THE INFLUENCE OF NAPHTHALAN OIL EXTRACT ON CHANGES IN THE EPIDERMIS DURING LOCAL α-IRRADIATION

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Translated from Byulleten' Éksperimental'noi Biologii i Meditsiny, Vol. 51, No. 3, pp. 121-125, March, 1961
Original article submitted February 11, 1960

During local injury to the skin with ionizing radiation it has been shown [1-3, 6, 8] that certain substances (or measures) possessing the general property of stimulating the proliferation of the epithelium of the skin have a beneficial effect. From the practical point of view one such substance which merits attention is naphthalan oil extract (NOE), which has been found to have a beneficial effect after local γ-irradiation, exposure to x-rays and β-irradiation [8, 9].

In order to complete the picture of the efficacy of the proliferation of the epithelial cells of the skin obtained by means of NOE, we tested the effect of this substance during irradiation with α-particles, especially in view of the fact that their action from an external source is limited to the epidermis.

EXPERIMENTAL METHOD

Tests were carried out on 21 rabbits. The source of external irradiation with α-particles was applicators containing fission products of thoron – thorium B, thorium C, thorium C' and thoriumC". Besides α-particles these radioactive products emit a small number of β-particles and γ-rays. About 90% of the radiation energy absorbed by the tissues, however, is attributable to α-particles, the biological effects of which are predominant [6, 10]. The applicator, measuring 5 × 5 cm, was applied repeatedly to the shaved skin of the dorsal region of a rabbit for 20 hours. The applicators used had an initial content of α-emitting isotopes (thorium C + thorium C') of 0.06-6 $\mu c/cm^2$ surface area.

At different periods after the beginning of the experiment skin was excised from the experimental and symmetrically opposite control areas of the body. Sections were stained with hematoxylin-eosin, by Van Gieson's method, with Heidenhain's iron hematoxylin, and impregnated by Campos's method.

In the first variant of the experiments a few drops of NOE were applied once or occasionally twice (on two successive days) to the shaved area of skin immediately after irradiation or after six or 12 days.

EXPERIMENTAL RESULTS

Painting the healthy skin of rabbits with NOE causes capillary hyperemia, edema and inflammatory infiltration of the dermis next day, and on succeeding days an intensification of proliferation of the cells of the stratum germinativum of the epidermis and of the follicular epithelium, with thickening of the cutaneous epithelium to 200 μ or more, with hyperkeratosis, granulosis and acanthosis. An increase is found in the staining properties of the keratinous material, and cysts are formed from the proliferating epithelium of the follicles. These phenomena gradually subside in the course of six weeks.

After irradiation with an applicator with an initial content of thorium C + thorium C' of 4-6 $\mu c/cm^2$, the histological changes in the intact skin of the dorsum of the rabbit were mainly confined to the epidermis on account of the low penetrating power of the α-particles – about 35 μ into the tissues [4, 5]. These changes consisted of dystrophy and necrobiosis of the cells, expecially the basal cells, with the accumulation of pigment, pyknosis and gigantism and their nuclei, and of a considerable thinning of the epidermis. These phenomena, which began on the 2nd-3rd day after irradiation, reached their maximum usually in the middle of the second week, soon after which the structure of the epidermis gradually became restored over a period of 1-1.5 months.

If the skin was painted with NOE immediately after irradiation with the applicator as mentioned above, next day it was possible to observe severe and massive dystrophy of the cells of the epidermis, with the almost continuous involvement of the basal cells, in which were observed enlargement, vacuolation and, sometimes, pyknosis of the nuclei, and swelling and the eccentric position of the nucleolus. The dermis showed a well marked inflammatory infiltration. On the second, third and fourth day after irradiation and painting with NOE we found progressive dystrophy and necrobiosis of the elements of the stratum germinativum of the epidermis, with an abundance of giant, pyknotic and mainly mononuclear cells in this layer, with deformed, horizontally arranged nuclei. In some sections a serous fluid appeared among the degenerating cells, collecting in the form of an intra-epidermal vesicle (Fig. 1). Starting with the fourth day mitotic activity reappeared in the basal layer of the epidermis. The dying, deformed, pyknotic cells were displaced to the skin surface by small epithelial cells with a palisade arrangement of their nuclei, proliferating in the basal layer. On the following days marked thickening of the epidermis, characteristic of the action of NOE, was observed, together with the rapid desquamation of the dead, irradiated epidermal cells. At the end of the second week and later, the epidermis closely resembled in thickness the epidermis of the unirradiated areas of skin, untreated with NOE, and showed no signs of dystrophy (Fig. 2).

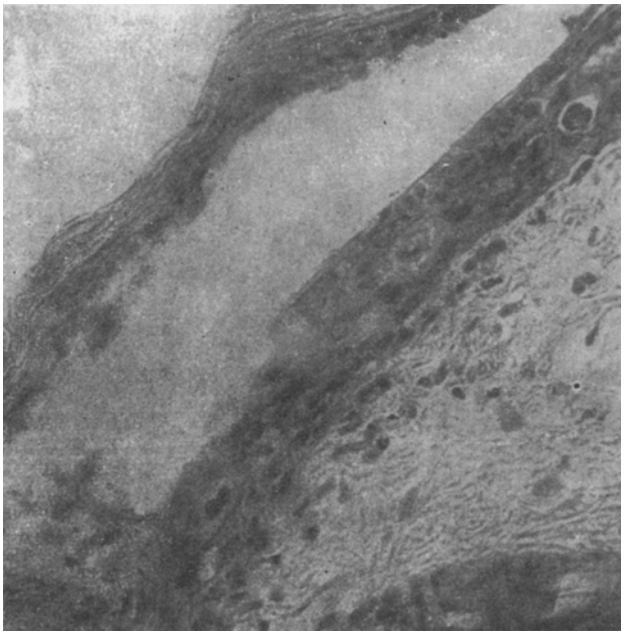

Fig. 1. The skin of a rabbit 48 hours after painting with naphthalan oil extract. Skin preliminarily irradiated with α-particles. Marked dystrophy of the cells of the stratum germinativum of the epidermis. Formation of vesicles. Stained with hematoxylin-eosin. Magnification: ocular 15×, objective 40×.

Similar changes were found when the skin was painted with NOE immediately after irradiation with applicators of lower activity (initial content of α-emitting isotopes 0.3 and 0.06 $\mu c/cm^2$). In these cases, in contrast to the action of applicators of higher activity, the dystrophy of the epidermis although developing equally early did not, however, affect all the cells of the basal layer. During the action of radiation from these

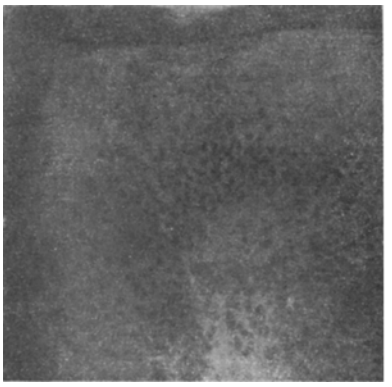

Fig. 2. The skin of a rabbit two weeks after irradiation with α-particles and subsequent painting with naphthalan oil extract. Thickening of the epidermis without signs of dystrophy. Stained with hematoxylin-eosin. Magnification: ocular 10×, objective 40×.

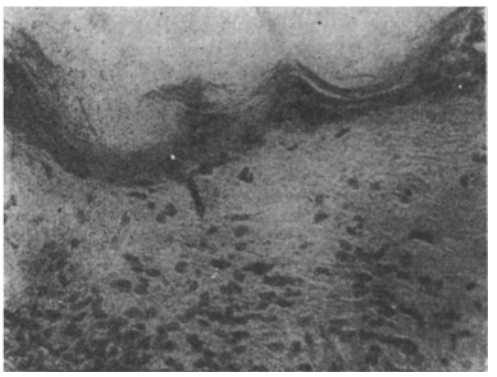

Fig. 3. The skin of a rabbit on the second day after irradiation with α-particles and painting with naphthalan oil extract immediately before irradiation. Dystrophy in the stratum germinativum of the epidermis. Stained with hematoxylin-eosin. Magnification: ocular 15×, objective 40×.

applicators, the radiation changes were also observed to be more rapidly overcome, with restoration of the normal structure of the epidermis, which took place at the beginning of the second week when the content of thorium C and thorium C' on the applicator was 0.3 $\mu c/cm^2$, and on the 7th-8th day of the experiment was 0.06 $\mu c/cm^2$.

When painting with NOE was carried out six days after α-irradiation, proliferation of the epidermis took place against a background of moderate dystrophic changes in the epidermis, taking the form of swelling and vacuolation of the cells in the basal layer, the presence of individual giant, pyknotic cells, and also the formation of pigment along the nuclei and cell borders. On the day after painting with NOE there was a sharp increase in the number of damaged cells in the epidermis, and mitoses were absent. On the 2nd-3rd day, besides the large numbers of dying polymorphic and giant cells, many normal mitoses were present in the cells of the basal layer, and on subsequent days proliferation of epidermal cells took place, causing the quicker desquamation of the disintegrating epithelial elements. The same effect was produced by painting with NOE on the 12th day after irradiation: a rapid and marked increase in the number of degenerating cells and an equally rapid proliferation of normal cells in the stratum germanitivum, leading to desquamation of the disintegrating cells of the epidermis.

Painting the skin of a rabbit with NOE after local irradiation with α-particles thus led to an acceleration and apparent intensification of the radiation reaction in the epidermis, with the subsequent rapid repair of the changes.

When the skin in which proliferation of the epidermis was already developing (in the first week after painting with NOE the thickness of the epidermis was 100-150 μ) was irradiated once with α-particles, corresponding to the low penetrating power of the α-particles a practically complete protective action of the proliferation of the cutaneous epithelium was found, and was unaccompanied by changes in its stratum germinativum. Only in the prickle cells not deeper than 40-60 μ from the skin surface, and especially when the highest-activity applicators were used, were signs of dystrophy present in the form of individual large cells with deformed, pyknotic nuclei. Dystrophy, limited to only part of the prickle cells, was found on the 3rd-4th day after irradiation, i.e., much sooner than in the epithelium irradiated in a state of quiescence, thereby indicating the more rapid appearance of radiation changes in the epidermis when preliminarily treated with NOE. In the second week of the experiment hardly any degenerating prickle cells were found, and their desquamation was accelerated in the process of the more intensive renewal of the structure of the epidermis caused by the stimulus to its proliferation.

Consequently, after a single exposure to α-particles of skin in which proliferation of the epidermis has previously been induced by NOE, radiation injury is practically prevented. It is evident that the α-particles

are unable to reach the cells of the basal layer through the barrier of the thickened upper layers of the epithelium of the skin.

In the experiment with α-irradiation (applicator with an initial content of α-emitting isotopes of 6 $\mu c/cm^2$) immediately after painting the skin with NOE, i.e., before the thickening of the epidermis to protect the basal cells from radiation, the changes taking place in the epithelium were the same as those when the skin was painted immediately after irradiation. On the second day of this prophylactic variant of the experiment, widespread dystrophy took place in the basal layer of the epidermis, with swelling and vacuolation of the cells, and with enlargement, translucency and, later, pyknosis of their nuclei, and so on (Fig. 3). The further course of the process consisted of the speeding up of regeneration of the epidermis, which was fully restored during the second week after irradiation.

When α-irradiation was carried out 12 hours after painting the skin, i.e., when only insignificant thickening of the epidermis was present, the rate of development of the radiation injury and of regeneration of the epidermis was increased, to coincide in time with what happened in the case of irradiation immediately after painting the skin.

In the case of α-irradiation of the skin 36 hours after painting with NOE, when the thickness of the epidermis was about 60 μ, on the day after irradiation the epidermis was thickened as before, with numerous mitoses in the stratum germinativum and with isolated, larger degnerating cells scattered among the normal cells of the basal layer. On the second day after irradiation the number of such cells increased as the result of their appearance among the prickle cells of the continually thickening but otherwise little changed epidermis. On the following days of the first week, groups of large, pyknotic cells, becoming more and more displaced towards the skin surface, were observed mainly among the prickle cells; intensive mitotic activity continued in the basal layer, leading to the progressive thickening of the epidermis. Beginning in the second week of the experiment, no signs of dystrophy could now be seen in the thickened epidermis, their absence proving that the rate of repair of the radiation changes was increased under the influence of NOE.

The changes in the epithelium when a single dose of α-irradiation was given to the skin of a rabbit 2.5 days after painting, i.e., when the thickness of the epidermis was 100-120 μ, corresponded completely to the changes from α-irradiation one week after painting with NOE; the thickening of the epidermis taking place during 2.5 days almost completely protected the radiosensitive stratum germinativum from the action of the α-particles.

SUMMARY

In connection with the favorable effect exerted on radiation injuries by substances capable of stimulating proliferation, including the naphtalane-oil extract (NOE) it was deemed interesting to study the action of the latter in radiation injuries of the skin provoked by α-rays.

As shown experimentally, an acceleration of radiation reaction of epidermis and of its recovery occurred, consequent upon application of NOE to the rabbit's skin directly after its local irradiation with α-rays of thorium fission. Rabbit skin irradiated in 2.5 days and later after NOE application gave practically no radiation reaction. α-irradiation directly or within the first 2 days after NOE application to the skin provoked an accelerated radiation reaction and recovery.

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