MORPHOLOGY AND PATHOMORPHOLOGY

MORPHOLOGICAL CHANGES IN THE SKIN IN RESPONSE TO EXTERNAL α-IRRADIATION

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The biological action of α-rays and, in particular, the morphological changes resulting from external α-irradiation have been inadequately studied. For this reason it is not yet clear whether external α-irradiation is harmful, and if it is, how its action differs qualitatively from that of other types of ionizing radiation. There are reports in the literature [2, 4, 14] of the extremely limited harmful action of α-irradiation from external sources, such as: "α-Rays, when acting externally, may have a harmful effect only in exceptional cases, for example when they act on the mucous membranes" [2]. In contrast to this view, there are reports [6] of the development of deep necrosis and ulceration after irradiation of the skin of rabbits with α-rays from polonium.

In view of the scanty and controversial information on the pathological changes in the tissues in response to the action of external α-irradiation, we considered it of interest to investigate these changes over a period of time, varying the doses of radiation absorbed.

EXPERIMENTAL METHOD

Experiments were carried out on 35 rabbits weighing 2.0-2.5 kg, to the shaved dorsal skin of which were applied radioactive binders containing fission products of thoron (thorium B, thorium C, thorium C_I and thorium C_{II}). These radioactive isotopes emit α-, β- and γ-rays, but it can be considered that their action is due mainly to α-rays which account for more than 90% of the radiation energy absorbed by the tissues [1, 15, 16, 19]. The activity of the applicator was 4-5 $\mu C/cm^2$ in the first series of experiments, 0.3 $\mu C/cm^2$ in the 2nd series and 0.06 $\mu C/cm^2$ in the 3rd series. The applicator, 8 × 8 cm in size, was placed in position for a single period of 20 hours or 5-6 times at intervals of 1 week. In the same conditions a binder free from radioactivity was applied to 5 rabbits. The animals were sacrificed at various periods of time (from 1 day to 8 months from the beginning of the experiment) with subsequent morphological examination of the skin and inspection of the internal organs. In some animals biopsy of the skin of irradiated and unirradiated symmetrically opposite areas (as controls) was performed.

EXPERIMENTAL RESULTS

Before estimating the morphological changes after irradiation it had to be ensured that this was external, i.e., that the radioactive isotopes incorporated in the applicator had not penetrated into the skin tissue. For this purpose biopsy specimens of skin taken from the experimental rabbits immediately after irradiation at intervals of 5, 24, 48, 72 and 96 hours, were investigated by the histoautoradiographic method of mounting [7, 20].

Microscopic examination of the histoautoradiograms (11 experiments in all, and 15-20 sections of skin investigated in each case) showed that the characteristic "stars" of the isotope emitting α-rays were present on the

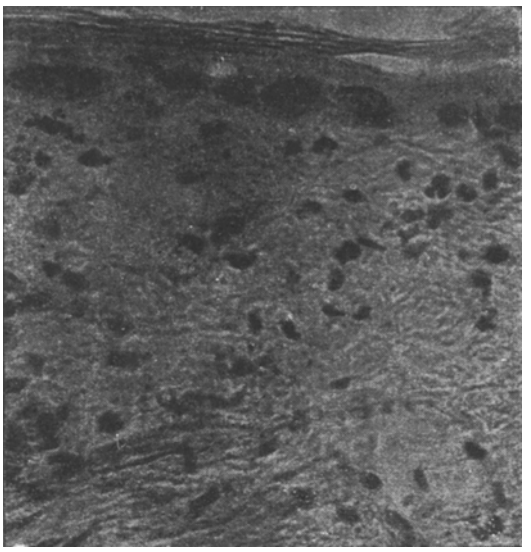

Fig. 1. Changes in the skin of a rabbit three days after a single exposure to α-rays. Gross thinning of the epidermis, with gigantism and a transverse disposition of the nuclei in the cells which are left. Ocular 15×, objective 40×.

surface of the skin only, which was evidence of the transfer of a known quantity of radioactive material from the applicator to the skin. No radioactive material was found in the thickness of the epidermis and dermis. The largest quantity of isotopes on the surface of the skin was found immediately after removal of the applicator. Later on, on account of the rapid fission of the isotopes (maximum half-life period about 11 hours), their quantity progressively fell, so that after 3-4 days the skin was practically free from radioactivity. Judging by the data from histoautoradiography, therefore the radioactive substances tested did not penetrate into the skin or were practically completely disintegrated before they could possibly penetrate the skin. For this reason the action of the radioactive applicators on the body was entirely due to external irradiation. The length of penetration into the tissues by α-particles emitted by the fission products of thoron, from measurements with the ocular micrometer, from our findings was 50-60 μ which is only very slightly more than the thickness of the epidermis in the dorsal region of the rabbit's skin.

During the period of irradiation and for a year after its conclusion, the general condition of the animals appeared normal. Histological investigation of the internal organs also revealed no pathological changes. Macroscopic changes in the skin were manifest in the form of hyperemia, pigmentation, and desquamation, varying in accordance with the size of the dose absorbed. With whatever dose was used, the microscopic changes were mainly found in the epidermis. In the first series of experiments, for instance, immediately after removal of the applicator, individual cells of the basal layer of the epidermis were seen with swollen and unusually light nuclei and

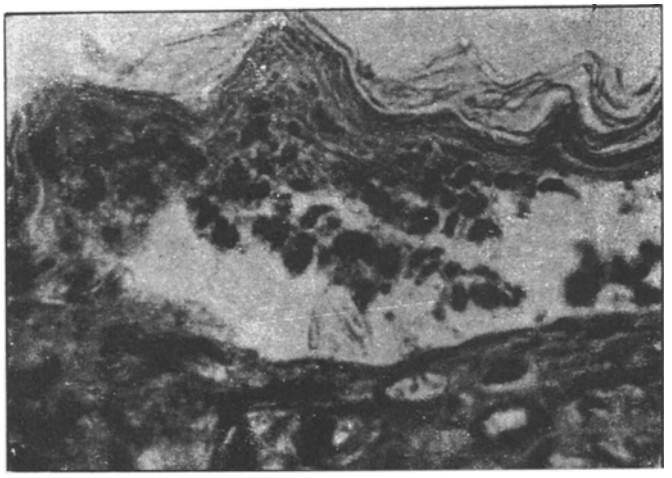

Fig. 2. Changes in the skin of a rabbit after repeated exposure to α-rays. Formation of a vesicle in the epidermis. Severe dystrophy of the epithelium at the base of the vesicle. Objective 40×, ocular 15 ×.

large, eccentrically situated nucleoli within them, arranged against a background of the main mass of unchanged cells. The number of these cells later increased, and this was accompanied by abnormalities of differentiation of the cells of the epidermis and vacuolation of the cells of the stratum spinosum. Three and 4 days after irradia-

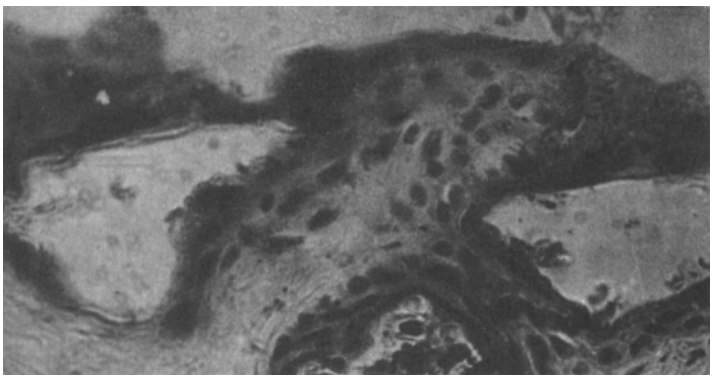

Fig. 3. Imperfect regeneration of the epidermis of a rabbit. Obliteration of the cell borders and the formation of ridges. Ocular 10×, objective 40×.

tion, cells with giant, deformed nuclei, arranged parallel to the skin surface, and also isolated small pycnotic cells were observed in the basal layer (Fig. 1). Staining by Feulgen's method at this period showed a sharp fall in the content of desoxyribonucleic acid in the nuclei of the swollen and giant cells and an increase in the content of DNA in the pycnotic cells.

One week after irradiation, the epidermis presented a picture of severe disturbance of differentiation, with pycnosis and karyocytosis of many cells of the basal layer, severe hypertrophy and deformation of the nuclei in the cells which were preserved and with the onset of desquamation of the stratum corneum together with the underlying dead epithelium. Pigment formation began at this period, in the form of the appearance of fine granules of melanin in the perinuclear zones and alone the cells borders in the basal layer. The degree of the dystrophic changes in the epidermis and of deposition of pigment were unevenly expressed over the skin surface. This "spotted" character of the changes was evidently connected with distinctive properties of this source of radiation — the uneven distribution of radioactive material on the surface of the applicator and the criss-cross structure of the applicator itself, which was made of gauze.

Two weeks after a single exposure to irradiation, even more marked dystrophic changes were present in the epidermis, which in some areas was thinned to three, two or even one layer of cells, with huge polymorphic nuclei, situated in various positions. An abundance of pigment was present in the cytoplasm of three cells. In these areas the stratum corneum was usually absent, but sometimes it was observed to be desquamated together with the underlying of dead epithelium, in which the outlines of giant pycnotic nuclei could vaguely be distinguished. Three and four weeks after a single exposure to irradiation, signs of progressive regeneration were observed in the skin, with proliferation of the epidermis in its basal layer and desquamation of the superficial layer of abnormal epithelium.

After the course of irradiation was completed, the changes in the epidermis in the 1st series of experiments were more noticeable. The thinning and the deposition of abundant pigment were almost diffuse. Desquamation of the stratum corneum together with the underlying necrotic epidermis was accompanied by penetration of edema fluid into this layer, together with a few leucocytes, and the formation of vesicles (Fig. 2). The base of the vesicles was often formed by dermis, in which there was obvious leucocytic infiltration. In the areas of the hair follicles next to the epidermis, dystrophy of the epithelium was present, and here and there the hair was shed and the follicles dilated and deformed. One week after the course of irradiation, the dystrophic changes in the epidermis were accompanied by imperfect regeneration of that structure, with obliteration of the cell borders and the basal membrane and the formation of characteristic ridges (Fig 3). Only two weeks after the course of irradiation, however, the regeneration of the epidermis was normal again; proliferation of an epidermis of typical structure was observed, slightly thinner than in the control animals. Areas of severe dystrophic changes could still be seen at this period against the background of intensive regeneration.

After a single or multiple exposure to irradiation, the dermis in the 1st series of experiments in the course of the first week showed a moderate capillary hyperemia in the stratum papillare against a background of very

slight edema, palisading of the leucocytes in the small vessels and slight perivascular leucocytic infiltration. To this was subsequently added a slight, diffuse and nodular (beneath the epidermis) histiocytic proliferation, accumulation of pigment in the histiocytes of the dermis, and isolated giant histiocytes. No changes were found in the argyrophilic collagen and elastic fibers of the skin after a single exposure to the radiation; after repeated exposure, at the end of the course, impregnation by the Tibor-Pape* method showed a transient coarsening of the subepidermal argyrophilic membrane and swelling of the collagen fibers in the stratum papillare. Restoration of the skin structure after a single exposure to irradiation in the 1st series of experiments began in earnest after one month; after repeated irradiation – after 3-4 months, although at this period too, traces of its effect could still be seen in the form of the presence of pigment in the dermis and small areas of epidermis in which the basal layer was irregular in its structure.

After the absorption of smaller doses of radiation (2nd and 3rd series), dystrophic and necrobiotic changes were also observed in the epidermis, although these developed much more slowly. In the 2nd series, for instance, after 3-4 exposures, isolated hypertrophied cells with vacuolated cytoplasm and eccentrically situated nuclei were found in the epidermis. To these were subsequently added, in turn, maldifferentiation and polymorphism of the epidermis, gigantism and transverse disposition of the nuclei, and thinning of the epidermal layer to 1-2 rows of cells. After the conclusion of irradiation in the 2nd series of experiments, the changes thus resembled those which took place during the 2nd week of the experiment in the 1st series. In the 3rd series of experiments, it was only at the end of the course of irradiation that foci of dystrophy and necrobiosis of the epidermis were seen, with thinning of the epidermis in these areas and excessive accumulation of melanin in the cells. Changes in the dermis in the 2nd series were shown merely by a transient dilatation of the small vessels in the stratum papillare and by slight perivascular leucocytic infiltration. In the 3rd series no morphological changes were observed in the dermis.

Consequently, external α-irradiation, although leading to obvious dystrophic changes in the epidermis, was not accompanied by any significant involvement of the dermis, and for this reason did not produce sclerosis nor atrophy of the skin. If we compare these changes with those described after the action of x-rays [5, 9, 10, 21, 22] and β-rays [11, 12, 17, 18, 23], we can observe that doses of x-rays and β-rays which led to such marked changes in the epidermis inevitably caused in addition a severe inflammatory reaction in the dermis, with (especially after the action of x-rays) subsequent atrophy of the skin appendages and sclerosis of the dermis. The distinction which we found in our experiments between the degree of the significant changes in the epidermis and the slight changes in the dermis is very probably connected with the physical properties of this radiation, and especially with the fact that α-particles, which posses a high ionization density (and, hence, high biological effectiveness) have a low penetrating power, so that the bulk of the α-particles are absorbed in the epidermis and do not enter the connective tissue layer of the skin.

The absence of any severe inflammatory reaction in the dermis after external α-irradiation also accounts for the fact that, in our experiments, no atypical proliferation of the epidermis and follicular epithelium took place in the later stages of the experiment, with the development in isolated cases of carcinoma of the skin, as is observed after β-irradiation [17]. This is understandable in the light of the work of V. G. Garshin [3], who showed conclusively that proliferative processes in the epithelium are largely dependent on the degree of the inflammatory reaction of the stroma.

As has already been pointed out, the skin changes after α-irradiation are completely reversible. The active course of the regenerative processes in our experiments was undoubtedly due to the superficial localization of the changes and also to the unevenness, the "spotted" nature of the lesions in the epidermis, so that areas which were only slightly affected acted as sources of regeneration. These findings are in agreement with the statement by G. S. Strelin [13] that when a source of radiation is in the form of grid, the areas which are least exposed to irradiation have a stimulating effect on the regeneration of the areas of skin which absorb a larger dose of radiation.

We also studied the morphological changes in the nerve elements of the skin after external α-irradiation. For this purpose, biopsy specimens of skin of experimental and control animals were stained for myelin by Spielmeyer's method and impregnated with silver by Campos' method. It was found that, corresponding to the slight inflammatory and dystrophic changes in the dermis, the nerve trunks of the stratum reticulare and the stratum papillare, as well as the receptors of the sebaceous glands and hair follicles situated in these layers, underwent no

* Name not verified.

morphological changes. So far as the palisade-like receptors terminating in the epidermis are concerned, when their terminal ramifications were intact, the prereceptor fibers at the height of the skin changes in the 1st and 2nd series of experiments showed increased argentophilia and irregular thickenings and spiking of their contours. These changes in the receptors of the epidermis disappeared 1-2 months after the cessation of irradiation, i.e., they were reversible. The neurohistological examination of the skin thus also emphasized the superficial localization of the pathological changes during external α-irradiation.

SUMMARY

The author studied the changes occurring in the skin of the rabbit in external alpha-irradiation. The latter has a pronounced injurious effect, the morphological manifestations of which are analogous to those observed in the action of other types of ionizing radiation. Besides this, the reaction of the alpha-irradiated tissue has a specific feature in the form of a sharp contrast between the degree of affection of the superficial and deep layers. The injury mostly involves the epidermis. This is due to the physical properties of alpha-radiation.

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