THE THEORY OF INDIVIDUAL VARIABILITY OF OSTEOTROPIC RADIONUCLIDES METABOLISM.

N.LYUBASHEVSKY, V.STARICHENKO, A.GOLUBEV, E.SHISHKINA.
Institute of Plant & Animal Ecology, 620219, Ekaterinburg, RUSSIA.

The greatest radiation accidents - Kyshtym (in the Urals), on the Three Miles Island, in Chernobyl led to increased accumulation of artificial radionuclides in organisms of tens of thousands of people, and also in animals. Unfortunately, new similar and even more dangerous accidents are possible. Health condition examination and controlling of such great population contingent are unlikely possible. The only rational way is to reveal and to analyze groups of the increased risk. Individual dose overloading or prognosis of dose overloading from the internal radiation is one of criteria of these groups. Obviously, revealing of individuals with the increased defeat possibility has great medical , social, agricultural and economic importance.

Osteotropic radionuclides are of specific danger for human being long time after accident. This is connected first with such fact that most of them have a long half-life period and secondly, they can be selectively accumulated in the skeleton, being tightly bound with bones, Reaction to the inner irradiation by incorporated radionuclides depends on their kinetics that defines the dose load besides of individual radio sensitivity.

Despite the fact that thousands of works and dozens of mathematical models [5] are devoted to osteotropic radionuclides metabolism only isolated ones promise satisfactory reconstruction of individual absorbed doses in future and no one leads to their individual prediction.

The aim of this paper is to study mechanisms of individual peculiarities of osteotropic radionuclides skeletal metabolism, and to develop approach for dose value prediction. Some regulations explaining the importance of skeleton in radionuclides metabolism and showing the direction of search of its quantitative regularities are taken as a basis of these theory. The first, there are three evolution trends: universal significance of calcium in the cells in the row beginning from bacteria to highest organisms and increase of its regulator role in the multycellular on the level of organism; ability of calcium salts to increase mechanical strength of supporting tissues; growing connection of metabolic and supporting function. The second, bone is involved in metabolism of radionuclides as a structurally functional wholeness. The third, metabolic way of radionuclide from blood into bone consists of a number of stages. At each stage a life of radionuclide depends on its physical chemistry properties (alkaline earth, actinides and so on). The stages can be combined with respect to time and place. Radionuclides in blood are in ionized or colloid condition, they are partly fixed with proteins, blood cells, bioligands. At the same time they are mixed in circulation and are carried through capillary walls. Permeability is higher in the form of ions, high-dispersed colloids, complex compounds which are fixed neither with proteins nor with form elements of blood. "Deponing agent" of citrate type, breaking away radionuclid from proteins and cells and promoting permeability of capillary wall into extravascular space of a bone (20 $mm^3/gr.$) with its connective tissue and osteogene cells in which actinides are deposited appreciably, was found in bone capillaries. The next stage is bone surfaces having a number of local peculiarities. The processes of ion exchange, of adsorption and chemical combining, of diffusion are taking place here. Isotope is moving forward deep into bone along canaliculi-lacunar net. When in bone radionuclide is subjected to translocation, walling, resorption together with reorganized bone tissue. Their removal out of bone occur in the result of diffusion, desorption from the surface and cell resorption. Recirculation leads to new deponing. The fourth, radionuclides metabolism in skeleton is defined by 10 limiting morpho-physiological factors (LMPF). LMPF are physiological processes, physical chemistry reactions, biochemical substrata and hystological structures participating in the metabolism of radionuclides in skeleton tissues.

As a whole they are an integrated system which is necessary and sufficient for the complete description of radionuclides exchange in vertebrates skeletons. The influence of each of them is independent of the influence of others. They were distinguished from "innumerable" quantity of outward and inward factors influencing metabolism of radionuclides in skeleton. LMPF is: F_1 - blood circulating through skeleton; F_2 - ability to transcapillarity transfer; F_3 - deponing agent; F_4 -competitor role of intensity of radionuclide accumulation in soft tissues and its removal together with excreta; F_5 - desorbtional ability of the bone surface unit; F_6 - total area of skeleton; F7 - resorption; F_8 - growth leading to walling radionuclide being deposited on the surface and

accompanied by its local dislocation; F_9 - exchange inside of osteogenic cellular elements; F_{10} - surfacevolume correlation (effectivity of removing depends on a quantity of radionuclide deponed on the surface and in the volume of a bone). An individual variability can concern each of LMPF. Principle possibility of data using an individual kinetics of osteotropic radionuclides in dose loading retrospective evaluation and prediction has been studied by means of mathematical model (Fig. 1).

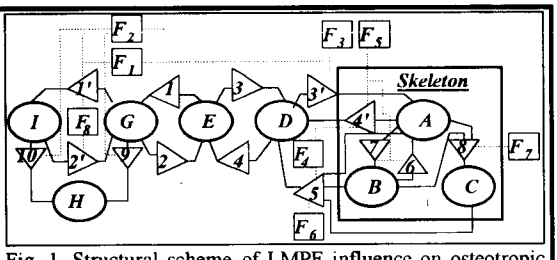

Fig. 1. Structural scheme of LMPF influence on osteotropic radionuclides metabolism.

Circles - chambers (A - bone surface; B - non-walled up; C - walled up volume; D - extravascular liquid of bone; E - blood; I - extravascular liquid of soft tissues; G - soft tissues; H - excreta. Triangles (arrows) - communications. Rectangles, F - LMPF.

Intercommunication of LMPF and their integral effect are represented in this model as an eight chamber model, in which the meaning of communication constants is defined by LMPF. A big number of chambers is justified by the fact that each of them reflects physiological reality. Thus chamber of extravascular space of bone and soft tissues introduced in the process of work turned out to be extremely significant. They allowed to describe processes of desorption taking place on the bone surface and in soft tissues more fully, that led to refusal from correction coefficients. The model is described by the system consisting of 8 linear differential equations having constant coefficients. In order to quantitatively characterize LMPF their parameters "a_1" were introduced. We illustrate specified approaches with some examples.

KO3 -is a velocity of transition out of extravascular space of a bone onto a bone surface which is defined by its sorptional ability and which is 88 times as high as permeability of capillary membrane KO3=58291.

K6,K7 - are the velocities of transition out of non-walled up volume onto the bone surface and from the bone surface into non-walled up volume, they are accordingly defined using the curves of washing off and accumulation of ^{90}Sr out of bone fragments.

Numerical values of parameters of LMPF of rats, mice, dogs, fish and men were defined. Qualitative agreement of radionuclides metabolism curves depending on their physical-chemical properties, species and physiological condition of organism (man, norm and Pedget illness) with real indexes was got with the help of this model.

An example of the results of study of individual variability of metabolism of osteotropic ^{91}Y and LMPF in the experiment and with the model is shown in the Fig. 2. The following parameters of LMPF were got: ability for permeability, part (0,16; 0,10; 0,22); skeleton surface area, cm^2 (569, 545, 731); desorptional ability, relative units(0,008; 0,017; 0,010); resorption, part/hour (0,015; 0,0009; 0,0009); surface-volume of a bone ratio, cm^{-1} (69;62;49). Average-species meanings of three other LMPFs are used in the model: blood-circulating, part (0,115), deponing agent, part (0,2), intensity of soft tissues metabolism and excretion, relative units (0,1). Satisfactory alignment of experimental points (vital registration) and calculated meanings of curves of removal is noticed.

In order to study the distribution of dose loading of internal β-radiationthe method of TLD-dosimetry was used (research are carried out in cooperation with dr.T.Betenekova, USTU-UPI). The distribution of ^{90}Sr in dog's and in rat's skeletons was measured TLD-dosimetric detectors of Al_2O_3 were used. TLD-indexes of absorbed dose for the unit of time (relative units) are shown in Fig. 3. You can see that ^{90}Sr is distributed along bone surfaces of a skull extremely irregularly (beginning from 6,4 relative-units in back part of a head till 22,6 relative units in the region of eye-sockets). Indications of TLD in the teeth (in enamel, dentine, cement) were also measured. They call for a separate discussion. Besides physiological aspects of metabolism of tooth, tissues the interest in tooth as to "an individual dosimeter" is very considerable. Interpretation of ESR-signal of enamel allows to evaluate adequately an absorbed dose of γ-radiation. However, this method is not adapted for β-radiation. β-source, including ^{90}Sr, in the result of peculiar structure, composition and physiology of different

reflected in the value of absorbed dose. Quantitative revealing of patterns of manifestation of these specific features for ^{90}Sr must become a bases for transition from absorbed dose in tooth tissues to the doses on the cells of skeleton surface, red bone marrow and inside the whole body.

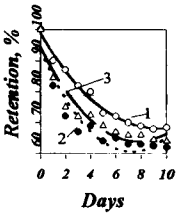

Fig. 2. Curves of retention of ^{91}Y with different individual parameters of LMPF in rats.

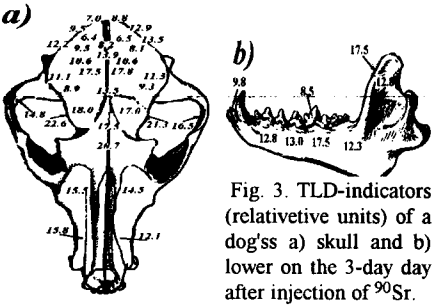

Fig. 3. TLD-indicators (relativetive units) of a dog'ss a) skull and b) lower on the 3-day day after injection of ^{90}Sr.

Specific features of radionuclide metabolism of teeth in our mathematical model are reflected in the following way: radionuclide comes from extravascular space of tooth pulp through the layer of odontoblasts to dentine surface and then to dentine canaliculi. In the framework of this model these stages are identical to extravascular space, bone surface, and bone volume. Radionuclide diffuses into enamel from dentine canaliculi which is described as a bone volume. Radionuclide also come into enamel from saliva (additional chamber and communicational constants: blood-saliva-enamel). Radionuclide moves along dentine canaliculi (analogy with bone volume) and from pericementary capillary net (in such a way as on the bone surfaces) into cement of tooth's root. An important peculiarity of tooth tissues is shown in removal of radionuclides deponed in teeth: normally they are subjected to remodeling very slightly (cement, dentine). Hence the most valuable in dosimetric relation quality of teeth: the most part of dentine and cement and practically all the enamel, being formed during the period of generation, are kept during the whole life, while any other area of bone is replaced repeatedly. Removal of radionuclides out of tooth tissue is made practically only by diffusion-desorption. Parameters of all LMPF of a tooth are quite accessed to quantitative definition and are identified now. Of course, not only kinetic data but steriometric relations between radiating tissues are taken into consideration when defining absorbed dose in tooth tissues with the help of ESR-method. So, dose loading is provided not so much by deponed isotope in it, as by the adjacent teeth and soft tissues, saliva and radionuclides of ration. Thus, the description of processes of radionuclides deponing in tooth tissues requires definite corrections in a structural scheme of a model and evaluations of parameters of appropriate chambers and communication constants.

Thus it is shown that individual peculiarities of kinetics of radionuclides in bones reflect quantitative differences of parameters of several limiting morphological and physiological factors (LMPF). This theory allows to hope that data of individual absorbed dose can be obtained from the results of living organism tests for LMPF parameters.

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