# LESSON 2

## RADIOBIOLOGY BASIS.
## PRINCIPLES OF RADIATION SAFETY CONTROL

### 1. Common mechanisms of the ionizing radiation biological action. Direct and indirect action. Molecular effects

The biological effects of ionizing radiation (IR) to all of living organisms from one-celled to the mammals have general patterns which are specific for this physical factor:

• the grave consequences for an organism appear of action the wretched amount of absorbed IR energy in the molecules of its tissues (at the even lethal dose of irradiation of man absorbed energy in his tissues is equivalent to thermal that directly would increase the temperature of the suffering body on 0,001°C);

• the certain time (latent period) have to pass after exposure of organism to an appearance of consequences which can has duration minutes, hours, weeks, months and even years depending on the dose of exposure and nature of the expected effect;

• different organisms can have specific and individual differences in a sensitiveness to action of IR *(radiosensitivity)* which can be differed at ten, hundreds and even thousands times;

• different functions and tissues of the same organism have different radiosensitivity;

• expected results of the IR effect can be considerably modified as in the side of their strengthening so of weakening till about complete prevention by influence on an organism by the factors of different nature before or after exposure.

Fully clearly, that the basic specific signs of radiation biological effects are linked with peculiarities of this physical factor:

- its to a certain extent «total penetrability»,
- a simultaneity of action on all of structures of organism in the site of irradiation,
- specificity of mechanisms of development of changes in an organism on principle of the chain branched reaction with gradual growth of their (changes) degree,
- ability of local energetic violations in biologically meaningful macromolecules to migrate outside a place of their primary origin.

It follows to add to it, that no one of biologically meaningful factors of environment of biological, chemical or physical nature attracted such attention of researchers and such deep and overall study from the side of conformities to the law of their influence on organized matter, as IR. Not by chance, that yet at the beginning of 40th of past century new science *radiobiology,* fully devoted to these problems, was officially acknowledged.

In the previous part it was already specified that the main feature of IR effect is two clear physical phenomena: excitation and ionization of atoms and molecules of the exposed matter which are initial in the chain of structural and chemical processes. These phenomena can finally be completed by the change of properties and composition of the matter.

When speech goes about exposure to ionizing radiation of the organized matter, these initial processes follows examine separately for a water phase and structural organic molecules, as changes of the last are give direct consequences related to radiation violations of functioning of the living system, while excitation and ionization of molecules of water does not have direct biological value, and only the products of these processes can stipulate violation of functioning of macromolecules with substantial consequences. Therefore ionization of macromolecules and molecules of water carry the name of «direct» and «indirect» effect of radiation, accordingly.

### Direct IR action

Any types of radiation: x-rays, gamma-rays, charged and uncharged particles can pass energy directly to critical targets in cells the atoms of which are ionized or become excited that begins the chains of events, which are completed by biological consequences (fig. 1). Such form of physical mechanism of IR action more, however, inherent to the heavy particles, such as alpha-particles, protons and neutrons with high-density ionization.

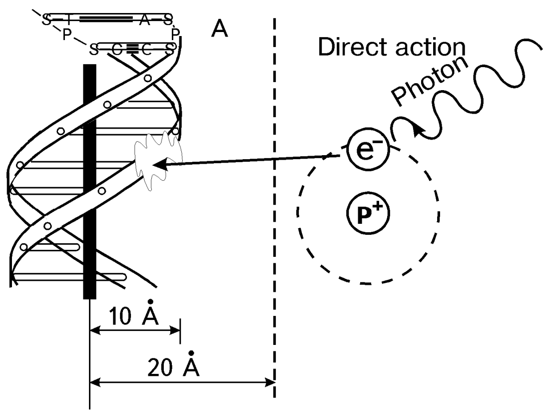


Fig. 1. Illustration of IR direct action: as a result of collision of photon with an atom, the last is ionized with tearing away an electron from its shell which becomes the instrument of destruction of structure of important macromolecules with the proper consequences for a cell; a photon can ionize and directly one of atoms of macromolecule with the same biological consequences.

### Indirect IR action

As known, from 70 to 90 % of the mass of tissues of organism are made by water that is why considerable part of absorbed energy of IR usually falls on this phase of internal medium of organism. Radiation transformations of water carry the name *of radiolysis*. The process of radiolysis of water takes place in a few stages:

- at first a molecule is ionized by a charged particle or photon (fig. 2):

$$H_2O \rightarrow H_2O^+ + e^-$$

- the ionized molecule is laid out on radical $OH^\bullet$ high of reaction ability and proton:

$$H_2O^+ \rightarrow H^+ + OH^{\bullet}$$

- a "breaking" quickly interacts with one of surrounding molecules of water with the origin of the strongly excited molecule of $H_2O^-$, which, in same queue, dissociates on two radicals: $H^{\bullet}$ and $OH^-$

$$H_2O + e^- \rightarrow H_2O^- \rightarrow H^{\bullet} + OH^-$$

- a hydrogen peroxide appears from two radicals of $OH^-$:

$$OH^{\bullet} + OH^{\bullet} \rightarrow H_2O_2$$

- and *at presence of oxygen* there is the reaction:

$$2H^{\bullet} + O_2 \rightarrow 2HO^{\bullet}.$$

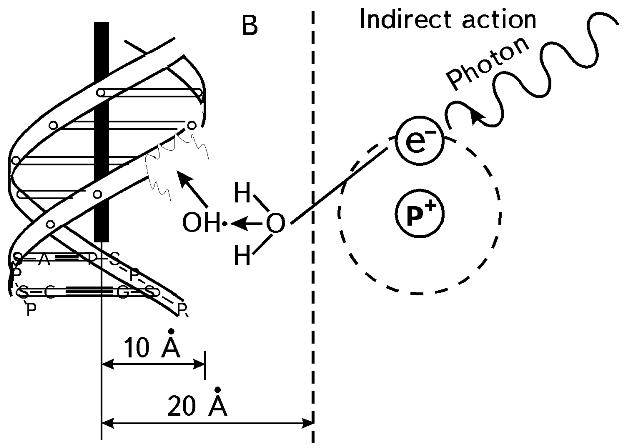


Fig. 2. Illustration of the IR indirect action: in the result of ionization of water molecules radicals $OH^{\bullet}$ and hydrogen peroxide are forming, which chemically destruct macromolecule

Hydrogen peroxide ($H_2O_2$) and radical $OH^{\bullet}$ diffuse in an environment, oxidizing and destroying organic structural molecules: DNA, proteins, pyrimidine and purine bases (fig. 2).

Unsaturated fat acids and phenols also are undergone to oxidizing, as a result of what lipidic and chinchonous radiotoxins appear. Radiotoxins repress the synthesis of nucleic acids, act on the molecule of DNA as chemical mutagenes, change activity of enzymes, react with lipidic-protein intracellular membranes. Purine and pyrimidine bases are undergone to deamination, oxidizing of rings and opening of heterocycle, i.e. to considerable destructions of molecules, carbohydrates to oxidative disintegration with formation of uronic acids and cleavage of aldehydes from the molecules.

Under act of radiation the molecules of simple proteins are undergone to the following changes (fig. 3):

- configuration changes without change of molecular mass, but with weakening or loss of physical and chemical, and biological properties;
- formation of «seaming» inside molecules and between molecules with their aggregating and increasing of molecular mass;
- destruction of molecules with disintegration on fragments with small molecular mass;

- chemical transformations of functional centers of molecules of protein with loss specific properties by them: inactivation of protein, in particular enzymes.

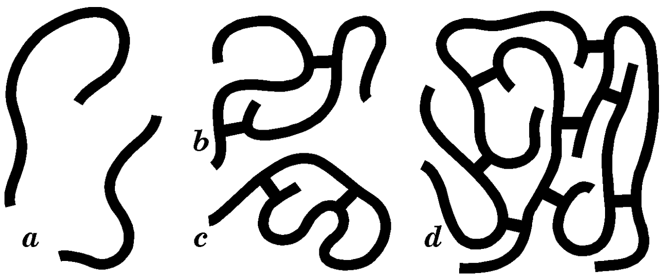


Fig. 3. Illustration of morphological radiation damages of albumens. **a** — the native molecules of proteins, **b** — intermolecular bridges which connect two molecules by chemical bond, **c** — internal molecular bridges, **d** — formation of net from a few molecules

At nucleic acids IR can cause breaks of one or rarer two fibers of spiral or formation of bridges between separate molecules (fig. 4). Fully clearly, that structural violations will be accompanied by functional insolvency of the molecules.

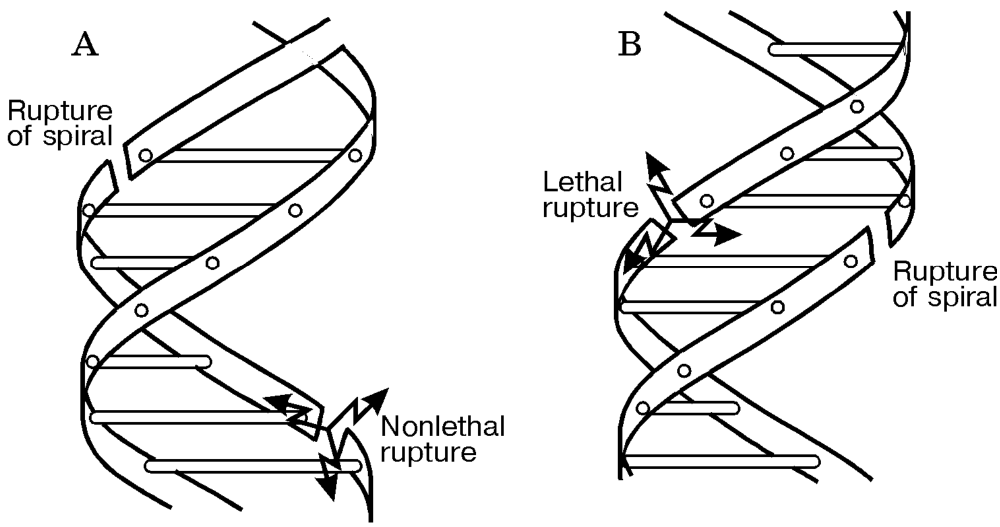


Fig. 4. Radiation breaks of spiral of DNA: A — single, B — double

Consequently we see that any of molecules which enter in the composition of structural elements of cells, at the radiation effect can be undergone direct or mediated destruction with the loss of function and formation of chemically active radicals. Another matter, that such destructions are possible at insignificant doses of exposure by rare and refurbished factors of internal or external origin.

Thus primary radiochemistry reactions cause direct and mediated (through the products of radiolysis of water and radiotoxins) damages of the most important biochemical components of a cell: nucleic acids, proteins, enzymes. In subsequent enzymes reeffects are changed stormily: enzymes disintegration of proteins and nucleic acids increases, the synthesis of DNA goes down, the biosynthesis of proteins and enzymes is violated.

## 2. Modification of radiosensitivity

At the beginning of 50th years of 20th century the first reports appeared in relation to possibility of real attenuation of IR effect, even lethal, by previous introduction to the organism of some chemical compounds which got the name of *radioprotectors* (from *latin* protector). The process of radiation damage attenuation was named a *chemical protection.*

Matters, which contain SH-groups (cystamin, glutathione etc.), active regenerators, inactivators of oxygen behave to the most effective protectors.

A reverse problem is strengthening of effect of IR is developed at the same time. It is important for radiation oncology, as radiosensitivity of many tumors hinders the effective use of radiation therapy in such cases, and an artificial increase of their sensitivity to the effect of IR can be a way to the improvement of result of radiation treatment.

For the estimation of degree of radiosensitivity modification three criteria are used:

- absolute value of difference between the indexes of research of radiosensitivity in experience (experiment with a modifier) and control (experiment without a modifier);
- index of effect is relation of the indexes in experiment and control;
- factor of dose change (FDC) is relation exactly of effective doses in experience and control.

*Oxygen effect* is phenomenon of radiation damage strengthening at the increase of concentration of oxygen. A quantitative index of it is *OER* is *oxygen enhancement ratio*, analogue of FCD for the modifiers of radiosensitivity (fig. 5). The phenomenon is universal and appears at the effect of sparsely ionizing IR in all types of the organized matter. The effect appears even at substituting of anaerobic terms by air.

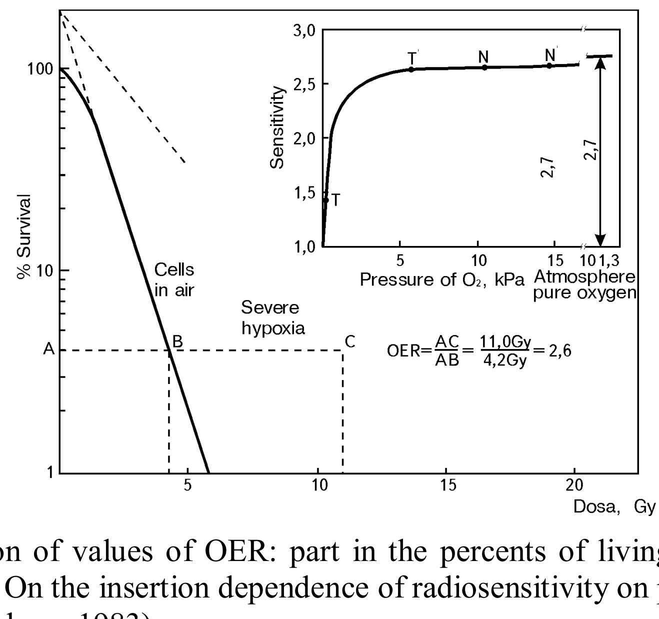


Fig. 5. Illustration of values of OER: part in the percents of living cells at a presence and absence of oxygen ($O_2$). On the insertion dependence of radiosensitivity on partial pressure of $O_2$ (for H. Johns and. J. Cunningham, 1983)

On the scheme (fig. 6) the chronologic sequence of the physical and chemical, and biological phenomena in the exposed tissues is presented. On the first stage (during the first $10^{-18}$–$10^{-12}$ sec) there are especially physical processes of radiation energy absorption by ionization and excitation of molecule atoms of environment.

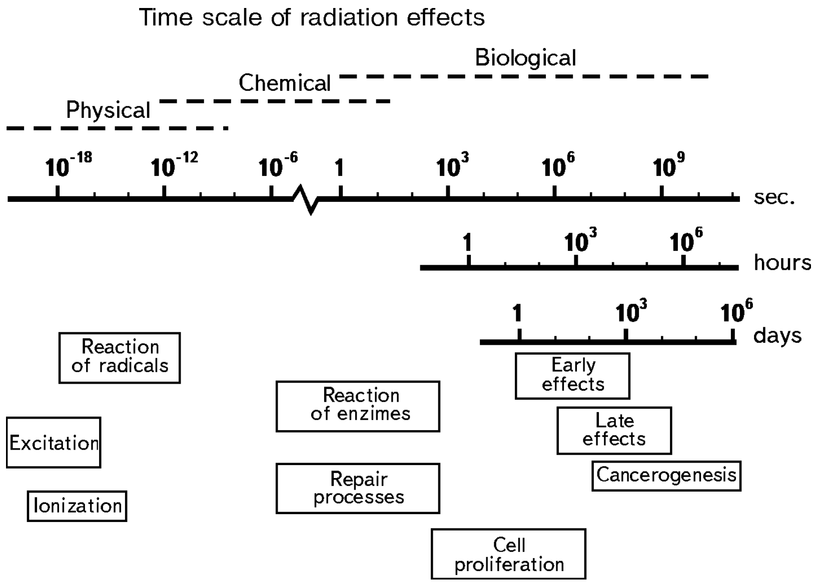


Fig. 6. Chronologic sequence of the physical and chemical, and biological phenomena is in the radiation-exposed cells and tissues

This phenomenon is not specific for the organized matter and it is taking place identically in any environment. Then through the millisecond interval radiochemistry reactions begin with formation of free radicals. Chemical protection (radioprotectors) starts acting exactly on this stage, from one side, and oxygen effect of the strengthening of future radiation damage from other. Next stage is beginning of damage of macromolecules, enzymes reactions renewal of damages. Duration of this stage (if exposure finished) are seconds or dozens of minutes: such time is exactly necessary all formed radicals to react with macromolecules with development of the proper consequences for the last (damage of genetic material of cell, biochemical damages, possible early physiologic effects). Thereon the initial period of physical and chemical changes in atoms and molecules actually finishes, and especially biological, pathophysiological and pathomorphological changes begin to develop:

- delay of cells division,
- metabolic disturbance morphological damages.

### 3. Cellular effects. Bergonie-Tribondeau's low.

### Latent period

The most important difference between the effect of IR and other chemical and physical agents consists in that an initial effect in the first case can be so weak, that some time in general it does not appear. This period between exposure and appearance of signs of damage is named *latent*. During latent period growth of amount of structural and functional violations in the view of chain reaction goes.

Duration of latent period depends on the numerous factors of biological nature, however mainly related to the size of absorbed dose. The greater it is, the shorter latent period, up to the almost immediate display of effect of irradiation. But after exposure in the most ordinary absorbed doses, between 1 Gy and 10 Gy, latent period makes a few hours or even days. Such period for some effects of exposure can be too long, even decades, and that is why is hard to say is there complete renewal of cells and tissues after exposure.

**Variants of a cell death**

At exposure to ionizing radiation, all of intracellular structures are damaged without an exception, as a result of what it is possible to register a lot of various responses of a cell: delay of division, oppression of synthesis of DNA, damage of membranes and organelles etc.

Intensity of these reactions depends on that, at what stage of cellular cycle an irradiation took on a place.

*The life cycle of cell (cellular cycle, mitotic cycle) consists of the successive stages (fig 7):*

- mitosis (M) — process of division of cell and
- *interphase,* which is divided into successive:
    - *presynthetic (G1),*
    - *synthetic* (S) and
    - *postsynthetic* (G2) periods.

There is a process of synthesis of DNK in synthetic stage.

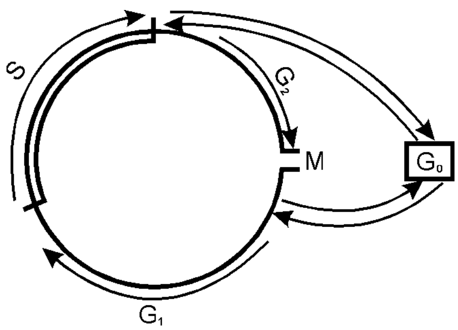


Fig. 7. Mitotic cycle of a cell. M is mitosis, $G_1$ is presynthetic period, S is period of synthesis of DNA, $G_2$ is postsynthetic period, Go is phase of rest (a cell passes for it or after completion of synthesis of DNA, or on completion of mitosis; in the phase of rest a cell is until a certain stimulus will not wake up it again to enter in $G_2$ or $G_1$ periods)

Duration of each stage of cellular cycle varies in relation to each other, usually, disposes in such sequence:

$$M < G2 < S < G1$$

In tissues with an active update (epithelium of intestine, bone marrow, skin, etc.) and also in malignant tumours with high proliferative ability the term of cellular cycle makes 10−48 hours. Protracted periods are $G_1$ and S, the shortest is M with duration of 30−60 minutes.

In little updatable tissues most of cells are in $G_1$-period, the term of which can arrive at distinguish weeks, months or even years, as for example in CNS. It is also observed in occult malignant tumours and latent metastases which can clinically show up through many years after as though treated tumour. Because of this circumstance the additional stage of cellular cycle is now selected G0. If a cell is in such state, it is accepted to consider it out of limits of cycle, or in *a state of rest.* Such cells are a reserve of repopulation of tissue in case of death for diverse reasons of part of pool of cells, for example, renewal of growth of tumour after radiation treatment.

At 1906 Bergone and Tribondo (Bergonie, Tribondeau) formulated a law which became classic:

«X-rays acts on a cell with greater intensity if:

- its reproductive activity is greater,
- it will be more divided during its life and
- its morphology and function is less certain».

Actually the major conformities of biological IR effect were formulated at cellular level in these positions in integrated form.

Many the radiation reactions of cell are completed by renewal because they are result of the structures damage, a loss of which or built quickly or remains unnoticed. Such transient cellular reactions are named *the physiology* or the *cumulative* of *exposure effects.* Usually, similar reactions show up in the nearest time on exposure and disappear in course of time. The most universal their form is *a delay (suppression) of cellular division* or *radiation blocking of mitoses.* Duration of division delay depends on the dose of exposure to ionizing radiation and shows up in all cells of exposured population independently of subsequent fate of each them it will survive or perish.

Time of division delay also depends on the stage of cellular cycle, in which it was exposured. Protracted division delay can be in the cases of exposure in the stage of synthesis or postsynthetic stage. Exposure during mitosis in most cases or insignificantly affects his duration, or mitosis is completed without a delay.

Among many signs of IR effect on the vital functions of cells the suppression of division is the most important. In this connection under *a cellular death* or *the lethal effect of exposure* in radiobiology the loss by cell of ability for proliferation is understood. And opposite the cells are considered survived when they only retain of ability to an unlimited division, i.e. to *forming of a clone.* Thus, in this case they suggest *reproductive death of cell* which is the most widespread form of radiation inactivation of cells.

But after the effect of exposure in high doses *complete suppression of mitosis* comes, when a cell continues to live, but irreversibly loses a capacity for a division. Giant cells can appear as a result of such reaction, sometimes even with a few sets of chromosomes the result of their replication within the limits of undivided cell *(endomitosis).* Such cells are non-viable.

Main reason of reproductive death of cells is structural damages of DNA from the IR effect. They are revealed by cytological methods as *chromosomal aberrations* as fragmentation of chromosomes, forming of chromosomal bridges, dicentrics, circular chromosomes, intra- and interchromosomal exchanges. Part from them mechanically hind the division of cell, other result in the loss of genetic material, which causes deficit of metabolites and, as a result, biological death of a cell (fig. 8.).

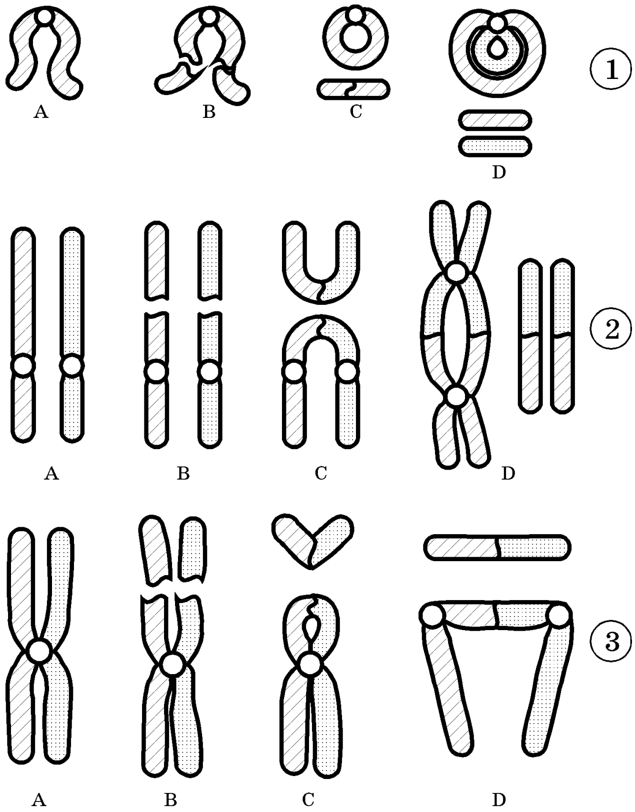


Fig.8. Radioinduced chromosome aberrations: 1 — formation of rings: A — chromatid in early interphase, B — radioinduced break of every arm of the chromatid with formation of «sticky» ends, C — «sticky» ends united to form a ring and a fragment, D — after chromosome replication — doubling of a ring and a fragment; 2 production of a dicentric: A — separate chromatids of two isolated chromosomes, B — radiation breaks in both chromosomes, C — «sticky» ends of chromosomes united with formation of exchange between chromosomes, D — replication during the synthetic phase of DNA with formation of dicentric chromosome and fragments; 3 — forming of anaphase bridge: A — a chromosome in the phase of $G_2$ after replication, B — radioinduced breaks of both chromatids, C — «sticky» ends united, D — at anaphase the section of chromatin between the centromeres stretched across the cell between the two poles (E. Hall, 1978).

Another form of radiation inactivation of cells is *interphase death* comes up to beginning of mitosis. At too high doses of exposure (dozens and hundreds Gy) the death is observed directly «under a ray», or soon (during 2–6 hours) after exposure. There is a hypothesis, that interphase death of a cell is the mitochondrial way of *apoptosis,* which is induced by the damage of DNA by the effect of radiation in high doses. *Apoptosis* is special programmable type of elimination of a cell cage by division of it into pieces («apoptosis corpuscles»), which farther are phagocytized by macrophages and neighboring cells.

In the nucleus of cells a few dozens of molecules of DNA are contained with general length of 1–2 m. They have permanent connection with proteins, which take part in support of structure of interphase chromatin, forming of chromosomes and transfer of genetic information. Exposure causes the various damages of DNA, that will become the main reason of inviability and death of a cell:

- breaks of its molecules,

- formation of alkaline-labile connections,
- loss of bases and changes of their composition,
- change of nucleotide sequences,
- sewing together of DNA—DNA and DNA—protein, etc.

Already at a dose in 1 Gy approximately 5000 bases of molecules of DNA in every cell of man are damaged, 1000 single and 10–100 doubling breaks appear, each of which can become reason of aberration. Doubling breaks of molecules of DNA are usually fatal for a cell. But the damage of a cell is not limited by only the damage of nuclear apparatus. There are structurally metabolic changes also at organelles of cytoplasm: mitochondria is power «stations» of cells, ribosomes is «factories» of the synthesis of proteins, lysosomes is «depositories» of enzymes, etc. The damages of organelles have various character and different consequences for functioning of cell depending on its setting in tissue and organism. It is important and damage of superficial membrane of a cell with the increasing of its permeability and, as a result, violation of exchange of matters with an extracellular environment.

## 4. Tissue and organism effects

If we pass to the examination of radiation effects in an isolated cell to the level of tissue or organism, all of the phenomena are complicated that is caused by the next factors:

- not all cells are damaged in the equal degree
- tissue effect doesn't the sum of cellular effects
- for the aggregated reactions of tissues and organism as a whole it is hard, if in general possibly, to select various local effects and varieties of general reactions.

Tissue cells are extensively dependent one from another and the environment. The physiology and functional state of any cell is not indifferent not only for «neighbors» but also for all of population of them in tissue. It is well known, for example, that cicatrization of wound is provided by speed-up reproduction of remaining cells for substituting for the lost part, whereupon the rate of cellular division is normalized. In the mechanism of such stimulated and damp influences which cells are undergone, not only local factors but also systems of general support of homoeostasis of organism take part. There is not a doubt in participation of those universal mechanisms in realization of tissue and system reactions on exposure. In addition, on tissue radiosensitivity other factors have a large influence, such as a degree of blood flow, size of the exposed volume and others like that. Consequently, it does not follow to examine radiosensitivity of tissue only from position of radiosensitivity of components of cells, not having regard to general pathological and morphological factors. As an example: erythroblasts have different radiosensitivity depending on their place in the organism in spleen or bone marrow. All of it, sure, complicates the estimation of radiosensitivity of tissues, but however does not cast aside the leading role of cytokinetics, which determines a type and degree of radiation reactions on all of levels of biological organization.

Conformities of the damage of integral organism are determined by two factors: *radiosensitivity* of tissues, organs and systems, substantial for the survival of organism, *value of the absorbed dose* of exposure and its distribution in a space and time.

*Each of them separately and in combination determine the overwhelming type of radial reactions (local or general), specific and time of their appearance (early, delayed or late) and their meaningfulness for an organism.*

The classic example of radiation damage of organism of an animal and a man is *acute radiation sickness* which appears after a general, even a single external exposure. In such case exposure simultaneously acts on all of the systems, organs, tissues and cells in the identical dose. But the best comprehension of basic signs of radiation damage is provided by comparison of them with absorbed dose exactly in «critical organs», under what vitally important organs and systems are understood which in the range of dose of present radiation influence fall out the first, that and draws death of organism in certain terms after exposure.

Thus, *there is strict dependence between the level of absorbed dose and mean life-time*, which is defined by the radiosensitivity of the separate critical systems.

Comparison of radiosensitivity of separate tissues must be done only on the basis of adequate criteria. For example, bone marrow and liver have very different radiosensitivity, at the same time it is possible to see in their cells the almost identical amount of chromosomal aberrations at the equivalent doses of exposure. However, at comparison of remote consequences of these organs exposure, we see striking differences. Consequently, the concept of radiosensitivity of tissues or organs is very relative. General radiosensitivity of an organism must be equated with radiosensitivity of bone marrow, because its radiation aplasia is sufficient for death of the organism.

For the quantitative estimation of radiosensitivity of organism they use the *survival curves* or *mortality curves,* on abscissas axis of which there is shown dose of total irradiation and on the ordinate axis is percents of lost through certain time (fig. 9). For all mammals species such curve has a S-like form: in the range of low doses death of animals is absent at all, the first cases of death are observed at a dose which is named *minimal lethal,* at subsequent growth of the dose frequency of death of individuals grows, and at the level of certain dose which is named *absolutely lethal,* all radiation-exposed animals are perished.

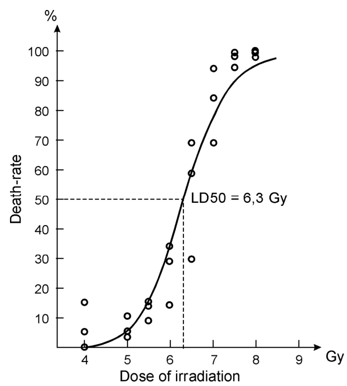


Fig. 9. The curve mortality-dose for mammals at a total external irradiation. LD50 is numeral index of lethality of animals of certain kind, which makes the value of dose at which in certain time the half of the irradiated individuals die.

It is possible to use the curves of death-dose comparison of radiosensitivity of tissues of the entire organism (for example, man), conducting research on the cultures of the isolated cells, tissues of different types. Exactly in such experiments the practically important row was created from tissues in order of diminishing of their radiosensitivity: *1) embryo,* 2) *fetus,* 3) *lymphatic cells,* 4) *bone marrow,* 5) *epithelium of digestive tract,* 6) *ovaries,* 7) *testicles,* 8) *endothelia of capillaries,* 9) *epithelium of salivary glands*, 10) *epithelium of hair follicles,* 11) *areas of growth of bones,* 12) *breast,* 13) *lens of an eye,* 14) *sweat and sebaceous glands,* 15) *epidermis*, 16) *liver, kidneys,* 17) *bones of adults,* 18) *cartilage,* 19) *epithelium of alveoli of lungs,* 20) *CNS,* 21) *muscles.*

But there is also rating of radiosensitivity of tissues after other criteria, namely after their functional and morphological replays on exposure in an integral organism. The difference of the range of radiosensitivity of tissues after such criterion in comparing with the previous one consists in that *CNS, adrenals, thyroid and autonomic nervous system* stand at once after an *embryo* and *fetus.*

There are an individual, species, sex (females, usually, are less sensible to an irradiation) and age-old differences in radiosensitivity.

Fig. 10 shows of dependence of radiosensitivity of mice from their age. As an index of radiosensitivity $LD_{50/30}$ is used, that dose due effect of which 50% exposed individuals die during 30 days. It is possible to see that 50% of the youth die at a low dose, i.e. their radiosensitivity is high. Than with the age $LD_{50/30}$ grows, goes out on a short plateau and at senescence diminishes again.

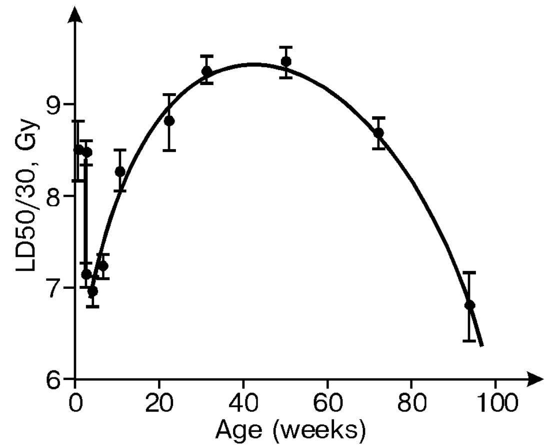


Fig. 10. The curve of the dependence of radiosensitivity from age of organism. As an index of radiosensitivity is taken $LD_{50/30}$ back proportional to radiosensitivity.

Some researchers are inclined to explain also and interspecies differences in organisms of mammals by the features of kinetics of cellular populations of the critical organs, the determinants of damage of which are the proper stem cells.

In relation to the radiation damages of organism two systems hemopoietic and digestive have a major value with high-rate of the cellular renewal.

The bone marrow has too high radiosensitivity. The damage of the system of hemopoiesis of that or other degree as typical phenomenon is observed always after a general exposure and even local, in particular at radiation therapy of oncologic diseases. As it is known, the main setting of bone is producing of the mature high-differentiated cells of blood. In the norm the elimination of every cell of peripheral blood or of the other site of organism is compensated by forming on the average of one analogical cell in bone marrow. Passing one or a few divisions, a cell gradually differentiates, loses a capacity for a subsequent division and includes in *a non-proliferating pool*, where finally becomes functionally valuable, in a state of maximal preparedness to substituting for the cell of blood which was eliminated from function under any circumstances. Such a way the functioning system is self-keeping, constantly substituting for losses which become the original stimulus of activating of all of the previous stages of development of the specialized cells, due what *the permanent cellular renewal of organism* is carried out.

In any cellular system of renewal under the effect of exposure violations of dynamic equilibrium between the separate pools of cells, drawing heavy functional disorders in the system and, obviously, proper consequences for an organism, appear. Clear comprehension of mechanisms of such violations is possible to get from the analysis of reactions of the exposed isolated cells, conformities of which are saved for the tissue systems of integral organism. These are the basic radiobiological reactions of cells which determine typical violations of every system of renewal:

- temporal delay of division of all cells regardless of next each fate or it will survive or not;
- death of the low-differentiated cells and those which are in the stage of division;
- minimal changes of duration of process of the cellular maturing, and also a duration time of life of the most matured cells and speed of arriving of them in the functional pool.

As a result three pools of cells the stem cells, cells in the division and maturing cells are devastated at once and quickly (in the nearest days after an irradiation), and the pool of the mature functioning cell is devastated gradually, later, when their natural losses will stop to be compensated from the devastated previous pools. Exactly to it at an irradiation in doses up to 10 Gy the typical *bone marrow syndrome* develops in an organism.

The mechanisms of radiation damages of hemopoietic system are typical for all systems of cellular renewal, in particular for the cells of the digestive system in which the *intestinal syndrome* of radiation damage develops on the analogical scenario.

General radiation reactions of mammals as the function of the dose and time is determined by four cardinal parameters of cellular populations:

- size of pool of stem cells;
- radiosensitivity of cells and ability of them to next renewal;
- cellular proliferation and
- term of functioning of mature elements.

The taking into account of these factors enables enough reliably to forecast development of events after the irradiation of separate sites of a body, if certainly parameters of the exposed tissues are defined. In addition, leaning against the considered conformities, it is possible to plan the course of radiation therapy with the least extraneous consequences and to forecast its efficiency.

At the total exposure of a metazoan in many tissues it is possible to find out not necrocytosis, but changes of cell's functions, appearance in tissue quantitative and qualitative changes in composition of metabolites. The last, operating on nervous receptors, spreading in a humoral way, cause deep changes in the neurohumoral regulation of exchange of matters and, as the result, *generalization of pathophysiology violations.* The changes of exchange of matters in ductless glands drawn the release of inadequate amount of hormones in the blood, causing violation of proteins, carbohydrates and lipids exchanges. One of universal and specific signs of a radiation damage of an integral organism is common increase of permeability of blood-tissue barriers in all, without an exception, tissues and organs, in particular the blood-brain barrier, as a result of what disorganization of regulation of exchange of matters between cells and extracellular environment become, change of alkaline-acid and electrolyte equilibrium in tissues and blood appears.

Endocrine glands are radioresistant, although at general exposure their reactions are well-known. But it is difficult to define, whether these reactions are the result of damage directly of cells of gland, or they represent operating of radiation on other systems and the whole organism. It is possible to assume that violations of balance of hormones, especially of the thyroid, after general exposure can be consequence of the known reaction of the hypothalamo-hypophysis system, taking into account the connection between thyro-, adrenalo- and gonadotropic factors of hypophysis.

## 5. Post-exposure reparation

Radiation damages are partly restored depending on the dose of exposure. This ability of tissues, organs or an organism is related to the capacity of cells for renewal from damages caused by exposure. The phenomenon of the post-exposure is predefined by the fact that, at the certain terms, lethal damages of cells can be liquidated by the restored systems. For example, dose of x-rays exposure in 700 rad per hour causes the certain degree erythema of skin. To cause the same erythema by two exposures with an interval between them in 24 hours every dose from these two exposures must be 535 rad that consists 1070 rad in the sum. It means that for 24 hours between exposures partial renewal after the effect of the first dose of exposure takes place. As the second exposure in 535 rad causes erythema of the same degree as well as dose of single exposure in 700 rad then it means that from the first exposure from the two ones through 24-hr interval only 165 rad «remained» and thus the skin restored from the effect of 370 rad of the first from the both exposures.

However if cells perished the damage can be removed only by the way of replacement of them by the new ones. One of the factors of the survival of an organism after exposure in a high dose become the presence of remain of viable stem cells of the critical hemopoietic, digestive, immune systems. In particular the medical effect of a transplantation of the bone marrow is determined exceptionally by a presence in it of stem cells.

Consisting of permanent dynamic equilibrium of any cellular population in living organism that is necessary for normal vital functions supported the systems of renewal of cells. The loss of the part of cells in the system on any reason particularly under the effect of exposure is restored by the appearance of the proper amount of the new ones. Cells of each type have the characteristic middle duration of life cycle and accordingly differ by the rate of renewal. Consequently, an organism of adult is constantly in the state of the strictly balanced cellular renewal which takes a place continuously in the row of its vitally important systems. Every minute in each of them dozens and hundreds of thousands of ‘obsolet’ cells die, exchanging by new, what are ready through the certain term to ‘sacrifice’ by themselves, and this way up to the end of life of organism. This stable equilibrium of the system of cellular renewal, too important for reliable support of viability of organism, is named *a cellular homeostasis*. *The phase of renewal* in future is provided by the two-bit of saved stem cells in the bone marrow, which after devastation can manifest the capacity for unlimited reproduction. In this they not only product cells similar to themselves for addition of the own pool but also cellular elements which are necessary for repopulation of the differentiated cells. As these processes need a time the renewal of cellular composition delays and the first stage of beginning of the renewal pass slowly.

If to divide the dose of exposure into a few fractions its biological efficiency diminishes. It is predetermined by two main factors:

- the reparation of sublethal damages in the interval between fractions and
- the replacement of the lethally damaged cells by repopulation of the stored ones.

The replacement of the cells can be also carried out by migration of the healthy cells from the non- exposured areas.

## 6. Determined and stochastic effects of IR. Low doses of exposure. Hormesis. Hypotheses of threshold of effect of low doses

The varieties of all somatic character reactions and damages of an organism for example erythema, dermatitis and ulcers etc. are accepted to name *determined or non-stochastic effects.* They are determined *as such that have the threshold of appearing and degree of their gravity increases with a dose.* Such damages can appear only after the effect of high doses of exposure which exceed *tolerant* dose for exposured tissue (fig. 11a).

Unlike of the somatic the genetic (teratogenic and carcinogenic) IR effects do not depend on a dose on the sign of their gravity (the effect appears on principle «all or nothing») only *probability of their appearance* depends on a dose: the higher dose the higher frequency of their appearance (fig. 11b). Such effects got the name of *stochastic* (*probabilistic*).

The threshold dose of the determined effects is the dose value which the certain radiation effect appears at least in 1–5% the exposured individuals. Accordingly term the *threshold of radiation effect appearance* or simply *the threshold* means the presence of the ability of a tissue to maintain exposure in an *up to threshold doses*, that is below than threshold, without the signs of development of the certain radiation effect. For different radiation effects the threshold dose is different. Thus, in the case of a skin erythema the threshold dose makes 6–8 Gy of single gamma-irradiation, that is higher than dose, minimum necessary for the appearance of temporal depilation (3–5 Gy), but below, than doses which cause such skin effects as a dry and moist desquamation, ulcer and others like that.

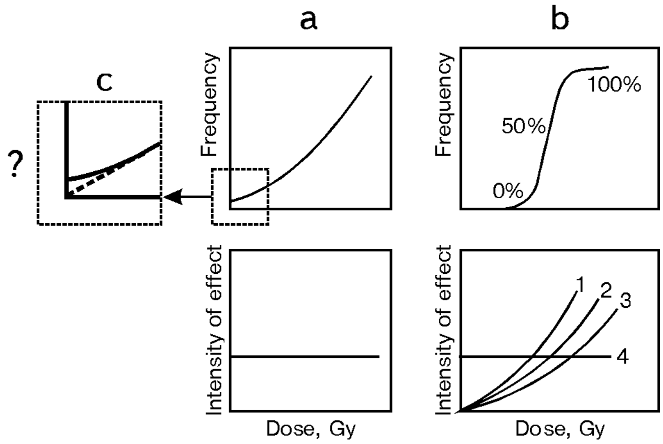


Fig. 2.11. Differences between the curves of dose–effect for non-stochastic and stochastic effects: a) non-stochastic effects, b) stochastic effects, c) area of doses of hypothetical threshold of stochastic effects; 1, 2. 3 are individual differences of radiosensitivity for non-stochastic effects, 4 is threshold of origin of pathological state (from the publication of ICRP 41, 1987)

A term the *tolerant dose* is used for denotation of maximal radiation dose in which tissue can bear without development of the *clinically meaningful determined effect* in it. By analogy the term *tolerance of tissue* reflects ability of the tissue to bear exposure without development of such effect.

In pathogenesis of the determined effects a decisive role played a cell death that is associated of these effects with a dose and with time passed after exposure, in a large measure depends on the survival of cells in the damaged tissue. Most the important effects appear only after the long latent period. In this connection they distinguish *early effects* which appear up within *one hundred days* and *late* or *delayed* those appear in a few months or years.

*Stochastic effects* are the gene mutations appearance of which in *gametes* (ovules or spermatozoa) causes the *congenital defects* of development (teratogenic effect) from a non grave colour-blindness to such grave conditions, as Down syndrome, Huntington's chorea and others like that. Congenital defects can be related also to exposure of embryo *in utero.* Except for congenital somatic defects after exposure of an embryo there can be a delay of mental development.

Another form of stochastic IR effects is observed after exposure of *somatic cells* is causing *blast-cell transformation* in them, that is the transformation of the differrentiated cells in the undifferentiated ones with the loss of control of the reproduction, that clinically appears in the view of malignant tumours. This stochastic effect carries the name of the *carcinogenic radiation effect.*

The morphological type of such radioinduced tumours depends on the morphological type of «maternal» that is the initial cell which was undergone to mutation and as a result gave beginning to the malignant growth. From the cells of epithelial origin carcinomas of different morphological variants are developed, the mesenchymal cells give the beginning to the sarcomas. Leucosis are derivatives from the cells of hemopoietic tissues.

There are different looks in relation to the presence of dose threshold of the stochastic effects. Looking after the exposed people and experimental data allow to be expressly determined in relation to correlation of size of dose and probability of biological IR effect of stochastic character at the large doses of exposure. However, there are a few data and they are mainly uncertain in relation to such correlation for the level of low doses (fig. 12A). Usually, hypotheses about their stochastic effects are accepted on the basis of extrapolation of information for high doses on the level of low ones. Till now there are no grounds for the certain choice of one of the three hypotheses in relation to correlation of dose and probability of effect as the true one:

- 1- linear ratio without the threshold,
- 2- linear ratio with the threshold
- 3- non-linear ratio with the threshold but the initial IR effects slowly grow with next acceleration of their rate.

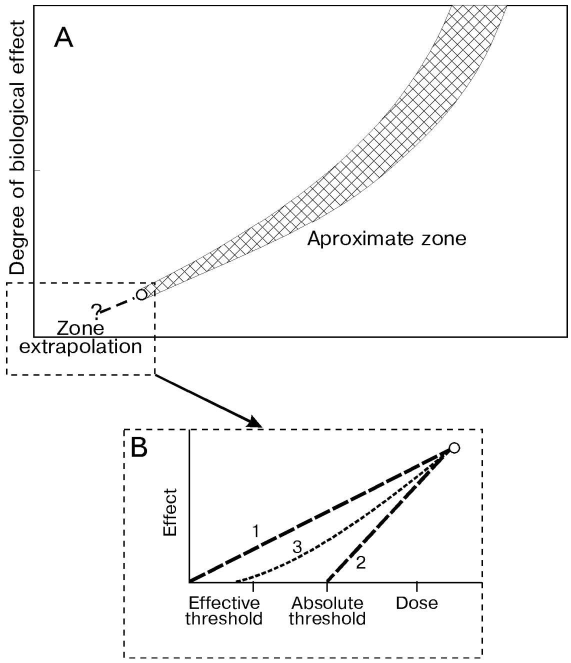


Fig. 2.12. Problem of the threshold of stochastic effects of low doses of irradiation. A) Conclusions in relation to absence of the threshold of such effects of low doses are making by extrapolation of information of the data set probably for a high-dose irradiation. B) But there are three hypotheses in relation to this problem, presented schematically on a lower chart: 1) linear ratio of dose-effect without the threshold, 2) linear ratio n with the threshold, 3) non-linear ratio with the threshold but the initial IR effects slowly grow with next acceleration of their rate (M.Tyubiana et al., 1969)

*Linear ratio without the threshold* means direct linear dependence of frequency of origin of the IR examined effects on the dose value, beginning from a 'zero' dose. Oppositely *linear ratio with the threshold* assumes the presence of the dose threshold of stochastic effects appearance.

From the humane considerations in radiological defense it is accepted as an official the *hypothesis of non-threshold phenomenon of stochastic radiation effects*.

Necessary for development of the radiation induced tumours to the clinically meaningful sizes time depends on a speed of proliferation of the initial cell. The first cases of solid tumours usually can be registered in 10–12 years after exposure to ionizing radiation and maximum of them occurs at the term in 25–30 years. Leukemias in the victims of the atomic bombardments of Japanese cities were registered yet in 2–3 years (first cases) with a maximum on $7^{th}$ year.

The stochastic effects appearance after exposure in low doses has low probability that is why risks of their appearance can be meaningful only at exposure of large groups of people. The output of these effects is determined by a collective dose unit of which is Sv-man and appearance of them at a separate individual has an unforeseeable event. It is set that the risk of these diseases makes from data of ICRP 5.5 cases on 100 Sv-man.

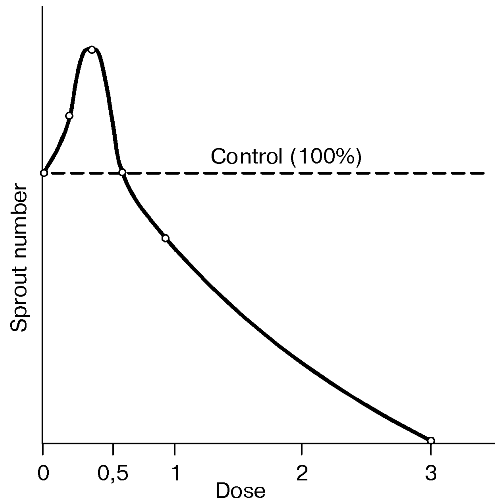


Fig. 13. Chart of development of plants on depending on the absorbed dose. Stimulation of their development at ultra-low doses, that diminishes to the extent of growth of dose; at subsequent growth of dose stimulation changes by the oppression.

In experiments on plants and cells of warm-blooded animals in behalf of threshold hypothesis the phenomenon of *radiation hormesis* was established favorable effect of ultra-low doses (fig. 13). The term was offered in 1980 by T.D. Lukki. The mechanism of this phenomenon at the level of cells consists in initiation of synthesis of proteins, activating of genes and reparation of DNA in reply to the IR effect, near a dose to the level of natural background. This reaction eventually draws activating of membrane receptors, proliferation of splenocytes and stimulation of the immune system (Publication of UNSCEAR, 1994).

Fully clearly, that the problem of threshold of stochastic effects belongs to the level of the *low doses* the values of which are subjacent lower of the threshold of the determined effects. The National Commission on radiological protection of the USA determines high doses, as “such, which exceed a level for which most biological events deviate from linear dependence on the dose of irradiation”. As the border between low and high doses the value of dose in 200 mSv is accepted. “High power of dose is determined as the power at which the reparation of radiation damages is impossible (approximately 100 mSv/year)” (Publication 116 NCRP, 1993).

### 7. Regulation of man radiation safety

Determination of the man exposure risks is not simple medical problem, as too much factors of physical and biological nature influence on the origin of reactions and damages of tissues and organs. Without regard to more than centenary experience of contacts of man with all varieties of IR in the most various conditions (in professional activity, at medical exposure, at radiation accidents, military application of nuclear weapon and others like that) and great number of experimental researches on the different types of animals, and until now there are an overstatement (more frequent) or underestimations of that or other character of the IR effect risks for a man.

The necessity of protecting from x-rays was firstly expounded in 1915 in the publication of the British roentgenologic society “Recommendations in relation to protection of persons those work with x-rays”. But two problems were not solved: 1) after what criterion or criteria to determine the level of safe exposure and 2) in what units and how at the certain conditions of exposure to measure the level (by then there was not even confessable unit of exposure and method of measuring of its level). Only in 1928 in Stockholm on 2$^{th}$ Congress of non-state the International Commission on radiation measurements and units (ICRMU), created on the initiative of prominent radiologists of that time pioneers of radiology, the unit of the dose roentgen was inculcated, and the method of its measuring is offered. In the same 1928 the International Commission on protecting from x-rays was also founded, later renamed in the International Commission on Radiological Protection (ICRP).

Up to 1934 years as the *permissible dose,* i.e. such that, as considered, does not harm to a man at an of long duration effect, 1/1000 part was accepted from the erythema dose was accepted. As it was established later, this dose approximately answered 0.1 R per a day. In 1950 ICRP revised the level of possible dose, reducing it to 0.3 R per a week.

Then the problem of allowed dose remained under permanent attention of ICRP, WHO and IAEA, looked over repeatedly, specified and complemented by new approaches in connection with the introduction firstly of a concept of the equivalent, and then the effective dose. In 60$^{th}$ the maximum allowed dose of occupational exposure was set the equivalent dose in 5 rem per year, i.e. 50 mSv per year.

*The modern norms of radiation safety are required the unexceeding of the basic limit of the effective dose, which makes in middle 20 mSv per year for any successive 5 years, but not more than 50 mSv per year.*

For the calculation of the effective dose of exposure the coefficients of radiation risk of different tissues exposure and organs were established presented on fig. 14.

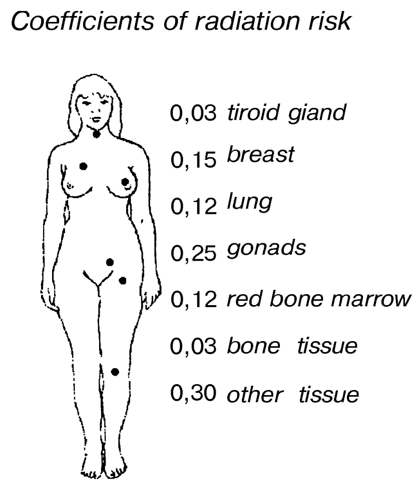


Fig. 2.14. Coefficients of the radiation risk of different tissues

The modern system of recommendations on radiation protection of a man, developed by the international organizations (IAEA, the International Commission on Radiological Protection (ICRP), the United Nations Scientific Committee on the Effects of Atomic Radiation (UNSCEAR) on the basis of irrefutable scientific data and present international experience of radiation incidents and failures minimizes the radiation risks of a man (personnel, population) to the maximally reasonably possible levels (the principle of ALARA As Low As Reasonably Achievable). ALARA shows by itself the practice of requirement of the observance of the principle of support of doses of exposure of patients and personnel so low as far as reasonably accessible. This principle touches organization of radiological protection of all contingents of persons: personnel, patients and population.

On the basis of international recommendations every country develops national documents which regulate any activity with the use of IR sources.

Radiation Safety Standards of the Ukraine (RSSU-97) measures on *radiation safety* and *radiation protection* for the situations *of practical activity* terms of contact of man with IR linked with implementation by it any technological processes with the use of IR sources, and *interferences* — activity, directed “on a decreasing and avoiding out of control and unforeseeable exposure or probability of exposure” emergency, chronic from the technogenic enhanced sources of natural origin and other situations, those require interference.

For the both situations radiation safety and radiation protection are built on three principles:

- justification of practices
- optimization of protection and safety
- dose limitation (dose constraint).

***Justification of practices.*** The government or the regulatory body shall ensure that only justified practices are authorized (BSS). Except for justified practices involving medical exposures. In medicine the process of justification is a balance between the risk of radiation health effects and the clinical benefits of the medical exposure to individuals: it includes the consideration of the risks and benefits of alternative diagnostic and therapeutic techniques.

***Optimization of protection and safety*** requires for the conditions of practical activity providing of so low level of the individual doses of persons irradiation as far as it can be provided taking into account economic and social factors, and for the conditions of interference the choice of his form, scales and duration of such "that a difference between a total *benefit* and a total *loss* be not only adequate, but also maximal".

***Dose limitation (dose constraint)*** is implicated impermissibility of exceeding *of limits of doses* those are defined for the terms of practical activity with the purpose of maximal decreasing of the level of risk of stochastic, and limitation of individual doses, at the level beneath the threshold of the determined effects, for the conditions of performing of the interference. For medical exposure, dose constraint levels should be interpreted as guidance levels, except when used in optimizing the protection of persons exposed for medical research purposes or of persons, other than workers, who assist in the care, support or comfort of exposed patients.

Radiation Safety Standards of the Ukraine (RSSU-97) includes four exposure groups for regulated magnitudes:

- **the first group** is control regulations in *practical activity,* the purpose of which is maintenance of *occupational* and public exposures on the accepted for an individual and society levels,
- **the second group** is regulations with the purpose of limitation of medical exposure,
- **the third group** is regulations which determine the size of *dose* of public exposure, what is turned away as a result of an interference in the conditions of a *radiation accident,*
- **the fourth group** is regulations which determine the size *of dose* of public exposure from the *technogenically enhanced sources of natural origin,* which is turned away as a result of an *interference.*

The radiation regulations of the first group are defined for such categories of persons:

*category A (personnel)* are persons from personnel, those are directly busy at a work with the sources of IR,

*category B (personnel)* are persons from a personnel, those are not busy directly at a work with the sources of IR, but from the location of workplaces can get more irradiation in comparing with natural radiation background,

*category C (population)* is whole population.

Limitation of exposure of the persons *of category A and B* (personnel) is carried out by introduction *of limits* of *individual annual effective* dose of external and internal exposure and *equivalent doses* of external exposure.

Limitation of exposure of persons *of category C* (population) is carried out by introduction *of limits of annual effective* and *equivalent doses* in *the critical group* of persons. The last means that the value of annual exposure dose of persons which are included in the critical group must not exceed *the limit of dose*, set for *category B*.

In accordance with the requirements of RSSU-97, to work with the IR sources persons above 18 are prohibited.

At a reception to work of persons from the personnel, subsumed to the category A, in particular bringing in temporally to works with radiation sources, pass previous (before the job placement) and next periodic health surveillance (not rarer 1 time per a year). The persons are assumed to if they have no medical contraindications. This requirement spreads also on:

- persons, which enter to the special educational establishments (in particular on courses), where they prepare specialists for work with IR sources,
- persons, which are brought over to emergency workers of consequences of radiation failures, persons with exceeding of annual limit of dose of exposure, regardless of tis reasons and terms and levels of previous exposure.

Persons from the personnel of category A necessarily are under permanent individual dosimetry control (IDC), and their workplaces annually are passed the attestation on the accordance to the norms of radiation safety.

## 8. Medical exposure

Medical practice, linked with the use of ionizing radiation gives the most contribution in the irradiation of a population from the anthropogenic (created artificially by a man) radiation sources: in the whole world about 95% of the general dose are from such sources. That is, except for the natural background a medical exposure presently is the biggest source of ionizing irradiation of the population of the Earth (table 1), and that is why the measures of radiological protection must be used for prevention of unjustified increased the population and individual doses of medical exposure.

*Table 1*

*Middle annual effective doses are per capita in 2000from the natural and anthropogenic sources of exposure on data of UNSCEAR (2001) (mSv)*

| | |
|---|---|
| Natural background | 2.4 |
| Medical exposure | **1.2** |
| Atmospheric nuclear tests | 0.005 |
| Chernobyl accident | 0.002 |
| Nuclear energetics | 0.0002 |

Current estimates put the worldwide annual number of diagnostic exposures at 2500 million and therapeutic exposures at 5.5 million., and this tendency steadily goes upwards. Such numbers testify the undoubted benefit for the health of a patient, which can be from the medical use of radiation, and abandon no doubts concerning its necessity.

Radiological risks, related to diagnostic procedures, as a rule, are low for an individual (after some exceptions), while for the whole population can become the substantial at neglecting by requirements of providing of optimum level of exposure during realization of diagnostic procedures. Consequences of emergency irradiation are in radiotherapy [*], moreover, can be very serious for a patient and, consequently, exposure must be carried out thus, that a dose will be high enough for achievement of the desired therapeutic results in a targeting focus, but at the reasonably accessible low level in other organs and tissues.

[*] The emergency irradiation (in accordance with the International basic standards of safety in relation to protecting from the ionizing radiation and safe handling the sources of radiation there) is the next: "Any therapeutic irradiation or not that patient, or not those tissues, or by using of an erroneous radiopharmaceutical, or in a dose or with freffectating of a dose, substantially different from appointed by a doctor, and which can result in superfluously acute or secondary effects".

In any table of statistics of probabilities of death from different factors (automobile accidents and air crashes, falling from a height, domestic accidents, drowning, bullet wounds, electrical injuries, fires, tornados and hurricanes and others like that) the medical exposure as factor of such similarity is not remembered. Usually it is accepted as an obvious thesis that medical radiation procedures are so needed and a benefit from them is so considerable, that a small risk can be not taken into account. However, radiologists as doctors to whom, firstly, public respecting is not indifferent and, secondly, which responsibly perceive the medical duty «do not harm», must weigh all possibilities and apply all facilities of diminishing of the risk of harm to the minimum which reasonably accessible, otherwise speaking, to reduce a medical diagnostic exposure to the level, at what receiving of the necessary information on the state of health or character of disease it is possible without the loss of quality, and do not allow the overexposure of a patient.

It is proved in experiments and population researches of people that stochastic risks (cases of mortal oncologic diseases, congenital diseases and defects) are made 0.055 cases on 1 Sv-man of the collective dose of exposure per year, and they are realized inevitably. It is the substantial level of risks, taking into account the considerable population dose of exposure from radiation diagnostic procedures and that is why it is so important to do all dependent upon a medical personnel which carries out radiological investigations to decline these risks up to the reasonably accessible level. Otherwise speaking, the **culture** of radiological examination or treatment of a patient in practice of medical exposure is especially important, that makes the principle of the radiological protection of patients.

It is well-proven that there are possibilities of the decreasing of risks as diagnostic so medical application of radiation without the decreasing of medical benefit, and the whole medical association must play its own role in this process. Education and professional education of personnel, organization of the proper guarantee of the quality are the necessary components for the achievement of this purpose.

International document from radiological protection the Medical Exposure Directive (MED) (97/43/Euroatom) specifies that the limits of doses are not set for such cases of *medical exposure*:

- patients as the part of their direct diagnostics or treatment;
- persons at the professional medical examination;
- persons as the part of the screening programs;
- healthy persons or patients who voluntarily take part in medical or biomedical, diagnostic or therapeutic experimental researching programs;

- persons as the part of forensic medical procedures.

In all these cases a radiologist has the right independently after the situation to determine necessary diagnostic procedures on a type and amount, taking into account a necessity to get reliable diagnostic information. However, on the other side, his professional duty and responsibility is the observance of principles of ALARA. In addition, a patient must be informed by the personnel in relation to a benefit for him of the appointed procedures and degree of their risk.

Consequently, from all above-mentioned it is following that it is necessary and important to take care of the measuring of patients exposure, because, from one side, a radiologist however must be oriented in the levels of doses, in which he exposes the patients, and degrees of risk related to them, and he must to search the ways of its decreasing, for what quantitative criteria are needed. From the other side, the knowledge of the level of is no less needed for the obtaining of the exact diagnostic information.

"The profession of physician is highly valued by a population in the whole world. We assume that we can be deceived by a car mechanic, we are ready to the overpayment at a necessity of a help to our television set, but in the majority of cases trust our doctor! Without regard to difficulties which he, certainly, as well as others, he has in relation to the payment of a tax, charges on providing of the living necessities, we are sure on the whole, that our doctor is not subject be influenced by economic pressure and he will act in our interests. Probably it is not quite how it was a generation ago, but we still hope, that a doctor lives on the laws of moral, and his ethics exceeds ethics of other people.

It is a result rather not advertisings or indoctrination from the side of professional association of physicians, but direct expression of our love to life, to helplessness before pain, suffering and death and wish to trust to the person, who is able to return a health to us. In the most cases we are trusted to a man of worth. Radiology in that behalf is not an exception.

From the medical point of view an insignificant danger, related to [diagnostic] irradiation of patient, must be with surplus compensated by the information got a doctor, necessary for diagnostics and treatment of a disease."[**].

[**] Note: Cit. E. J. Hall. Radiation and life. Second Ed., Pergamon Press Inc., 1984.

By the directive of Euroatom (MED) introduction from May, 13, 2000 in the national legislations of the countries of European Union of the *diagnostic reference levels* of medical exposure was recommended.

Determination and ground of diagnostic levels and methodology of their establishment were thoroughly described in the special document of European Commission on the problems of radiological protection «Radiation Protection 109 EC».

*Diagnostic reference levels (DRL) are the levels of patient exposure doses at x-ray diagnostics or, in the case of a radiopharmaceutical the level of radioactivity for typical investigations and groups of standard patients or standard phantoms for the types of equipment acknowledged in general lines.*

*It is accepted, that these levels will not be exceeded at standard procedures, if* *the proper and normal practice of organization of diagnostic and technical work is used. As the DRL for radiography the entrance superficial dose (ESD) or the product area-dose (PAD) is accepted, and for fluoroscopy a general time of the investigation.*

*If the DRR are substantially exceeded, it is necessary to perform local verification necessarily (article 6).*

Diagnostic reference levels can be *international*, for example, for countries of the European Union, *national* i.e. national in every country, and *local.* The validity of existence of the last must be thoroughly grounded by worthy factors. For example, in difficult case, when conditions of the investigation require greater duration and complication, than standard, a higher dose on a patient can be justified. Nevertheless, local DRL the higher, than equivalent national values, cannot be justified only through the use of off-grade equipment and/or technology.

Thus, by these documents the internal and external audits of radiation doses were founded on patients from x-ray and radionuclide diagnostic procedures.

It follow to underline that the DRL are not only the way of optimization of diagnostic irradiation of patients, but at the same time and the control of quality of radiological diagnostics, and on the whole are the marker of *culture of medical exposure.*

Another important function of the DRL is that they allow to compare the degree of exposure of every patient at certain radiological diagnostic procedure with the size of exposure from such universal source, as a natural radiation background (NRB), and to estimate risks in the sizes of this natural phenomenon.

The national DRL of Great Britain for radiography of separate anatomic areas of “standard man” there are such values of the entrance superficial doses (mGy): skull (direct) — 4, skull (lateral) — 2, chest (direct) — 0.2, chest (lateral) — 0.7, thoracic spine (direct) — 5, thoracic spine (lateral) — 16, lumbar spine (direct) — 7, lumbar spine (lateral) — 20, lumbar spine (oblique) — 35, abdomen (direct) — 7, pelvis (direct) — 5, for intravenous urography — 25, for barium investigation of upper digestive tract — 17, for investigation with barium enema — 35.

The resulted values of DRL can be compared with the middle level of NRB in 2.4 mSv/year (in this case it is possible to accept the equivalence of mSv and mGy). Consequently, 1 craniography in the direct projection is equivalent to the additional exposure from NRB during 1.5 year. There are all grounds to assert that an additional risk from such research is enough low, that they must take care of. But such investtigations as the barium enema and the oblique x-ray film of lumbar spine create an additional risk on an order higher, which needs the certain attention and justification.

It is worth paying attention at the level of exposure from those radiation diagnostic procedures, for these from each of them separately additional risk is insignificant, however taking into account the high frequency of their application it becomes too substantial. For example, the radiography of a thorax creates the exposure in 0.2 mGy, that makes only a 1/10 part of annual exposure from NRB (the risk is possible to ignore), the fluorography of a thorax gives a dose in five times higher, than at the radiography (1 mGy). However, as fluorography is executed to hundreds of thousands of healthy persons, if to not millions annually, then as though an insignificant additional risk grows on many orders and becomes the real threat for hundreds of people in general population.

"Radiography of thorax, appointed to the people with suspicion on any disease, carries in itself a benefit which obviously exceeds the risk related to it. A similar investigation, appointed for the universal control of the state of health of population, does not have such correlation of a benefit and the risk. Millions of fully normal healthy individuals are exposed without any benefit for them, only, by chance to discover in someone from them any violation. Tuberculosis presently is rare disease, and then it could be revealed at the general survey of population by the ordinary skin test. Therefore the radiography of a chest for this purpose is not justified. It follows to appoint it only under special circumstances. The attitude to the general radiography of thorax in a population with the purpose of exposure of lung cancer is contradictory. The subject of the discussion consists in a doubt in relation to the possibility of an ordinary radiography of thorax though to increase (on any degree) the survivability of a patient. And that is why, indisputably, it does not justify the irradiation of millions of people, if the result of their investigation will be negative. The rational compromise can be limitation of annual radiography of thorax only to the zealous smokers and workers, whose profession is related to the risk, for example, such as miners of uranium mining camps or workers of asbestine productions". [***]

The prophylactic surveys of population with the application of the fluorography are not recommended by the WHO yet in 1994, taking into account their inefficiency for diagnostics of tuberculosis and especially lung cancer.

[***] Note: Cit. E. J. Hall. Radiation and Life. Second Ed., Pergamon Press Inc., 1984.

If patients disturbed by the possible risk of necessary radiologic investigation, they apply to the doctor for giving hope, that the investigation is necessary indeed, and that it can give useful diagnostic information. All the rational measures must be accepted for minimization of these risks, and also the confidence is necessary, that radiologic investigation is justified from point of benefit for the health of a patient. In most cases a risk for the health of a patient from an inexact diagnosis, put before, or limitation of application of x-rays will be far more than very small risks, related to the irradiation for the exact diagnosis. Patients expect they will be properly familiar with character of the offered procedure, about a benefit and risks, alternatives and duties of medical personnel.

A doctor must be sure, that diagnostic information expected from the new x- ray investigation is not already accessible from any of previous researches, even if they were appointed by other doctor or conducted in other hospital. If he or she are sure, then a requirement in a new roentgenologic investigation must be determined by prestige of doctor and in connection with current status of the health of a patient. There is no necessity to examine previous irradiations from the point of view of risks, if the new investigation is fully justified and optimized thus, that the benefit for a patient prevailed the risks of low irradiation from this research. The size of additional risks (and the advantages) from this new research does not depend on previous irradiations, even if they were conducted only the short time ago.

«The amount of radiograms on a 1 million of population varies severely in the different states. It is desirable to think that medical practice, as it is expounded in Oath of Hippocrates, serves exceptionally to the interests of a patient. But, obviously, it is not so. In some states up to one-third of radiograms executed from other grounds, than exceptionally medical. There are two main reasons. At first, necessity to turn to the account. In private practice, when a considerable capital is inlaid in acquisition of new medical equipment, it is difficult to hold back from temptation to do superfluous radiograms with the purpose of to plug them in an account to the patient! Other, «medical defense». A doctor performs superfluous radiograms, as they say, looking around on an advocate of a patient, i.e. superfluous films are done for the sake of guarantee in a case of the court claim. These too oppressive for doctors problems mainly are absent in the Great Britain. However here, in opposite, there is dependence of the amount of the performed x-ray investigations from the assignation by the state of certain region of the National health protection. »[****]

[****] Note: Cit. E. J. Hall. Radiation and Life. Second Ed., Pergamon Press Inc., 1984.

Plenty of high-dose investigations (for example, computer tomography of a body) during one year fully can be justified for diagnostics and estimation of treatment of the states dangerous for life.

It is needed to take into account and the circumstance that as possible development of a cancer after exposure will last many years and even decades, these risks are especially decreased for people, aged in the moment of exposure. For many persons above sixty simply will not be a sufficient time of life for the development of radiation induced cancer. And vice versa, children undergone to roentgenologic investigation, can have to two times greater probability of becoming of the middle term of development of cancer from this x-ray examination.

The important measure for the decreasing of the doses of medical exposure is the arrangement of the performing of radiological researches. Foremost, each such investigation must be *justified,* that is grounded by clinical indications, especially for children. This norm provides for, that in a hospital chart or ambulatory card the proper record will be done by a treating doctor in relation to the purpose of research and expected results in the benefit of a patient.

The important ways of reduction of the dose of patients is providing of:

- the proper control of quality of the film processing;
- the proper collimation of the radiation beam for the avoiding of the influence on other, comparing with the area of interest, tissues; the filtration to limit influence of low energy radiation, which does not have a diagnostic value;
- the exception of the use of fluoroscopy without the image intensifier;
- the use of the voltage on a x-ray tube (kVp), which answers the purpose of the certain performed investigation, and
- regular revision of protocols of fluoroscopy with the special accent on the duration of its performing.

Unlike simple radiography, the dose of exposure of a patient during fluoroscopy depends on the professional preparation of an operator, his experience in fluoroscopy and his efficiency in the completion of a diagnostic investigation. The range of the exposure doses of sick children from fluoroscopy is wide, because this research is conducted by not only pediatric radiologists but also general roentgenologists.

Conception of ALARA is resolutely supported by radiologists, especially pediatric, in the use of procedures and methods with the greatest doses of exposure, such as CT and fluoroscopy of pediatric patients. There is not a doubt, that medical images undergone enormous technical achievements in the last decades are the inalienable constituent of care for patients, but they must be optimized for the decreasing of the pediatric patients exposure doses, which can be in dozens times more radiosensitive, than adults.

It follows to spare the special attention to babies and children, because, at first, the risk of stochastic effects for them is more high, than for adults, and secondly, because of wide range of weight of their body which does standardization of procedures more difficult; and thirdly, because the amount of child's diagnostic procedures, executed in the world annually, makes over 250 millions.

The gonad exposure creates the increased risk of appearance of mutations for the descendants. At a consideration of the question about the possible exposure of patient's gonads, the minimization of the dose by the correct positioning of the beam, the collimation and the shielding of gonads, always practically will diminish the possible inherited effects to the minimum. The risk of the appearing of new mutations which became apparent as the congenital diseases for the descendants of the exposed patients is estimated as small by comparison to a risk of those which arise up in natural way. Inherited and oncologic risks for next generations after the gonad irradiation of conceivable parents are small by the comparison to natural risks.

All main medical organizations recommend screening mammography for women above 40. Such reduces the death rate from the breast cancer on 20%–35% for women in the age of 50–69 years and some less among women in the age of 40–49 years. On 100 000 women, each of which got the dose in 3.7 mGy on the both breasts from the annual screening mammography in the age of 40–55 years and farther twice on a year to 74 years, the origin of 86 induced cancers and 11 deaths from them is foreseen. This risk is small by comparison to the predictable death rate which is turned away by mammographic screening that is why the risk of radiation-induced breast cancers cannot be cause for the refusing from the mammographic screening for women above 40.

Without regard to the substantial exposure doses, related to the generally accepted practice of dentists to perform x-ray films of all teeth to the patients, there are grounds to accede categorically to rationality of such approach to the supervision on the teeth state for adults. The point is that cavity of a damage of a tooth on the initial stage it is impossible to discover by other methods, except for the roentgenological, and that is why the film of tooth can rescue it, that it is too important, as prosthetic appliances cannot compete with natural teeth. But it is impossible to justify such approach to the treatment of teeth for children. A cavity in milk tooth does not have substantial value, because such tooth at one time will be replaced by the permanent one.

Each time, for the possibility, up to the decision-making about the use of ionizing radiations for the patients of the reproductive age the alternative methods of research, unconnected with ionizing radiation, must be considered. When the radiological investigation at which the direct beam exposes a pelvic area, or procedure with introduction of radionuclides is appointed to the woman of reproductive age, a woman must be asked, whether she is or can be pregnant. If a patient cannot exclude the possibility of pregnancy, it follows to ask, how long is delayed her menstrual cycle. If the pregnancy set or credible, the ground of the offered investigation about delaying of the examination up to the birth, but weighing and that procedure, clinically useful to the mother, will have also an indirect benefit for its unborn child, and that a delaying of the important procedure on later during the pregnancy can increase a danger for a fetus. If procedure is conducted, the dose of exposure of a fetus must be decreased to the minimum in accordance with a diagnostic purpose.

For such circumstances there is the «rule of ten days»: a woman of reproductive age during the first ten days from the beginning of menstruation (normal after intensity) can be certain, that she is not pregnant. Exactly in this period it is required to conduct any roentgenologic investigation of stomach and the pelvis area without doubt in relation to the risk of exposure of an embryo.

The diagnostic levels of doses can make the substantial risk of genetic effect for an embryo only in a view of induction of cancer. None other potential risk (death, defect of development, deceleration of growth, heavy mental backwardness and inherited effects) does not show by itself serious problem in connection with the low levels of exposure, which they use for the majority of diagnostic procedures. But, however, additional effects, for example malformations and delay of growth, can be related to the before childbirth exposure at exceeding of threshold in 100 mGy at some CT-investigations of a stomach or pelvis. In the case of genetic inclination which is rare, a malformation also can be caused on the stage before implantation.

After exposure of an pregnant woman at a high-dose diagnostic procedure (exposure of fetus up to a few dozens of mGy, for example, CT of a pelvis or any barium investigation) a risk of the induction of a cancer for a yet unborn child can be more than in two times higher, than natural risk. So, by the retrospective inspections of *children with leukemia,* it was set that in the considerable quantity of cases their mothers were exposed during pregnancy with the including of the fetus in the area of effect of IR. It was also set that even a dose on a fetus in 50 mGy doubles the risk of the congenital leukemia, and it's irradiation in the dose of 100 mGy must become the indication for terminating of the pregnancy.

***Radiation is the stars flame giving the weal to us***
***regard to it with awe so it warms but not incinerate.***