INTERPRETATION OF EXPERIMINTAL DATA ON POLONIUM-210 METABOLISM FOR COMPUTING ADMISSIBLE LEVELS

Yu.D. Parfenov

Institute of Biophysics of the USSR Ministry of Health
Moscow Union of Soviet Socialist Republics

Abstract

Experimental data on ^{210}Po metabolism in animals show that there are some uncertainties for the value of absorption into the blood from the gastro-intestinal tract and from the respiratory system; for the choice of the critical organ and for assessment of the nonuniformity of the internal irradiation. However there is no real basis for radical changes in the existing admissible levels of ^{210}Po intake into the huma body.

^{210}Po is one of the most highly toxic radionuclides /1/. Th existing ICRP recommendations are based on the admissible ^{210}Po content in the body of the professionals equal to 0.03 μCi, and the spleen is taken as a critical organ with ^{210}Po content equal to 0.002 μCi/2/. This paper sets out to analyse experimental data on ^{210}Po metabolism in animals fo calculating admissible levels of this radionuclide intake i man.

Absorption from the gastro-intestinal tract

ICRP recommendations are based on the value of ^{210}Po absorption from gastro-intestinal tract into the blood equ to 0.06. This value was obtained by administering inorgani compounds of ^{210}Po to animals /3, 4, 5/. Our data for dogs and rats confirms this value. However Morrow et al. /6/ ha

shown already that absorption into the blood depends on physico-chemical properties of the ^{210}Po compound administered. According to their data for cats the rate of absorption from intestinal tract for soluble polonium citrate was 10 times higher than for colloidal polonium. It was Hill /7/, Litver /8/, Kauranen and Miettinen /9/, who first drew attention to the fact that the assessment of the natural ^{210}Po intake by people from the Arctic regions who eat reindeer meat gives a value of ^{210}Po absorption from the intestinal tract, which is much higher than was assumed from experiments. Our indirect assessment of the natural ^{210}Po absorbed into the blood, which enters the human body from the environment mainly through food, is 0.35 /10/. This high absorption into the blood may be explained by the fact that ^{210}Po which enters the body with meat or other food stuffs is in form of organic compounds, where it is bound with highly soluble aminoacids. Another reasonable explanation for this fact is that the ^{210}Po natural intake into the body is 10^5-10^6 times less the amounts of ^{210}Po administered to experimental animals. This difference may influence the physico-chemical state of ^{210}Po microquantities with pH in the intestinal tract, and thus the level of absorption into the blood. Johnson and Watters' latest data /11/ show that ^{210}Po entering rats in the form of organic compounds with milk from exposed cows is absorbed from the gastro-intestinal tract into the blood in much higher levels than with administration of inorganic compounds. This may serve to confirm the first proposition. Thus the level of absorption of ^{210}Po in the form of organic compounds in food stuffs is higher than that in the form of inorganic compounds. It would thus seem that there is no reason to increase the value of the ^{210}Po absorption coefficient in order to calculate the admissible intake for professionals, as they are dealing with inorganic ^{210}Po compounds. However, when calculating the ^{210}Po intake via food chain it is necessary to take into account the fact that organically bound radionuclide is more easily absorbed into the blood.

Absorption from the respiratory system

The level and rate of radionuclide absorption from the lungs into the blood are mainly determined by the degree of solution of the inhaled compound.

Berke and DiPasqua /12/ consider that ^{210}Po absorption into the rats' body after multiple inhalation amounts to 20-26% of the radionuclide inhaled. The ^{210}Po absorption coefficient for rabbits' lungs which was obtained through comparison of ^{210}Po retention after intravenous and intratracheal administration, the retention being measured by histoautoradiography and counting tracks, is 27-48% of the total amount of radionuclide retained in the lungs /13/. For rats, 29,4% of the ^{210}Po administered intratracheally is absorbed into the blood. Smith et al. /14/ obtained a value of 20.3-32.3% for the ^{210}Po absorbed by dogs inhaling polonium chloride. Little and McGandy /15/ studied the ^{210}Po absorbed into the blood through smoking. According to their assessment at least 38% of the total amount deposited in the lungs is absorbed

into the blood. Thus the probable quantity of the inhaled compound, assessed on the basis of above-mentioned data, allows us to say that about 19-34% of the ^{210}Po inhaled is absorbed into the blood.

The dynamic lung model for retention and clearance of radionuclides inhalaed into the respiratory system /16/, which was developed by ICRP, is an important step forward compared with their former recommendations. According to this model polonium and its compounds belong to the "W" class (moderately soluble compounds). This model's parameters, characterizing the ^{210}Po behavior in the respiratory system, correspond to the actual process of ^{210}Po clearance from the lungs. Our data for rats and other experimental data /14/ fully confirm that the longest biological half life from lung is 50 days.

According to the ICRP model the quantity of radionuclide absorbed into the blood from respiratory system is determined by the following expression:

$$\frac{D_3 f_a \lambda_a}{\lambda_a+\lambda_r} + \frac{D_4 f_c \lambda_c}{\lambda_c+\lambda_r} + \frac{D_5 f_e \lambda_e}{\lambda_e+\lambda_r} + \frac{D_5 f_h \lambda_h f_i \lambda_i}{(\lambda_h+\lambda_r)(\lambda_i+\lambda_r)}$$

where D_3, D_4, D_5 - the corresponding coeffecients for deposition in three regions of the respiratory system (nasopharynx, tracheobronchial region and pulmonary region) which depend on the aerodynamic diameter of the particles; f - corresponding fractions of radionuclide in each region cleared with the according constants of biological elimination - λ (f and λ do not uepend on the particles' size); λ_r - the constant of radioactive decay. Substituting the corresponding figures for D, f and λ for the "W" class and $\lambda_r = 0.005$ for ^{210}Po and solving this expression, we obtain an absorption coefficient of 9.4-14.5% for the particles in size range of 0.01-10 μm. As can be seen from the above, this calculated value is substantially less than the absorption value for ^{210}Po obtained from actual experiments. This divergency can be explained by the fact that ^{210}Po in the body can not be considered a homogeneous, moderately soluble compound, because in pH in the body polonium can be found in two fractions simultaneously - aggreggated (insoluble) and ionic (soluble) - which have their own rates of clearance from the sustem.

Analyzing the routes of ^{210}Po metabolism in the respiratory system according to the ICRP model, it can be seen that 80% of the material deposited in the pulmonary region is transported by the cilia through the tracheobronchial tree to the gastro-intestinal tract and only 15% with $T_{1/2}(biol.)=50$ days is absorbed through alveolar membranes into the blood. It would seem that the value of f_e - fraction transported from the pulmonary region into the blood, for ^{210}Po amounts to 0.45 instead of 0.15. There follows a parallel reduction in the values for the f_f and f_g - fractions transported to the gastro-intestinal tract, to 0.3 and 0.2 respectively. Once the parameteres have changed in this way the absorption coefficient will be equal to 15.8-32%, which corresponds more closely the actual experimental data.

Distribution in the body

^{210}Po in the blood is found in two forms - in an ionic, highly dispersed state and in an aggregated state simultaneously.

The highlydespersed ionic form of ^{210}Po probably bound with organic acids, is easily soluble and transportable; ^{210}Po in this form is distributed in the body correlating with sulphur distribution, being its analogue and possible substitute in organic compounds. ^{210}Po in this form is easily excreted through the kidneys with urine.

The other fraction is the aggregated form of ^{210}Po. Its basis is the colloidal or pseudocolloidal forms of ^{210}Po with the body pH. This form of ^{210}Po can be nonspecifically bound with protein. The aggregated ^{210}Po is not diffusable because it is in the form of large aggregates which cannot enter the membranes and the walls of blood capillaries. They are phagocit ized by macrophags and the cells of the reticulo-endothelial system. That is why this form of ^{210}Po is mainly deposited in the liver, spleen, lymphatic nodes and, partly, in the adrenal glands. This form of ^{210}Po is excreted through the intestines with the bile. These states of ^{210}Po do not appear to be stable. ^{210}Po can transfer from one state to the other. Thus, for example, aggregated ^{210}Po can be destroyed transferring to the highly dispersed form under the influence of complex-formation with organic ligands.

A part of ^{210}Po (apparently in the dispersed form) is adsorbed to the surface of the erythrocytes, and when the latter are destroyed it is deposited in the spleen and liver. The ratio of these two forms of ^{210}Po depends on many factors: the pH environment, the presence of other chemical compounds (phosphates, citrates, thiols et al) and, finally, on the concentration of polonium atoms.

Critical organ

Though at present the spleen is considered as a critical organ for ^{210}Po, there exist at least three more organs with the same radiosensitivity level, where ^{210}Po retention is 2-3 times higher than in the spleen-that is the kidneys, liver and lymphatic nodes. At the same time ^{210}Po concentration in the gonades, regarded as belonging to the first group of radiosensitivity, is only 2-3 times less than in the spleen. We observed that the relative ^{210}Po retention in the spleen decreases in the following succession: mouse-rat-rabbit-dog-man. This speaks for the fact that it is hardly reasonable to choose the spleen as a critical organ.

The earliest changes under the influence of minimal ^{210}Po quantaties exeeding admissible levels 10-50 time, may be found in the function of the liver enzymatic system, in the skin and endothelial capillaries, in the blood system and in the state of enzymatic systems and bile secretion function of the liver. Those changes are as follows: transient bilirubinaemia, increased aldolase content in the blood serum, changes in the volume of renal plasma flow; displacement of adsorbtion exponents of ^{131}I bengal-rose by the liver cells /17/. With higher

levels of radiation after ^{210}Po administration to experimental animals the liver and kidney also show more signs of serious damage compared with other organs. However, the relatively umform ^{210}Po distribution with prevailing retention in the reticulo-endothelial system leads to the irradiation of practically all the organs and tissues. In connection with this, damage to the neuro-endocrinal systems is characterestic for ^{210}Po; this damage in its turn indirectly furthers the development of radiation damage in various organs stemming from the direct impact of α-irradiation /18/. The essentially adaptive reactions of the sympatho-adrenal system and the pituitary-adrenal cortex system may exceed the physiologically expedient level and aggravate the progression of radiation sickness. One should bear in mind that the direct impact of ^{210}Po on the hypothalamopituitary region and on the reproductive system is more important than its effects on the reticuloendothelium, where the radioisotope preferentially accumulates. The concept of "the critical organ" or the preferentially irradiated organ is in adequate for analysis of the pathological process following exposure to ^{210}Po. It is probably fair to say that the critical organ concept is valid only when we consider the reaction of the body as a whole that develops as a result of the direct impact of the isotope on tissues and its indirect effects. An this considerably complicates the choice of the critical organ for ^{210}Po. However calculation of admissible irradiation levels taking various systems as the "critical organ" (kidneys, liver, spleen, reproductive system, the whole body) reveals no essential divergencies for assessing admissible intake.

Non-uniformity of irradiation

In spite of the generally uniform ^{210}Po distribution in the body, the difference between the highest concentration (in kidneys) and the lowest (in the skeleton) constitutes two orders. In the homogeneous tissues the ^{210}Po distribution is fairly diffusive and relatively uniform. However in some organs (kidney, spleen) the distribution of ^{210}Po is non-uniform. Thus, for example, the ^{210}Po concentration in the renal convoluted tubules is approximately 30 times higher than in the medulla, as was obtained by the histoautoradiographic method used for rabbits /13/. Even with the regular intake of radioactivity by man at uranium mines the ^{210}Po concentration in the renal cortex is 4.2 times higher than in the medulla /19/. In rabbit spleen after a single administration of ^{210}Po the ratio of red pulp/phollicule concentrations is about 5/13/. On the whole, the maximum concentrations of the radionuclide in the kidney and spleen are usually 2-3 times higher thas the mean concentration for organ, which is used to calculate admissible levels. In connection with this fact one should take into account the non-uniformity of distribution while assessing the maximum levels of irradiation on the basis of the mean concentration for the organs (or the total content in the body divided by the organ's weight).

Elimination half-life from the organs

The decrease of ^{210}Po in the organs after a single administration is well described by one exponential function during a long-term observation. Only in the initial phase, which is limited to several days after administration, it is possible to determine for certain organs one more rapidly eliminated fraction with a short half-life (lymphatic nodes, liver, kidney). The rate of decrease for ^{210}Po amounts, as a result of biological elimination and radioactive decay expressed through T_{eff}, can be taken as similar for all organs and tissues. The T_{eff} differences in the experimental data can be explained by the insuffecient number of measurements, by individual deviations and by the range of measurements. This speaks for a similar mechanism of ^{210}Po metabolism in tissues. The T_{eff} value ranges from 29 to 42 days /18/ as was confirmed by experimental data on dogs, rats and mice after a single ^{210}Po administration. The value of 37 days may be generally accepted. This value corresponds well to the data for man which range from 22 to 47 days /21-24/. The rate of ^{210}Po excretion from rabbits is considerably higher. T_{eff} for rabbits is about 6-19 days /25/.

Conclusion

Thus after analyzing the experimental data on ^{210}Po metabolism obtained from animals, it is possible to conclude that there are some uncertainties regarding the coefficient of absorption into the blood from the gastro-intestinal tract (organically bound compounds of ^{210}Po) and form the respiratory system; regarding the choice of the "critical organ" and the assessment of non uniform internal irradiation in organs. However at present, these uncertainties do not provide adequate ground for substantially modifying existing admissible levels of ^{210}Po intake for man.

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