ЗМІСТ

Means of Protecting the Body from the Effects of Ionizing Radiation: study guide

Про книгу

The study guide is committed to provide current information about the human body protection against acute and chronic ionizing radiation. The study guide concerns the issues on applying radioprotective chemical agents and natural food items to increase the body resistance against the ionizing radiation in unfavourable environment as well as in the course of radiation therapy. Special attention is paid to the novel conception of radiation protection nutrition. This study guide is designed in accordance with the Curriculum of Radiation Medicine and Radiology to meet the academic, professional needs of medical interns and medical residents of higher medical establishments. It is intended for use by delivering the course of Radiation Medicine and Radiology to medical students.

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STUDY GUIDE

RECOMMENDED
by the Academic Council of Higher State Educational Establishment of Ukraine "Ukrainian Medical Stomatological Academy" as a study guide for students of higher educational establishments of Ministry of Health of Ukraine

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Introduction

Ionizing radiation has since the origin of life been part of the natural environment surrounding all living matter on Earth. Since 1945, when the atomic and later hydrogen bombs were developed, when their intense testing and the extensive development of nuclear energy has started and a range of modern human activities associated has expanded, the amount of energy causing irradiation has been gradually increasing. When released into atmosphere and reaching its upper layers in different ways, radionuclides can distribute fast throughout the globe, falling onto the land surface, oceans and seas.

This has resulted in an increase of environmental background radiation that, it is important to stress, has remained relatively stable over the last few thousand years. Thus, due to growing human activity, all living organisms throughout the planet began to experience additional radiation burden.

That is why the mankind inevitably faces the necessity to design and conduct measures aimed at providing effective radiation protection and safety. In this regard, the researchers worldwide are searching for the best ways to protect from both acute and chronic exposure to ionizing radiation, as well as working out the radioprotective agents to decrease the side effects of radiotherapy.

In Ukraine, the problem of the biological impact of ionizing radiation, particularly in small doses, and protection against is still remaining one of the fundamental issues of medical and biological sciences. Nowadays, the problem is extremely relevant because the Chornobyl nuclear power accident led to huge releases of radioactive materials into the atmosphere deposited over large areas of Ukraine. The consequences of this grievously known accident were associated with the significant environmental radiation pollution of different intensity.

Today we can confidently state that no one doubts the importance of using complex protection, which along with the methods of physical protection, and screening in particular, should involve the appliance of radiation protectors.

All radioprotective agents are divided into two classes — radioprotectants and agents for the treatment of radiation damages.

Radioprotectors are drugs (mostly synthetic) that have the greatest effect when given within some period before the radiation exposure. They

are present in the radiosensitive organs (often in the maximum tolerable and subtoxic doses) and prepare the body to develop high radioresistance. The agents for the treatment of radiation damages are usually applied following the irradiation and the development of the main syndromes. They are aimed at overcoming the potential damages by substitution and supportive therapy.

One of the new directions of radioprotective researches is the medium of early pathogenic therapy. This is a special class of compounds that are able to influence on the development of pathologic process under the impact of ionizing radiation on early stages. Analysis of available literature allows us to consider a long-term chronic exposure to ionizing radiation as a lingering radiation stress, backed up by the set of environmental and psychosocial stress agents. Key role in the pathogenesis of the stress is played by the activation of free radical oxidation, increasing antioxidant deficit, immune and neuroendocrine deregulation. Effective means for correction of these changes include antioxidants, anti-stress drugs (adaptogens) and immunomodulators.

Currently, chemical methods of radiation protection embrace the following areas

1. Individual prevention by using radiation protectors that protect the body from external irradiation that causes acute radiation syndrome.
2. Applying means that enhance human body radioresistance during radiation therapy.
3. Applying nutritional supplements and drugs that increase the resistance of biological objects during chronic exposure to ionizing radiation in natural conditions.
4. The removal of radionuclides from the body.

Existing radioprotectors and radioprotection measures are far from being perfect. Literature review points out the fundamental properties of new chemical agents, so-called perfect radioprotectors that must meet the following requirements:

- to provide high efficiency causing no or little toxicity;
- to be manufactured in dosage forms, which are easy to use and are effective delivering the medication as needed;
- to be cost-effective and to have good storage stability;
- to be effective when used at different types of ionizing radiation;
- to provide the protection that must start from the first minutes after the administration and last for a few hours.

Only few radioprotective chemical compounds are widely used in medical practice, but they are ineffective at high lethal doses of radiation. Radioprotectors as means of individual chemical protection may be used in cases of emergency at nuclear power plants to make urgent repairs in conditions of increased radiation exposure or while being in a radiation contaminated environment, for example, during space missions and when taking the course of radiation therapy.

Chapter 4

CLASSIFICATION OF RADIOPROTECTIVE MEANS

Nowadays, radioprotectors are presented by a wide range of substances different by their origin and chemical composition, thus their classification by pharmacological action seems to be very difficult. In this regard, in radiobiology protective drugs can be classified according to the duration of their effect and the timing of the development of radioprotective effect.

All radioprotectors are divided into two main groups: short-term and long-acting substances.

Short-term radioprotectors include drugs, which show their protective effect for 0.5—4 hours after the administration. They are the most effective when a body is irradiated to maximally tolerated doses. As an individual protection means, these drugs can be used to protect against nuclear weapons, before the session of radiotherapy, during space exploration missions with long-term protection from solar flares. The long-term protection drugs include agents with radioprotective effects lasting from one day to several weeks. They generally show less effectiveness than short-term radioprotection agents under pulsed ionizing radiation. Practical application of these protectors may be occupational and typical of professionals dealing with ionizing radiation, e.g. astronauts during long space flights, long-term course of radiotherapy. Thus, it is possible to select the appropriate class of radioprotectors for a particular case. But the selection and administration of the agents should keep some regulations.

1. The medicines must be sufficiently effective and do not induce adverse reactions.
2. The medicines must have a fast effect (within the first 30 minutes) and this effect must last for a relatively long period (at least for 2 hours).
3. The medicines must be non-toxic.
4. The medicines must not have a negative short-term impact on the ability to work or reduce the acquired skills.
5. The medicines must be manufactured in an easy-to-use dosage form.
6. They should not reduce the body resistance to other adverse environmental factors.

7. They should produce no harmful effects upon repeated administration or possess cumulative properties.

8. The medicines should have good storage stability preserving their protective and pharmacological properties for at least 3 years.

Radiotherapy raises less strict requirements to radioprotectors. But they are complicated with an important condition, and namely the necessity to provide differential protective action. This means they are to provide the highest level of protection for healthy tissue and to produce minimal effects upon the tumor tissues. This separation makes it possible to enhance the action of topically applied therapeutic dose of radiation toward the tumors without serious damages to the surrounding healthy tissues.

The short-term medicaments are classified into the following groups, according to the structure and mechanism of their protective effect:

1. Sulfur-containing compounds (ß-mercaptoethylamine (IEA), cystamine, L-cysteine, gammafos, cystophos, etc.).
2. Biologically active amines (serotonin, 5-methoxytryptamine, adrenaline).
3. Preparations that impair the oxygen transportation through the body or oxygen utilization by cells (cyanides, nitrites).
4. Imidazole derivatives.
5. Arylalkylamines.
6. Indolylalkylamines.
7. Other radioprotectors.

At present sulphur radioprotectors are known as the most effective. Most of the compounds of this group are derived from one of the first of radioprotective drugs — ß-mercaptoethylamine. Radioprotective effect of sulfur-containing radioprotectors is associated with the presence of free or easily released SH-group. More favorable pharmaceuticals are thiophosphates, derivatives of thiophosphoric acid. Their SH-group is "covered" with phosphoric acid residues that determine their slight hypotensive effect and less toxicity.

Indolylalkylamines (serotonin, tryptamine, 5-methoxytryptamine) yield to sulfur radioprotectors only when they are used to protect from the irradiated with neutrons. Their protective effect lasts for shorter time intervals compared with SH-radioprotectors. Obvious advantages of this group are the rapid development of the protective effects and greater efficiency in small doses. It should be noted that the study of derivatives of indolylalkylamines was conducted mainly by Soviet scientists. Cyanides are able to

block the activity of iron-containing respiratory enzymes such as cytochrome oxidase, which provides the transfer of electrons from cytochrome to oxygen.

Radioprotectors of prolonged action. Disadvantages of available chemical radioprotectants (mainly toxic side effects and the limited duration of their action) served as the basis for the study of radioprotective properties of low-toxic substances of biological origin. The researches within this direction focus on searching substances and compounds, which would increase the overall body stability and resistance to infections and stimulate the active functioning of the hematopoietic system. Currently, metal-complexes of porphyrins can be regarded as substances demonstrating desired properties.

A wide variety of substances of natural origin have been studied to be used as possible radioprotective agents. Various extracts from plants, microorganisms and other biological objects without extraction of their active substances, and sometimes without control over their purity have been the most often in the scope of the scientists. For example, there were attempts to use such biologically potent substances as snake venom, bee venom, bacterial endotoxins, and estrogens in small doses to provide radiation prevention.

Melittin (polypeptide of bee venom, consisting of 26 amino acid residues, M-2840) demonstrated pronounced and statistically significant radiopreventive action in both short-term and prolonged irradiation (low energy dose of 0,1Gy / min). Bacterial endotoxin isolated from *Salmonella typhi*, alleviated post-radiation damages when administered within 30 minutes after the radiation exposure.

Zymosan, a polysaccharide isolated from yeast cells and polysaccharides isolated from bacteria *Salmonella paratyphi* and *Proteus vulgaris* were also observed to have protective effects. The most statistically significant effect was demonstrated by estradiol when compared with methyl testosterone, diethylstilbestrol, and estradiol dipropionate.

Metabolite products including nucleic acids, vitamins, coenzymes, carbohydrates, lipids, flavonoids, amino acids, exchange intermediates are often used as radioprotective drugs and in combination with effective radioprotectors.

Intraperitoneal administration of 1.5 ml of boiled cow milk for 1—2 days to the total X-ray irradiation is known to have non-specific radioprotective effect. Other reports describe radioprotective effects resulted from paren-

teral administration of whole citrated blood, solcoseryl, benzene extract of human blood cells. Application of serum globulins with normal autoantibodies before the irradiation (or as a therapeutic measure after the irradiation) was proven to increase the survival of mice, guinea pigs, rats, rabbits, exposed to lethal γ-radiation in LD doses of 80—100 / 30.

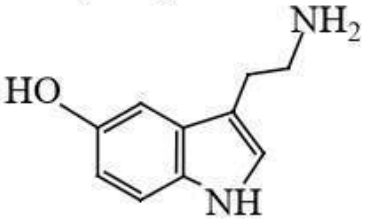
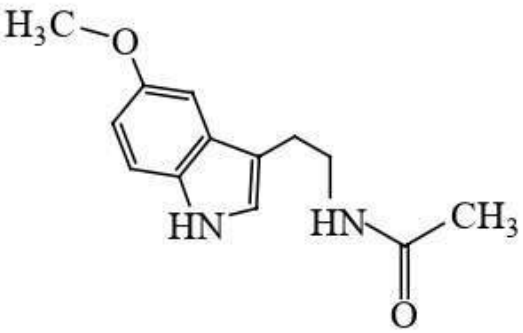
Radioprotective drugs of prolonged action also include natural adaptogens. Unlike radioprotectants, they produce a non-specific effect, enhancing the overall body resistance to various adverse factors. Adaptogens show radioprotective effectiveness when administered repeatedly over many days before the irradiation in doses lower than lethal. They are effective when used in cases of acute irradiation, but in cases of prolonged or fractionated irradiation they provide the highest effect.

It is necessary to stress that no adverse reactions caused by using radioprotective doses of adaptogens occur. The most effective drugs of this group are extracts of ginseng, Eleutherococcus, Schisandra chinensis, Echinacea. The apparent decrease in the sensitivity of the laboratory animals was detected when dry extract of buckwheat was administered orally as well as by blockade of the reticuloendothelial system with coal particles, polystyrene, latex or glycogen. However, the mechanisms of radioprotective effects provided by adaptogens are still unclear. Some effective radioprotectors are presented in table 1.

Table 1

Some effective radioprotectors (*S.P. Yarmolenko, 1969*)*

Drug	**Chemical formula**	**Effective doses (intraperitoneal, mg/kg)**
ß-mercaptoethylamine (cysteamine, mercamin, MEA)	Mercaptoethylamines $SH–CH_2–CH_2–NH_2$	120—150
Disulphide ß-mercaptoethylamine (cystamine)	$S–CH_2–CH_2–NH_2$ $S–CH_2–CH_2–NH_2$	150—180
β-aminoethyliso-thiouronium (AET)	–NH H2N–CH2–CH2–S– –NH2	200—250

Drug	Chemical formula	Effective doses (intraperitoneal, mg/kg)
2,3-aminopropyl, aminoethylthiophosphate (gammaphos, WR 2721)	H2N–CH2–CH2–CH2–NH– –OH CH2–CH2–S–P =O –ONA	300—400
5-hydroxytryptamine (serotonine, 5-HT)	Indolylalkylamines 	10—60
5-methoxytryptamine (mexamin, 5-MT)		10—60

*Clinical trials involved laboratory mice and rats

It is worthy to say that a balanced diet has been proven to provide beneficial effects upon radioresistance of laboratory animals that offers the prospects of effective long-term protection of the body from the lethal effects of ionizing radiation.