

LESSON 4

INTERNAL EXPOSURE. STOCHASTIC EFFECTS OF INTERNAL EXPOSURE

1. INTERNAL EXPOSURE

Internal exposure is exposure with incorporated radioactive substances. Usually internal exposure is combined with exposure of the skin from its contamination with the same radionuclides.

Incorporation of radionuclides might develop under different circumstances, in particular:

- nuclear reactor accidents (mainly cesium and iodine radionuclides),
- infringement of rules or instructions concerning principles of work with powder and liquid radioactive materials,
- accidents with depressurization of radionuclide sources (^{60}Co , ^{137}Cs , ^{192}Ir , ^{226}Ra),
- errors in radionuclide dosage in medical practice during nuclear medical diagnostic or treatment procedures,
- accidents in sites of nuclear fuel production and processing and also during radioactive waste transportation and recycling.

Radioactive substances may get into the organism via the *lungs, digestive tract, skin, and wounds*.

Inhalation pathway is the most widespread. Radioactivity of the air may be caused by content of radioactive substances in the form of gases, vapor (fog), aerosols (smoke), and dust. Retention of a radioactive contaminant in the upper airways or lungs will depend on its aggregate state, the size of aerosol particles of the radioactive substance, minute volume, and respiratory rate.

Gaseous radionuclides easily penetrate into the alveoli of the lungs, and are also quickly removed. That is why the doses absorbed by the lungs in these cases are mainly formed when a person is in the radioactive cloud. When someone is inhaling, for instance, radon-222 for a long time, his/her lungs are accumulating absorbed doses sufficient to cause bronchitis, pneumosclerosis or even lung cancer.

The depth of penetration of aerosols into the airways and precipitation in them depends on the degree of aerosols dispersity. When one inhales superdispersed aerosols with a diameter of particles of 0.01 micrometer, about 70–100 % of them may precipitate in the alveoli. Bigger particles get into the alveoli to a lesser extent and

almost all of them are precipitated on the epithelium of the nasopharynx, trachea and bronchi.

Gaseous radionuclides are removed from the lungs by means of expiration and diffusion through the alveolar epithelium and endothelium into the blood and lymph vessels and are spread through the organism via blood flow, precipitating in the tissues, for which they have tropism, or being removed from the organism through natural channels (digestive tract, liver, kidneys, lungs, skin). Such radionuclides include ^3H , ^{32}P , ^{137}Cs , iodine radioisotopes and some chemical compounds of ^{90}Sr .

Sparingly soluble compounds inside the particles that have penetrated the alveoli remain there for some time until macrophages transfer them into the pulmonary interstitial tissue along the bronchi and lymph vessels, where they are accumulated in some areas or migrate further to the lymph nodes, staying in them for months and years. For example, the so-called “hot particles” containing plutonium, which were formed in the incandescent destroyed 4th block of Chernobyl NPP, were discovered after many years in the lymph nodes of the chest cavity of disaster fighters that fell ill with leukemia.

Also radioactive aerosols are partially accumulated under the visceral pleura.

Particles that settle in the respiratory tracts above the level of the alveoli are removed by the ciliated epithelium into the pharynx and then, if they are swallowed with secretion, enter the digestive tract.

Radionuclides reach the *digestive tract* with food and water, and are also reabsorbed from the lungs. Part of radionuclides that remain in the lumen of the digestive tract depend on their *transportability*. This term is used according to ICRP recommendations to indicate the probability of compounds with radionuclides in their composition to be absorbed from the lumen of the digestive tract into the internal environment.

When radioactive material is swallowed, the digestive tract undergoes the same transformations as in case of nonradioactive elements. Soluble compounds of rare earth elements, transuranic in particular, transform into insoluble hydroxides, which are almost not absorbed and are removed as “transit” from the digestive tract. And, vice versa, insoluble compounds can transform into soluble and enter the blood by means of intestinal epithelium absorption. Iodine and cesium are absorbed quickly, and plutonium, radium and strontium — slowly. Usually, in any situation only part of all radionuclides enter the internal environment of the body from the intestine, and the rest are excreted by means of transit.

During elimination of Chernobyl accident consequences examination of

disaster fighters showed cases of “native” *pulmoscintigraphy* and *colonoscintigraphy*, i.e. scintigraphic lung or colon images by gamma-radiation after a person was exposed to radiation from radioactive substances taken from contaminated environment through inhalation of aerosols or food.

Quite often, radionuclides penetrate into the body through *wounds*, *scratches*, or *abrasions*. Any wound should be considered contaminated until the contrary is proved. Therefore, if a wound is received during an accident, it must be debrided and kept under radiometric control of contamination.

The rate of absorption of a radioactive substance from a wound is determined by its solubility, particle size, pH and reactivity of wound tissues. Small insoluble particles are transferred by phagocytes into the lymph flow. Acid substances-contaminants coagulate tissue proteins, thus reducing their transportability. This phenomenon was observed in Gulf War veterans who received depleted uranium shrapnel wounds. Examination showed that uranium from wounds slowly entered the blood stream, and from it — the liver and kidneys.

Under certain circumstances radionuclides from liquids and gases can be rather quickly absorbed directly through the skin in quantities sufficient to become significant as a radiopathogen. Tritium oxide (heavy water) vapor with gaseous radioactive iodine penetrates through the skin as easily as through the respiratory tract. Dissolved radon from water easily gets through the skin into the body in large quantities. Skin contamination with plutonium compounds is also accompanied with its entering into the organism in the same relative quantity as in case of entering the digestive tract with food or water. Transdermal absorption usually has the form of passive diffusion. The epidermis plays the role of a physical barrier for penetration of contaminant particles. The rate of transdermal absorption of any substance is determined by its fat and water solubility. Soluble radionuclides diffuse through the epidermis to the basal layer. There they can stay for a long time causing a significant dose of radiation. During hydrolysis their transportability increases, thus leading to transition of such further into the blood and lymph and passing it over to the tissues.

Skin permeability can increase if it is irritated during too thorough decontamination by mechanical friction and under the influence of chemicals such as dimethyl sulfoxide. Chemical burns and mechanical scratches also become an epidermis portal for entry of a contaminator directly into the subcutaneous tissue.

The risk level of radionuclide incorporation is determined by:

- the quantity of radionuclide,
- type and energy of its radiation,

- length of stay in the body, and
- the presence of critical organs.

Critical organs in internal exposure are:

- those receiving the largest amount of radionuclides,
- those playing the vital role in support of organism functioning and those having high radiation sensitivity.

A whole organ can be critical, as well as its certain part or certain cell populations, such as intestinal or bronchial epithelium, or active osteoblasts of the skeleton.

After inhalation of untransportable substances containing short-lived radionuclides, especially alpha-emitters, the lungs become the critical organ. At large doses of exposure and massive intake of radionuclides radiation-induced pulmonitis may develop as it was observed in Chernobyl accident liquidators; it should be differentiated from infectious pneumonia in order to choose adequate treatment of such patients.

The digestive tract is a critical organ for insoluble radionuclides. The colon is exposed to the highest radiation because of the low rate of its contents passage. The radionuclides, which travel through the digestive tract, are removed from it in about 24 hours in persons with normal digestion. The rate depends on the content of vegetable fibers in food. But in some cases passage can be delayed by up to 5 days, and *decorporation* needs appropriate medical procedures in such a case.

During skin exposure the critical organ is the skin itself, and thereafter — the organs that were exposed through the blood flow. The pathogenetic role in determination of the degree of radiation damage to the skin and its remote consequences is played by absorbed radiation doses in the basal layer of the epidermis, where stem and proliferative cells are concentrated, and in the zone of hemo- and lymphomicro-circulation of the dermis.

A radionuclide in the body is involved in metabolism as well as its stable version, i.e. according to chemical properties of the element. Excretion from the body is subject to the same laws — it is excreted either unchanged or in metabolites. The time of radionuclides stay in the body influences the most the level of radiation effect and determines the accumulated dose of tissue exposure.

The vast majority of radionuclides are excreted by the kidneys. Radionuclides of heavy metals taken orally are excreted unchanged through the digestive tract. They can also be excreted through the liver and lungs. To a lesser extent, radionuclides are eliminated by the sweat, salivary and mammary glands (with milk during lactation).

Usually, the kidneys excrete water, and the liver — fat-soluble radionuclides

and radioactive compounds. Elimination processes are characterized by variability caused by many factors, including peculiarities of metabolism, functional state of the body systems, nutrition, etc.

The greatest threat at external contamination comes from low energy emitters of beta particles that can cause severe radiation skin burns. For indication of such radiation one should use special radiometers, therefore examination of people contaminated with radionuclides should be carried out by an experienced radiation physicist.

Indication of an incorporated radionuclide, determination of its type and quantity is a very important part of aid to the victim, because this establishes the very fact of incorporation and determines the choice of adequate care and subsequent patient management. When radionuclides enter the body, the worst consequences are caused by alpha-emitters, because their track length in tissues does not exceed 40 micrometers, which is comparable with the cell size, and therefore all the energy emitted by the particle is absorbed almost completely by one cell with its fatal damage. Detection of alpha-radiation of radionuclides that have entered the human body is a difficult task, but an error in this case may cause fatal consequences. For this purpose one should take a swab from both nostrils, open skin and oral mucosa. After some time (1–2 days) the urine and feces should be subjected to radiometry. Radiometry is performed on special devices.

Early detection of the fact of incorporation allows to remove most contaminants from the body and thus substantially reduce the injured person's risks.

Quantitative assessment of potential radiobiological effects from intake of radionuclides is a complex problem. To solve it one must take into account the following factors:

- type and possible amount of a radionuclide,
- how long the radionuclide stays in the body,
- its distribution in organs and tissues (the radionuclide may be characterized by specific tropism as a chemical element or compound to specific organs or cells),
- cell kinetics of the tissue that receives most radiation and is vital in terms of physiological and pathophysiological functions in the body (critical tissue).

Radiation injury of the internal organs does not depend on the pathway of radionuclides entering the body, it is determined solely by their spatial distribution and absorbed dose in tissues.

Radionuclides of chemical elements enter the body in different physical and chemical states, in the form of simple inorganic compounds, or as part of organic

molecules, or particles of different degree of dispersion. Obviously, all these peculiarities of the radionuclide containing material influence the time of its residence in the organism environment, and this circumstance together with the amount of radionuclide that has entered the body forms the dose of critical organs exposure.

The time of radionuclide exposure of the organism tissues depends not only on its kinetics in the internal environment, but also on a purely physical factor — the rate of atomic decay. From short-lived radionuclides the dose of tissue exposure grows faster than from long lived ones.

According to the type of distribution in the organism, there are differentiated radionuclides tropic for:

- bones,
- reticuloendothelial system,
- kidneys,
- liver,
- thyroid gland, and
- with diffuse distribution in the parenchymal organs and muscles.

Osteotropic chemical elements include calcium (Ca), strontium (Sr), barium (Ba), radium (Ra), some compounds of plutonium (Pu) and thorium (Th).

Reticuloendothelial accumulation is characteristic for nuclides of praseodymium (Pr), zinc (Zn), americium (Am), and also colloidal forms of nuclides (e.g. radioactive collaurin).

Alkaline elements like potassium (K), sodium (Na), cerium (Ce), rubidium (Rb), and also hydrogen (H), carbon (C), and nitrogen (N) are almost evenly distributed in all environments of the organism.

Obviously, radionuclides, which are characterized by high tropism for a particular organ or type of tissue, constitute the highest threat of extensive exposure with severe consequences.

The tropism of a radionuclide may largely depend on the type of the compound, into which composition it enters. Sodium orthophosphate can be cited as an example; it is mainly distributed in cells with high proliferation potency, such as bone marrow cells, tumor cells, etc.

The extent and nature of radiation injury caused by incorporated radionuclides depends not only on the average internal exposure dose, but also on its unevenness, when cells with high radiosensitivity are affected by the highest dose. Unevenness of internal exposure may be associated with the type of emitter distribution in the tissue, especially of microdistribution of alpha-emitters.

As has been noted above, in case of internal exposure alpha-emitters constitute the greatest threat, because their radiation has a high linear transfer of energy to the medium and thus creates such ionization density in the structures of cells and, consequently, such destruction, that reparative processes are made impossible. Radiotoxicity of alpha-emitters is 100 times higher than radiotoxicity of beta- and gamma-emitters, which are distributed in tissues similarly to the former ones.

Toxicity of radionuclides that enter the organism has certain features:

1. In contrast to chemical substances, toxicity of radionuclides declares itself when their mass is very small. For instance, biologically significant amounts of radionuclides have a mass of 10^{-14} — 10^{-11} g, which is million times less than natural exposure to isotopes of corresponding elements.
2. Toxicity of radionuclides is mainly conditioned not by their chemical properties, but by their physical properties — the ability to irradiate cells during radioactive decay.
3. Pathophysiological mechanisms of radionuclide toxicity differ slightly from those of any chemical toxicants due to peculiarity of ionizing exposure effect and this difference is denoted by the term *radiotoxicity*.

The most widely used in industry, medicine and scientific research are the radionuclides: ^3H (tritium), ^{32}P (phosphorus-32), ^{60}Co (cobalt-60), ^{90}Sr (strontium-90), ^{131}I (iodine-131), ^{137}Cs (cesium-137), ^{192}Ir (iridium-192), ^{198}Au (aurum-198), ^{210}Po (polonium-210), ^{226}Ra (radium-226), ^{238}U (uranium-238), ^{235}U (uranium-235), ^{239}Pu (plutonium-239).

A doctor may face any radionuclide, which has caused contamination. In practice, there have been encountered such radionuclides as: ^3H , ^{60}Co , ^{90}Sr , ^{137}Cs , ^{131}I , ^{226}Ra , ^{235}U , ^{238}U , ^{238}Pu , ^{239}Pu , and ^{241}Am . The treatment for radiation injury caused by internal exposure requires knowledge of potential threat of these radionuclides.

Elements of the 1st group of the periodic table are mainly hardly soluble and are distributed in the organism rather evenly. Skeletal distribution is typical of elements of the 2nd group. Elements of the 3rd group are prone to hydrolysis and complex formation. Hydrolyzed forms are mainly accumulated in the liver (in the mononuclear phagocyte system). Some radionuclides are concentrated in the cortical layer of kidneys (^{106}Ru , ^{210}Pb , ^{207}Bi , ^{203}Hg) and red bone marrow (^{32}P , ^{90}Sr , ^{241}Am). Distribution of radionuclides in tissues may be diffuse even or spotty. The latter is observed in the pulmonary tissues, liver, kidneys, thyroid gland and skeleton, where radionuclides are accumulated in the form of “hot spots”, in which concentration of a radionuclide may be 5—20 times higher than on average in the tissue. Accordingly,

exposure doses in these foci of nuclide concentration will also be increased.

The rate of nuclide excretion from a tissue or organism in whole is determined by the value of *effective excretion half-time* T_{eff} (Table 1), which is the time of nuclide amount reduction by half due to its radioactive decay and biological elimination from the organism.

Table 1

Effective Half-Life T_{eff} of Some Radionuclides from Depositing Organs

Nuclide	Organ, Medium	T_{eff}, days
³ H	Aqueous phase	12
³² P	Skeleton	14.1
⁴⁵ Ca	Skeleton	164
⁹⁰ Sr	Skeleton	6400
ni!	Thyroid gland	7.6
¹³⁷ Cs	Muscles	138
²¹⁰ Pb	Kidneys	46
²²⁸ Th	Skeleton	16000

It is clear that long-term incorporation of a radionuclide exposes to risks of malignant tumor development. It is believed that radionuclide must constitute a dose of 0.5–1 Sv for beta-emitters and 0.025 Sv for alpha-emitters for this purpose.

Treatment for lesions caused by incorporated radionuclides is first of all aimed at measures of radionuclide elimination from the body and its removal from the skin. Different approaches and means are used for this purpose depending on the type of radionuclide, its pathway and type of distribution.

Tritium is heavy hydrogen. It emits beta particles with energy of 18 keV, which are used for static elimination, for example in textile industry. It is widely used as a tracer of organic compounds and water in biological studies of metabolism. Tritium can enter the organism, like water, through the skin, lungs and gastrointestinal tract in the form of heavy water or gas (steam) and further it can be uniformly distributed in body fluids. Only a small portion of tritium is fixed in organic compounds. Partial elimination of tritium on average lasts for 12 days. Taking into account low permeability of tritium beta particles, all the energy of which is absorbed in a short distance in tissues, and its homogeneous distribution at incorporation, there quickly occurs acute homogeneous exposure of tissues, which is comparable by biological effect with homogeneous total external gamma-exposure of corresponding dose.

A dangerous dose for an average person may be 1 curie. Exposure to such

amount of tritium causes subacute or even acute reaction of the organism with all signs of acute radiation sickness syndrome. Tritium incorporation can be determined by urine radiometry using standard techniques with liquid scintillator.

Elimination of tritium from the organism depends on the state of water metabolism: cooling, reduced liquids consumption result in its delay. Therefore, the first measures to reduce radiation injury caused by incorporated tritium are warming of the injured person, drinking of large volumes of fluid up to 3–4 liters per day (water, juices, compotes, tea, milk), and use of moderate doses of diuretics. These measures may accelerate elimination of the radionuclide 2–3-fold and accordingly reduce the absorbed dose in tissues.

It has been established that tritium concentration in the urine of 10 $\mu\text{Ci/L}$ is not a sign of danger. Only when its concentration in the urine is 20 $\mu\text{Ci/L}$ and higher, the employee should be suspended from work where he is exposed to tritium for the period required to reduce it to the level below 10 $\mu\text{Ci/L}$.

Diffuse distribution of the radionuclide in tissues and easy determination of its concentration in the urine, which corresponds to such in body fluids, makes it possible to correctly determine the dose absorbed by tissues of the victim's body due to ingress of this radionuclide into the body.

Treatment for manifestations of exposure injury in case of tritium incorporation is the same as treatment for acute radiation sickness caused by total external gamma exposure.

Phosphorus-32 is a beta-emitter. The energy of beta particles is 680 keV, which ensures their way of a few millimeters in soft tissues of the human body.

The radionuclide is used in medical practice for erythremia treatment, beta-therapy of erosive keratitis and superficial dermatitis of various etiology (application beta-therapy), and diagnosis of melanomas and intraoperative diagnostics of metastatic lesions of lymph nodes in malignant tumors. Recently, it is also used as a palliative to relieve bone pain caused by disseminated skeletal metastases.

Entering the body by any channel the radionuclide is primarily accumulated in the bone marrow. Its half-life is 14 days, which coincides with its physical half-life (14.3 days). It testifies to the biological fixation of phosphorus atoms in body cells and further reduction of its amount is almost exclusively associated with its radioactive decay. The radiation dose is formed rather quickly. The main clinical manifestation of exposure injury caused by incorporated ^{32}P is disturbance of hematoipoiesis, mainly of bone marrow erythroblastic cell lineage. When substantial amounts of the radionuclide contact the skin, signs of radiation dermatitis develop on the

areas of direct contact, whose degree depends on the applied activity. Since phosphorus-32 is absorbed through the skin, in such cases there is also observed inhibition of bone marrow hematopoiesis, but in case of such a way of nuclide incorporation radiation dermatitis develops first.

The radionuclide can enter the organism through the mucous membranes of the mouth or nose, which is accompanied by specific symptoms of radioepithelitis (stomatitis, rhinitis, glossitis).

Exposure to phosphorus-32 at doses of up to 5 μCi does not cause systemic reactions. In case of exposure to the nuclide at a dose of 10 μCi there develops transient bone marrow hypoplasia, but generalized reaction is usually not observed. And only at higher levels of incorporation there develop persistent changes in bone marrow hematopoiesis against the background of systemic body reactions, whose intensity increases in proportion to the level of radionuclide dose.

Medical aid should be aimed at elimination of hematopoiesis suppression and systemic body reactions as in case of acute radiation sickness.

Cobalt-60 is an emitter of gamma rays with the energy of 1.17 and 1.33 MeV, its half-life is 5.27 years. Chemical compounds of cobalt are absorbed from the lungs and intestinal tract too slowly, that is why these organs become critical at early stages of incorporation. 30 % of the absorbed amount of the nuclide is accumulated in the liver and spleen, the rest is more or less uniformly distributed in the tissues and organism environments.

Effective half-life of ^{60}Co is 9.5 days. Most of it is excreted in the feces (up to 85 %), the rest is excreted through the kidneys. Medical aid may be required in case of exposure to the nuclide with the activity of 10 μCi or more.

Decorporation is performed using Co-EDTA (cobalt ethylenediamine-tetraacetate). Administration schedule: intravenously 0.6 g of Co-EDTA (2 vials of 300 mg/20 ml), 40 ml of the medication is slowly injected and then one immediately introduces 50 ml of hypertonic glucose solution. Blood pressure must be controlled.

Co-EDTA can be substituted by 0.9 mg cobalt gluconate (2 vials of 0.45 mg/2 ml). Another substitute is Ca-DTPA, which is administered at a dose of 1 g in the most acceptable way: intravenous injections of a concentrated solution for 3–4 minutes or of a solution diluted in 100–250 ml of 5 % glucose, or inhalation in the form of an aerosol (30 minute inhalation of aerosol of 4 ml of 25 % solution). During administration of the medication blood pressure should also be controlled. Contraindication is renal failure. In case of Ca-DTPA absence one uses Zn-DTPA, whose effectiveness is 10 times lower.

Strontium. Natural strontium is a mixture of stable isotopes: ^{84}Sr (0.56 %), ^{86}Sr (9.86 %), ^{87}Sr (7.02 %), ^{88}Sr (82.56 %). Radioactive isotopes have mass numbers 77–83, 85, 89–99. ^{85}Sr , ^{89}Sr and ^{90}Sr have the greatest toxicological significance. Strontium-90 is used in medical practice as a source of beta-particles for application beta-therapy and treatment for bone metastases.

Strontium-90 is a decay product of uranium-235 nuclei. Its half-life is 28.6 years. It emits beta-particles with the energy of 1.1 MeV.

The rate and relative amount of the nuclide that enters the blood from the lungs or gastrointestinal tract are different in various chemical compounds. In insoluble aerosol particles ^{90}Sr can persist in the lungs for a long time exposing them to exposure. Regardless of the route of exposure soluble compounds of radioactive strontium are selectively accumulated in the skeleton, because it is a chemical analogue of calcium. Its content in soft tissues is usually less than 1 %. In 100 days after intravenous injection into the human body (for medicinal purposes) approximately 20 % of the injected amount stays in the organism. In case of inhalation about 32 % of the nuclide gets to the skeleton, and only 7 % enters through the skin.

Minimum dangerous activity of ^{90}Sr for an adult is approximately 400 μCi . The first manifestations of strontium-90 entering the body are signs of its contact with the mucous membranes of the respiratory tract and/or oral cavity (epitheliitis), later — liver dysfunction, over a long period of time — bone marrow hypoplasia. Radiobiological effects occur slowly as slow chronic accumulation of absorbed dose is taking place in the critical organs. Sarcoma is likely to develop after a long period of time due to strontium-90 incorporated into bones.

When significant amounts of the nuclide enter the body, its exposure can cause radiation sickness.

To accelerate radionuclide elimination 2 g of ammonium chloride (4 tablets) three times a day is prescribed. Contraindications: metabolic acidosis, renal failure, and urine acid diathesis.

A possible alternative to ammonium chloride is calcium gluconate solution, 1 g intravenously (to be injected slowly during 10–15 minutes).

Absorption of strontium is reduced by alginates. One tablet of the antacid Gaviscon contains 200 mg of alginate. Administration of 10 g of this substance reduces radiotoxic manifestations of strontium tenfold.

Iodine-131 and **iodine-125.** Natural isotope of iodine is ^{127}I . Radioactive isotopes with mass numbers 115–126, 128–141 are well ^{125}I , ^{131}I , ^{132}I are of practical

importance. ^{131}I and ^{125}I are widely used in medicine for diagnostics and treatment purposes. Iodine is characterized by high migration ability, therefore its radionuclides upon entering the external environment are easily included in the biological migration chains and become a source of external and internal exposure of man. They can enter the human body through the gastrointestinal tract, lungs, skin, wounds and burns. Food stuffs such as vegetables, milk and dairy products are exceptionally important as a route of human body exposure.

Iodine-131 during decay emits beta particles with the energy of 70 keV (this energy is sufficient to cover a distance of 2–3 cells only) and gamma rays with the energy of 364 keV. Its half-life is 8.1 days.

The half-life of *iodine-125* is 59 days; its decay is of electron capture type with exposure of relatively low-energy photons (maximum 35 keV), Auger electrons (with energy of 50–500 eV), internal conversion electrons, and characteristic x-rays. Internal conversion electrons and Auger electrons impart energy almost exclusively to structures of the cell containing a nuclide atom, not affecting the structures outside it. Gamma rays and characteristic radiation also do not have enough energy to be able to create a large dose at a distance from their source.

Solutions and vapors of iodine radionuclides easily get into the blood through the skin from the respiratory and gastrointestinal tracts. Up to 90 % of the nuclide absorbed into the internal environment is accumulated in cells of the thyroid gland. ^{131}I is quickly accumulated in it: normally its content in 2 and 6 hours after incorporation of the radionuclide is 5–10 % and 15–20 %, respectively, and on the second day its content is 25–30 % of the incorporated amount. In case of hyperthyroidism, absorption of iodine by the gland is accelerated and in 24 hours it can reach 70–80 %, and in case of hypothyroidism, on the contrary, accumulation is decelerated to 5–10 % a day. ^{131}I is excreted primarily in the urine and feces, and in smaller amounts in the saliva and milk during lactation.

The critical organ for ^{131}I , as well as for other iodine nuclides, is only the thyroid gland, so even if it enters the human organism at a dose of a few dozen MBq, there are no significant systemic reactions. Acute radiation injury can be caused by ^{131}I in case of its ingestion in such amounts (MBq/kg):

- a) severe degree — 55;
- b) moderate degree — 18;
- c) mild degree — 5.

Common clinical manifestations of injury are similar to those developing in case of total external gamma exposure.

If smaller amounts of ^{131}I enter the organism, there is observed thyroid dysfunction, minor changes of blood count and indices of metabolism and immunity.

Toxicity of the inhaled radionuclide is approximately 2 times higher than in case of its entering through the gastrointestinal tract, which is associated with a greater area of exposure.

If ^{131}I dose is of a few hundred mBq, the function of the thyroid gland is impaired and follicular epithelial cells die.

Excretion of iodine radionuclides can be greatly accelerated by saturating the organism with compounds of its stable isotope — sodium or potassium iodide, orally, intravenously, or even by painting the skin with iodine tincture.

Cesium-137. Natural cesium has one stable isotope — ^{133}Cs . 23 radioisotopes of cesium with mass numbers 123—132, 134—144 are known. ^{137}Cs is of most practical importance.

Cesium-137 is an emitter of gamma rays with energy of 0.662 MeV and half-life of 30 years. It is used in chemical and radiobiological studies, gamma-ray radiography, and radiation technologies. ^{137}Cs is used as a source of gamma radiation for contact and beam radiotherapy and radiation sterilization of materials.

In 1987 in the Brazilian city Goiania there was a dramatic case of exposure of 249 persons to ^{137}Cs powder. The accident began when a scrap collector found a harmless looking metal container in an abandoned hospital. He had no idea that it contained a powerful source of radiation, which had been used to treat carcinoma. The container then was transferred to the scrap yard, whose owner cut the container shell made of steel and lead, and was surprised to find inside some white powder that glowed in the dark. It was ^{137}Cs chloride. Its glow fascinated all the workers of the scrap yard. Men, women and children being unaware of danger powdered their skin with that substance as if it was make up and presented it to their friends. Within two weeks 249 people contacted with the powder. 129 of them had combined contamination, both external and internal. “They burnt their skin. The bums were of varying severity, from minor to severe, which have not healed yet. Twenty-year lesions are still sore,” said Dr. Oliveira, who helped the injured. Four of them, including a little girl, died during the first month.

Spraying of a handful of radioactive cesium resulted in 3,000 cubic meters of contaminated materials buried in two green hills outside the city, which will be harmless only in 300 years.

After this dramatic case of population contamination with powdered ^{137}Cs from a medical source forgotten in the abandoned hospital the international organizations on radiation safety SCEAR, IAEA, and ICRP approved strict standards of radioactive sources safety. Now all countries of the world adhere to requirements of licensing each source so that one can trace its complete cycle from putting into operation to final burial.

Cesium is easily transferred to the blood both from the lungs and gastrointe-

stinal tract and distributed in muscles (up to 50 %) and other parenchymal organs. Its accumulation in the skeleton does not exceed 5 %. Its effective half-life is on average 140 days. Since cesium is a chemical analogue of potassium, it is localized mainly intracellularly, and its content in the blood is negligible. Cesium-137 is eliminated through the kidneys (60 %) and intestine (40 %).

Clinical signs of cesium incorporation according to the type of its distribution can include generalized reactions combined with changes in the functions of critical organs, the liver and muscles. Usually, the first manifestations of exposure are clearly detected only after 2–3 months from the moment of incorporation in the form of asthenic syndrome, vegetative vascular dysfunction, muscular dystonia, etc.

When a single dose of soluble compounds of cesium-137 (acute exposure) enter the body through the gastrointestinal tract in large amounts (about 10^8 Bq), there develops clinical presentation typical of acute radiation sickness. The latent period is 3–5 days, following which there appears sensation of distress, weakness, head noise, and hand tremor. There is an increase in pulse rate, blood pressure fluctuations, heart pain, dryness of the oral mucosa, and stomach pain with nausea. ECG shows mild symptoms of myocardial lesion. The liver is enlarged. After 2–3 weeks you start to lose hair, tendon reflexes are reduced, depression develops. Blood count changes: during the first 5–7 days there is noted leukocytosis followed by leukopenia. Blood clotting factors remain without changes. Combined treatment usually has a satisfactory effect and the victim returns to work, but carry-over effect of radiation injury can remain for a long time in the form of asthenic syndrome. Recurrence of the disease cannot be ruled out, which requires continuation of treatment. It is clear that during the entire period of treatment and later on it is required to exercise radiological control over the dynamics of radionuclide content in the organism.

Prussian blue accelerates elimination of radioactive cesium; it is prescribed by 1 g orally three times a day (0.5 g for children) in capsules during a couple of days. There are no significant contraindications. The injured is informed that the feces will acquire bluish tint. The agent eliminates up to 2/3 of the radionuclide. Prussian blue is a ferrocyanide. This compound is not absorbed in the gastrointestinal tract and is characterized by two mechanisms of action: it reduces absorption of many radionuclides from the gastrointestinal tract and eliminates some of them from the capillary bed in the small intestine. The maximum efficiency of the agent is demonstrated when one begins to administer it immediately after incorporation and continues for 2–3 weeks.

Nuclide elimination from the organism can be accelerated by saturating the

body with potassium and enhancing water exchange simultaneously.

Aurum-198 emits beta particles with the energy of 84–146 keV and gamma rays with the energy of 411 keV. The half-life is 2.7 days.

In medical practice colloid solutions of the radionuclide are used for gamma-scintigraphy of the liver, spleen, and lymph nodes. In carcinomatosis of the pleural or abdominal cavity this solution is injected into them as a medication (intracavitary radiation therapy). Moreover, in soft tissue tumors the solution is injected directly into the tumor. The radionuclide does not enter the blood through intact skin. Theoretically aurum-198 may enter the gastrointestinal tract, from which it is not absorbed either.

Polonium-210. The chemical element polonium is a very rare naturally occurring element due to the short half-life of all of its 29 isotopes. The nuclide polonium-210 is of greatest importance among them. Only about 100 g of polonium-210 is produced from bismuth every year by means of proton bombardment in a cyclotron, or from platinum by means of neutron exposure in a reactor. It is detected in the smoke of tobacco leaves grown on phosphate fertilizers. The air glows with blue light around a polonium-210 sample, because all the high energy of alpha particles emitted by this radioisotope is absorbed in the air at a short distance. The presence of this radionuclide is difficult to detect and identify since it can be done only by using alpha spectroscopy, which is a quite sophisticated method.

Scope of application:

- static discharge devices at textile factories, but now this method is replaced with safer de-electrification means,
- atomic heat sources for radioisotope thermoelectric generators providing spacecraft power supply (1 g of polonium-210 generates 140 W of electric power).

The nuclide polonium-210 is an alpha-emitter with half-life of 140 days. It is characterized by very high radiotoxicity. Entry of even a very small amount of this nuclide by weight into the blood (for example, through intact skin) poses a serious threat. Sources of environment contamination with possible subsequent radionuclide incorporation include damaged special devices containing it, laboratory samples of soluble compounds, as well as emission from destroyed reactors (mixed with radionuclides of other chemical elements). The critical organs are the kidneys, liver, and spleen. Alpha particles of the radionuclide create a high absorbed dose in a short period of time, therefore, when compounds of polonium-210 enter through the gastrointestinal tract, the first sign of toxic effect is severe enteritis. The nuclide is excreted in the urine (leaving out of account that part of the nuclide, which transits

through the gastrointestinal tract).

Mild injury caused by the radionuclide may result in impairment of liver and kidneys function, signs of vasculitis. When the nuclide is entering the body in the amount of 50–100 μCi or more, it results in severe liver and kidney injuries, whose severity degree correlates with the amount of incorporated nuclide.

First aid in case of incorporation of the powder of polonium-210 compounds shall include thorough washing of the skin, change of clothes, gastrointestinal lavage, drinking large amounts of fluid, and administration of diuretics, intramuscular injections of unithiol (dimercaprol). Further, medications for symptomatic treatment are prescribed, with particular attention to the liver and kidneys condition.

Recently, a case of application of polonium-210 as a poison has received much publicity. On November 1, 2006, businessman L. (43 years old) suddenly felt sick, his condition was getting worse. Eventually on November 3 he was admitted to Barnet General Hospital (London) in critical condition. There were no symptoms typical of any definite disease: normal temperature, functional disturbance of the liver and kidneys, hair loss. It was supposed to have been caused by thallium intoxication. One of the doctors said that “the symptoms were a bit strange for thallium intoxication, also we were able to detect levels of thallium, which are even less than intoxication level”. The patient died in 3 weeks. On December 1 thanatopsy and toxicological analysis showed that the deceased had been exposed to two separate polonium-210 doses. Doctors and Scotland Yard investigators had not been able to detect the element earlier, because polonium does not emit gamma rays as most isotopes do. The amount of the radionuclides detected in the deceased was approximately equal to 2 GBq (50 μCi) or 10 μg . It is 200 times more than an average fatal dose (238 μCi , or 50 μg for oral intake). Doctors said that L.’s poisoning “is an ominous landmark: the beginning of an era of nuclear terrorism epoch”. People who contacted with L. could have also been exposed to radiation, that is why all of them were thoroughly examined and remained under observation.

Calcium gluconate in the amount of 0.9 mg (2 vials of 0.45 mg/2 ml) accelerates radionuclide excretion. Ca-DTPA is an alternative that should be injected in the amount of 1 g in the most acceptable way: intravenous injection of a concentrated solution or diluted in 100–250 ml of 5 % glucose for 3–4 minutes, or inhalation (30-minute inhalation of aerosol from 4 ml of 25 % solution). One should control blood pressure during preparation introduction. Renal insufficiency is a contraindication. Zn-DTPA can be used in the absence of Ca-DTPA, but its efficiency is 10 times less.

DTPA effectively eliminates most heavy metals and multivalent radicals. Chelate compounds of DTPA with many heavy metals are water-soluble and thus are

excreted by the kidneys. These complexes are stable and do not lose trapped radio-nuclides until their excretion. After intravenous injection of 50 % solution it together with trapped nuclide atoms is excreted during the first hour. DTPA treatment efficiency, as in most other cases, depends on the time of its application after incorporation: the sooner it is injected, the better.

Radium-226. The nuclide radium-226 is an alpha-emitter used for luminophore production. Besides, in medical practice it is used as a source of radon-222. Its half-life is 1620 years.

Another isotope of radium is radium-224 with the half-life of about 3.64 days (alpha- and gamma-emitter). Radium is a chemical analogue of calcium, therefore it shows bone affinity when absorbed.

Incorporation routes include inhalation in the form of aerosol or via dirty hands to the gastrointestinal tract. Absorption of radium compounds from the lungs is rather slow, so the lungs might be exposed to a rather high dose. As a result at early terms there might develop such skin reaction as pulmonitis, and later on — pneumosclerosis and tumors. The latter are observed twice as often among people with incorporation of about 0.1 μCi radium than on average among general population. There mostly develop bone tumors — sarcomas, and also bronchial carcinomas. In the clinical picture one observes persistent anemia that can be life-threatening in case of a considerable entry of the nuclide into the organism.

The paints used in production of luminous dials of clocks and devices contain radium and thorium and one should be very careful working with them. Workers of such factories happened to develop bone sarcomas much more often.

In the period between 1920 and 1930 one practiced internal introduction of radium salts for treatment of some nononcologic diseases. Remote examination of such patients diagnosed 7 sarcomas among 50 patients. The amounts of radiation sustained by the bones were up to 10 Gy but in certain areas of the bones uneven distribution of the introduced radium could cause much higher radiation levels.

Uranium. Natural uranium consists of three isotopes: ^{234}U (0.0055 %, $T = 2.455 \times 10^5$ years), ^{235}U (0.7200 %, $T_{1/2} = 7.04 \times 10^8$ years) and ^{238}U (99.2745 %, $T_{1/2} = 4.468 \times 10^9$ years). Radioactivity of natural uranium is mainly determined by ^{234}U and ^{238}U . The isotope ^{235}U is the most widely used as fuel for nuclear reactors and explosive in nuclear weapons. Its separation from the isotopes mixture is a very complicated technological task. After separation of uranium-235 from the natural mixture there is a residue called “depleted uranium”, which is half as radioactive as natural uranium. According to available data only in the USA there are hundreds of

thousands of tons of depleted uranium. It is mainly used as radioprotective material and in some aerospace technologies. Each Boing-747 contains 1,500 kg technological depleted uranium. Besides, it is used as material for big flywheels, ballast in yachts and Formula-1 bolides and in oil-well drilling.

Depleted uranium is most famous as an armor-piercer core, which due to its high specific density is a most effective means of armor penetration. Besides, a heavy cap improves aerodynamic stability of the armor-piercer. Such piercers were used by NATO troops during combat operations on the territory of Yugoslavia, which led to a serious environmental problem of radioactive contamination of the territory. The matter was that the uranium core of such an armor-piercer after hitting the armor reduces to ultradispersed state and spreads over a large area contaminating it.

Depleted uranium is also used in modern tank armor and gamma therapeutic cobalt machines for distant radiotherapy as radioprotective material.

Uranium-235 that can decay by chain reaction type is used as a nuclear energy source in nuclear power plants. This very isotope is used in A-bombs.

Only a minor part of uranium is absorbed from the digestive tract, somewhat better from the lungs. Entry of uranium into the organism in the form of dissolved compounds causes chemical intoxication, whereas radiation effects are so insignificant in this case that they are not taken into account. Under such conditions critical organs are the kidneys and to a less extent the liver. If uranium enters the organism in the form of weakly soluble compounds, the organs where it is disposed are damaged: mucous membranes of the nasopharynx and upper respiratory tracts, the lungs, regional lymph nodes of the mediastinum, mucous membranes of the digestive tract and its lymphoid elements. Long after the accident in case of inhalation route the lungs, skeleton and kidneys become critical organs; if uranium entered the organism with water — the liver, kidneys and skeleton.

For uranium decorporation from the victim's organism intravenous injection of chelate compounds, e.g. pentacin, is used. A rather effective means of acceleration of uranium elimination from the organism is isotonic solution of sodium bicarbonate (1.4 % solution of NaHCO_3). 250 mg of such solution is introduced drop by drop intravenously every day during a couple of days until urine pH reaches 8–9. In case of skin contamination it is washed with the same solution.

Plutonium-239. A heavy toxic metal and emitter of alpha particles with the energy 5 MeV.

Inhalation entry of the radionuclide comprises high blastomogenic hazard. Experiments on different animals showed an increase in lung carcinoma incidence at

inhalation of nuclide compounds with different transportability. It has been also established that its forms with low motility, e.g. plutonium dioxide, are more hazardous than easily dissolved ones — citrate, pentacarbonate, etc. If an aerosol containing some plutonium is inhaled, aerosol particles deposit in the lungs. Later on part of them is removed from the upper respiratory tracts with mucus and enters the digestive tract. Those particles that have entered the bronchioles and alveoli are partially transported to lymph nodes with phagocytes, but mostly deposit in the interstitial tissue of the lungs, where nonspecific interstitial pneumonia gradually develops turning into pneumosclerosis. Chernobyl disaster liquidators, who had developed leukemia, had aerosol particles containing plutonium-239 in the mediastinal lymph nodes.

Later on there is a high risk of tumor development. Mortality from lung carcinoma among plutonium manufacture workers increased in 20 years after beginning work with the radionuclide. At that time manufacturing technique was just being mastered and respiratory organs protection was ineffective.

According to findings of Russian scientists, in 2005 it was offered to include into radiation safety regulations for those working with plutonium-239 the following requirements:

- monitoring of internal exposure of personnel must provide control of Plutonium content in the organism by means of high sensitive measurement techniques adequate to the modern manufacturing environment,
- control of plutonium content in the organism must include all the personnel of the main and auxiliary units with indication of its means and frequency,
- non-exceedance of the dose, which increases the risk of development of plutonium-induced lung carcinoma, can be provided only by cessation of work with the nuclide.

Plutonium compounds are slowly absorbed from the digestive tract lumen 1 %. Upon entering the blood the nuclide is deposited in the skeleton and liver. Later on the nuclide is gradually redistributed it is partly removed from the liver and moves to the skeleton.

Wound contamination with plutonium poses a considerable threat. In such cases plutonium easily enters the blood and is distributed all over the organism, still mostly depositing in the liver and bones.

For plutonium decorporation, as well as for uranium removal, intravenous injections of chelate compounds, e.g. pentacin, are used.

Sanitary and Medical Measures Taken in Case of Radiation Accident with Unsealed Nuclides

Therapeutic strategy requires skills and knowledge of physical and chemical properties of radionuclides, their metabolism in the human organism, and means of accelerating their removal from the organism. Treatment must involve a therapist, a medical radiation physicist, a toxicologist, and a dosimetrist.

At the accident site one should collect detailed information:

- concerning the time of the accident and possible routes of radionuclide entry into the organism of each victim (inhalational, through the mouth, eye conjunctiva, skin; if skin integrity is violated),
- concerning physicochemical properties of the radioactive compound,
 - concerning approximate amount of the radionuclide at the accident site.

The determinative principle of first aid and further treatment of victims with radionuclide incorporation is to decrease the level of radiation and thus to alleviate or even prevent the development of radiobiological effects. One uses means that decrease absorption of radioactive substances into the blood, prevent their depositing, and enhance their removal from the organism. The sooner after the accident first aid is provided, the higher probability of its considerable effectiveness.

Emergency measures are the following:

- change clothes after thorough washing of the victim's body, especially of open skin areas (with running water, shower),
- the mucous tunics of the nose, mouth and eyes are washed with 1—2 % soda solution,
- the stomach is lavaged with 2—3 liters of weak boric acid solution or water.

General medical measures depend on the routes of nuclide entry into the organism.

Nuclide incorporation in the respiratory tracts. It is very difficult to decrease absorption from the lungs. Administration of expectorants and mucolytics is ineffective. Lavage of the lungs is a difficult and rather dangerous procedure, because it is conducted under general anesthesia. The risk-benefit ratio in such a case is problematic.

Nuclide incorporation in the digestive tract. The digestive tract can be quite easily decontaminated. Stomach lavage, if conducted in time, is a rather effective measure of decreasing the radiotoxic effect of the contaminant. One can induce vomiting in the first place or as an auxiliary measure in different ways: give ipecac syrup,

inject apomorphine subcutaneously, or irritate the area of pharynx. Absorbents, e.g. activated carbon, can decrease absorption into the blood.

2. STOCHASTIC EFFECTS OF RADIATION

Carcinogenesis

Carcinoma is the most serious effect of low-dose radiation. Extensive examination of almost 100,000 survivors of Hiroshima and Nagasaki bombing in 1945 showed that carcinoma was the only factor of increased mortality rate and reduced life expectancy among these people.

The experience of studying radiation-induced human carcinoma can be summarized in the following way:

- a) skin carcinoma was frequently observed in physicists, radiologists and dermatologists who used radiation during the first years without paying proper attention to radiation protection,
- b) lung carcinoma is usually observed in uranium miners, who inhale radon and dust containing radioactive material during their work,
- c) bone tumors were found in people who had worked at plants manufacturing clocks and devices with luminous dials applied with paint containing radium or another radioactive material. It was common practice for these workers to use their lips to point small brushes with which they applied radioactive paint on the devices. During years there accumulated considerable amounts of radium in their organisms that deposited in the bones and lead to tumor development. This category also includes patients who were injected radium chloride for medical purposes during the 1930s,
- d) until the 1950s for liver examination there was used Thorotrast — a contrast liquid containing radioactive thorium. The patients that had it injected had a higher incidence rate of liver carcinoma,
- e) the Japanese who survived the A-bombing make up the largest group of irradiated people, among which the incidence of leukemia and other cancer types was increased,
- f) there was an increased leukosis incidence among the patients who received radiotherapy for Bekhterev's disease treatment,
- g) among the children, whose thymus was irradiated because of erroneous ideas of its size, there was a higher incidence of thyroid carcinoma,
- h) the women who had received radiotherapy for lactational mastitis and tuber-

culosis patients who often had had fluoroscopy done showed a higher incidence of breast cancer,

- i) the children with scalp dermatomycosis, whose scalps had been irradiated for epilation, showed a higher incidence of thyroid carcinoma and, possibly, encephaloma,
- j) a higher incidence of malignant tumors, leukemia in particular, was observed in the children prenatally radiated during X-ray examination of their mothers.

Although all these cases warn that radiation might induce carcinoma, most of them were sporadic, and just some of them are quite numerous to make quantitative assessment of radioinduced tumor risks possible.

Almost all the data concerning radiation-induced cancer incidence were obtained during examination of people irradiated at a relatively high level 1 Gy and more. There is little information on radiation effects at doses connected with professional activity, diagnostic exposure. And there is no direct information on the action of radiation doses on the world population in everyday life. Therefore there is no other way of population risk assessment at low radiation levels except extrapolation of risk assessment at high radiation doses (not much reliable as well) to the level of low radiation doses.

At first sight it might seem to be an academic question, but it becomes crucial when risk assessment is derived for low doses, e.g. effect of diagnostic x-ray examinations on people or impact of nuclear power stations. The greatest problem is that most data concerning radiation-induced carcinogenesis were obtained from the experience of high-dose exposure of quite small groups of people, whereas risk assessment is required for determination of low dose effects on large groups of people. That's why the hypothesis of thresholdless carcinogenic effects of radiation is officially accepted. The threshold hypothesis means that there is no risk for those irradiated at very low levels. Meanwhile, the linear model presupposes that risk per dose unit at low levels of radiation is equal to that at high levels, which makes it impossible to treat problems of radiation protection thoughtlessly.

There is always a long-lasting latent period between exposure and tumor appearance. It has been repeatedly shown that after radiation tumors will not be detected in irradiated population for a long time mostly for several decades. The most part of latent period between exposure and tumor detection is necessary for tumor to grow big enough to be clinically detected. That is tumor growth rate is the determining factor of latent period duration. But assessment of the delay period will depend on the sensitivity of the method used for tumor detection, accuracy of examination of

irradiated people, and simplicity of analysis of the morphological condition of the organ where a tumor might develop.

Leukemia

Leukemia is the first radiation-induced oncologic disease to develop in population. It causes death in about 10 years after the moment of exposure — much earlier than other cancerous diseases.

When radiation-induced leukemia is considered, it is important to take into account that incidence of different types of hematologic diseases varies depending on the victim's age and radiation dose. It seems that there is no link between cases of chronic lymphocytic leukemia and radiation, whereas chronic myeloleukemia is typical among irradiated grown-ups. Children mainly have acute myeloleukemia, whose incidence decreases with age. These and other reasons require one to be reasonable while assessing the dependence of leukemia risk on radiation dose.

In the period between 1929 and 1957 leukemia was detected in 4 % USA radiologists, which is 10 times more than among non-radiologists (0.4 %). Reconstruction of the doses, to which pioneer radiologists were exposed, indicates that they might have made 2000 rem over 40 years. Practically the whole body was being irradiated. Due to considerable decrease in permissible doses of professional exposure over the next years the incidence of leukemia among radiologists was the same as among other groups of population.

The Japanese who survived Hiroshima and Nagasaki A-bombing were examined very thoroughly, and the data obtained were analyzed repeatedly many times. Exceeding of leukemia incidence was observed in 5 years after exposure, reached its peak 10–15 years later and decreased afterwards. Unfortunately, it was impossible to reconstruct retrospectively the dose of each victim's exposure. Only estimated values can be set based on the distance of the victim from the explosion. It is proved, as expected, that leukosis incidence was inversely proportional to the distance, and for people from remote places it decreased to the level of common incidence. The latent period of disease development inversely correlated with the radiation level: an increase in radiation dose decreases the latent period. In both cities men, as always, appeared to be more sensitive than women. In the 1980s nothing indicated that the incidence of lymphatic leukemia still depended on that past exposure.

It has been determined that among children there are much more leukemia cases induced by exposure of prospective mothers during pregnancy compared to mothers from the control groups. Diagnostic radiologic examinations conducted at the

end of pregnancy and with a dose of fetal exposure up to 30–50 mGy might double the risk of newborn's leukemia.

Though one might consider the risks of such an increase in leukosis incidence after prenatal fetal exposure to be inconsiderable or have serious objections concerning the importance of the study of such cases, still one should be very thoughtful and treat the whole situation as if a considerable increase in leukosis incidence caused by intrauterine exposure has been proved.

During 1935–1944 in Great Britain 14,554 patients received x-therapy for ankylosing spondylitis. Radiation dose varied within 3.75–27.5 Gy. Limited parts of body were mainly irradiated but very often the spine and pelvis were included. Retrospective examination of the patients showed that till 1960 the number of those of them who died from leukemia was 12 times bigger than in the control group of the same age, sex, etc. The latent period lasted 5 years. It was also established that 1 Gy per half the total volume of the bone marrow doubles leukemia incidence.

Therapeutic exposure of the pelvis in women at a dose of 5–6 Gy for the purpose of conducting orchiotomy or relieving the course of benign gynecologic disease, e.g. hemorrhagic metropathia, also caused leukemia in some cases. The incidence is 17 cases of leukemia per 10^6 radiated patients per rem. On the contrary, there is no excess of leukemia cases after exposure of cervical carcinoma. It is possible that higher doses used for carcinoma treatment are lethal for lymphoid stem cells and this lethal effect prevails over leukemogenic effect at such doses.

There has been studied the possibility of leukemogenic effect of long-term exposure in patients from medical centres of the USA who had been treated for hyperthyroidism with iodine-131 that became most widely used in this disease. The control group was the patients treated by surgical method, the main alternative to iodine-131.

Iodine-131 bone marrow doses were 7–15 rad at a relatively low dose rate. Comparison of both groups of patients didn't show any leukemogenic effect of ^{131}I compared to surgery. However, the observed number of lethal cases from leukemia in both groups was higher than expected, which allowed arriving at a conclusion that patients with hyperthyroidism had a higher risk of leukemia.

According to UNSCEAR assessments, approximately two out of every thousand people exposed to 1 Gy will die from leukemia. In other words, if someone was exposed to 1 Gy of total exposure, he is running 1 to 500 risk of dying from leukemia (except for development of acute, but curable, radiation sickness).

Thyroid and Breast Carcinoma

Another most common type of radiation-induced cancer is thyroid and breast carcinoma. According to UNSCEAR about 10 out of 1000 persons exposed to 1 Gy will have thyroid carcinoma and 10 women will have breast carcinoma. However, both types of carcinoma are curable, mortality is especially low in thyroid carcinoma even in case of remote metastases.

Follow-up study of some infants, who received exposure of the thymus due to erroneous diagnosis of its hypertrophy, showed an increased incidence of thyroid carcinoma.

However, in adults carcinogenesis of radiation-induced thyroid carcinoma is quite problematic. Since the 1940s, radioactive iodine-131 has been used to treat hyperthyroidism in millions of patients, among which there were no cases of thyroid cancer afterwards. Lower carcinogenicity of high doses of radioactive iodine may seem paradoxical, but this phenomenon is probably explained by total ablation of the gland tissue at such doses and thus disappearance of substrate for malignant tumor development.

Breast carcinoma can be caused by exposure with a relatively high probability. The first cases of radiation-induced carcinoma are observed 10 years after exposure, and new cases continue to occur during 30 years or more. An average delay of tumor manifestation is probably 25 years.

Three different populations of women, who had been exposed to exposure, allowed estimating an excess of radiation-induced breast carcinoma cases in comparison with control groups of women.

The first of them is a large group of female patients of a sanatorium in New Scotland (Canada). It was found that the women who underwent multiple fluoroscopies during artificial pneumothorax in order to treat pulmonary tuberculosis consequently had breast carcinoma much more frequently than those who did not undergo pneumothorax. The total number of fluoroscopy procedures for each woman usually exceeded 100, and some of them underwent about 500. Development of carcinoma on the same side, where pneumothorax was performed, proved the fact that exposure had induced carcinoma. This observation is probably the most convincing proof of breast carcinoma induction by fractionated diagnostic exposure.

The findings of the Canadian study were confirmed by the results of a continuous follow-up of patients discharged from two antituberculosis sanatoria in Massachusetts (USA) from 1930 until 1956. These patients were examined by means of fluoroscopy (on average 102 fluoroscopy procedures) during the whole follow-up

period. Then, breast carcinoma occurred among them more frequently with an excess incidence of 80 % compared to unexposed population. This study confirms that there is an increased risk of developing breast carcinoma in persons receiving multiple exposures at diagnostic doses, i.e. exposure can accumulate and contribute to breast carcinoma induction. Excess carcinoma risk was higher among women exposed under the age of 30. Excess risk persists for 40 years.

In connection with these studies it should be noted that annual exposure of millions of people during chest x-ray when the central part of the thyroid gland (and breasts in women) is irradiated, significantly contributes to the development of two types of carcinoma in general population thyroid and breast tumors.

It has been established that therapeutic exposure of the breasts to about 2.0 Gy in order to treat lactational mastitis increases the risk of developing breast carcinoma twofold.

There has been detected a significant excess of breast carcinoma cases among the Japanese women who survived the atomic bombing compared with the incidence of this disease in women that were not in the city at the time of atomic explosion. However, these data are doubted, because there was no marital status and lactation duration parity between the groups of women, and these factors are known to affect incidence.

Bone Tumors

Bone tumors are rather rarely observed in man. In general, there were several groups of people exposed, who provided data on radiogenic bone tumors.

The first group belongs to the above-mentioned practice of Bekhterev's disease treatment by means of x-ray therapy in the United Kingdom. The doses ranged from tens to hundreds Gray. Subsequently, the incidence of malignant bone tumors in these patients was four times higher than in general population.

There were also skeletal sarcomas caused by external radiation therapy of inflammatory and dystrophic joint diseases, where much higher doses were given than it is practiced today. Until the 1950s during radiation therapy of benign tumors of the bones and soft tissues patients were exposed to 8–10 Gy.

Much more human bone tumors have been induced by radiation of radioactive isotopes. The first group includes about 770 people, mostly female workers of a plant producing luminous dial watches. Radium-226 entered the body due to the habit of the workers to point the brush, which they used to paint luminous figures, with their lips. In this group of patients there were 51 cases of bone sarcomas and 21 cases of

carcinomas of the epithelial cells of paranasal sinuses and nasal pharynx. None of these tumors was formed due to exposure at doses below 5 Gy, but at high level of radiation the incidence increased sharply, especially in the form of sarcoma.

Another group under study included about 900 patients treated with intravenous therapeutic injection of petheostor, a medication containing radium-224, which was used to treat bone tuberculosis and Bekhterev's disease in Germany. There were 53 cases of osteosarcoma in this group, mainly in young patients under the age of 20 at the moment of radium injection. The age of the exposed person is the most important factor of increase in the risk of radiation-induced malignant tumor development.

Skin Carcinoma

The first malignant tumor probably associated with the effect of ionizing radiation was squamous cell carcinoma on the hand of a radiologist, as reported in 1902. In the following years, hundreds of similar cases were registered among doctors, dentists, physicists and x-ray technicians at the time when there were almost no radiation safety standards at all. In most cases, skin carcinoma was preceded by long-lasting chronic radiation dermatitis. Squamous cell carcinoma and basal cell epithelioma were the most commonly occurring tumors along with sporadic subcutaneous tissue sarcomas. Along with the development of modern safety standards, squamous cell carcinoma has stopped being an occupational disease. It is believed that radiogenic skin carcinoma occurs after acute exposure at doses of 10 Gy after preceding severe radiation dermatitis.

Skin carcinoma with a latent period of 15 years or more may develop in 10 % cases of chronic local exposure with a total dose of 10–100 Gy. There have been cases of carcinoma development in the place of a scar 40 years after radiation dermatitis healing.

Lung Carcinoma

Lung carcinoma is considered an occupational disease of uranium miners in Saxony and Bohemia, but only recently it has been associated with radiation exposure. The number of lung carcinoma cases has significantly increased worldwide during the last few decades, it just indicates that respiratory epithelial cells are susceptible to carcinogen action of the environment. Smoking, air pollution and a great number of chemical elements such as: asbestos, chromium sulfate, sulfur mustard, hematite and asphalt's derivatives, obviously imply carcinogen role. Radiation is only one potent carcinogen in the long carcinogen list.

The great bulk of radiation-induced lung carcinoma is definitive for miners, who are impacted by radon in the mine atmosphere. The natural deposits of radioactive materials in the solids of the Earth are exposed to breakage undergoing many levels until they become a stable lead isotope. Radon is one of these levels, unlike the other elements of breakage range it is a gas. In the confined mine space, workers respire it and irradiating alpha particles some radon atoms decay to the next element of radioactive chain, which is solid and thus deposits in the pulmonary tissue. All other decay steps, which cause intense local tissue exposure, happen in the lung.

There is a clearly determined excess of lung carcinoma cases among uranium miners of Colorado plateau (the USA) and Czech Republic, workers of nonuranium mines in Sweden, and miners of Newfoundland fluorspar mines. It is difficult to adequately estimate lung carcinoma cases caused by smoking and radon, because there are very few non-smoking miners to form an adequate control group. It is quite possible that smoking is a cocarcinogen, not just another carcinogenic factor. It is also difficult to estimate the dose in the critical cells of the basal layer of pulmonary epithelium on the basis of radon concentration in the air respired by the patient.

Carcinoma of Other Organs and Tissues

In the 1940s–1950s for liver examination Thorotrast, a suspension containing radioactive thorium, was used as a radiocontrast agent. Hepatic carcinoma developed in 20 and even 40 years in such patients. Such a long latent period is obviously connected not with the biological properties of this type of tumor but with too slow thorium accumulation sufficient for carcinogenesis (slow disintegration of the radionuclide with alpha-particles emission) prevented from conducting a correct epidemiologic research. But at the end of the 1950s this suspension was withdrawn from use.

Total incidence of carcinoma of different localization in A-bombing survivors was as twice as high in comparison with other groups of Japanese population. As in leukosis cases, the incidence increased depending on the distance from the explosion epicenter, i.e. was connected with the size of radiation dose and probably little dependent upon the age of the victim.

Table 2 shows an expected incidence of mortal malignant tumors at exposure dose of 10^3 man-Sv.

Expected Incidence of Radiation-Induced Mortal Malignant Tumors and Genetic Defects

Critical Organ	Disease	Number of Cases per 10³ man-Sv
Whole body, bone marrow	Leukemia	2
Thyroid gland	Thyroid carcinoma	0.05
Breast	Breast carcinoma	2.5
Skeleton	Bone tumor	0.5
Lungs	Lung tumor	2
All other organs and tissues	Tumor of other organs	5
Genital glands	Genetic defects	4

Genetic (Teratogenic) Effects of Radiation

Studying genetic effects of exposure to radiation is even more difficult than studying cancer. Firstly, complete identification of all genetic defects can only be carried out by observing a few generations, and secondly, it is impossible to distinguish these defects from those that are caused by many other factors, or those that occur spontaneously.

About 10 % of all live-born infants have some albeit minor deficiencies, from color blindness to severe conditions such as Down's syndrome, Huntington's disease, etc. A significant number of embryos and fetuses with severe deficiencies do not survive until birth. Almost half of all cases of spontaneous abortion are associated with abnormalities of the genetic material. And even if a child with a birth defect is born alive, the probability of its survival until its first birthday is only 20 %.

Genetic disorders can be classified into two main types: chromosomal aberrations, such as change in the number or structure of chromosomes, and mutations in the genes themselves. The latter divide into dominant ones, which occur in the first generation, and recessive ones, which occur as phylogenetic manifestations only in those cases when the same gene has such mutation in both parents. Recessive mutations may not manifest themselves for many generations or be completely unnoticed. Both types of anomalies may result in hereditary diseases in subsequent generations, and may remain latent forever.

The data on ionizing radiation effects on human embryos and fetuses were obtained from the experience of therapeutic exposure of the abdomen of pregnant women and studies of children exposed in utero in Hiroshima and Nagasaki. The

general conclusion is not unexpected — radiosensitivity of the human fetus is high, and the younger the fetus, the higher its radiosensitivity.

The damaging action of radiation manifests itself in children that survived in the form of various anatomical and physiological abnormalities, physical and mental retardation, or their combination. The most common deficiencies include microcephaly, hydrocephaly, and cardiac abnormalities. Congenital abnormalities associated with exposure in utero are called *teratogenic effects of radiation*. They should be considered as stochastic effects, since the nature of their occurrence is probabilistic and they have no certain dose-dependent threshold for their occurrence.

The period of high radiosensitivity of human embryo is time-expanded. It begins from the moment of conception, that is, the time of merging of the genetic material from the sperm and egg, and ends in approximately 38 days after implantation. This period of embryonic development is characterized by the beginning of formation of all organs by means of differentiation of the primary cells. During this process the cells become high-sensitive to radiation, in particular with respect to chromosome affection, so birth defects can occur under the action of relatively low exposure levels. Later on the sensitivity of the fetus to the teratogenic effect of radiation decreases. Approximately 40 days after conception appearance of gross radiation-induced congenital malformations is highly unlikely. It should also be remembered that the embryo and fetus during almost the whole period of pregnancy have neuroblasts, cells with high radiosensitivity. The greatest risk of developing mental defects is observed when a fetus is exposed in the period between the 8th and 15th weeks of pregnancy.

There isn't any threshold for chromosomal mutations. Under any low levels of primary cells radiation there is a possibility of one or several genes exposure and development of one or several mutations. Any dose of intrauterine exposure increases the probability of primary cells mutations. Moreover, mutagenic radiation effects are being irreversibly accumulated. Natural mutations occur spontaneously: their quantity varies depending on the gene type, that's why it is difficult to assess. However, it is assumed there is approximately one mutation per 50,000 genes per generation. Radiobiologists took many efforts to determine the size of radiation dose that doubles this incidence and experimentally established it to be about 0.3–0.5 Gy. But these experimental data shouldn't be accepted unconditionally not only for the human being but even for animals due to many reasons. The main one is that radiation-induced mutations have no specific characters, i.e. cannot be differentiated from spontaneous natural ones.

Nevertheless the concept is practically convenient for assessment, though approximate, of possible radiation risks.

Observation of the descendants of people exposed in Hiroshima and Nagasaki showed no considerable increase of congenital effects. This proves the fact that experimental data extrapolation on people is not a serious disregard of protection. There have been determined changes in correlation of different sex of children of women, whose coxofemoral part was irradiated. This can be explained by genetic factors, in particular — more serious mutations incompatible with cell life develop in male embryos due to dimorphism of their chromosomes. It is not excluded that this very mechanism promotes a decrease in the number of congenital defects in descendants of irradiated women due to elimination of chromosomal mutations by means of embryo death. The same deviation in sex correlation of children is observed in descendants of women who survived Hiroshima and Nagasaki bombing and mothers who received radiation therapy or worked with ionizing radiation sources.

Thus, hereditary and oncologic risks for further generations after exposure of the gonads of prospective parents are not high in comparison with the natural ones. Such exposure cannot be the basis for reproduction restriction or termination of pregnancy. However, minimization of gonadal doses during medical exposure is recommended.