TRITIUM RADIOBIOLOGY

K.N. Muksinova, G.S. Mushkacheva, G.G. Rusinova, V.B. Shorohova,
V.S. Voronin, E.N. Kirillova, V.S. Revina, T.I. Uryadnitskaya

Branch No. 1 of Russian Federation State Scientific Centre Biophysics Institute
456780, Ozersk (Chelyabinsk-65), RUSSIA

INTRODUCTION

Actuality of the tritium biological effect researches is caused by its wide spreading due to accumulation of technogenic tritium in biosphere as well as the possibility of increasing of persons working with this nuclide because of real perspective of the thermonuclear energy production. Information about tritium effect in conditions, that is closely like the real conditions, i.e., under chronic isotope intake, is especially important.

The materials of many-years work of authors' group have been generalized in this paper on the kinetics of forming of early and late effects following the prolonged influence of tritium in broad range of doses including low level.

MATERIALS AND METHODS

Studying the chronic influence of tritium oxide (HTO) has been conducted for two species of laboratory animals on the different levels of integration (from molecular to population) by using the radiobiological, biochemical, hematological, cytogenetic, immunological, and pathomorphological methods. Animals were received the HTO during 3-6 months (dose rates of β-exposure ranging from 0.1 to 27 cGy/day, and absorbed doses ranging from 0.1 to 25 Gy).

RESULTS AND DISCUSSION

The study of tritium behaviour kinetics in chromatin of hematopoietic tissues under the prolonged HTO injections by 370 kBq/g per day has shown that 70-80% of nuclide were incorporated into DNA, and 20-30% of those were incorporated into chromatin proteins. The half-period of accumulation of tritium in DNA of hemopoietic tissues was 15-25 days. The excretion of label was being during two time period: 60-70% of label for 5-8 days; 30-40% of label for 12-18 days. Effectiveness of including tritium into carbon relations of DNA from water was 0.5-0.8, and if taking into account the easily exchanging tritium and tritium of 8th carbon of purine, it is approximately 1. Activation of the hematopoietic tissue proliferation (hemolytic anemia) did not influence on both the level of tritium incorporation into DNA and the effectiveness at the nuclide equilibrium period.

The common radiation burden on hemopoietic tissues as well as tritium inclusion into chromatin led to changes of DNA structure and reparation depending from dose, and also to nucleic acid metabolism changes. For prolonged injection of tritium oxide (37-1850 kBq/g per day, the absorbed doses of 1.2-28 Gy), the strong damages of DNA primary structure (by content of double-stranded DNA, and by single-stranded DNA molecular mass) were determined at and of nuclide injections in the animals, only which received moat amount of nuclide. The findings relate to DNA reparation at moment of tritium oxide intake in animals. The residual damages of DNA were remained after the intake end, and were found by additional test-exposure.

Content and rate of DNA biosynthesis depended from the dose rate and the absorbed dose. At first two months of β-exposure to incorporated tritium in dose range of 1-12 cGy/day, the DNA concentration in hemopoietic tissues was on subnormal

level, and that for high dose was on decreased level, despite the increase of absorbed dose. This was because of dose-depending activation rate of DNA synthesis from 14th day and practically during all period of nuclide injecting. However, under high values of rate of beta-exposure (the absorbed doses of 12 Gy), the decreasing of DNA content was indicated for studied tissues (thymus - 65% of control) at end of influence. After short-time recovery of this index, when radionuclide intake has finished, the secondary decreasing of DNA content was observed in animals of this group. The significant decrease of this index in hemopoietic organs corresponded the increasing of substances (polydeoxyribonucleases), that indicated to the DNA destruction, and reflected possibly the cell elimination with non-reversible radiation damages.

The DNA structure damage and their reparation developed to chromosome aberration. Cytogenetic studies of *Wistar* rats found the high sensitivity of myelocariocyte chromosomes to tritium damaging effect. During HTO injection (3.7-370 kBq/g per day, dose rates of 0.12-12 cGy/day, and absorbed doses of 0.24-25 Gy), the chromosome damages were mainly the aberrations of chromotide type in animals of all groups. The aberrations of chromosome type were being appeared with increasing the absorbed dose, which were mainly symmetrical exchanges. The time points of their appearance and frequency depended on the dose rate, and for maximum rate these damages began to be observed in 60 days after influence. At relatively later period the chromosome type aberration appearances and the absence of significant increase of chromosome damage in animal groups, when absorbed doses were being increased, evidence that there are adaptive processes under prolonged intake of tritium. The stable aberrations of chromosome type were being kept up to end of observation after cessation of HTO injections in animals, and the cell clones with atypical chromosome were determined for most of rats that were received the higher doses.

The nucleic acid metabolism changes developing under chronical effect of HTO in hemopoietic tissues made a basis for shifts of cell population kinetics in these tissues. It was found the dependence of hemopoiesis damages from nuclide dose burden under prolonged β-exposure to incorporated tritium with different dose rates (for rats -- 0.12-12 cGy/day, and for mice -- 0.04-4.4 cGy/day). The difference of tissue reactions of animals, which received the different HTO amounts, were expressing as different rates and depopulation. It was shown high sensitivity of multipotent and committed cells, that are precursors of myelo- and lymphopoieses, to tritium in comparison with morphologically recognized hemopoietic cells. The erythropoiesis damages under chronic effect of HTO was more clear, than granulocytopoiesis.

The clear dependence of character and fullness of recovery from radiation effect level was shown for bone marrow and lymphoid tissues after finishing of HTO injection. The recovery of cell content in these tissues of animals exposed to beta-radiation in dose of 12.5 Gy (dose rate of 12.0 cGy/day) was in 1-3 months later than after lower doses of exposure. The value of non-reversible decreasing of multipotent precursor compartment was being higher with increasing the absorbed dose. On this background, the recovery of lymphopoiesis, especially T-cell production, was defective. The population of committed precursors of T-lymphocytes stabilized on 40-60% level in comparison with B-lymphocyte precursors whose population reached the values of age norm in 3-6 months after the end of HTO intake. Also, the recovery of cellular structure in thymus and lymphatic nodes, which cells were mainly T-lymphocytes, was not full, and at the same time the cell content in spleen (B-cells) was being increased up to control level in 6-9 months.

HTO-induced changes of lymphopoiesis at different stages were being developed as the dose-depending damages of humoral and cellular immunity. During excretion of tritium oxide by amount of 370 kBq/g per day (mice, rats), the antibody production

was being lower up to 50% of control. Suppression of humoral response on the antigene at earlier time periods was caused mainly by insufficiency of T-helpers, and later of B-lymphocytes. Under prolonged intake of HTO by less amount, the antibody production changed during short-time period (for 185 kBq/g per day), or kept on level of age norm (for 37 kBq/g per day). The reliable dependence was obtained between the absorbed dose and the character and fullness of recovery of humoral and cellular immunity after the end of β-emitter intake. Antibody production, activity of normal killers, and T-inactivating lymphocytes recovered in 1-3 months after exposure to radiation in doses of 3-4 Gy, and in 9-12 months after the accumulated dose of 8.7 Gy (*CBA* mice).

The relative biological effectiveness (RBE) of tritium oxides in respect with γ-radiation (^{137}Cs) was determined basing on dependence of dose-effect after one-time injection of nuclide under the absorbed doses of 0.5-14.5 Gy. Taking into account the indexes of lymphoid organ's mass, the cell content in hemopoietic tissues, the damages of DNA structure and of nucleic acid metabolism, it may be indicated that RBE of tritium increased under decreasing of absorbed dose, and was 4-6 under minimum doses. The $DL_{50/30}$ value of RBE of tritium corresponded 2.32.

The late effects of tritium oxide intake are most important for assessment of its danger, particularly its cancerogenous influence. The publications on blastomogenous effects of tritium do not present the precise dose-depending outcome of malignant tumours at different sites (1,2). The late effects of prolonged beta-exposure to tritium incorporated were studied by us for following doses: 0.24; 2.02; 12.5; and 25.3 Gy. The frequency of malignant tumours in exposed *Wistar* rats exceeded the control level at 1.5-2.5 times. Revealed neoplasm at different sites may be divided on three categories by character of dose-effect dependence. Tumours of first category had the positive correlation with dose (leukaemia, lung cancer, skin cancer, osteosarcoma, and mammary gland cancer), at the same time tumours of second category had (lymphosarcomas of lung) were characterized by negative dose-dependence. The malignant tumours of endocrine organs, testicles, kidneys and urethra, gastro-intestinal tract did not have the reliable dependence on dose (3d category).

The difference of dose-effect dependence for frequency of different neoplasms induced by tritium makes the difficulty to use this criterion, as character of radiation danger. The non-stochastic index of dangerous effect for organism, such as lifetime shortening, is more integral and universal. The prolonged injection of tritium oxide by minimum amount (dose of 0.24 Gy) increased the mean lifetime (MLT) of animals by 12%, and in cases of injection of large amount of nuclide (dose of 2.02 Gy) the lifetime of animals did not differ from value of control. The further increasings of radiation dose up to 12.5 and 25.3 Gy led to decreasing of MLT of animals by 18% and 23%, respectively. However, decreasing of the MLT of animals was the same either in rats with malignant tumours, or in other animals. The absence of priority of malignant tumours for decreasing of the MLT makes possibility to think that there is single mechanism of thanatogenesis either for nature senescence, or for its acceleration, in particular, by radiation exceeding the specified level.

REFERENCE

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