FORMATION OF A CORNEA FROM HEAT-TREATED SKIN

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Translated from Byulleten' Éksperimental'noi Biologii i Meditsiny, Vol. 54, No. 7,
pp. 88-90, July, 1962
Original article submitted November 30, 1962

This work was devoted to further study of the question of sources of inductive effects, giving rise to the formation of a cornea from skin transplants and regenerating tissue in larvae of acaudal amphibia, which are particularly suitable for such experiments.

In contradistinction to the old and, it may be said, widely held, point of view, according to which the entire eye (retina, crystalline lens) stimulates young skin to transformation into a cornea, we were able to show that the leading role in the induction of a new cornea, in the post-fetal development of amphibia, is played by the photoreceptors of the retina: the rods and cones [5,6].

On the basis of a number of experiments, we established that induction of the cornea is directly dependent upon an appropriately timed discharge of a potential, related to an a wave and originating in the center of the photoreceptor cells, near their internal segments [4,9]. We were inclined to postulate that the formative effect of the eye on the skin, in the formation of the cornea, was of an energy nature, more precisely, electromagnetic. However, it seemed to us that to definitively elucidate the nature of the inductive relationship which interested us, it would be necessary to study not only the sources of the eye's formative influence, but also the norms of the formative reaction on the part of the skin transplanted to the eye or regenerating over it.

It seemed reasonable to carry out the study of the skin's formative properties according to the same scheme as was used in investigating the sources of the formative effect on the eye. It was established earlier that selective poisoning of the photoreceptors [4] and roentgen irradiation of the retina [7] suppress secondary induction of the cornea, and the action of certain light regimes on experimental animals enhances it notably [6]. A similar approach to the "reacting system" showed that irradiation of the donors with a dose of 1500 r increased the reactivity of their skin which, upon being transplanted to the eye of a nonirradiated recipient, was transformed into a new cornea significantly faster than normal skin [9]. In connection with this, we wondered about the use of certain other stimuli for increasing the reactivity of the skin transplants. In order to unify the degree of stimulation, it was decided to bring them to the point of reversible denaturation of the protoplasmic proteins in the transplanted skin, the endpoint being appearance of paranecrotic changes in the cells of the epidermis. We subjected the skin of the donor to such stimuli as elevated and lowered temperature, very dilute acetic acid, oxygen deprivation, etc.

The subject of this particular report is the experiments studying the effect of elevated temperature on the formative properties of the skin transplants.

EXPERIMENTAL METHOD

The experiments were carried out on tadpoles of Rana temporaria, in stage II of development [1]. The skin for replacement of the recipient's external cornea was always taken from the back of the donor.

Paranecrotic changes were obtained in the skin of the tadpoles by two means: either the tadpoles were stained in a solution of neutral red (1 : 10,000) over a period of 24 h at room temperature, and then transferred to the elevated temperature, or they were subjected to the elevated temperature at the start and then to the vital staining. After the animals were kept in small crystallizing basins containing a minimum amount of water for 1½-2 h at 35 to 37° incubator temperature, paranecrotic changes appeared with constancy in the epidermal cells, as evidenced by the

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diffuse staining of the protoplasm and the appearance of stained structures in the nuclear apparatus [2].

In addition to the experiments designed to elucidate the effect of elevated temperature on the reactivity of the skin transplants, we set up control experiments with transplanted normal skin and skin subjected to the action of roentgen rays.

EXPERIMENTAL RESULTS

We carried out 57 transplantations of skin subjected to the heat stimulus. In all cases, final transformation of the denatured skin into a new cornea took place in 11-14 days.

The skin of donors, irradiated with a dose of 1500 r, was transplanted at the end of the period of reaction (on the 2nd to 3rd day). We performed 45 of these transplantations, and transformation of the irradiated skin into a cornea was completed by the 10th-12th day after the procedure.

Normal skin was transplanted to 50 animals; its final transformation into a cornea was accomplished only after 18-20 days, and then not in all animals, but only 42 of the experimental subjects.

We did not observe any overlap of the beginning or the end time periods for transformation of the skin transplants into a new cornea between the animals of the first two series and those of the last series of experiments.

The results of these experiments completely coincide with the data obtained by us earlier [9]. It may be postulated that the indicated skin changes are related, above all, to the capacity of a number of substances, entering into the composition of the skin and the cornea, to form and break down multiple rings. It is very probable that, under the influence of an elevated temperature and certain other external agents, a depolymerization type of process begins in the colloidal system of the young skin. Then, against the setting of this depolymerization, the new aggregation, characteristic for the cornea, proceeds more easily and, possibly, also the polymerization secondary to the actual electromagnetic effects issuing from the photoreceptor cells of the retina.

Besides considerations of a general order, this hypothesis is supported by concrete investigations, showing that changes in molecular complexes are possible in living tissues [3].

SUMMARY

The authors' study concerns the mechanism of the effect produced by the eye on the skin transplants in experimental induction of the cornea. It was possible to demonstrate, with the aid of various morphological and physiological methods, that transformation of the skin into the cornea occurs under effect of photoreceptors of the retina Along with this, it was shown [9], and then confirmed in the present work, that irradiated skin is transformed into a new cornea much more rapidly than the intact one. But the main conclusion of the present work lies in the fact that not only the irradiated, but also the overheated (35-37°C) skin with paranecrotic changes in its cells, possesses an increased formative reactivity.

It is possible that under the effect of the mentioned factors there occur in the colloidal system of the young skin phenomena of depolymerization type. This being true, under the inducing action of photoreceptors in such skin there evidently takes place a new, more rapid aggregation, and possibly polymerization, characteristic of the cornea.

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