Metabolic peculiarity of ^{134}Cs and its radioimmunotoxicological effect on central and peripheral immune cells*

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Abstract A fitted equation with least square method to describe the retention of ^{134}Cs in whole body is obtained by a whole body counter. That is $R(t) = 18.04\exp(-9.3175t) + 45.13\exp(-0.0423t)$, where $R(t)$ is in %, and t in d. The equation consists of two half-life components, the fast component is $T_{1/2} = 0.07$d, and the slow is $T_{1/2} = 16.14$d. Study on the localization of ^{134}Cs at cellular level was carried out by freezing microautoradiography. The results indicate that ^{134}Cs was chiefly in ionizing form accumulated in red as well as white blood cells. In bone marrow cells ^{134}Cs predominantly deposited in young cells and less in mature cells. Distribution of ^{134}Cs in soft tissues such as muscle, liver and cerebrum was observed. It should be noted that ^{134}Cs penetrated quickly into the tissue cells. The observation of investigating radioimmunotoxicological effect induced by ^{134}Cs shows that the inhibition of thymocytes is higher than bone marrow cells, the spleen T lymphocytes are more sensitive to ^{134}Cs than B lymphocytes and lymphocytes of peripheral immune cells are more sensitive to radiation than central immune cells.

Keywords Signal nuclide ^{134}Cs, Metabolic peculiarity, Autoradiography, Radioimmunotoxicological effect, Central immune cells, Peripheral immune cells

1 Introduction

^{134}Cs is one of the most important produts in heavy nuclear fission. It is a signal nuclide released by the accident of nuclear power plant. ^{134}Cs emits β particles and γ rays simultaneously. The people are paying close attention to its internal contamination to human health through ecological environment[1]. ^{134}Cs is easily absorbed into blood through various ways[2], and induced radioinjury effect to organism. In recent years, with the continuous development of nuclear power plants and with the wide scope use of ^{134}Cs in production and research fields, persons contacting with ^{134}Cs were increasing constantly. It should be noted that the radioimmunotoxicological effect of ^{134}Cs is closely related to its retention characteristics and now is still a problem. Therefore, it is necessary to study the metabolic peculiarity of internal contamination of ^{134}Cs in whole body and in cellular level, as well as its radioimmunotoxicological effect on central and peripheral immune cells.

2 Experimental methods and results

2.1 Metabolic peculiarity of ^{134}Cs

2.1.1 Retention of ^{134}Cs in whole body

Experiments were carried out on 10 male Wistar strain rats of 122±12 g. The retention of $^{134}CsCO_3$ in whole body was observed after iv 9.25 kBq/g. Wistar rats were counted by whole body counter on 0.25, 0.5, 1, 2, 3, 4, 5, 6, 7, 8, 10, 12, 14, 17, 20, 23, 28 and 33 d after injection of ^{134}Cs, respectively (see Fig.1).

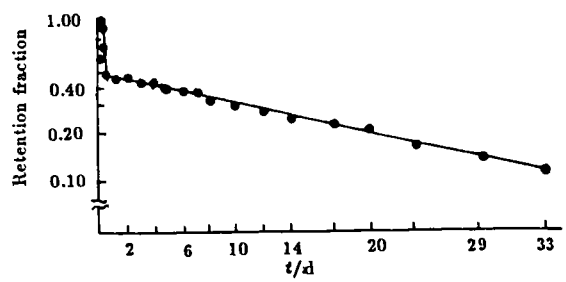


Fig.1 Retention dynamics in whole body after iv injection of ^{134}Cs

Fig.1 shows that the content of radiocesium in whole body was high at first, and then quickly reduced. Localization of ^{134}Cs in whole body obtained by whole body counter was well described by a two-exponential function[3]. A

* The Project Supported by National Natural Science Foundation of China
Manuscript received date: 1995–10–20

fitted equation to describe the retention of ^{134}Cs in whole body with least square method is obtained by a whole body counter as follows:

$$R(t) = 18.04\exp(-9.3175t) + 45.13\exp(-0.0423t) \quad (1)$$

where $R(t)$ is in %, t in d. The equation consists of two half-life components, the fast is $T_{1/2}$=0.07 d and the slow is $T_{1/2}$=16.14 d.

2.1.2 Dose estimation of ^{134}Cs in whole body

Thirty Wistar rats were divided into 5 experimental groups on an average. Doses of ^{134}Cs were estimated after iv 0.37, 1.85, 9.25, 46.25 and 231.25 kBq/g, respectively, by the formula[4]

$$D(t) = \frac{51.2\overline{E}\cdot f}{W}\int_0^t A(t)\mathrm{d}t \quad (2)$$

here D is in cGy, t in d, $\overline{E}$ the average energy for the ^{134}Cs (1.1 MeV), f fractional energy absorption by tissues, W mass of the whole body in g, $A(t)$ the amount of radioactivity of ^{134}Cs in kBq with respect to time, 51.2 calculative factor; on the 2nd d after injection, absorption doses in whole body are 0.64, 3.20, 16.02, 80.10, 400.52 cGy, respectively; on the 3rd d, 0.91, 4.56, 22.81, 114.02, 570.12 cGy, respectively; for corresponding injection dose.

2.1.3 Microautoradiographic study of ^{134}Cs at cellular level

Experiments are carried out on 20 male Wistar strain rats, weighing 122±12 g. Animals were divided into control and 3 experimental groups. Radionuclide ^{134}Cs was the same as that in 2.1.1. The localization of ^{134}Cs at cellular level is observed after iv injection of different doses of ^{134}Cs with 0.37, 1.85 and 9.25 kBq/g. Wistar rats were killed by decapitation after the 3rd d. The blood, and bone marrow were prepared as smear microautoradiography. The liver, muscle and brain were taken out of the experimental rats quickly and cut into a piece of tissues about 10 mm^3. Then the pieces of tissues were cut into sections with 6μm thick freezing slices[5]. Thereafter the tissue slices were fixed by the vapor of absolute alcohol, and prepared for freezing microautoradiography[6].

After absorption of ^{134}Cs into organism, it appears rapidly in erythrocytes as shown in Fig.2a. At the same time, ^{134}Cs also penetrates into lymphocytes (Fig.2b) and neutrophil leukocytes (Fig.2c).

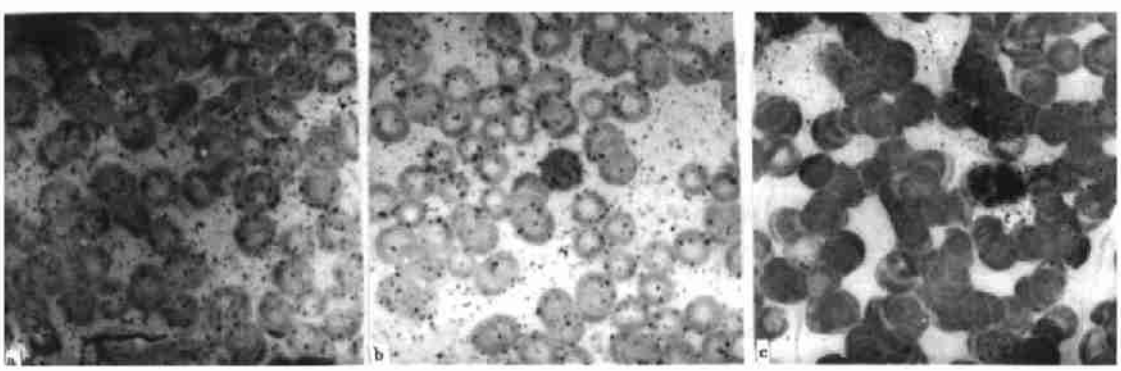


Fig.2 Microautoradiography of blood cells after iv ^{134}Cs 1.85 kBq/g, ×800

The intake of ^{134}Cs in bone marrow cells was mainly deposited in immature cells as shown in Fig.3. It should be noted that relatively less autoradiographic tracks appeared in mature cells.

The autoradiographic studies show that ^{134}Cs mainly accumulated within muscular cells. While less tracks appear in the interstitial of muscle fibers (see Fig.4).

The internal contamination of ^{134}Cs in the body was predominantly and quickly deposited in liver cells. Fig.5 shows autoradiographic tracks in nucleus as well as in plasma.

The localization of ^{134}Cs in structure of brain is relatively ununiform. As shown in Fig.6, it is relatively more in gray cortex and

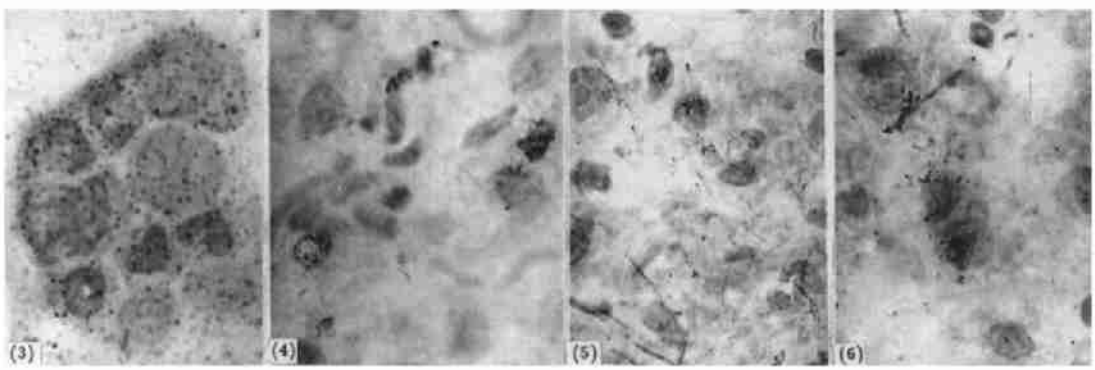
less in white cortex.

2.2 Radioimmunotoxicological effect of ^{134}Cs on central and peripheral immune cells

2.2.1 The effect of ^{134}Cs on the proliferation ability of central immune cells

$^{134}CsCO_3$ with radioactive and chemical purity was used in this study. Sexually mature Wistar rats were divided into control and 5 experimental groups. Rats of experimental groups were injected i.v. 0.37, 1.85, 9.25, 46.25 and 231.25 kBq/g of ^{134}Cs, respectively. ^3H-TdR with a specific activity of 37 MBq/mmol was from Shanghai Institute of Nuclear Research.

The cell culture medium, known as complete RPMI 1640, was composed of RPMI 1640 (J.R. Scientific), supplemented with 20 mmol/L Hepes, 2 mmol/L L-glutamine, 3.6 g/L glucose, 2.0 g/L sodium bicarbonate, 5×10^{-5} mol/L 2-mercaptoethanol, 100 μg/ml streptomycin, 100 U/ml penicillin, and 10% new born calf serum.



Figs.3—6 Autoradiography of bone marrow cells (3) and muscular cells (4) after iv ^{134}Cs 1.85 kBq/g, ×800; and of liver cells (5) and brain cells (6) after iv ^{134}Cs 0.37 kBq/g, ×800

Rats were sacrificed by decapitation and the femurs and thymus were immediately excised under aseptic condition. Bone marrow cells of the femurs were flushed out with RPMI 1640 using a syringe and a 25 gauge needle. Thymocytes were obtained by squeezing the thymus with forceps. Finally the cells were dispersed through a 25 gauge needle to give a suspension of single cells and their concentrations were adjusted with RPMI 1640 to 2×10^6 cells/ml for bone marrow cells and 5×10^6 cells/ml for thymocytes. To each ml of the cell suspensions 37 kBq of ^3H-TdR was added and cultured in a humidified 5% CO_2, 37°C incubator for 24 h. After 24 h culture, the cells of each sample were gathered onto a No.49 glass fibre filter, dried at 50°C, dropped into 5 ml scintillation cocktail (0.4% PPO plus 0.04% POPOP in xylene), and their radioactivities were determined with a Beckman LS 6800 liquid scintillation counter.

The contrast of the proliferation ability of thymocytes and bone marrow cells on the 3rd d after i.v. injection of different doses of ^{134}Cs are shown in Fig.7. The ^3H-TdR incorporation in thymocytes and bone marrow cells increased significantly after low doses of ^{134}Cs injection, while dropped to a lower value after higher doses injection.

It should be noted that the inhibition of thymocytes induced by ^{134}Cs to ^3H-TdR incorporation is more powerful than that of bone marrow cells.

2.2.2 The effect of ^{134}Cs on the transformation ability of peripheral immune cells

In this experiments radionuclide ^{134}Cs, reagent ^3H-TdR and animals all are from the same source as in 2.2.1. Treatment and grouping of rats are also the same as those in 2.2.1.

Mitogenic PHA was from Shanghai Medical Test Institute, LPS and ConA were from Sigma.

Fig.8 illustrates the action of ^{134}Cs on peripheral blood T and B lymphocytes proliferation. It can be seen that the transformation ability of T lymphocytes stimulated by PHA mitogens as well as that of B lymphocytes stimulated by LPS mitogens all were depressed obviously by ^{134}Cs. The inhibitory effect is a dose-effect relationship. The PHA conversion of T lymphocytes is more sensitive to the radiation of ^{134}Cs than the LPS transformation of B lymphocytes.

Fig.9 shows that spleen T lymphocytes are more radiosensitive to ^{134}Cs than spleen B ones.

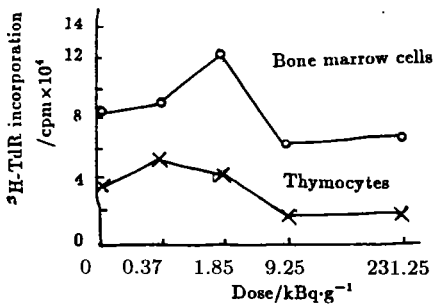


Fig.7 Contrast of DNA syntheses of bone marrow cells and thymocytes after different iv doses of ^{134}Cs

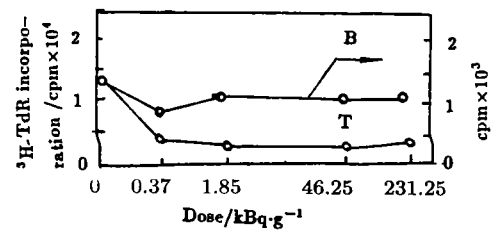
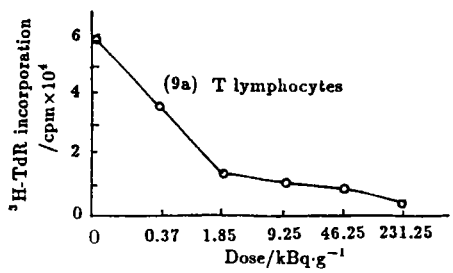


Fig.8 Contrast of transformation abilities of peripheral blood T and B lymphocytes after different iv doses of ^{134}Cs



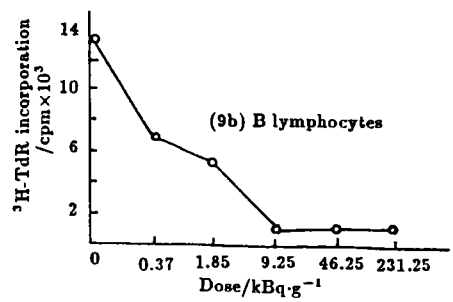


Fig.9 Contrast of transformation abilities of spleen T and B lymphocytes after different iv doses of ^{134}Cs

3 Discussion

Immune system is the important part of defense mechanism in organism. Studies have demonstrated that the immunocytes have the high radiosensitivity to internal exposure radionuclides. It is evident that serious disturbances and morphological changes are induced by internal contamination of different radiators, including suppression of division and proliferation of immunocytes, occurrences of sequelae and immunoinjury effects of both central and peripheral immune cells.

The bone marrow contains various precursors of immune cells. It is a mature place of mammalian B lymphocytes[7]. Therefore, the bone marrow is an important central immune organs. Thymus is a place where pre-T lymphocytes of bone marrow were further divided into mature T lymphocytes. They moved from the pulp of thymus, then into the peripheral immune organs. Studies have demonstrated that the immune organs possess high radiosensitivity to radionuclides exposure[8].

Our experimental data show that the ^{3}H-

TdR incorporation rate of bone marrow cells cultured in vitro indicated not only the proliferation ability of the various immature cells in bone marrow, but also suggested the proliferative ability of the lymphocytes growth system. At the same time, the ^{3}H-TdR incorporation rate of thymocytes showed the DNA synthetic function of various immature lymphocytes from pre-T lymphocytes to mature T lymphocytes.

The mature T and B lymphocytes are sensitive cells to radiation[9]. But the comparasion of radiosensitivity between T and B lymphocytes still needed to be further studied[10]. Our current results show that at lower doses of ^{134}Cs 0.37 kBq/g, PHA induced T lymphocytes transformation reduced 0.302 of that in control, and LPS induced B lymphocytes transformation reduced 0.674 of that in control in the peripheral blood; at dose of ^{134}Cs 1.85 kBq/g, PHA or LPS induced splenic lymphocytes transformation were depressed 0.218 and 0.405, respectively, suggesting that the radiosensitivities of T lymphocytes were higher than B lymphocytes.

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