THE MUTAGEN EFFECT OF THE IONIZED RADIATIONS

RAMONA LINDA PĂTRUŢOIU

Abstract: The radiations are the most known and utilized physical factor for inducing mutations. Classified by their nature, the radiations are of two types: non-ionized and ionized. The non-ionized ones are: infrared radiations, ultraviolet radiations, while the ionized ones are: electromagnetic, represented by X radiations and gamma radiations; corpuscular, represented by neutrons, alpha radiations, beta radiations, accelerated nuclei fluxes, HYE particles etc. Some of the sequels produced by exposure to radiations are: lung cancer, thyroidal cancer, osteosarcoma, skin cancer, acceleration of the ageing process.

Key words: radiation, mutagen effect, diagnosis, treatment

Rezumat: **Efectul mutagen al radiaţiilor ionizante.** Radiaţiile sunt cei mai cunoscuţi şi mai utilitizaţi factori pentru inducerea mutaţiilor. După natura lor, ele se clasifică în: radiaţii neionizate şi radiaţii ionizate. Cele neionizate sunt: radiaţoo infraroşii, radiaţii ultraviolete, iar cele neioniyate sunt: radiaţii electromagnetice, reprezentate de radiaţiile X şi radiaţiile gamma, şi radiaţii corpusculare, reprezentate de meutroni, radiaţii alfa, radiaţii beta, fluxuri de nuclee accelerate, particule HZE etc. Câteva din urmările produse de expunerea la radiaţii sunt: cancerul pulmonar, cancerul tiroidian, osteosarcomul, cancerul de piele, accelerarea procesului de îmbătrânire.

Cuvinte cheie: radiaţie, efect mutagen, diagnostic, tratament

The mutation notion was introduced by *Hugo de Vries* (1901) who elaborated the mutation theory after researches made over *Oenothera lamarckiana*.

The discovery of the radioactivity at the beginning of the 20th century and its effects over the cell was followed by the appearance of a new domain, the radio genetics. The researches of H.J. Műler concluded that the genes suffer mutations with a higher frequency, under the influence of the radiations rather than under the influence of natural phenomena.

The **radiations** represent the most known and utilized factor in inducing mutations. Classified by their nature, the radiations are of two types:

1. Non-ionized radiations, that are not generating photochemical reactions directly and they are represented by infrared and ultraviolet radiations.

The **infrared radiations** are a component of the atmosphere, found at the superior limit of the visible light specter. They can increase or decrease the effects of the mutagen factors when they are administrated together with them, dependent on the administration type (before or after the irradiation with X radiations).

The **ultraviolet radiations** are also a component of the atmosphere, found at the inferior limit of the visible light specter. The have the wave length between 136Å - 4000Å. They are formed of photon with energies of 3-5 ergi/m^2. They present mutagen effect, especially the ones with the wave length of 2580Å, which corresponds with the wave length absorbed by the nitrate alkalis from the nucleic acids structure.

The UV radiations can induce mutagen and lethal effects. Those are caused by the chemical modifications at the nitrate alkalis level in the DNA molecule, due to the absorption of energy. After the DNA irradiation with UV it is formed a thymine dimer, if there are two adjacent T nucleotides in the same chain. In the T-T thymine dimer's region, it can be formed a curl determined by the breaking of the H bonds in the considered region, followed by the elimination of a sequence of nucleotides (with the alteration of the genetic material), or the breaking of the of the DNA molecule (genetic mutation), sometimes the breaking of the chromosome (chromosomal mutation).

2. Ionized radiations, that generate directly photochemical reactions in the living tissues, are after their nature, of two types:

-electromagnetic radiations, represented by the X radiations and gamma radiations;

-corpuscular radiations, represented by neutrons, alpha radiations, beta radiations, accelerated nuclei fluxes, HYE particles etc;

Electromagnetic ionized radiations

The **X radiations** (Roentgen radiations) were discovered in 1895, by bombarding a target (metal plate, tungsten) with high speed electrons (freed by an overheated filament). The X radiations impress the photo plate. They are electromagnetic radiations similar with the light ones, but having higher energy. They have the wave length of 0.06-100Å, and energy between 0.01-0.1 MeV.

The g**amma radiations** are emitted in the same time with the disintegration of the radioactive elements. They are not deviated into a magnetic field. They have the wave length between 0.005-1.4Å, and the energy between 1-1000 MeV.

Electromagnetic ionized radiations

The a**lpha radiations** are helium nuclei, formed by 2 protons and 2 neutrons, being liberated after the radioactive disintegration. They are attracted by the negative pole of a magnetic field, because of their positive electric

charge and high mass. Their penetration power is very low. Their effect is high if they are liberated in the organism by radio nuclides.

The b**eta radiations** are electrons liberated after the radioactive disintegration of unstable radio nuclides. Their penetration power is low. They are attracted by the positive pole of a magnetic field, because of their negative electric charge.

The n**eutrons** are neutral elementary particles, emitted by the disintegration reactions of the heavy metals (uranium, plutonium etc.). They are classified, after their energy, like this: thermal, slow, medium, fast. They have high ionization and penetration power.

The **accelerated nuclei fluxes** are obtained in heavy particles accelerators (cyclotron, synchrophasotron etc.).

The **HZE particles** are found in the cosmic space and are the result of the stellar reactions. They have a very high speed and penetration power (they can cross the planet).

The ionization of the living matter takes place after the interaction of ionized radiations with it. The ionization reactions are due to the water radiolysis at its interaction with an electromagnetic particle, followed by the creation of radicals filled with high energy:

$$H_2O \rightarrow H_2O^+ + e^-$$
$$H_2O^+ + e^- \rightarrow H_2O^-$$
$$H_2O^* \rightarrow H^+ + OH^-$$
$$H_2O^- \rightarrow H^* + OH^-$$

By combination, the free radicals resulted in this manner can yield the following reactions:

$$H^* + H \rightarrow H_2$$
$$H^* + OH^* \rightarrow H_2O$$
$$OH^* + OH^* \rightarrow H_2O_2$$

The free radicals, H*, OH*, and H_2O_2, loaded with energy and resulted due to the ionization reactions, interact with the cellular structures (membrane system) and with the organic substances in the cell (in the nucleic acids and proteins case, there is induced serious damage), being responsible for the radio induced effects. They destroy the membrane systems of different cellular organs; they break the purine and pyrimidine rings, determining the induction of a large number of mutations and many other modifications.

The ionized radiations effect unit of measure is Gray (Gy). 1 Gy represents the energy of 1 Joule absorbed uniformly by 1 kg of mass of living matter from an ionized radiations field:

$$1 \text{ Gy} = 1 \text{ J}/1 \text{ Kg}.$$

In medical practice it is utilized the old unit of measure **rad (r),** because the dose of 1 Gy is too high.
1 rad is the radiation dose absorbed, in which 1kg of living matter absorbs uniformly from the ionized radiations field energy of 0.01 Joule. Analogously, it can be said that the rad is the energy of 100 ergs absorbed by 1 gram of living matter from the ionized radiations field.

$$1 \text{ r} = 10^{-2} \text{ J/kg or } 1 \text{ r} = 100 \text{ ergs/g}$$
$$1 \text{ Gy} = 100 \text{ r}.$$

Gy replaces the old measure called Roentgen. 1 Roentgen (R) represents the quantity of radiations capable of producing $2{,}08 \times 10^9$ pairs of ions in $1 cm^3$ of air at the atmospheric pressure of 760 mmHg.

The ionization density is represented by the number of ion pairs produced on the unit of capacity by different types of radiation. After their value of ionization density, the radiations are of two types:

-radiations with low ionization density (called also low-LET radiations, are with low energy linear transfer). They produce a low number of ion pairs on the capacity unit, inducing a low ionization and a low biological effect. The X radiations and gamma radiations are included in this category.

- radiations with high ionization density or high-LET radiations have a high energy linear transfer. They produce a high number of ion pairs on the capacity unit, their radiobiological effect being much higher. For instance, the ionization density of the neutrons is about 10-20 times higher than the one induced by the X radiations or gamma radiations. The biologic importance of the ionization density is logically explained: the number of points where there are impacts (and possibly breakings) between free radicals and biologic structures or molecules is much higher, because the ionization density being higher. In these points there are breakings in the DNA molecule, in chromosomes, cellular membranes etc; the effects being much important in the case of high density of ionization radiations.

If there is a relation without threshold between the genetic effect of the radiations and the irradiation dose, the dose of irradiation must go beyond certain threshold to induce a form of cancer.

The ionized radiations induce an evident genetically instability, a radio induces cancer being frequently linked with other mutations too, fact that determines the function loss of one or more genes. The mutagen process is composed of many phases and it is of long period of time through specific translocations or loss or deletion of chromosomes.

The most frequent radio induced neoplasies are leukemia, lung cancer, thyroidal cancer and osseous cancer.

In the first place of radio induced cancers it is found the leukemia, being frequently found between radiologists, survivors of the Hiroshima and Nagasaki bombardments, radioactive contaminated persons after nuclear hazards, sick people with ankylosing spondylitis which are irradiated etc.

The induction of leukemia in experiments on mice shows the two main factors:

- the age of the animals in the time of the exposure, the younger individual are more exposed then the adults

- the dose of irradiation and the manner of exposure of the fractioned irradiations administrated to the whole body are more efficient, the males being more exposed than females.

The causes of irradiations:

- professional (radiologists)
- nuclear explosions (Hiroshima, Nagasaki)
- exposure in therapeutically purpose

Lung cancer

It is the most found form of cancer induced by radiations. It was found frequently to miners, the cause being the exposure to radioactive gases (radon, radio nuclides of the radium, uranium etc.).

Thyroidal cancer

It can be induced by internal or external irradiation (with radioactive iodine from the environment, assimilated after by the thyroid). The threshold dose for inducing the carcinoma is 200 R. Externally; the iodine source is represented by nuclear accidents (Chernobyl explosion).

Osteosarcoma

After the radioactive contamination it can be constituted deposits of radium and thorium in the bones, which can realize in time high cumulative doses. The values for the appearance of these effects are of 30 kR, accumulated by summing the effect. SR 90 can participate in the forming of the radioactive deposits. It can get in the animals food and then in the human organism, especially through milk.

Skin cancer

It appears after many years of irradiation with high doses (over 1000 R in the case of unique sources and over 4000 R in the case of fractional cumulative doses). The risk of appearance is linked with the age at which the exposure took place: the lower the age, the higher the risk.

The acceleration of the aging process

Through experiences on mice, it was observed that the irradiation shortens the survival duration, by cancer appearance or by inducing degenerative phenomena in the structure of organs and tissues. It can be said that these phenomena of accelerated aging are similar with the physiological ones.

The effects of aging acceleration depend of:

- Sex
- Professional activity
- The type and dose of radiations (the thermal neurons have more power than gamma radiations, X rays etc.)
- Irradiation conditions

The mechanisms through the aging processes are accelerated, are:

- Cellular death
- The wound of stem cells
- The affectation of the defense mechanisms through antibodies
- Perturbations in development
- Somatically mutations

The irradiation disease

It comprises the modifications produced in the organism under the influence of the ionized radiations.

Etiology: the irradiation disease is produced by ionized agents (that produce ions), like the electromagnetic radiations (Roentgen rays) or corpuscular radiations (a, b with neutrons).

The irradiation disease can supervene in the following circumstances:

- in medical explorations (radioscopy, repeated radiographies or explorations with radioactive isotopes);
- in the treatment, especially of malignant tumors, with ionized energy (Roentgen rays, radioactive isotopes);
- in other explorations, in industry, where with the help of ionized radiations it can be verified the quality of some materials;
- by explosion of atomic bombs.

Pathogenesis: the irradiation can be external (Roentgen rays, gamma radiations) or internal (through radioactive powder, which can get inside the organism by digestion, inhalation or much rarely by wounds).

Through irradiation, metabolic, endocrine or nervous disorders can be produced. The symptomatology is variable and can take many clinical forms, depending on the irradiation quantity induced, on the surface and volume irradiated, on the individual sensibility, on the manner of irradiation (fractional etc).

We can distinguish, two clinical forms:

a) the acute form that can be produced by limited and general irradiations

The local effects prevail in the limited irradiations: dermatitis, vesicles, ulcerations and necrosis. The general irradiations are more important than the partial ones, especially when they are unique and with a big dose. They can produce the following clinical forms:

- the mild form (at 200 – 300 r) which is characterized by vomiting, cephalic disorder, diarrhea, anorexia, leucopenia, hair loss;

- the medium form (at 400 r) is characterized by agitation state, cephalic disorder, vomiting, diarrhea, anorexia, hair loss, leucopenia etc and it is deadly in 50% of the cases;
- the critical form (at 600 r) and
- the instantaneous forms are deadly and are characterized by hallucinations, intense excitation state.

b) the chronic form appears after general, small, repeated irradiations

There are three degrees depending on the gravity of the disorder, which in some cases can succeed one another being progressive phases.

- First degree: general disorders, reversible – asthenia, cephalic disorder, vasomotor disorders, insomnia, sanguine modifications (eosinophily, leucopenia)
- Second degree: at the disorders from the first degree there can be added: diarrhea, anorexia, pruritus etc.
- Third degree: same symptoms as in the first and second degree, but there are more accentuated acute crises and local lesions.

The **diagnosis** of the irradiation disease is determined taking in consideration the symptoms presented by the patient and of the circumstances.

The **prognosis** depends on the intensity of the disorders and on the complications that can supervene.

The prophylactic **treatment**:

- must include avoiding the futile radiological investigations and radioactive isotopes investigations;
- must include the rigorous respecting of the labor protection rules in the radiological system and isotopes system, or in other working places where ionized radiation sources intervene.

The **curative treatment** must include: first of all, the patient must get out of the influence of the radioactive substances. The local lesions (radio epidermatitis, radio epithelium diseases, scars etc) are treated by medicines (calming pomades etc), physical agents (infrared rays 20 – 30 sessions) or chirurgical (extirpating the lesion, eventually plasty).

Radiations doses in the irradiation disease

<table>
<tr><th>Exposition time</th><th>Supra lethal dose
10 Gy</th><th>Medium dose
5 Gy</th><th>Sublethal dose
2 Gy</th></tr>
<tr><td>First week</td><td colspan="2">Nausea and vomiting in the first day</td><td rowspan="2"></td></tr>
<tr><td>Second week</td><td rowspan="2">Nausea, vomiting, diarrhea, fever, neck swell, depression, dehydration, asthenia, decease</td><td></td></tr>
<tr><td>Third week</td><td>Bad general state, loss of appetite, alopecia, bleedings, pallor, diarrhea, neck swell, asthenia, decease</td><td>-Loss of appetite, alopecia, neck swell, pallor, bleedings, diarrhea;
-the patient enters in the recovery period;
-no decease if there aren’t any complications</td></tr>
</table>

REFERENCES

CHIOSILĂ I. 1998. *Radiațiile şi viața*.Societatea Română de Radioterapie. Bucureşti.

CIORBĂ D., COSMA V., MORARIU V., RISTOIU D., COSMA C. 2006. *The emvironment and Cancer***.** Environement & Progres **8**: 73-76.

DINU ALEXANDRA, DICU T., COSMA C. 2006. *Efectele biologice ale radiațiilor*. Environement & Progres **6:** 149-155.

DORDEA MANUELA, COMAN N. 2005. *Ecologie umană*. Casa Cărții de Stiință. Cluj Napoca. 489 p.

ONCESCU M.1996. *Conceptele radioprotecției*. Edit. Horia Hulubei Bucureşti-Măgurele.

PĂTRUȚOIU RAMONA LINDA. 2006. *Efectele radiațiilor asupra organismului uman*. Referat doctorat - Universitatea de Medicină şi Farmacie Craiova.

PETRI DOINA. 2007. *Cancerul pulmonar şi radiațiile ionizate*. Ecoterra. 12 an IV. Cluj Napoca: 32-33

RAICU P.1997. *Genetica generală şi umană*. Edit. Humanitas. Bucureşti. 357p.

RĂILEANU C. & RĂILEANU MOȚIU IOANA. 1974. *Atlas de Hematologie*. Edit. Acad. Bucureşti: 25, 340.

TAHÂŞ S., RISTOIU D., COSMA C. 2007. *Influența radiațiilor cosmice asupra climatului terestru*. Environement & Progres **9**: 535-540.

ȚOLEA I., 2000. *Dermatologie Clinică.* Edit. Sitech. Craiova.

Pătrutoiu Ramona Linda - Resident doctor –Spitalul Clinic Universitar Craiova
ramona_patrutoiu @ yahoo.com

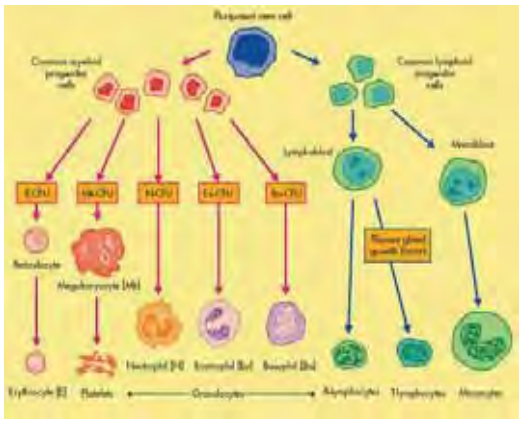


Figure 1. Sanguine elements filiation
Figure 1 Filiația elementelor sanguine
(after RĂILEANU C & RĂILEANU MOȚIU I-1974)

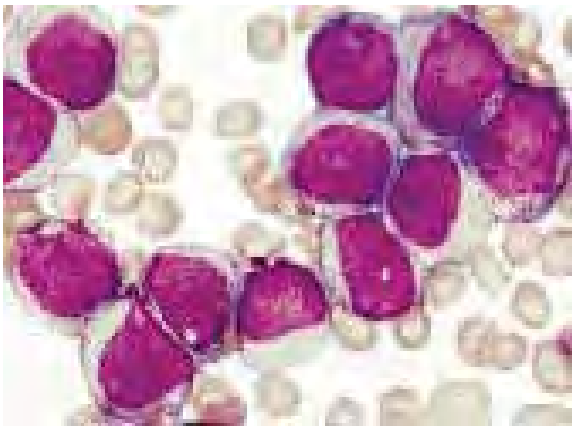
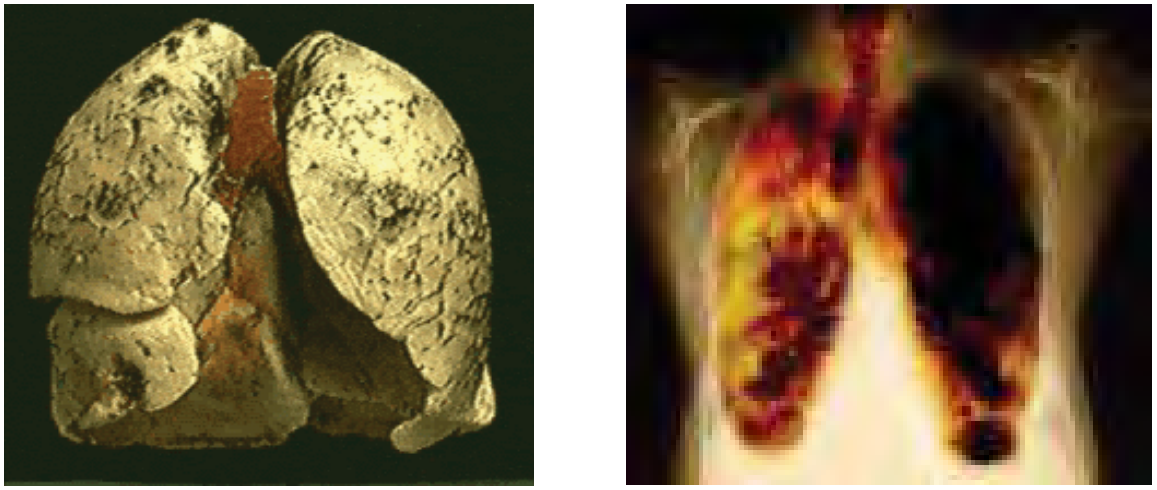


Figure. **2** Sanguine smear – leukemia
Figure. **2** Frotiu sanguin – leucemie
(after RĂILEANU C & RĂILEANU MOȚIU I-1974)



a **b**

Figure 3 Lung cancer aspects a-macroscopically b-radiological
Figure 3 Aspecte de cancer pulmonary: a-macroscopic, b-radiologic
(AFTER RĂILEANU C. & RĂILEANU MOȚIU I-1974)

Figure 4. Malignant melanoma
Figure 4. Melanom malign (after TOLEA -2000)