THE EFFECT OF CHEMICAL PROTECTION ON THE POSTIRRADIATION RECOVERY OF SYSTEMS RESPONSIBLE FOR "MARROW" OR "INTESTINAL" SYNDROMES IN MAMMALS

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The process of recovery of the whole organism of mice after totalbody irradiation with sublethal doses has been studied by the method of split-dose irradiation with "marrow" or "intestinal" death as criteria. Male and female I2-I6 week-old mice F_1 (CBA x C57BL) were used. Whole-body exposure to ^{137}cesium gamma rays was performed at a dose rate of 450 R/min. The second irradiation (with 3-7 doses) was given at intervals of I to 30 days after the first dose of 350 R or 500 R without protection or 595 R following an i.p. injection of 350 mg/kg of cysteamine-S-phosphate.

In order to study the rate of recovery the residual injury was estimated (as the difference between isoeffective doses under single or split-dose irradiation).

A comparison between the patterns of haemopoiectic endogeneous CFU recovery and the whole organism recovery with "marrow" death as a criterion was done. In both cases the postirradiation recovery curves are undulating. A characteristic feature of both processes is the maximal rate of recovery within the first 24 hours. As to the population of haemopoietic stem cells, it can be interpreted by the transition of the quiescent (G_0) part of the cell pool to the proliferative state. During several successive days the decrease of the residual injury level is slower, but also equal in both cases, in the interval from 4-5 to I5-I6 days after irradiation the curves diverge and subsequently the difference disappears again.

Our survival data obtained from the study of "intestinal" death we compared with the data of Withers and Elkind concerning the dynamics of recovery of CFU in the small intestine. In both cases the postirradiation recovery curves are undulating and completely coincident. The small intestine crypt proliferative pool does not contain such a great fraction of quiescent cells as the haemopoietic stem cell pool. So the maximal recovery rate within the first 24 hours after irradiation in this case might be related with greater repair of sublethal cell damage. The strict coincidence of the pattern of whole organism radiosensitivity changes concerning the "intestinal" death with the pattern of crypt CFU number changes allows us to consider the crypt CFU as a substrate of the whole organism recovery for the cased the gastrto-intestinal syndrome.

The divergence of analogical curves in the case of the haemopoietic syndrome in our opinion may be interpreted by the superposition of the secondary rise of residual injury in the gastro-intestinal system to the recovery process in the haemopoietic system.

Thus according to our own and reference data the postirradiation

recovery process appeared to be complex involving three stages with different cell mechanisms as a basis:
I) Rapid recovery within the first 24 hours owing to sublethal damage repair in stem cells and also by activation (in the haemopoietic system) of the quiescent cell fraction.
2) Whole repair to the initial level die to repopulation of the stem cell pool.
3) Overshot and succesive undulations of radiosensitivity near the control level due to regulatory processes in stem cell pools. The different rates of recovery form a characteristic feature of the considered process. The gastro-intestinal system recovers I,3 times more quickly than the haemopoietic system, this, apparently contributes to a greater relative radioresistance of the gastro-intestinal system (the LD 50/7 is I,2 times greater than the LD 50/8-20).

So, the response of the organism of mammals to irradiation under moderate exposure is essentially determined by the recovery process.

In the radiation protection experiments the residual doses in the case of haemopoietic system were counted in per cents to the dose of 350 R in the control and protected animals, because the DRF was I,7. After irradiation of protected mice with a dose of 595 R the residual injury within the first 24 hours (the first stage of recovery) is mainly the same as under irradiation of unprotected mice with a dose of 350 R. In subsequent days (the second stage of recovery) the decrease in residual injury in protected and unprotected mice is the same.

During the third stage the recovery of the protected animals leaves slightly behind the recovery of the unprotected mice and the undulations of corresponding curves are not quite synchronous. The recovery of gastro-intestinal system was studied under irradiation with the same dose. But because the DRF for the intestinal death is only I,3 the residual doses were counted in per cents to a dose of 460 R in protected animals versus 350 R in unprotected.

After irradiation of protected mice with a dose of 595 R the residual injury becomes equal to that of unprotected animals irradiated with a dose of 350 R within the first stage of recovery. During the second stage the residual injury disappears in both cases. The subsequent dynamics of recovery was studied up to the 8th days, when the residual injury is quite different in protected and unprotected mice.

The sharp decrease of residual injury within the first 24 hours may be accounted for by that the action of the protector consists in either decreasing the primary damage during the exposure or enhancing the recovery process in stem cells of the corresponding system. The protection does not influence the second stage of the recovery process, which means, that the proliferation rate of survived stem cells is not changed.

In the third recovery stage of gastro-intestinal system of protected animals there was not registered a secondary rise of residual injury on the 7th-9th days, as in unprotected animals. A more early overshot in this stage of haemopoietic recovery was also noted in protected mice.

The reason of this later fenomenon might be the of superposition of the secondary rise residual injury in gastro-intestinal system

to the pattern of haemopoietic recovery in unprotected animals. As the protection eliminates this secondary rise, it is naturally, that the residual injury following the pattern of haemopoietic stem cell recovery.

Thus, the observed differences in the recovery curves of protected and unprotected animals additionally confirm the cell mechanism of mammalian radiation death.