy, Belrad provided Gomel State Medical Institute with automated Rug-92M gamma radiometers. The duration of measurement is one minute for samples >100 Bq/kg and 10 minutes for samples of 50–100 Bq/kg. Below 49 Bq/kg precision decreases. Samples were also doubled-checked in France to validate the findings.

In areas with the ^{137}Cs soil contamination over 15 Ci/km^2 , the whole body ^{137}Cs concentration of more than 80 Bq/kg led to the occurrence of electrophysiological changes in the heart in more than 80% of the children.

By their nature, the pathological processes can be divided into the following two categories: the arrhythmia and the ischemic injuries resulting from disruption in the redox-sensitive signaling pathways. The most commonly observed arrhythmias were related to the conduction disturbance of the electrical impulses in the myocardium (bundle-branch blocks, atrioventricular blockades). In most groups, it was predominantly arrhythmias that were observed (Table 2).

Table 2
Nature of ECG changes in children of the examined groups

The group name	Arrhythmias	Ischemic injuries	Ischemic injuries and arrhythmias	Normal ECG
	(n=sample) %	(n=sample) %	(n=sample) %	(n=sample) %
1. Gomel	(n=113) 49.76%	(n=51) 22.47%	-	(n=63) 27.75%
2. Vetka	(n=46) 60.53%	(n=20) 26.32%	-	(n=10) 13.16%
3.Svetilovichi	(n=32) 58.18%	(n=12) 21.82%	(n=8) 14.55%	(n=3) 5.46%
4. Grodno	(n=41) 39.42%	(n=28) 26.92%	-	(n=35) 33.65%
5. Minsk	(n=23) 46.00%	(n=5) 10.00%	(n=4) 8.00%	(n=18) 36.00%
6. Zhlobin	(n=48) 40.68%	(n=18) 15.25%	-	(n=52) 44.67%
7. Children	(n=7) 4.50%	(n=81) 52.26%	(n=64) 41.30%	(n=3) 1.94%
Mothers	(n=18) 29.02%	(n=7) 11.29%	(n=31) 50.00%	(n=6) 9.68%
8. Children with disorders of the GT	(n=149) 70.62%	(n=30) 14.22%	-	(n=32) 15.68%
9. Students	(n=88) 40.36%	(n=8) 8.33%	-	(n=111) 51.3%

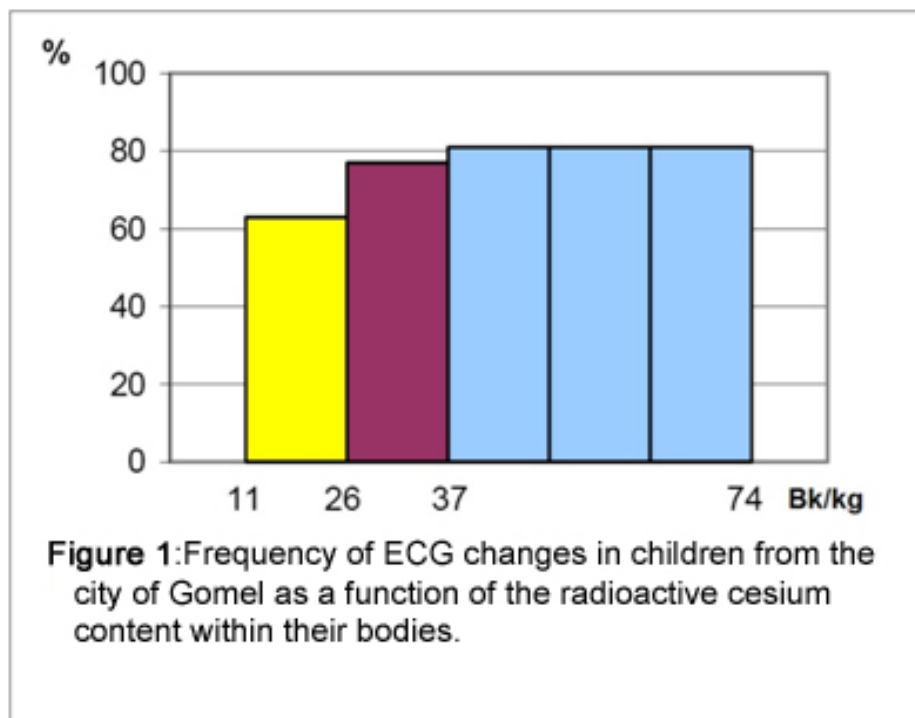
Depending on the range of the whole body ^{137}Cs incorporation in children, each group was divided into five subgroups (Table 3).

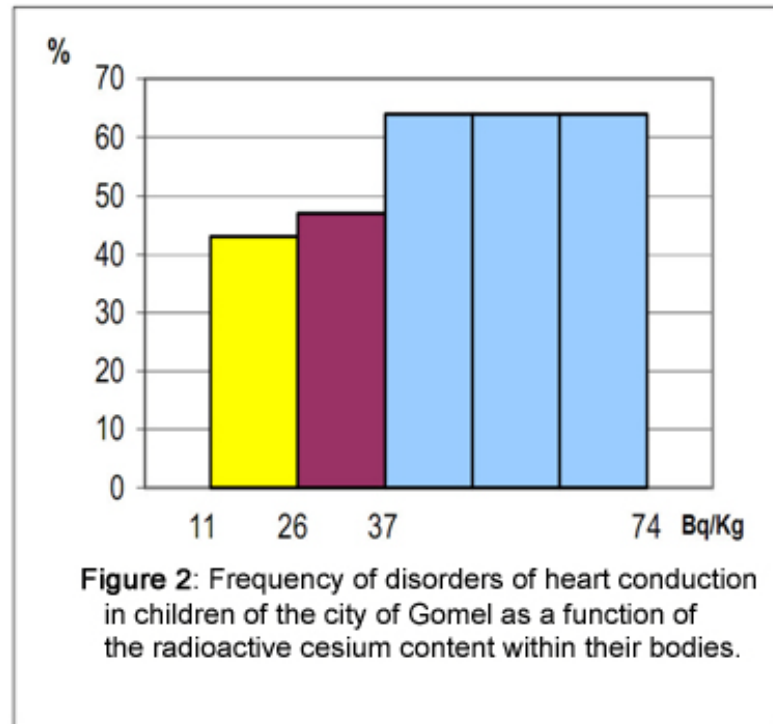
Table 3
Frequency of ECG changes, depending on the level of ^{137}Cs incorporation

Group	^{137}Cs Concentration in children, Bq/kg [Editor's note: as measured using Whole Body Counts]				
	0 Bq/kg	11-25.9 Bq/kg	26-36.9 Bq/kg	37-74 Bq/kg	>74 Bq/kg
1. Gomel	-	62.8%	77.6%	80.7%	-
2. Vetka	-	-	82.4%	92.3%	87.9%
3. Svetilovichi	-	-	100%	92.3%	96.0%
4. Grodno	-	62.5%	65.5%	78.6%	-
5. Minsk	18.8%	83.8%	100%	-	-

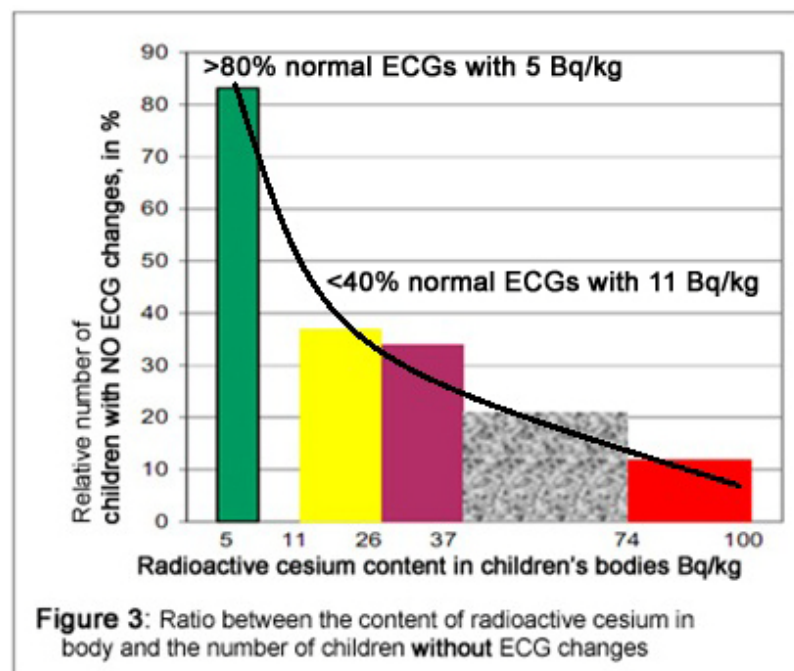
The testing revealed the ECG changes were directly proportional to the amount of incorporated ^{137}Cs .

This correlation is most clearly seen in the first group (from the city of Gomel), mainly caused by the abnormalities of intraventricular conduction (Figures 1 and 2).





It should be noted the radionuclide ^{137}Cs was generally absent from 16 of the 50 surveyed children (32%) in the city of Minsk, whereas in the other groups the internal concentration of ^{137}Cs did not drop below 11 Bq/kg. ECG changes occurred in 19% of the cases in children who had no internal ^{137}Cs accumulation, and these changes were represented by the right bundle branch block. If we take into account only the parameters of ^{137}Cs incorporation and the frequency of ECG abnormalities, we can establish that children with the smallest amount of incorporated ^{137}Cs exhibit the smallest percentage of ECG changes. [Editor' note: *As ^{137}Cs incorporation increases, the percentage of children that exhibit normal ECGs rapidly decreases at a logarithmic rate.* There are >80% normal ECGs in children that average 5 Bq/kg of ^{137}Cs in total body weight, versus <40% normal ECGs in children that average 11 Bq/kg of ^{137}Cs in total body weight.] (Fig. 3).



Children in the Svetilovichi village, with an average accumulation of ^{137}Cs at 100 Bq/kg of body weight, showed significant clinical signs of heart failure: heart pain, faint heart sounds, and a systolic murmur on auscultation. Attention is drawn to the presence of both arrhythmias and ischemic injuries in the same ECG. It is noted that the level of ^{137}Cs incorporation in this case was significantly higher than those with the presence of either arrhythmia or ischemic injuries alone – 165.10 ± 8.47 Bq/kg (for children with arrhythmias - 84.61 ± 9.29 Bq/kg, $p < 0.05$).

Accumulation of ^{137}Cs is recorded also in young children and their mothers (Table 1). ECG changes were detected in 98.1 % of the children and 90.3 % of the mothers, and these consisted mainly of metabolic disorders of the myocardium and arrhythmias. In children, metabolic myocardial disorders accounted for 88.4% (47.1% in isolation, and 41.3 % in combination with disorders of intraventricular conduction). Conduction disorders, presented mainly as incomplete right bundle branch blocks, were observed in 45.8 % of the children. The normal ECG was recorded in only 3 children (1.9 %).

ECG changes in mothers also included metabolic abnormalities and arrhythmias (automaticity and conduction disturbances). In 83.2 % of the tested children hypocalcemia was observed; 39.5 % of the children showed an increase in the activity of alanine aminotransferase and 74.6% showed an increase in aspartate aminotransferase, indicating disorders of the metabolic processes in the liver and the heart.

Studies have shown a high sensitivity of a mother and a fetus to the effects of ^{137}Cs . In this case relatively small amounts of ^{137}Cs caused damage to the cardiovascular system of both the mother and the fetus, interfering with its normal development in the fetus.

Administration of "Belosorb-2" enteric adsorbent for 5-6 days in these children led to a reduction of ^{137}Cs up to 25.43 ± 2.54 Bq/kg (baseline - 34.93 ± 3.30 Bq/kg) and a decrease in the number of cases with metabolic disturbances in the myocardium.

The study of ECGs of children with chronic pathology of the gastrointestinal tract, living in conditions of constant ^{137}Cs incorporation in the body, showed a high frequency of cardiac disorders at 84.9 %.

[Editor's note: It was through the routine ingestion of foodstuffs contaminated with "low-dose" ^{137}Cs that the "constant incorporation" took place – and still takes place. Almost all foodstuffs that are harvested in ecosystems contaminated with ^{137}Cs will contain ^{137}Cs . Dairy products and meats will contain higher quantities of water-soluble ^{137}Cs , which bioaccumulates and biomagnifies as it moves up trophic levels in the food chains. Also, any foodstuffs that are naturally high in potassium, such as mushrooms and berries, will also tend to bioaccumulate high concentrations of ^{137}Cs .]

The most frequently reported were metabolic disorders in the myocardium (54.5 %), impaired automaticity of sinus node (36.0 %), and conduction disturbances in the form of the incomplete right bundle branch block (32.7 %). It should be noted that in children with the level of ^{137}Cs accumulation of more than 20 Bq/kg, disorders of automaticity occurred in 73.3 % of the cases, while they were seen in 21.0 % of the children with the lower accumulation level. Metabolic disorders were found in 66.6 % of the higher and 42.1 % of the lower ^{137}Cs accumulation levels. Normal ECGs were recorded in 6.7 % of the higher and 19.3 % of the lower ^{137}Cs accumulation levels. At the same time, hyperactivity of the sympathetic nervous system was noted in 83.8 % of the children with the level of accumulation higher than 20 Bq/kg (per kg of

body weight), while it appeared in 50.8 % of the children with the accumulation level less than 20 Bq/kg.

Thus, in children with chronic pathology of the gastrointestinal tract who are living in areas contaminated with radionuclides, the adaptive and compensatory mechanisms of the autonomic nervous system regulation are under stress. This is reflected in the predominance of hyperactivity of the sympathetic nervous system, with direct dependence on the amount of ^{137}Cs in the body. There is an increased cortisol level and a reduced free thyroxine level in blood serum (Table 4). Clinically, symptoms of autonomic nervous system dysfunction are manifested as neurocirculatory dystonia and biliary dyskinesia, the frequency of which also depend on the amount of ^{137}Cs in the body. These symptoms appeared in 93.3 % of the children with ^{137}Cs incorporation of more than 20 Bq/kg, and in 68.8 % of the children with ^{137}Cs incorporation of less than 20 Bq/kg.

Table 4
Cortisol and Thyroxine serum levels
in children with different sympathetic nervous system reactivity

Variant of the sympathetic nervous system reactivity	Normal n=48	Hyperactive n=47	Hypoactive n=28
Cortisol, nmol/l	622.49 \pm 42.10	771.19 \pm 50.67*	706.16 \pm 89.29
Free thyroxine, mmol/l	13.40 \pm 0.49	12.21 \pm 0.29*	12.90 \pm 0.31

* - $p < 0.05$

In young people ages 18-20 years, living in the city of Gomel, with an average whole body ^{137}Cs concentration of 24.5 Bq/kg, changes in ECG occurred in 48.7 % of the cases. They were predominantly arrhythmias, primarily intra-cardiac conduction disturbances, constituting 56.3% of all ECG changes.

It is worth noting that the early repolarization syndrome of the left ventricle was found in 7 students (7.3 %). This condition can contribute to ventricular fibrillation without previous tachyarrhythmia and cause sudden death. These young people had increased levels of thyroxin - 13.44 ± 0.01 mmol/l (control – 11.35 ± 0.26 mmol/l, $p < 0.05$). In this regard, it is possible that thyroxin participated in the disorder of the cardiomyocyte function, through effects on the mitochondrial complex and energy system that regulates the ion balance. The concentrations of thyroid stimulating hormone, triiodothyronine, thyroxine and cortisol in the blood of persons with symptoms of arrhythmia on the ECGs, were not significantly different from the control group.

Studies have shown that a high frequency of ECG changes (over 50 % of the total surveyed) was seen in both groups of children, living in the areas contaminated with ^{137}Cs and in the clean areas. Levels of ^{137}Cs incorporation in children are correlated with the contamination levels of their areas of residence.

However, in control areas (Grodno and Minsk), there also are cases of significant whole body ^{137}Cs concentrations in children [Editor's note: this could reflect the widespread distribution of

contaminated foodstuffs]. Regardless of the area of residence, contaminated or clean, the frequency of occurrence of ECG changes at different whole body ^{137}Cs concentrations revealed a clear linear dependence of the ECG changes on the level of the whole body ^{137}Cs concentration. Even a low concentration of ^{137}Cs - over 10 Bq/kg - can cause a high frequency of the above disorders, while its absence almost precludes their occurrence.

Particular attention should be paid to the state of the cardiovascular system in children with ^{137}Cs incorporation above 150 Bq/kg. The combination of metabolic disorders in the myocardium of a growing child with an impaired electrical impulse conduction is a result of the long-term chronic effects of ^{137}Cs , suggestive of an ominous prognosis. Assuming that the myocardium incorporates ^{137}Cs more intensively than other organs and systems [8], one can imagine what the ^{137}Cs concentration is in the myocardial tissues (in the rats, the concentration of ^{137}Cs in the heart is 10 or more times higher than in skeletal muscles). It is not surprising that after exhibiting full (100%) pathological signs on ECG at the ^{137}Cs concentration of 100 Bq/kg and above, the clinical signs and symptoms of the heart disease arise.

Studies have also shown a link between the frequency of the ECG changes and the amount of ^{137}Cs incorporated into children of different ages. When you consider the linear relationship between the ECG changes and the ^{137}Cs concentration, the long half-life of ^{137}Cs and therefore its prolonged existence as a chemical element, and its accumulation in the body having small radiation effects, we can assume it is not so much the radiation that affects the cardiac muscle but mostly its chemical toxic effects. In addition, interrelated disorders of the energy system and ion transport and metabolic disorders take place, leading to dystrophic and necrobiotic processes. This hypothesis allows us to consider the problem of impact of long-lived radionuclides on the human body from other perspectives. This is very important in terms of understanding the mechanisms of their deleterious effects upon the vital systems and organs, in particular the cardiovascular system. The results obtained suggest that, in the prolonged chronic exposure to ^{137}Cs , the cardiovascular system of a growing child is the most vulnerable. This should naturally determine the development of appropriate medical treatment as well as preventive and rehabilitative measures.

Chapter 2

STRUCTURAL CHANGES IN THE MYOCARDIUM IN GOMEL REGION RESIDENTS ACCORDING TO AUTOPSIES

In order to prove the damaging effects of ^{137}Cs on the heart, a study of the myocardial tissues taken from children and adults (a total of 408 cases) was conducted on the residents of the Gomel region who died from various causes. During the study, the ^{137}Cs concentration in the autopsied tissues were measured. In 99% of the 408 cases, microscopic examination revealed the presence of diffuse injury to the myocardial cells, in the form of contractures or overcontractions of muscle fibers, primary cluster disintegration of myofibrils, degenerative processes with varying degrees of severity, and necrosis. There is no doubt that regardless of the underlying disease, changes in the myocardium caused by the exposure to ^{137}Cs that had been incorporated into it (with concentrations from 20 to 500 Bq/kg), was one of the main causes of death. This is especially true for a child's body. Here is one of the examples:

Baby L., a 7-month-old living in the Kormjansk district, was taken to a hospital with signs of acute respiratory viral infection. With time, cardiopulmonary insufficiency and sepsis developed. Death from septicemia occurred on the eighth day after admission to the hospital. In the internal organs, including the heart, significant accumulations of ^{137}Cs were found (Table 5).

Damage to cardiomyocytes was shown through degenerative changes in the form of hyaline droplets and focal hydropic dystrophy. Muscle fibers were separated from each other and had vague outlines and weakly expressed striation. A focal lysis of myofibrils with their fragmentation had occurred. The nuclei of cardiomyocytes showed hyperchromia and polymorphism and also karyopyknosis and karyolysis in some areas. Myocardial vessels were sharply plethoric, dilated and engorged with blood. There had also been plasmorrhagia and proliferation of vascular endothelium.

Table 5.
Amount of ^{137}Cs in the internal organs of the child L

Organs	^{137}Cs (Bq/kg)
Lungs	450
Heart	2410
Stomach	250
Small intestine	1250
Large intestine	1200
Kidney	710
Pancreas	240
Thymus	80
Thyroid gland	470
Spleen	130
Brain	650
Liver	670
Adrenal glands	2500

The stroma showed intermuscular edema and perivascular infiltration with lymphocytes and plasma cells (Fig. 4).

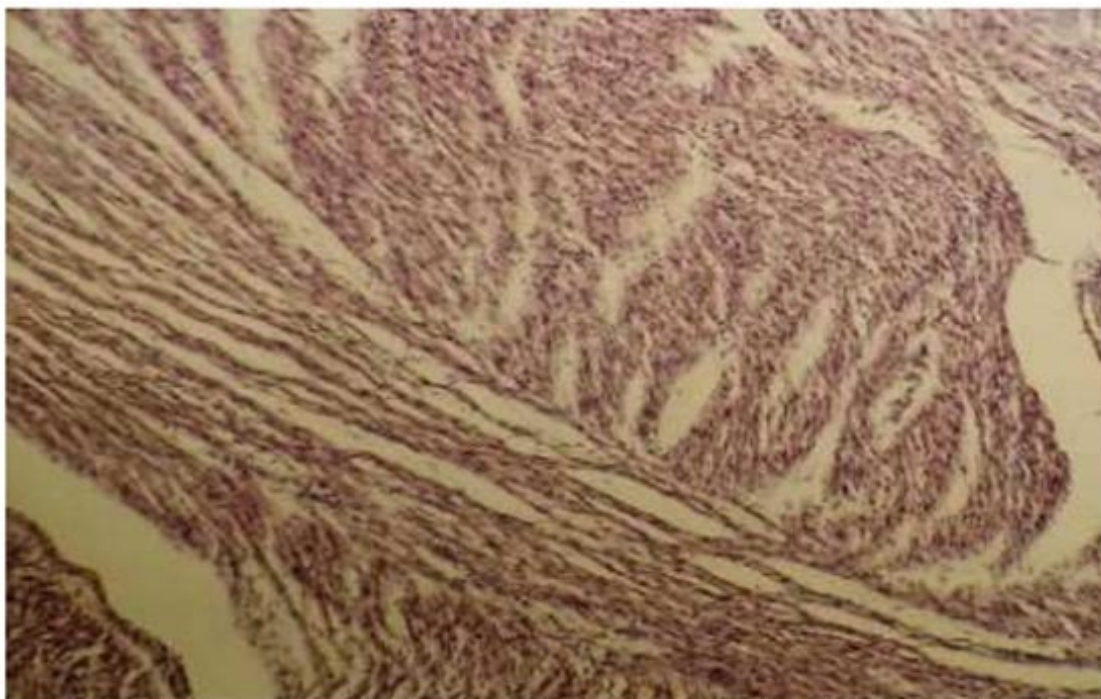
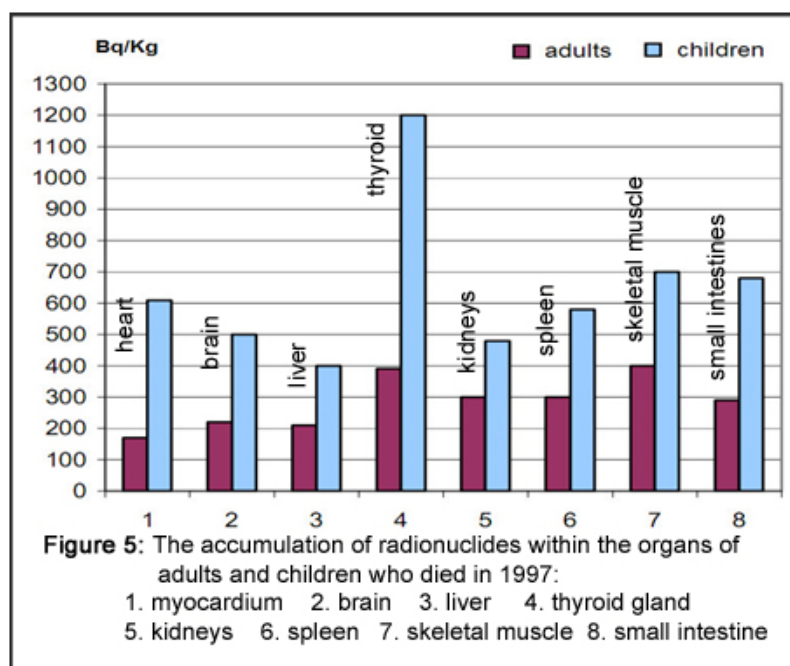


Figure 4. Histological section of the myocardium of a 7 month old child. ^{137}Cs concentration in the heart was 2,410 Bq/kg. Marked intermuscular edema. Muscle fibers separated from each other, with vague outlines and weakly expressed striation. Focal lysis of myofibrils with fragmentation. Polymorphism and hyperchromia of cardiomyocyte nuclei, with some areas of karyopyknosis and karyolysis. Stained with hematoxylin and eosin. Magnification x 250.

It should be emphasized that the ^{137}Cs accumulates much more intensively in the internal organs of children than in adults (Fig. 5), affecting their formation and proper functioning at the different stages of the development.



Chapter 3

STRUCTURAL AND METABOLIC CHANGES IN THE BODIES OF LABORATORY ANIMALS INTERNALLY EXPOSED TO ^{137}Cs

In an experiment on laboratory animals (albino rats), the structural and metabolic changes were studied in the heart, liver, kidneys, and lungs, which developed during internal exposure to ^{137}Cs . This radionuclide entered the rats through ingestion, either in aqueous solutions administered orally or in oats fed to them.

A total of 121 male albino rats and Wistar rats, weighing 180-200 grams, were kept in a vivarium. The first series of experiments included keeping animals in the experimental group on the diet of oats with the ^{137}Cs concentration of 400 Bq/kg (the daily intake of oats for each animal in both groups was 35 grams) for 45 days. Animals in the control group during this period were given oats with the ^{137}Cs concentration of 40 Bq/kg.

39 animals from the experimental group and 29 from the control group were sacrificed after they inhaled ether anesthesia on the 11th day of the experiment; 10 rats from the experimental group and 10 from the control group were also sacrificed on the 45th day. Before being euthanized, all the experimental and control animals were subjected to measurement of the whole body ^{137}Cs concentration, with the gamma radiometer, RUG-2 (manufactured by the Belarusian Institute of Radiation Security, "BELRAD").

The second series of experiments consisted of daily oral administration of 45 Bq of ^{137}Cs in aqueous solution (5ml) for 6 days for 19 animals of the experimental group. 20 animals in the control group in the same period received daily oral administration of physiological saline (5 ml). The amounts of the whole body ^{137}Cs accumulation in the animals were regularly measured throughout the experiment using the radiometer RUG-2.

On the 4th, 6th and 8th days after the start of the experiment, some of the animals of the experimental and control groups were sacrificed.

A third series of experiments consisted of daily oral administration of 180 Bq of ^{137}Cs in aqueous solution (5 ml) for 6 days for 12 males of the experimental group. 12 animals of the control group in the same period received daily oral administration of 5ml of physiological saline solution. The whole body accumulation of ^{137}Cs in the animals was checked during the entire experiment using the radiometer RUG-2. On the 8th day after the start of the experiment, the animals of the experimental and control groups were sacrificed.

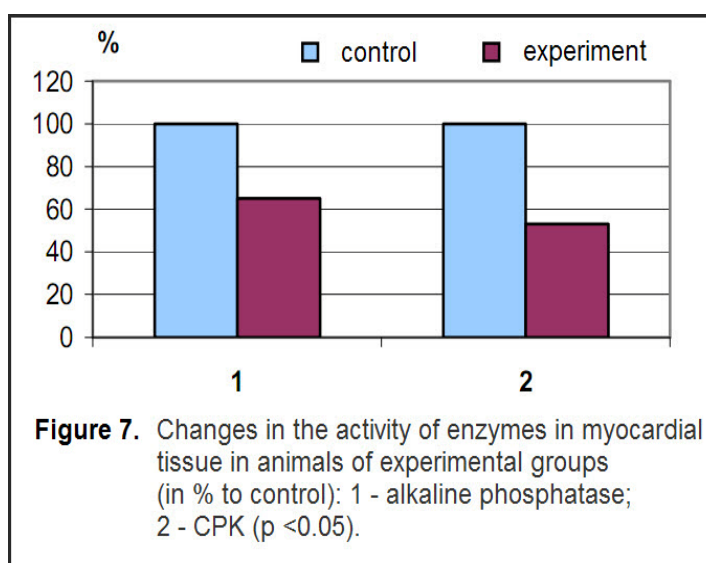
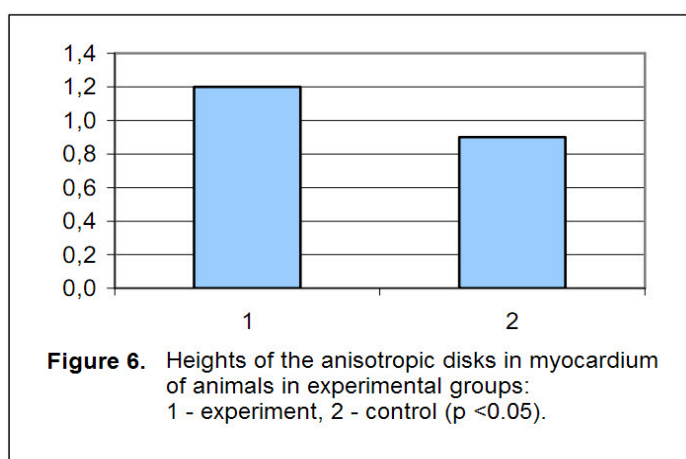
After all the experimental groups were sacrificed, the macroscopic study of internal organs was performed. Liver, kidneys, myocardium and lungs were sliced into pieces with thickness of 0.5-1.0 cm, fixed in 10% formalin solution and embedded in paraffin. The results were histological preparations with a thickness of 5-8 microns stained with hematoxylin and eosin. Histological preparations were studied using a binocular microscope. In order to determine changes of the contractile apparatus of cardiac muscle in animals of the first series on the 11th day of the experiment, a method of polarization microscopy was used with the definition of the size of A-disks through the Vidas-video morpho-optic system, manufactured by the Opton company (Germany). Muscle tissues were sampled from the hearts of 8 animals of the experimental and control groups; these tissues were then processed into a homogenate and analyzed for the activities of alkaline phosphatase, acid phosphatase, lactate dehydrogenase,

creatine phosphokinase, alanine aminotransferase, aspartate aminotransferase, and gamma-glutamyltransferase.

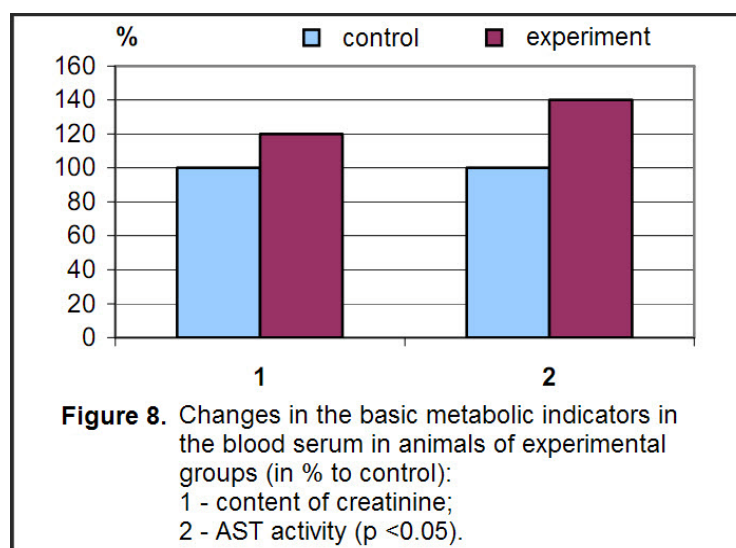
For all the animals in the series, the blood sampling was performed by separating the serum and determining the levels of total protein, albumin, urea, creatinine, aspartate aminotransferase and alanine aminotransferase with the “Synchron” analyzer from the Beckman company. The results were then subjected to statistical analysis.

The research showed that the daily intake of the ^{137}C in food by albino rats caused its progressive accumulation within their bodies. In particular, the ^{137}C s concentration on the 11th day of the experiment was 63.35 ± 3.58 Bq/kg in the experimental group, and 5.43 ± 0.87 Bq/kg ($p < 0.001$) in the control group.

Microscopic examination of the internal tissues of animals of the experimental group on the 11th day of the experiment did not reveal gross changes. However, they did register a change of the polarization properties of the cardiomyocytes, in the form of an increase in A-disks compared with the control group (Fig. 6). Reduced activities of alkaline phosphatase and creatine phosphokinase (Fig. 7) were noted in the cardiomyocytes.



In the blood serum of these animals there were increased levels of aspartate aminotransferase and creatinine (Fig. 8). The liver tissues exhibited signs of protein dystrophy and circulatory disorders.



In the kidney tissues, along with the infiltration of glomerular loops with lymphohistiocytic cells, the fragmentation and destruction of glomeruli were observed in a number of cases. Accumulation of ^{137}Cs in the amount of 101.05 ± 1.69 Bq/kg caused significant changes in the bodies of albino rats. Pathological changes noted in the kidney included the proliferation of mesangial cells, the infiltration of glomerular loops with lymphohistiocytic cells, and the fragmentation and loss of glomeruli. Granular and hyaline droplet degeneration of the epithelium of the straight and convoluted tubules was observed.

Microscopic examination of the liver tissues found granular and vacuolar degeneration of hepatocytes, and the expansion of the space of Disse (perisinusoidal space). Moderately marked impairments of circulation were seen as dilated and engorged central intralobular veins. Diffuse myocytolysis, focal lymphohistiocytic infiltrations, and engorged vessels was seen in the myocardial tissue. The serum of these animals had a significant increase in creatinine at 41.20 ± 1.60 nmol/l, as compared with controls at 33.11 ± 2.45 nmol/l ($p < 0.001$).

Daily oral administration of 45 Bq of ^{137}Cs resulted in the ^{137}Cs concentration in the rats of the experimental group on subsequent days as follows: 40.91 ± 10.62 Bq/kg (control group 2.67 ± 1.05 Bq/kg, $p < 0.005$) on the 4th day; 104.55 ± 24.73 Bq/kg (control group 12.13 ± 4.75 Bq/kg, $p < 0.001$) on the 6th day; and 150.58 ± 52.06 Bq/kg (control group 10.66 ± 4.82 Bq/kg, $p < 0.001$) on the 8th day.

Microscopic examination detected dystrophic and necrobiotic changes in the myocardium, liver and kidneys, corresponding to the changes identified in the effects of ^{137}Cs entering the bodies of the animals through ingestion of the oats. With increasing amounts of ^{137}Cs incorporated into the bodies of the rats came an increase in creatinine and the progressive reduction of the total protein content, mainly due to reduction of the alpha-1 and alpha-2 globulin fractions (Table 6).

Table 6
Values of protein fractions in laboratory animals (albino rats)
with different concentrations of ^{137}Cs in their bodies

Protein Fractions	^{137}Cs , Bq/kg		
	[Editor's note: Bq/kg as determined by Whole Body Count]		
	group №1	group №2	group №3
	40.91±10.62	104.55±24.73*	150.58±52.06*
Total protein g/l	65.56±3.74	62.98±3.26	49,08±2.01*
Albumin (%)	36.32±1.70	39.95±2.26	41.68±0.97*
α_1 - globulins (%)	13.84±1.01	12.93±1.93	10.16±0.54*
α_2 - globulins (%)	15.63±0.91	11.65±1.23	12.12±0.45*
β - globulins (%)	14.52±0.88	13.78±2.18	14.76±0.76
γ - globulins (%)	19.69±1.41	21.70±1.40	21.28±1.24
The ratio of albumin to globulin (a/g)	0.58±0.04	0.67±0.06	0.72±0.3*

* p<0.05

The daily oral administration of a 180 Bq solution of ^{137}Cs , administered for 6 days, resulted in the average ^{137}Cs concentration in the albino rats of 991.00 ± 76.00 Bq/kg (control group 6.70 ± 2.36 Bq/kg, $p < 0.01$) on the 8th day of the experiment. It should be noted that in the experimental group, 5 (41.7%) animals died on the 5th and 6th days of the experiment, with the ^{137}Cs accumulation in the bodies equaling more than 1,000 Bq/kg. In the macroscopic study, a marked hemorrhage in the internal organs was revealed. In the microscopic study of kidney tissues, damage of structural elements of the glomeruli was recorded. Majority of the damage was necrosis of the epithelium and the vascular network, resulting in their complete disappearance and the subsequent formation of a cavity. In the tubules, vacuolar and granular degeneration was detected as well as necrosis of the epithelial cells.

In the liver there was venous congestion, more pronounced in the central parts of the lobules, with protein and fat degeneration, as well as necrosis of hepatocytes. In the lungs there was a pronounced dilation and engorgement of the blood vessels, the presence of erythrocytes in the alveolar lumen, and inflammatory changes of the pleura. In the myocardium, a pronounced manifestation of interfiber and intracellular edema, with the lysis of the majority of cardiomyocytes along with their nuclei. In some cases, inflammatory infiltrates in the area of the epicardium and pericardium were detected.

Thus, the ^{137}Cs incorporation into the bodies of albino rats through the gastrointestinal tract, as an oral administration of solution and as part of the oats feed, causes structural and metabolic changes in the vital organs. The degree of expression of these changes is determined by the

amount of the incorporated ^{137}Cs , with such expressions ranging from manifestations of protein malnutrition to severe necrobiotic and degenerative changes. This demonstrates the toxic effects of ^{137}Cs on the vital organs such as the heart, liver, and kidneys.

It should be noted that the toxicity of this long-lived radionuclide affects, first of all, highly specialized cells that have no or very little proliferative capacity. In the case of the myocardium, significant changes occur in the structure of the mitochondria [9], with a corresponding decrease in the activity of creatine phosphokinase, which is a key enzyme of energy exchange, catalyzing reactions involving high-energy phosphates and creatine. Disruption of energy-producing processes in the heart and the development of intracellular hypoxia lead to a change in its contractile apparatus, namely a change in the myofibrils, as various degrees of contractures, or their disaggregation and lysis [30].

Changes in the ultrastructure of the contractile apparatus are manifested as the changes of polarization properties of muscle fibers. An increase in the ^{137}Cs concentration in the body leads to the death of cardiomyocytes. It should be noted that in the case of a ^{137}Cs accumulation in the range of 100-150 Bq/kg, lymphohistiocytic infiltrates can be seen in the myocardium as the reaction of the immune system. The accumulation of 1,000-1,500 Bq/kg of ^{137}Cs , which is 10 times more, becomes incompatible with life, as this causes the total dystrophy and loss of many of the cardiomyocytes.

Damage of cell structures under the influence of ^{137}Cs was seen in the liver and the kidneys, in addition to the myocardium. Of particular note is a degenerative process occurring in the glomerular apparatus of the kidneys. Even at a relatively low level of ^{137}Cs incorporation at 30-50 Bq/kg, a loss of cellular elements of individual glomeruli was seen, along with the formation of characteristic cavities. We could not rule out that the primary mechanism of this process is the formation of vascular lesions at the level of arterioles and capillaries. Damage to the tubular epithelium led to different types of protein degeneration and necrosis of cells.

Given that the kidneys are the main organ for the excretion of radioactive cesium from the body, it can be argued that the disruption of their excretory function leads to the accumulation of both metabolic waste products and radioactive cesium in the body. Such metabolic waste products have toxic effects on vital organs, particularly the myocardium.

Disruption of the excretion of ^{137}Cs from the body increases its concentration in the blood, and thus drives radioactive cesium to concentrate within cells such as cardiomyocytes that exhibit the highest metabolic activity as well as the structural and functional specialization. In this case, there is an impaired permeability of the cytoplasmic membrane, resulting in an increased movement of Na^+ ions and water into the cell. Here intracellular edema develops, followed by cytolysis. The consequence of this process is the disruption of cardiac activity, resulting in the death of the affected individual.

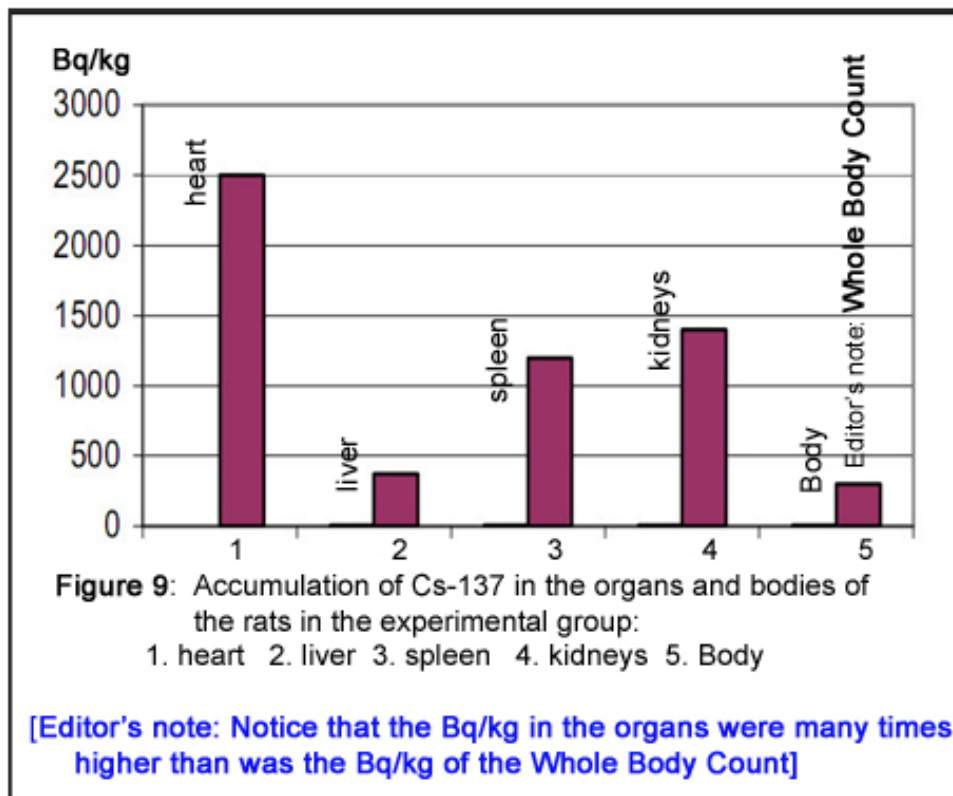
Thus, impaired excretion of radioactive cesium results in the death of the nephron structures and leads to the development of toxic cardiomyopathy, which is the leading cause of death. Morphological manifestation of this pathological process exhibits the same pattern of inflammation in the pleura and pericardium as in renal failure. ^{137}Cs has a toxic effect on liver tissues, which undoubtedly affects the state of the metabolism. These results suggest that the incorporation of small concentrations of ^{137}Cs into the body of a laboratory animal has toxic effects on cells of the myocardium, liver and kidneys, which can be a major cause of death.

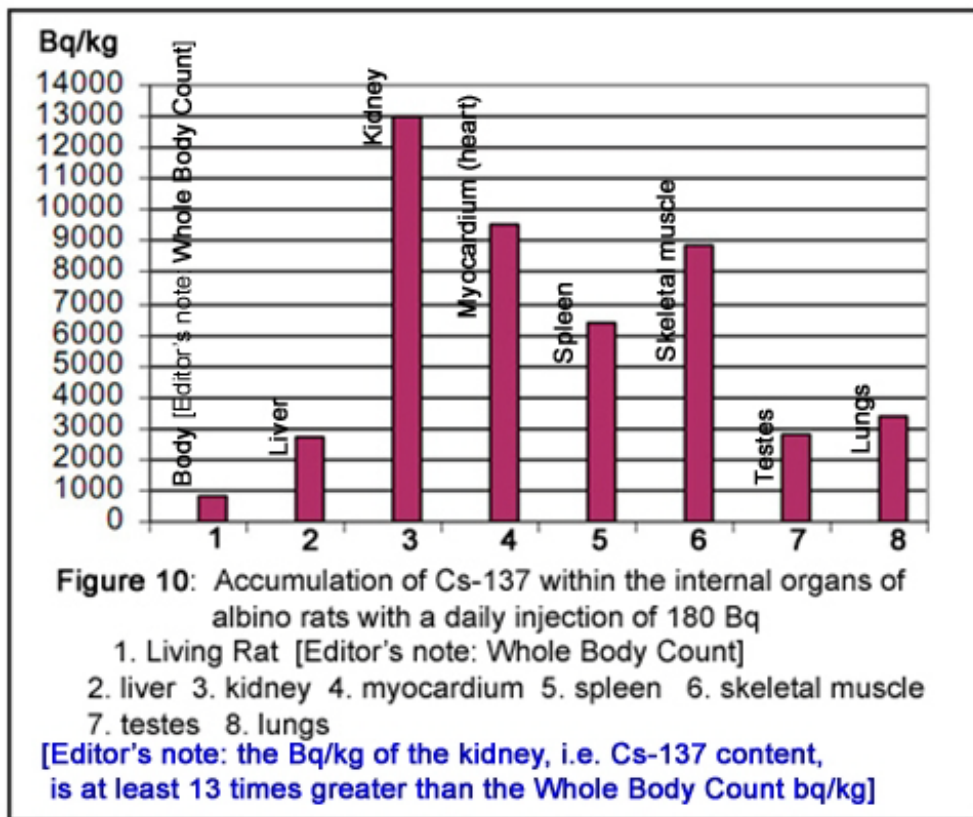
Chapter 4

PATHOPHYSIOLOGICAL CHARACTERISTICS OF EFFECTS OF RADIOACTIVE CESIUM ON THE HEART

Thus, after the analysis of the results of ECG examinations of children of different ages with different levels of the whole body ^{137}Cs incorporation, the microscopic studies of persons living in areas affected by the Chernobyl disaster, and the experiments on laboratory animals, it is possible to conclude that ^{137}Cs has an adverse effect upon the cardiovascular system. This effect is manifested through its direct impact on cell structure, as well as its indirect influence through a number of systems, particularly the nervous and endocrine systems.

The direct influence of ^{137}Cs on the heart is due to its selective accumulation within the myocardial cells, as compared with other organs and tissues (Figures 9, 10). This is due perhaps to the intense operation of the sodium-potassium pump; since ^{137}Cs is in the same atomic group as potassium, it can easily enter into the cardiomyocyte. This process involves the structures of cellular membranes, and this radionuclide actively interacts with them [15]. This is accompanied by the suppression of the activity of the important enzyme creatine phosphokinase (CPK), which is involved in the energy exchange of cells: accumulation, transport and utilization of high-energy phosphates. CPK catalyzes the reversible phosphorylation reaction, which involves the transfer of a phosphate group from ATP to creatine and from phosphocreatine to ADP [1].

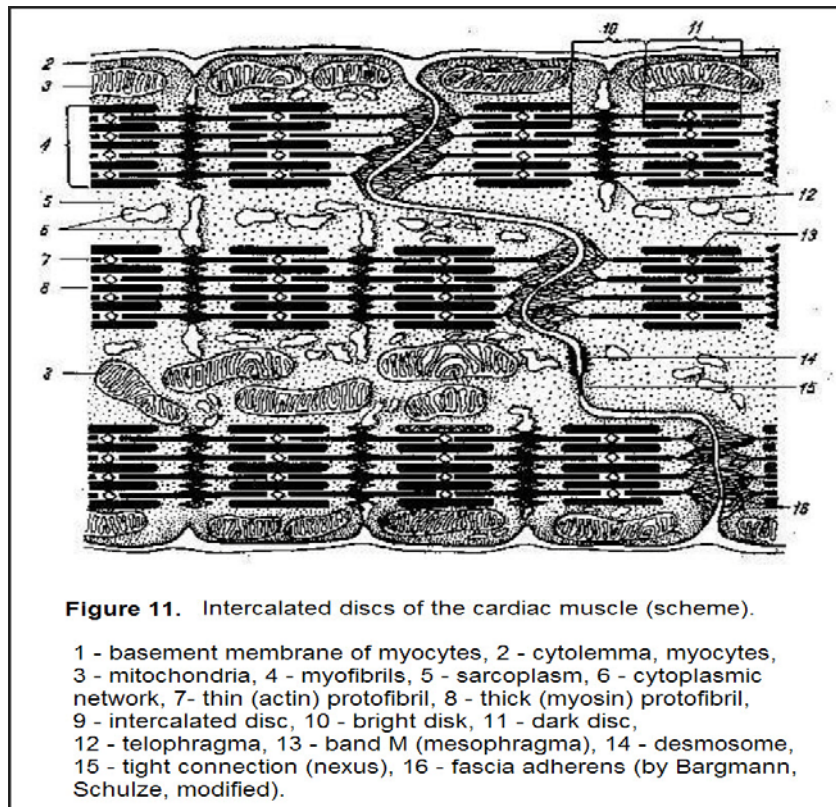




CPK is localized in different subcellular structures such as the cytoplasm, mitochondria, microsomes, nucleus, sarcoplasmic reticulum, and myofibrils. According to current thinking, mitochondrial CPK catalyzes the formation of creatine phosphate from ATP, produced within the mitochondrial matrix as a result of oxidative phosphorylation. The resultant creatine moves to the cytoplasm in accordance with the concentration gradient or by rapid diffusion to certain isoenzymes of CPK, and in particular those:

- associated with the structures responsible for muscle contraction - M-line of myofibrils.
- associated with the sarcoplasmic reticulum and Ca^{2+} adenosine triphosphatase.
- related to the sarcoplasm and the Na^+ / K^+ adenosine triphosphatase.
- associated with the postsynaptic membrane, rich in acetylcholine receptors and ATPases.

Mitochondrial CPK holds together the external and internal surfaces of the mitochondrial membrane, creating its structure. [1]. Localization of CPK in the M-line area creates conditions for the continuous renewal of ATP to ensure the proper contractile function of myofibrils (Fig. 11). The resulting creatine returns to the mitochondria to become again a substrate for phosphorylation.



Note about the Figure 11: 2 should be sarcolemma of cardiomyocyte. 3 is technically “mitochondrion” as it is just one of them. 10 should be light disc (I-band). 11 should be dark disc (A-band). 12 is fragma of body. 13 is M disc. 14 is desmosome (macular adherans). 15 is nexus (gap junction).

Thus, a decrease in the activity of CPK indicates serious structural and metabolic defects in the energy metabolism of the cardiomyocytes. This is observed in changes of the mitochondrial system, in the form of an increased number and size of mitochondria, and an increased number of lamellar cristae and their subsequent destruction. It is also observed in the aggregation of mitochondria and changes in the number of intermitochondrial contacts (Fig. 12).

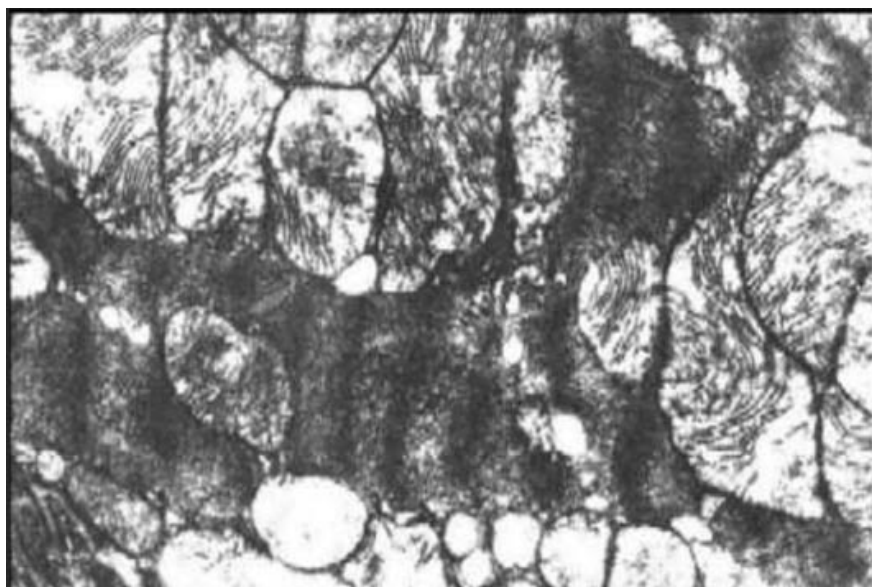
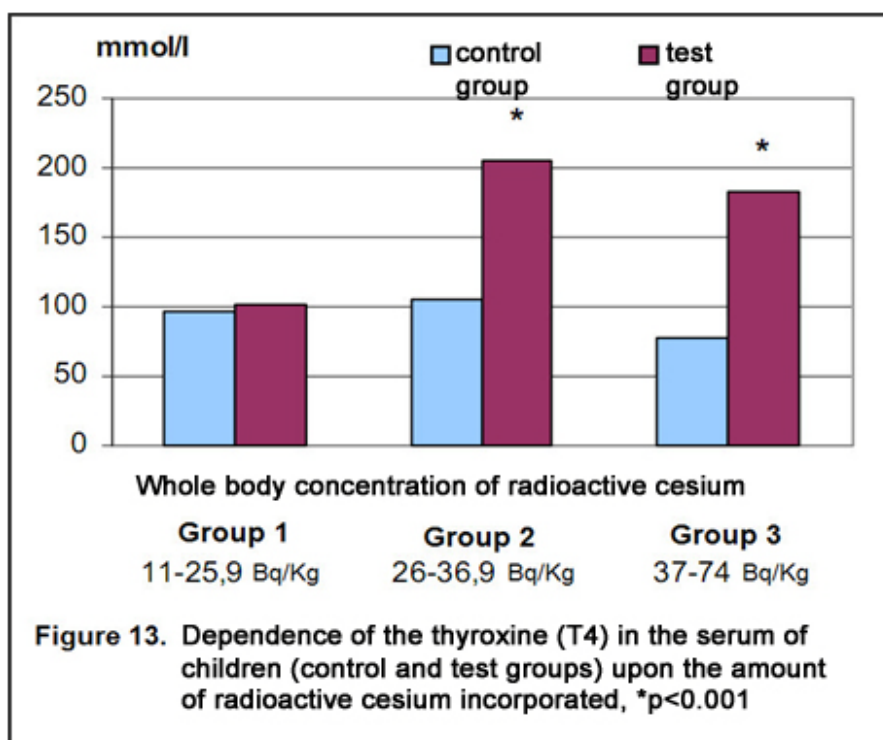


Figure 12: Aggregation, increase in the number and size of mitochondria of rats following the ^{137}Cs incorporation of 45 Bq/kg into their bodies. Magnification X 30,000

Inhibition of the energy metabolism can be connected to the direct influence of ^{137}Cs on the membrane structure, as well as from the effects of some metabolites, including thyroid hormones, given that the latter exert a toxic effect on the mitochondrial system [13]. In this regard, as with Graves' disease, or in experimentally induced hyperthyroidism, there is an inhibition of the CPK activity [1]. It is also possible that in the course of ^{137}Cs exposure, the increased amount of free thyroxine causes damage to myocardial cells by affecting CPK. This view is confirmed by a parallel increase in the frequency of ECG changes and the level of free thyroxine in the blood of children with ^{137}Cs incorporation of more than 37 Bq/kg (Figure 13). Thus it is possible to assume a certain role of thyroxine in the occurrence of arrhythmias.



In men, the CPK activity is greater than in women [1]. The possibility cannot be ruled out that the vulnerability of this enzyme in myocardial cells under the influence of ^{137}Cs , is the main cause of sudden death in men.

Note the decrease in activity of alkaline phosphatase in the structures of the myocardium, indicating the development of degenerative processes, which is specific for exposure to ionizing radiation [36].

The nature of structural changes in the myocardial cells, observed in laboratory animals that had incorporated ^{137}Cs and also in persons living in the areas contaminated with ^{137}Cs , indicates an impairment of the permeability of the sarcoplasmic reticulum membrane for Ca^{2+} . This may be connected with the direct impact of ^{137}Cs on the structure of cell membrane, as well as to the radioactive emissions produced as it decays [8, 29, 41]. The resulting peroxidation of fatty acid chains of phospholipids leads to changes in their structure and permeability for different ions, including Ca^{2+} . At the same time, this naturally changes the activity of membrane-bound enzymes. The hyperproduction of free hydroxyl radicals and an amplification of lipid peroxidation contribute to the destruction of cell membranes.

The Ca^{2+} transport system of sarcoplasmic reticulum of the myocardium is actively involved in the process of the contraction-relaxation of myofibrils, through the release and accumulation of

Ca^{2+} . If there is damage to this system by various agents, including ^{137}Cs , then the level of free Ca^{2+} in cardiomyocytes increases, and the relaxation of myofibrils is disrupted.

Changes in the contractile apparatus are reflected in changes observed in the double ray refraction of myofibrils: appearance of segmental and sub-segmental contractures, intracellular myocytolysis, primary cluster disintegration of myofibrils, cytolysis, and eventually coagulation or colliquative necrosis [32].

Contractive alterations of the segmental and sub-segmental type are defined in the polarized light by enhancement of the anisotropy of the A-disk of myofibrils. They look like glowing transverse stripes, with cross sections of striated myofibrils that can be seen between them. When examined under the light microscope, they are visible due to the greater density and eosinophilia.

Ten days' worth incorporation of ^{137}Cs in the body of Vistar-line rats (^{137}Cs concentration 60-100 Bq/kg) also led to these changes (Figure 14). In the primary cluster disintegration of myofibrils, isotropic spaces are found between anisotropic lumps (Fig. 15). This is in contrast to contractures of severe and irreversible damage of the cardiomyocytes, indicating their death. It should be noted that primary cluster disintegration is often found in acute heart failure [30, 31].

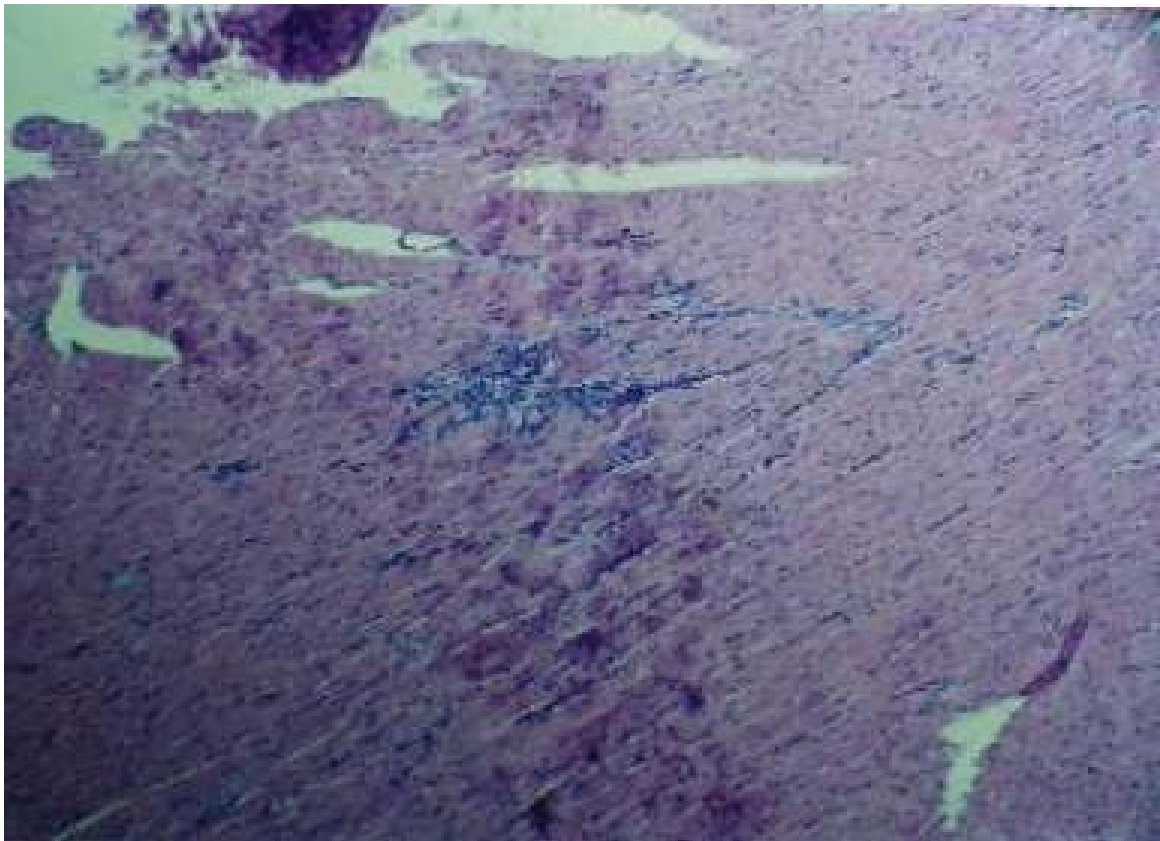


Fig. 14. The histological section of animal myocardium [rat] after incorporation of radioactive cesium in the food (concentration in the body at 100 Bq/kg). Diffuse contracture in myofibrils of cardiomyocytes. Diffuse myocytolysis. Focal infiltration by lymphohistiocytic cells. Stained with hematoxylin and eosin. Magnification X 125.

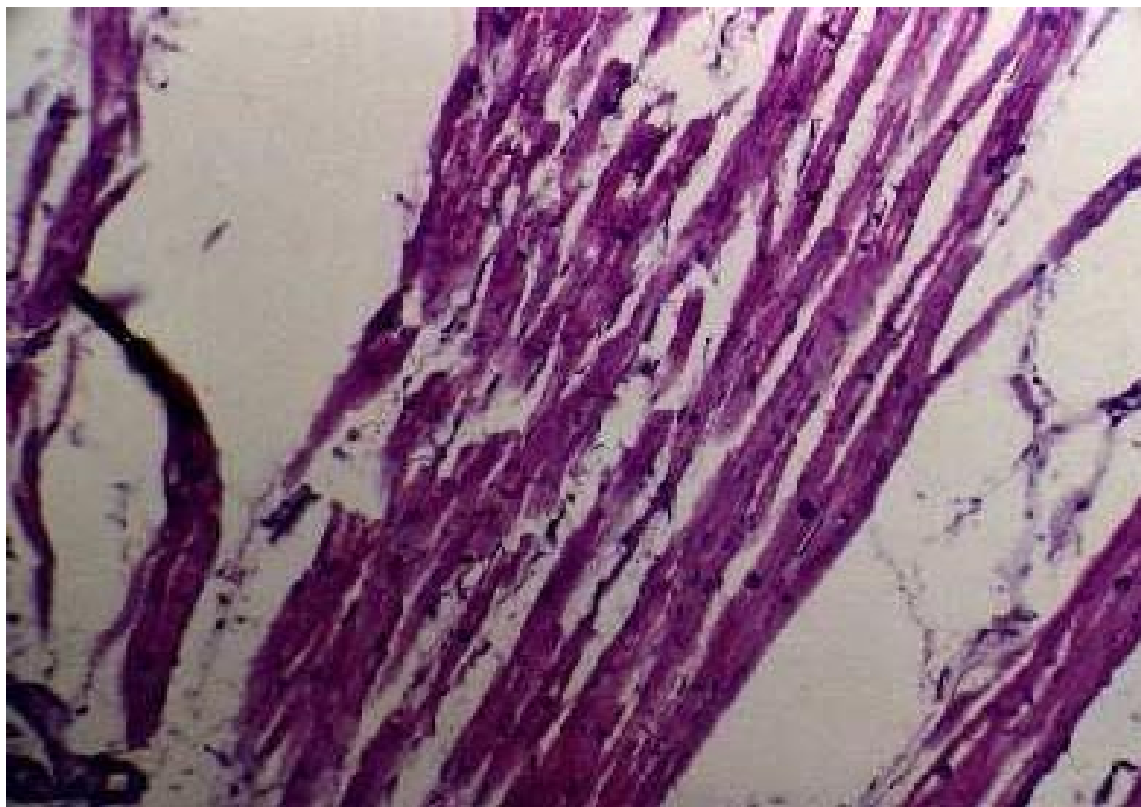


Figure 15. Histological section of the myocardium of a woman who died in childbirth. Concentration of ^{137}Cs in the heart at 105 Bq/kg. Primary cluster disintegration of myofibrils. Separation of muscle fibers, intermuscular edema. Stained with hematoxylin and eosin. Magnification x 250.

Cytolysis, or in vivo autolysis of cardiomyocytes, is also an irreversible condition. It tends to be diffuse under the influence of ^{137}Cs (Fig. 16, 17).

The above changes are observed not only under the exposure to ^{137}Cs , but also when metabolic damage occurs due to intoxication, hypoxia, and functional overload [14, 24, 40], and under the influence of extreme environmental factors contributing to the development of stress reactions [27, 28, 31]. It is observed that in these reactions the Ca^{2+} concentration in cardiomyocytes increases [28].

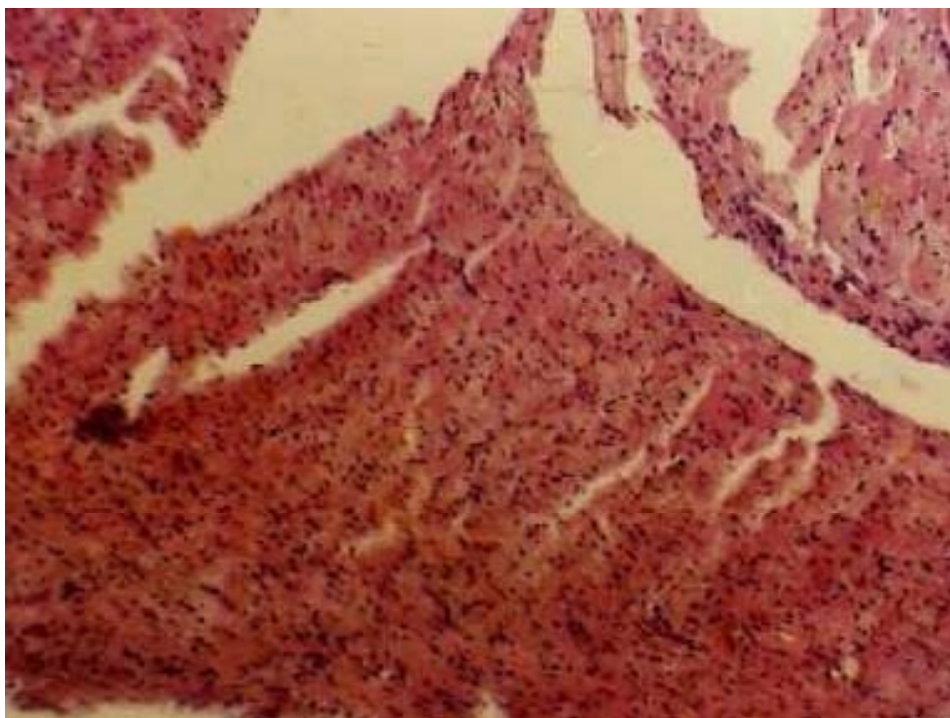


Fig. 16. The histological section of the myocardium of an animal that has received ^{137}Cs (concentrations in the body of 900 Bq/kg). Diffuse myocytolysis. Pronounced intertissue edema. Stained with hematoxylin and eosin. Magnification x 125.

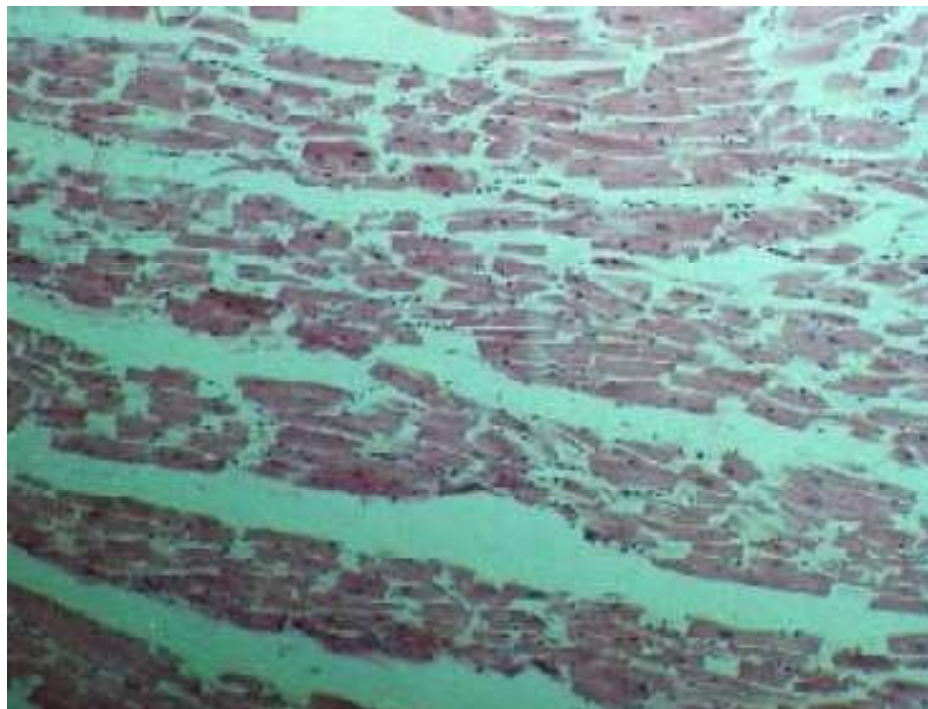


Fig. 17. The histological section of the myocardium of a 43-year-old Dobrush resident who died suddenly. The ^{137}Cs concentration in the heart: 45 Bq/kg. Diffuse myocytolysis. Intermuscular edema. Fragmentation of muscle fibers. Stained with hematoxylin and eosin. Magnification x 125.

The leading role in the mechanism of injury is played by the effects of catecholamines (noradrenaline, adrenaline) on the beta-adrenergic receptors of the myocardium. This does not have any connection with ischemic damage to the heart [28].

The total scheme of the effects on the heart is influenced, by a wide variety of factors, through stress reactions. High concentrations of catecholamines increase the number and timing of openings of voltage-dependent and receptor-dependent calcium channels, resulting in accumulation of Ca^{2+} in the cardiomyocytes. Cells of the conduction system are damaged earlier and to a greater extent, since they have low resting potential and the input ion current, which is responsible for the action potential, is primarily calcium [10]. Moreover, this system has predominantly adrenergic innervation [28].

As a result of this process, a high concentration of Ca^{2+} is formed within the cells. Arrhythmias or rhythm disturbances can occur when Ca^{2+} is inappropriately released from the cardiomyocytes. We emphasize that this is directly related to the function of the cationic pump. A significant role in the energy supply for the pump is played by the creatine phosphokinase and glycolytic systems [28]. In order to cause the relaxation of myocardium and break bridges between thin actin and thick myosin myofibrils, it is necessary to coordinate the work of these systems. This includes the sarcoplasmic ATPase, which transports Ca^{2+} back into the cistern of the sarcoplasmic reticulum. It should be noted that this is the energy-dependent process in which the heart muscle spends 15% of its total energy consumption [25].

Considering the constant exposure to and influence of ^{137}Cs upon the people living in the contaminated territories and the suppression of noradrenaline production in the cells of the cerebral hemisphere [23], it is not difficult to imagine that catecholamines play a leading role in causing the contractures of muscle fibers. This could just happen in cases with strong stress reactions. In reality, the accumulation of Ca^{2+} in the cells, under the influence of ^{137}Cs exposure, can occur due to energy shortages, caused by damage to the energy supply system within the cell membranes, including mitochondria and structures of the sarcoplasmic reticulum. That is why cells cannot release Ca^{2+} in a timely manner. Calcium ions enter the cells very intensively due to the destruction of membrane phospholipids by free hydroxyl radical groups. In this situation, significant myocardial damage can be caused with little effort. Death of cardiomyocytes may occur with prolonged energy deficits, caused by physical exertion, acute infectious processes, and alcohol intoxication.

Cardiac activity can be stopped by increasing the ^{137}Cs concentration in the body. In particular, the rapid injection of large amounts of ^{137}Cs (reaching a concentration of 1,000 Bq/kg within 5 days) caused cardiac arrest in rats. In this case, the radioactive agent itself became the immediate cause of death. To a lesser degree, the source of reconstructions of myofibrils of cardiomyocytes in the presence of ^{137}Cs could be an emotional stress, resulting in the release of catecholamines. This is due to the fact that in long-term cesium toxicity, there is progressive inhibition of the function of the sympathetic nervous system, reducing adaptive reserves of the body [17]. At the same time, it is impossible to completely exclude the role of catecholamines in cardiac damage under the influence of ^{137}Cs .

This has been confirmed by the results of clinical examination and laboratory testing of children with chronic gastrointestinal pathology. There was a directly proportional relationship between the frequency of hyperactive sympathetic nervous system and the amount of ^{137}Cs in the body. Based on the above information, one can conclude that the energy deficit in the calcium transport system, arising during the ^{137}Cs incorporation, leads to disruption of cardiac rhythm, damage to the contractile apparatus of cardiomyocytes and, in the end, to cardiac arrest.

Injuries to the cardiovascular system cannot be considered in isolation from other organs and systems, particularly the kidneys. As the main organ of excretion of ^{137}Cs from the body [16], the kidneys are significantly affected even at a small ^{137}Cs concentration of. Kidneys also undergo similar damaging effects as the cardiovascular system, first and foremost in the glomerular apparatus [6,7]. In muscle fibers within the arterioles, there are changes identical to those observed in the myocardium. Contractures of myofibrils lead to a prolonged spasm of arterioles and hence the cessation of circulation in structures of the nephron. Deaths of cellular elements form a specific structural change in the glomeruli, a phenomenon called 'melting icicles'. Dystrophic and necrobiotic changes gradually appear, accompanied by shrinkage and fragmentation of glomeruli (Fig. 18, 19).

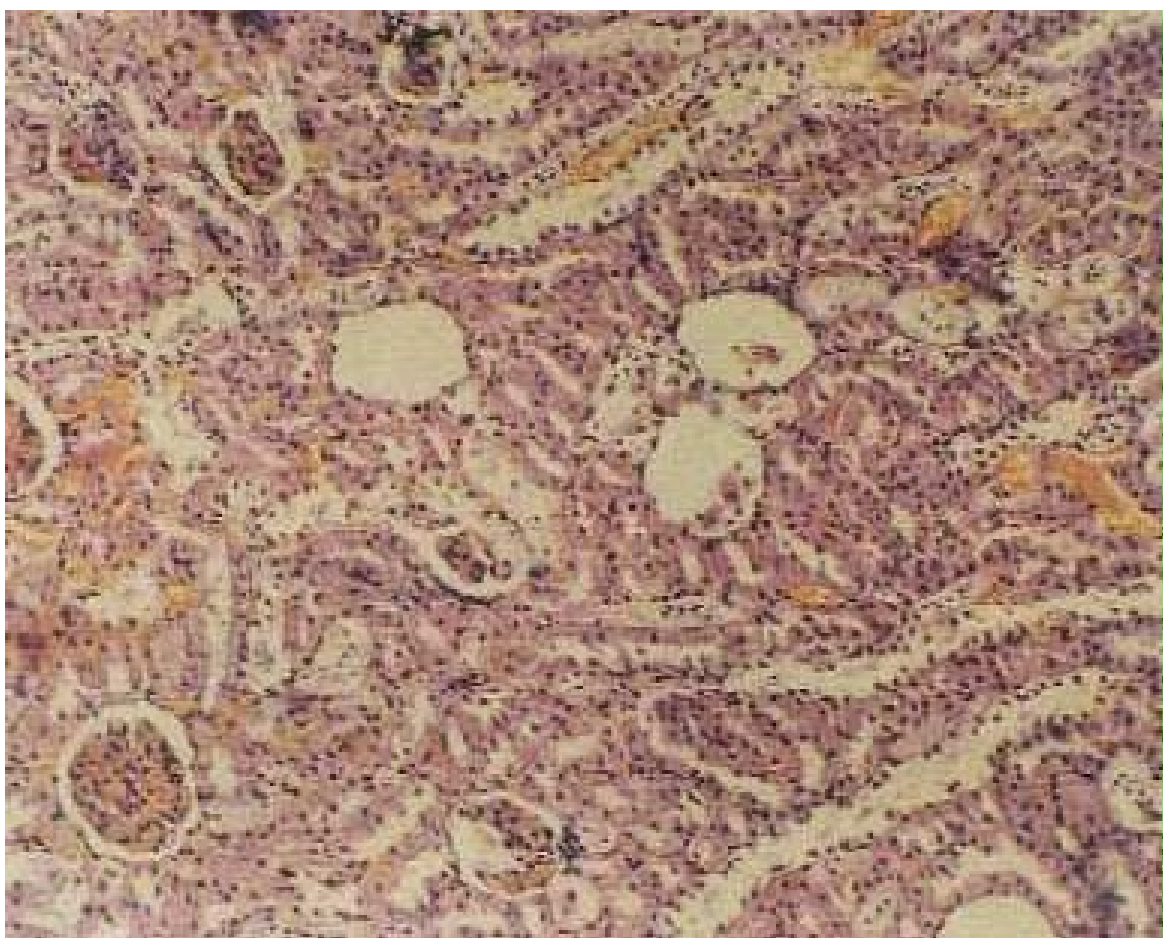


Fig. 18. Histological section of albino rat kidney with a ^{137}Cs concentration in the whole body of 900 Bq/kg. Necrosis and fragmentation of the glomeruli with the cavity formation. Necrosis and hyaline droplet dystrophy of tubular epithelium. Stained with hematoxylin and eosin. Magnification X 250

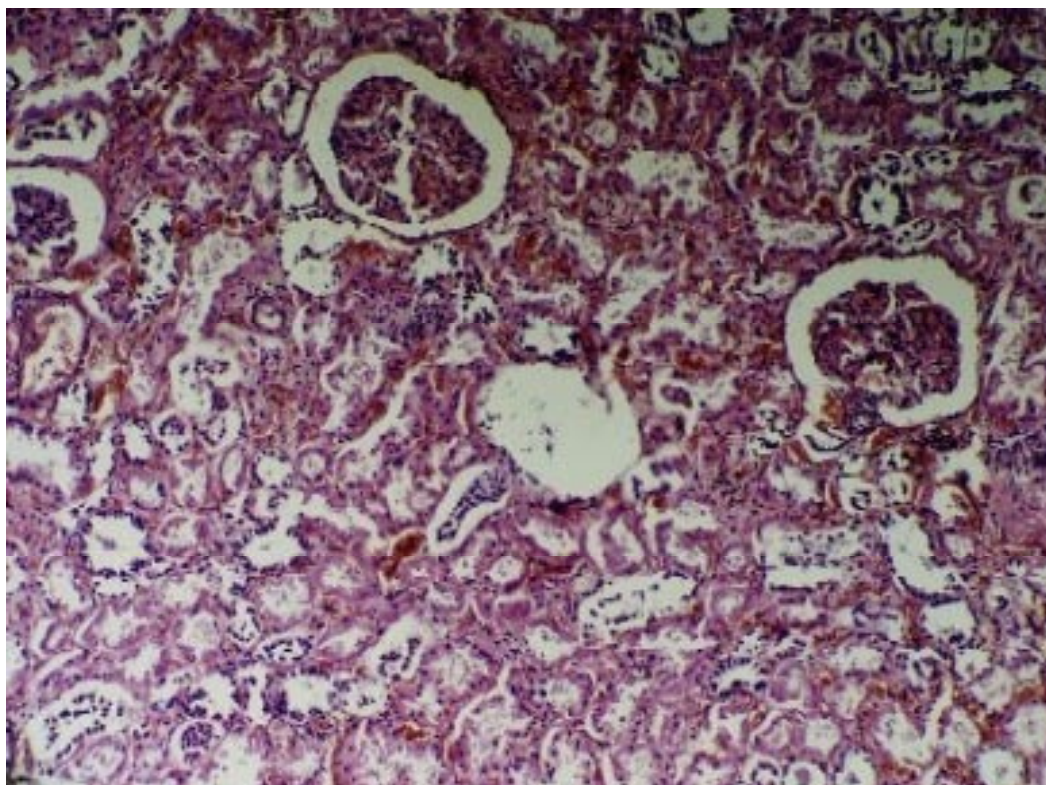


Fig. 19. Histological section of the kidney of a 71 year-old female patient in Gomel. She died of adhesions of the abdominal cavity and acute upper-lobe pneumonia of the right lung with consolidation and fibrino-purulent component, complicated by bilateral pulmonary edema. ^{137}Cs concentration in the kidneys was 300 Bq/kg. Fluid accumulation in the glomerular cavities. Hyaline droplets and hydropic dystrophy of the tubule epithelium. Interstitial tissue edema. Stained with hematoxylin and eosin. Magnification x 250.

Cavity formation without any marked cellular reaction is characteristic of the effects of ^{137}Cs on the kidney tissue. With the ability to cause hyper-contractions (excess contractions) of muscle fibers in arterioles, ^{137}Cs damages the process of vascular microcirculation in the kidneys. It must be emphasized that there is a lack of proper inflammatory reaction of the body in response to damage in the kidneys and other organs. In our opinion, this is due to the suppression of the synthesis of biologically active substances, such as inflammatory mediators in specialized cells.

Damaged glomeruli cease to function. It is not a coincidence that the histological characteristics of kidneys, when exposed to ^{137}Cs , are the same as those of thrombotic microangiopathy [2]. In both cases, the microcirculatory channeling system of the nephron is blocked at the level of the arterioles, leading to necrobiotic processes.

Development of renal insufficiency is the reason for the accumulation of metabolic waste products and wastes in the body. These have toxic effects, along with the impact of ^{137}Cs itself, upon the vital organs and systems. Also characteristic are inflammatory processes of the serous membranes, particularly pericardium (Fig. 20) and pleura (Fig. 21).

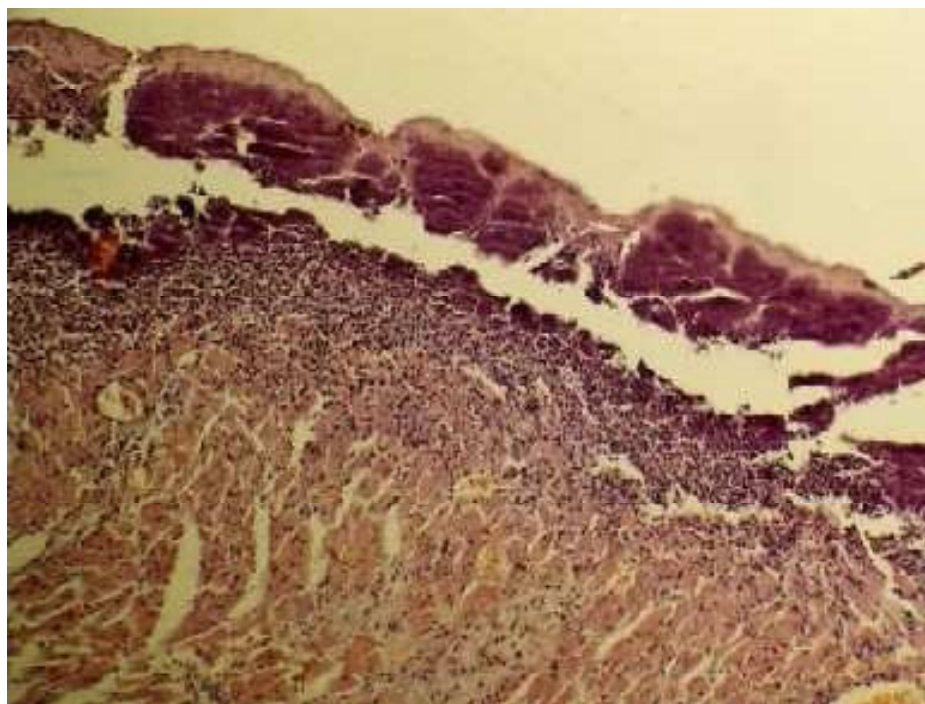


Fig. 20. Histological section of an animal myocardium with ^{137}Cs incorporation of 900 Bq/kg in the body. Infiltration of the epicardium and pericardium by neutrophils and lymphocytes. Pronounced myocytolysis. Stain hematoxylin and eosin. Magnification x 125.

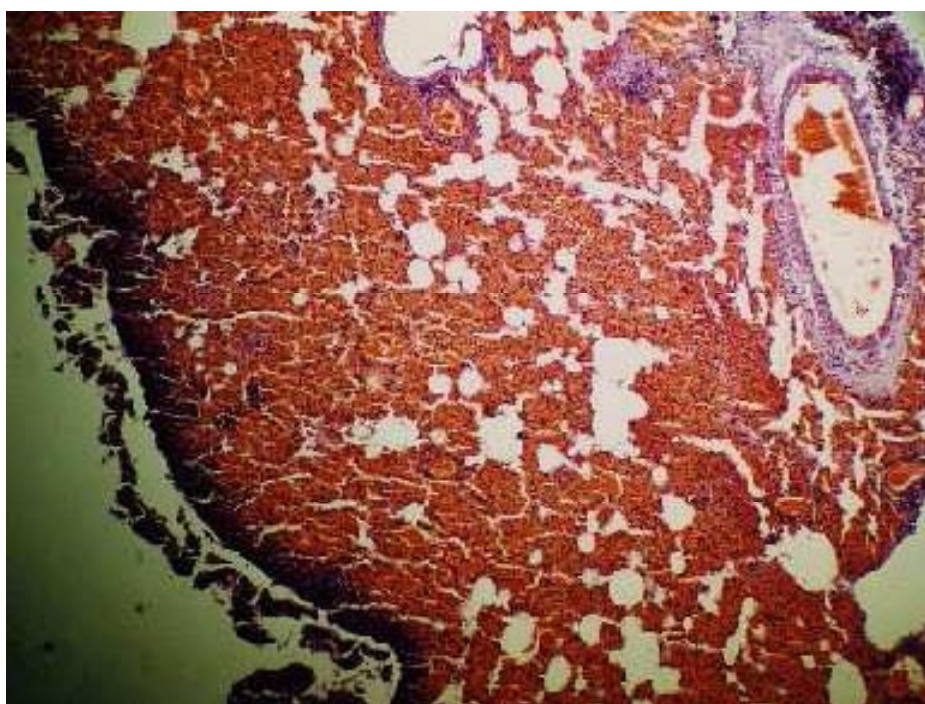


Fig. 21. Histological section of animal lung with ^{137}Cs incorporation at 900 Bq/kg in the body. Engorgement of alveolar lumen with blood due to the rupture of blood vessels. Infiltration of the visceral pleura with neutrophilic leukocytes, lymphocytes and histiocytes. Stain hematoxylin and eosin. Magnification x 125.

Injuries to the vascular system of the kidneys may be one of the main reasons for the increase in blood pressure, especially the diastolic pressure, in children. However, given the hidden, latent course of this pathological process, it only can be found after ordinary medical treatment fail to bring any tangible results. Therefore, a continual assessment of both renal and heart function in children, living in regions contaminated with ^{137}Cs , should be made with the use of modern laboratory and technological diagnostic methods.

The liver is also negatively affected under the influence of ^{137}Cs . Individuals who lived in the Gomel region were found to have significant levels of ^{137}Cs in their liver [6]. In most cases, histological examination revealed marked dystrophic and necrobiotic changes in the hepatocytes (Fig. 22).

Similar changes were found in experimental animals exposed to ^{137}Cs . There was an immediate disruption of hepatocyte functions, in particular synthetic and detoxification (neutralization) functions.

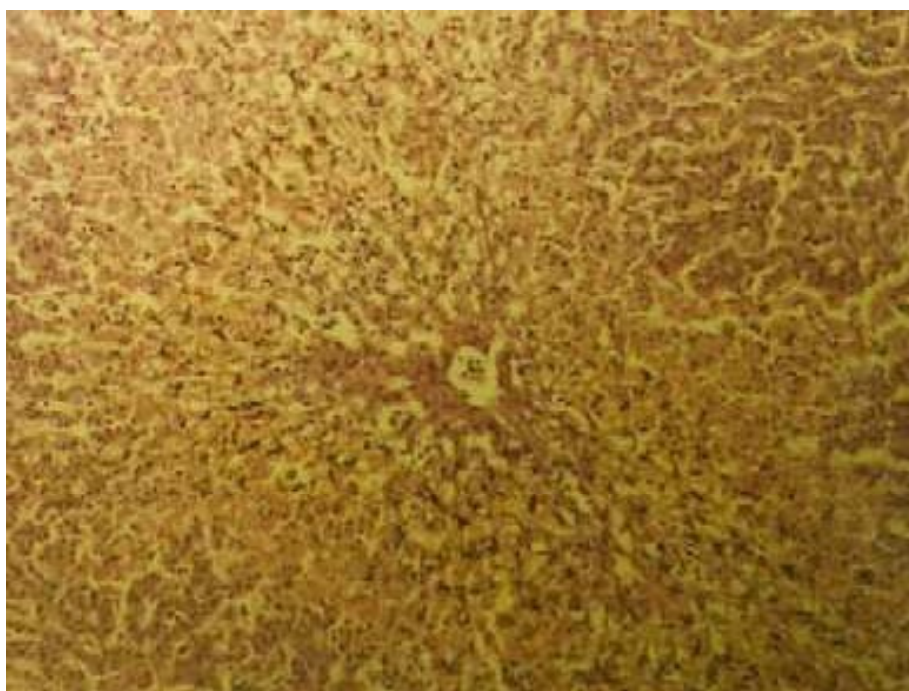


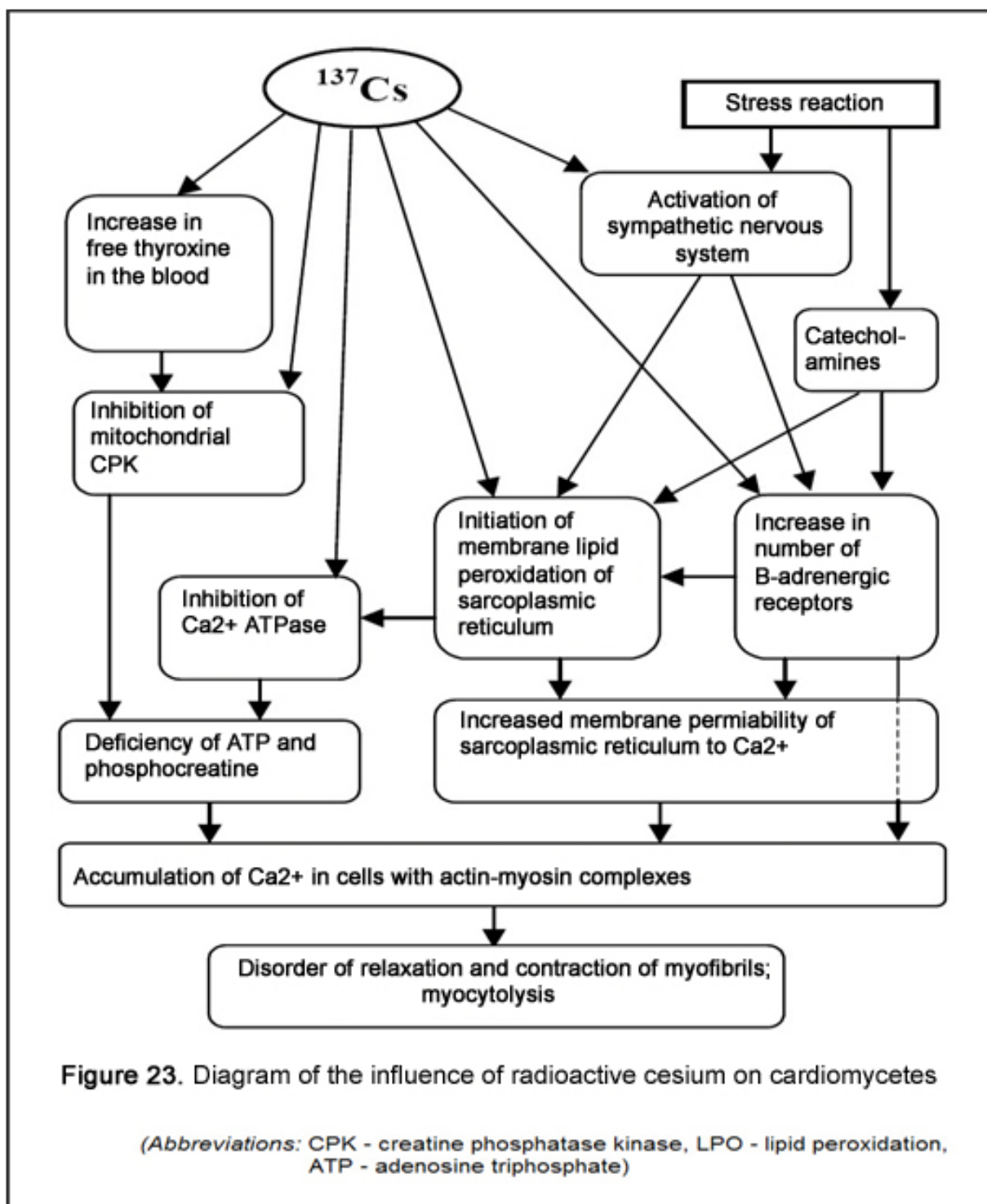
Fig. 22. Histological section of the liver in a 40-year-old Gomel resident, who died suddenly. ^{137}Cs concentration in the liver: 142 Bq/kg. Fat and protein degeneration, with necrosis of hepatocytes. Stained with hematoxylin and eosin. Magnification $\times 125$.

Impairment of the synthetic function of hepatocytes is manifested through a progressive decrease in the synthesis of L1-globulin and L2 globulin, with increasing concentrations of ^{137}Cs in the body. This will undoubtedly affect the state of metabolism in other organs, including the heart.

Oxidation of steroid hormones, especially the adrenal cortical hormones, takes place in the liver. Also the breakdown of the catecholamines, the hormones of the adrenal medulla, noradrenaline and adrenaline can take place by way of methylation reaction. The liver plays a huge role in detoxifying ammonia, by utilizing it in the synthesis of urea. An insufficiency of

the synthetic and detoxifying functions of the liver leads to the emergence of metabolic dysfunction, which adversely affects the condition of the myocardium.

Thus, metabolic dysfunction, occurring in the body as a result of the incorporation of ^{137}Cs , may contribute to disturbances in the structure and function of cardiomyocytes.



Conclusion

Working on this book, I kept thinking about the need to inform every civilized person of the dangers posed by radioactive elements absorbed and ingested into the human body.

Unfortunately, society today is, at best, indifferent towards this issue. And for this indifference we are paying the highest price - in human lives. The ignorance of intelligent people leads to tragedy. To a great extent, the blame rests upon medical scientists, who not only are not trying to raise awareness among the people using previously obtained data, but also do not study the adverse changes that occur in the body due to the incorporation of radionuclides.

I understand that this little book cannot compensate for a general lack of information on the existing problem. Nevertheless, I hope that it will generate interest to this topic and further discussion of the situation. And this will undoubtedly be useful.

Based upon the presented information, we can arrive at a number of conclusions.

Whether we like it or not, radionuclides – especially ^{137}Cs – exist in our environment. Without any protective measures, they will enter the human body, mainly through food and water, and are subsequently incorporated into organs and tissues.

The incorporation of radioactive cesium into myocardium of the developing organism is most dangerous for a human life.

When ^{137}Cs enters myocardial cells, structural and metabolic changes follow, leading to energy shortages and disruption of their main functions, and in some cases, death. A series of changes occur, indicating direct damage of the cardiac muscles as well as damage to many organs and systems regulating cardiac activity.

Cardiomyocytes are not only damaged directly by radioactive cesium, but also suffer injury when there is a disruption in the production, transport, binding, excretion or breakdown of natural metabolites (Fig. 23).

The degree of the severity of pathological changes is directly dependent upon the amount of ^{137}Cs within the body and cardiac muscle. The long-term incorporation of ^{137}Cs in the body, totaling more than 30 Bq/kg, is highly undesirable, possibly leading to serious consequences.

In most cases, the impact of existing ^{137}Cs concentrations in the body (10-20 Bq/kg) does not lead to death. However, the influence of ^{137}Cs upon the energy apparatus of cardiomyocytes significantly reduces their adaptive capacities. As a result it can become impossible for individuals to function properly in various stressful and even ordinary situations, such as during physical and mental stress, hypoxia, extreme temperature fluctuations, drinking alcohol, infectious and allergic diseases.

It should be recognized that ^{137}Cs is a highly toxic agent and we must regard it as a slow-acting poison to the cells [Editor's note: This is particularly true when so-called "low-dose" ^{137}Cs is routinely ingested in contaminated foodstuffs, as evidenced by the laboratory studies and tissues of the autopsied patients.]

^{137}Cs undermines the energy mechanism of cardiomyocytes and causes cardiomyopathy, characterized by cardiac arrhythmias, abnormalities in myocardial contractility and spasms of peripheral vessels. It is important to mention that the influence of the incorporated radioactive

cesium on human and animal organisms presupposes its participation in anabolic and metabolic processes, first of all, as a chemical element, but not as a source of radioactivity. However, one cannot completely exclude the latter.

This is especially pronounced with prolonged exposure to small amounts of ^{137}Cs . The main reason for the pathological changes of the kidney under the influence of ^{137}Cs is the arteriole spasm, which causes necrosis of the glomerular loops and destruction of the nephron structures. The vasoconstrictive effects of cesium were noted in 1888 by S.S.Botkin [11].

Therefore, ^{137}Cs is one of the major etiologic factors in high blood pressure in children, living in the contaminated area. This has been confirmed by numerous observations [20].

As a basis for prevention of cardiovascular diseases in populations living in the area affected by the Chernobyl accident, the relevant issues include the reduction in the amount of radionuclides, and above all ^{137}Cs in the body, through the reduction of its content in foods, as well as its removal from the body with the help of adsorbing agents. These measures will play an important role in the improvement of metabolic processes in the myocardium.

List of Abbreviations:

ATP - adenosine triphosphate
 CPK – creatine phosphokinase
 LPO - lipid peroxidation
 GIT – gastro intestinal tract
 ECG – electrocardiogram
 WBC- whole body count

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