Influence of a Mixture of Chemical Protectors on the Lymphopoietic and Hematopoietic System of Mice Irradiated with a Dose of 2000 R of X-Rays

Mice irradiated with lethal and supralethal doses of X-rays, which survive more than 3–6 days, die between the seventh and the thirtieth day of hemorrhage, infection or progressive anemia[1]. This mode of death is called hematopoietic death. Sulfhydryl radioprotectors and mixtures of radioprotectors are known to protect mice against hematopoietic death[2,3].

The present communication reports data on the influence of a mixture of radioprotectors on the hematopoietic and lymphopoietic systems in mice exposed to 2000 R of X-rays.

Materials and methods. Twelve-week-old male mice of the BALB/c strain weighing 25–30 g were used. The treated mice were given 16 mg of reduced glutathione via stomach intubation, 25 min before irradiation with 2000 R of X-rays. Fifteen minutes later, the mice were injected i.p. with 15 mg of cysteine and 10 mg of AET (neutralized to pH 7.2 with NaOH) and 20 min after the administration of glutathione, with 1 mg of serotonin creatinine sulfate. The conditions of X-irradiation were: 300 kV, 20 mA, 1 mm Al, 2 mm Cu, dose rate 100 R/min. The mice were killed by cervical dislocation at various time intervals after X-ray exposure. The spleen, the lymph-nodes, the thymus, the femurs and the small intestine were fixed in Bouin or neutral formalin and stained with hematoxylin eosine safran, or, for bone-marrow, with Giemsa.

Results and discussion. A few hours after a dose of 2000 R of X-rays, damage in the bone-marrow is evident from oedema and hemorrhages. On the fourth day, the bone-marrow is atrophic, but among the few nucleated bone-marrow cells, large numbers of megakaryocytes are still visible. The atrophy of the bone-marrow is maximal between day 5 and 7 and only a few reticular cells and histiocytes persist. Sometimes on the ninth day, but usually on the twelfth day, large areas of regenerating cells and some megakaryocytes appear. Twenty days after 2000 R, the recovery of the bone-marrow has progressed, mitoses and small dark cells are numerous, but some hemorrhages and cell debris are still visible. Thirty days after irradiation, the bone-marrow shows an apparently normal histological and cytological picture (Figure 1).

In the spleen, cell damage is mainly present in the germinal centre during the first 12 h after the irradiation. One day after exposure, the number of cells in the white and the red pulp is markedly reduced and cell debris have in part been cleaned up. By day 4, the atrophy of the germinal centre is very marked and blood pigments are deposited in the red pulp; megakaryocytes are rare, but reticular cells and fibroblasts are numerous; mitoses are few, cell debris are scarce. Regeneration of the white pulp with small dark cells and mitoses is visible in some mice on day 5; in the others, on day 7, but during following days, this regeneration of the white pulp apparently proceeds much more slowly or not at all.

In the red pulp, nodules of regeneration consisting of small dark cells and/or cells with large pale nuclei are numerous 12 days after irradiation. In some cases, rows of regenerating cells are formed below the capsule, along the trabeculae or around the small vessels. Between the zone of regeneration, germinal centres are visible but are still atrophic. After 30 days, the spleen shows almost a normal histological picture with numerous mitoses and a preponderance of the red over the white pulp (Figure 2).

Twelve hours after irradiation, the thymus shows marked damage, especially in the cortical area. From day 3 to day 7, the cellular debris are rare and only a few small thymocytes and large polymorphic cells are present. The reticulum is hypertrophic. On day 12, marked regeneration of the thymus is seen and the cortical and medullar zones are well distinguishable (Figure 3). Thirty days after irradiation, some but not all mice display a full regenerated thymus.

The regeneration of the lymph nodes and of the Peyer's patches seems to proceed at a lower rate than in the thymus. Thus, 30 days after exposure, the reticulum of

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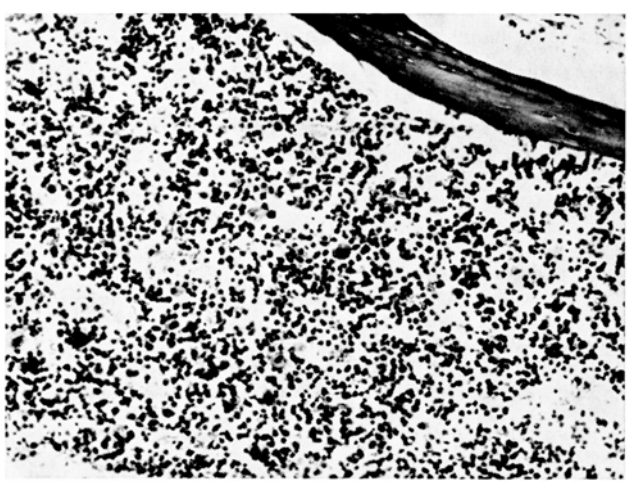

Fig. 1. Histologic aspect of the bone-marrow of a BALB/c mouse, 30 days after a dose of 2000 R of X-rays and pretreatment with a mixture of chemical protectors. × 240.

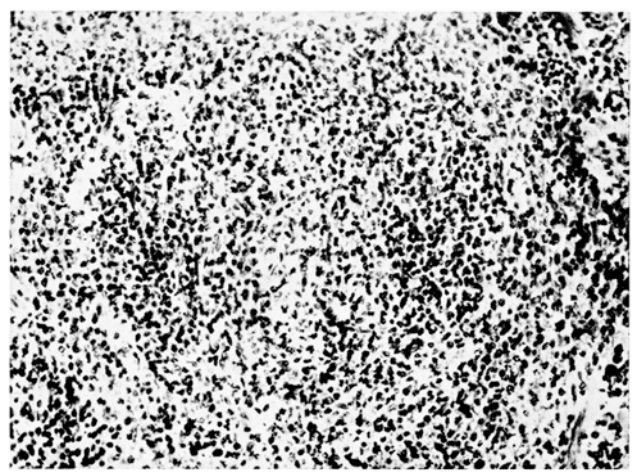

Fig. 2. Histologic aspect of the spleen of a BALB/c mouse, 30 days after a dose of 2000 R of X-rays and pretreatment with a mixture of chemical protectors. × 400.

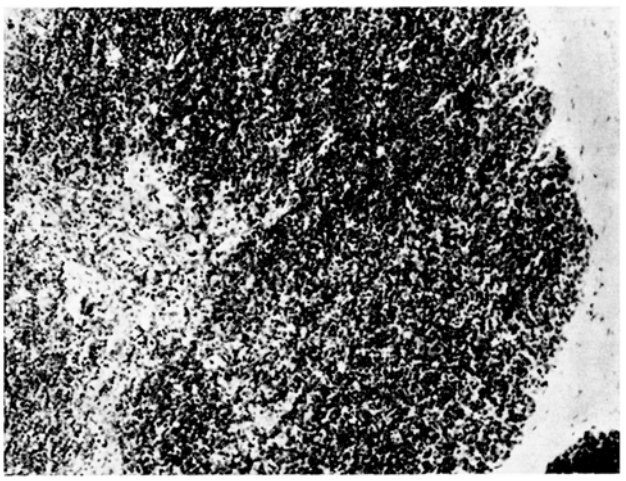

Fig. 3. Histologic aspect of the thymus of a BALB/c mouse, 12 days after a dose of 2000 R of X-rays and pretreatment with a mixture of chemical protectors. × 160.

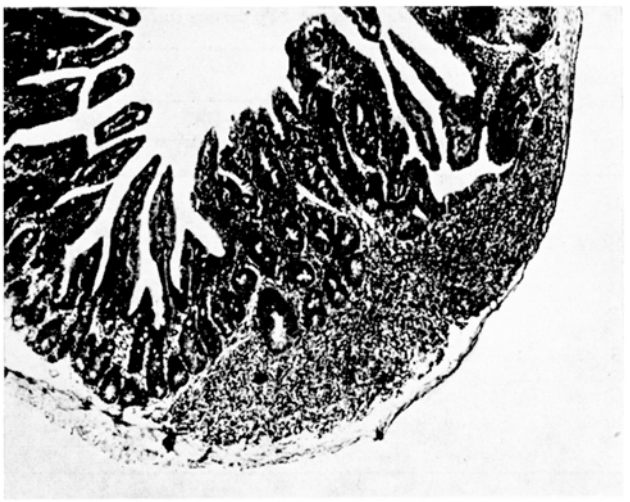

Fig. 4. Histologic aspect of the Peyer's patches of a BALB/c mouse, 30 days after a dose of 2000 R of X-rays and pretreatment with a mixture of chemical protectors. × 65.

the lymph nodes is hypertrophic, the sinus dilated; mitoses are rare and some cell debris and many plasmocytes are present. The germinal centres are not well discernible. At this time, the regeneration of the Peyer's patches is more advanced (Figure 4); some cell debris and many young lymphatic cells are visible. All lesions in the different tissues appear sooner until the death of the animal on the fourth day and are more pronounced in the X-irradiated non-protected than in the protected irradiated mice.

Conclusions. The bone-marrow spleen and thymus show, 30 days after a dose of 2000 R of X-rays and pretreatment with AET + glutathione + 5-HT + cysteine, an almost normal histologic and cytologic picture. At the same time, regeneration in the lymph nodes and the Peyer's patches has set in, but is less advanced[4].

Résumé. La moelle osseuse, la rate et le thymus montrent, 30 jours après une dose de 2000 R de rayons X et un traitement préalable avec une association d'AET, de glutathion, de 5-hydroxytryptamine et de cystéine, un aspect histologique et cytologique normal. Au même moment, la régénération des ganglions et des plaques de Peyer est bonne mais moins avancée.

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Increase in Urocanate Concentration in Human Epidermis Following Insolation

Since the formulation, by Ženíšek et al.[1], of the hypothesis that urocanic acid (UA) has a physiological role of protecting the skin against the damaging effect of the erythema-producing range of solar radiation, considerable circumstantial evidence has been presented in favour of this proposal by a number of authors. It has only been objected that patients with histidinemia, whose epidermis lacks histidine ammonia-lyase and UA, are not abnormally sensitive to sunburn[2]. These views might be reconciled by the suggestion that UA is not the sole protecting mechanism operating and that these mechanisms may, if necessary, compensate for each other; it has long been known that albinos can adapt themselves to repeated insolation by the thickening of the horny layer. We wish now to report on experiments which add further support to the conception of the physiological role of UA as a natural sunscreen by showing its increase after insolation.

Three male subjects exposed one upper arm to solar radiation for the first time after the winter season. The other arm served as a control and remained covered. Erythema which followed the insolation ranged from just perceptible (subject H) to fairly strong with subsequent peeling (subject S and C). Suction blisters were produced by the method of Kiistala and Mustakallio[3] and the epidermis was then removed with scissors. Its extract was chromatographed on Kieselgel HF_{254} thin-layers in a propan-2-ol-concentrated ammonia-water (17:1:2) mixture, *trans*- and *cis*-UA spots were scraped off separately, eluted, and UA estimated by spectrophotometry.

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