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TO BURNS OF IRRADIATED RABBITS
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- USSR -

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HISTOLOGICAL CHANGES IN SKIN FOLLOWING HOMOPLASTY
TO BURNS OF IRRADIATED RABBITS

- USSR -

[Following is the translation of an article by L. B. Berlin and V. F. Zhupen in the Russian-language publication Doklady Akademii Nauk SSR (Reports of the Academy of Sciences USSR), Vol. CXLVI, No 1, Moscow, 1962, pages 242-245.]

Numerous research has shown that skin homotransplants in mammals and man survive only temporarily, and then perish (1-7). Through acting upon the recipient (8-12) or the transplanted flap (13-16), it is possible to prolong the survival of the homotransplant tissues. One such method is the administration of cortisone (17-20). Skin homoplasty is one of the best treatment methods for severe burns, particularly those in radiation sickness (21). The histological changes in skin transplants, however, have received little attention.

Acute radiation sickness in rabbits was produced by a total single irradiation by x-ray of 600 r (current, 15 ma; voltage, 195 kv; filter Cu 0.5; skin-focus distance, 50 cm; dosage strength, 20 r/min). On the same day 80 rabbits were subjected to thermal trauma by water heated to 82.5-83° on the inner skin surface of both ears. A round burn was produced, 3 cm in diameter. Twenty animals were studied in terms of histological changes in the skin following radiation sickness burn; while 60 rabbits, at various periods of acute radiation sickness, had necrectomies and homoplasty by graft taken from the external surface of the ear, infiltrated with V. I. Popov's preservative liquid (22) and stored in the same solution at 4-6° temperatures. Cortisone was administered intramuscularly in 1.0 mg/kg daily doses. At the same time complex treatment was given for the radiation sickness. Specimens were fixated at intervals of several minutes to 17 days following burns, and from several minutes to 47 days following homoplasty.

The epithelium and connective tissue show little change immediately following the burn. An insignificant oxyphilia occurs in epithelial cell cytoplasm, external vaginal capillaries, and intercellular substance of the cartilage. During the first hour, necrobiotic changes occur. There is pyknosis of the cell nuclei of epithelium and dermal adnexa; the cytoplasm becomes acutely oxyphilic with perinuclear vacuoles. A wide homo-

geneous lightly-staining line an hour below the basal epithelial layer (Figure 1a). Connective cell nuclei, particularly in the papillary layer, become hyperchromatic. Burn trauma produces severe edema in the outer part of the ear; the skin thickens; collagenous nodules are severely divided by edemic fluid; and the edemic fluid begins to show pseudoecsinophilic leukocytes.

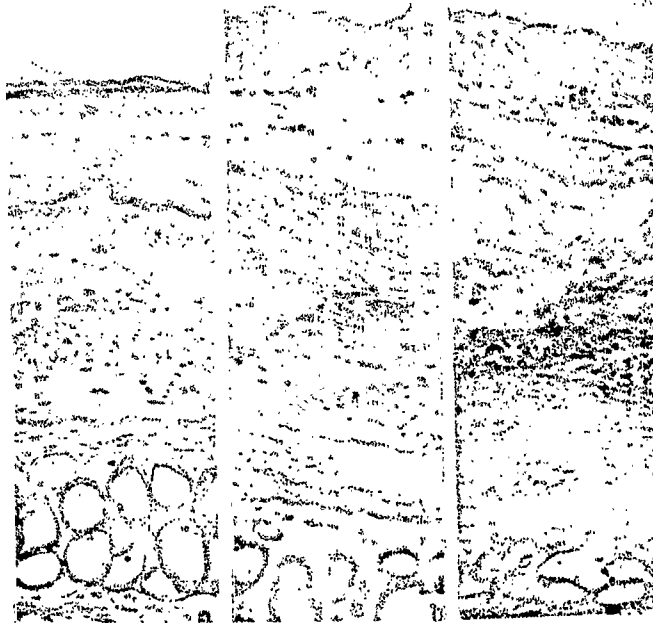


Figure 1. Burn lesion areas of external surface of rabbit ear.
Formalin, hematoxylin-eosin.

Legend: a --- 1 hour; b --- 48 hours; c --- 4 days following burn.
Additional explanation within the text.

The burned epidermis of the inner ear surface exfoliates in many places by the 12th hour following trauma, while a leukocyte-containing fluid accumulates beneath (Figure 1b), -- burn blisters of various sizes begin to form. Gradually the necrobiotic dermal changes become more and more manifest. Collagenous nodules lose their fibrillar structure; nuclei become pyknotic; and by the end of the first day the whole area of burn is surrounded by a narrow demarcational agger, separating the necrotic epidermis and the outer part of the dermis, composing the scab, from the bordering and underlying skin. In places the skin is necrotic to the very cartilage. The surface side of the demarcational agger shows in-

flammation, leading to the development of granulated tissues, while the side areas show the formation of multi-layered epidermal regeneration growing under the scab (Figure 1c). The further course of burn wounds in irradiated rabbits, even to the 17th day, is characterized by the formation of numerous hemorrhages in the granulated tissue; insignificant infiltrational phenomena; delayed separation of the burn scab; and the slow development of regenerative epithelial changes in the connective tissue.

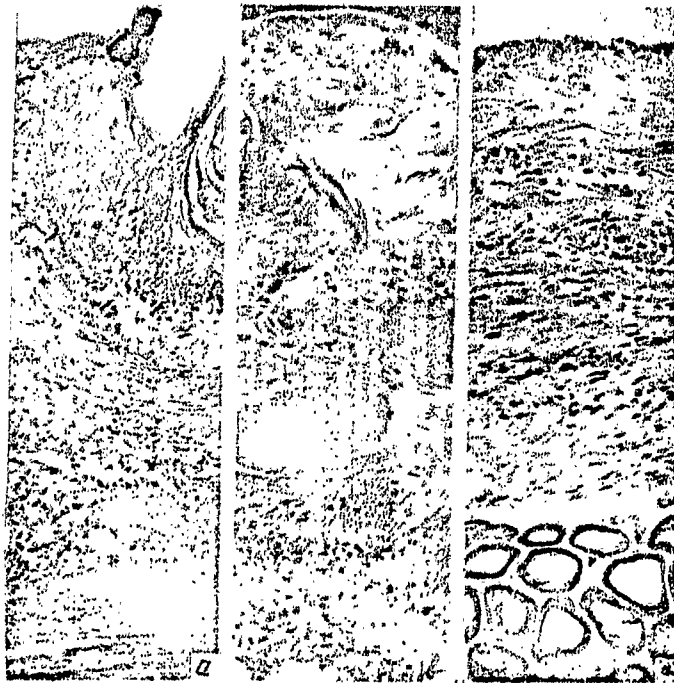


Figure 2. Homotransplantation areas. Formalin, hematoxylin-eosin.

Legend: a — 25 days after transplantation in the latent period.
 b — 22 days after plasty in the climactic period
 c — 47 days after transplantation in the recovery period.
 Further explanation within the text.

Skin homotransplants, grafted in the latent period of radiation sickness, retain a viable character nearly throughout for a period of 4 weeks. At the end of the first week following plasty, despite significant hemorrhaging into the dermis and bed of the transplant, the flap epithelium becomes severely thickened; its cell cytoplasm and the epithelium of the pilar follicles becomes basophilic; and mitoses appear. Only

the most marginal areas of the skin flap perish. The number of dermal cells somewhat increases, particularly at the expense of lymphocytes. During the course of the following two weeks, some areas of the transplant epidermis show foci of necrosis and small ulcerations; the flap, however, remains covered on the whole with completely viable epithelium (Figure 2a), formed, in the case of epidermal necrosis, as a consequence of proliferation and displacement of pilar follicles on the epithelial surface (16). The last, moreover, form cystoid cavities, covered with multi-layered epithelium. The marginal areas of the graft show a marked junction between its epidermis and the recipient's epithelium, growing over the partially exposed transplant dermis. This epithelium is very thin, as its substratum is alien to it, and it is, apparently, destined to perish. The graft dermis is visually very little changed. It has some increase in the number of cell elements: in the external areas -- at the expense of lymphocytes and pseudoeosinophils, and in deeper areas -- in consequence of infiltration between collagenous nodules of the transplant of granulated tissue fibroblasts under the graft, the so-called commissure layer. In later intervals following plasty in the latent period (30 days), there is an absence of transplant epithelium in many areas, while the deeper layers of the graft show the ingrowth of numerous rods of connective tissue cells and endothelial branches from the commissure layer.

In homoplasty in the climactic period of acute radiation sickness, hemorrhages are more marked into the transplant dermis and bed. The graft epidermis gradually perishes throughout, and a new continuous epithelial plast forms underneath (Fig. 2b). This is first formed at many points at the expense of proliferation of the pilar follicle epithelium, replacement by regenerated tissue on the dermal surface, and their fusion into the general stratified tegmentum. Dermal connective tissue has a viable appearance throughout the course of observation -- to 45 days. There is more severe change of the dermis in deeper tissues of the graft, where rods of connective tissue cells from the commissure layer together with the endothelium penetrate deeply between the transplant's collagenous nodules. As a consequence, initially in the deep layers, and later, closer to the epidermis, the dense connective tissue of the donor is supplanted by the recipient's cell elements, which gradually form their intercellular substance. Accumulations of hemosiderin are observed at hemorrhage sites (Fig. 2b). It also fills the necrotic blood vessels of the graft. The commissure layer achieves significant development. The cartilage, which has been drawn into the inflammatory process from the moment of the burn, displays the destructive changes of resorption and proliferating processes, with the formation of new groups of cartilage cells. Marginal homotransplant areas at late intervals (30-45 days) manifest either necrosis and separation of small areas with an undergrowth of recipient's epithelium, or the formation of a continuous extension of the recipient's epithelium into the homotransplant epidermis. In some rabbits the dystrophic processes in graft tissues transplanted during the climax of acute radiation sickness prevail over proliferation processes. In these cases, necrosis of the epithelium and external dermis occurs earlier, by the 15-20th day,

and is accompanied by scab formation on the ulcerated skin.

Nectrectomy and graft transplant during the period of recovery from acute radiation sickness occurs within conditions of prolonged inflammation induced by burn trauma and sustained by necrotic tissue structures, which frequently had a secondary infection. The graft, therefore, from the first hours and days is surrounded by tissues with inflammatory changes distributed in the area of the bed, cartilage lamina, and the skin of the outer surface of the concha auricularae. Suppurative inflammation, as well as the by now disappearing leukopenia, which occurred in the latent period and particularly in the climax of the radiation sickness, leads to pseudoeosinophilic leukocyte infiltration of the transplant by the 9-10th day following transplantation. This infiltration, particularly epidermal, has a focal character. The transplant epidermis greatly thickens in some parts, while in others, particularly where leukocyte infiltration is occurring underneath, perishes and becomes part of the composition of the scab. The epithelium of skin appendices in developing forms cystoid cavities, sometimes filled with perished leukocytes. At later intervals, a wide commissure layer develops. Graft infiltration by pseudoeosinophils disappears, but lymphocytic infiltrates remain. The prolonged contiguity of burned and necrotic tissues in these experiments lead to particularly severe cartilage changes. In some places areas of newly-formed cartilage are distributed somewhat to the side of the basic cartilage lamina. Along its length is observed an alternation of old surviving cartilage, and newly-formed cartilage. Even at the latest time periods (47 days following transplantation), homotransplants preserve their viable character. The stratified epithelial covering is distributed on the connective tissue deprived of skin appendices (Fig. 2b). Their cambial elements form, in earlier intervals, an epithelial plast instead of the perished epidermis, while the differentiated ones are eliminated. The deeper layers of the graft, enriched with recipient's cells, merge without abrupt demarcation into the recipient's granulated scar tissue (Fig. 2b), here in the role of a commissure layer.

The data obtained permits our considering that graft tissues, influenced by cortisone, preserve their viability for a very long time, while following conservation in identical conditions without cortisone they perish in 12-15 days (16). The inhibition of reactive resources through irradiation and particularly through cortisone (23, 24) is the reason for the decrease in the recipient's immunological reaction to the homotransplant (25, 26), and for the very slow separation in only marginal graft areas, weakly overgrown by the host's epithelium.

These experiments confirm the observations made earlier in homotransplants of rat skin concerning "settlements" of the host's fibroblasts in the dense connective tissue of the graft, the so-called "partial adaptation" (27, 28). For final resolution of the problem, which has great practical significance aside from its theoretical interest, very prolonged observation is necessary.

What merits attention is that it is not so much the condition of the organism at any period of radiation sickness, as the various local conditions (29), for example the depth of thermal trauma, the presence of

absence of secondary infection in the wound, the necrectomy time interval, etc., that significantly influence histological changes in skin transplantation.

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