EFFECT OF SITE OF DEFECT ON COMPLETENESS OF REGENERATION OF THE RAT'S SKIN

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Healing of skin wounds on the tail and head of rats ends with the formation of regenerated areas which differ from the connective-tissue scar arising as the result of healing of skin wounds on the dorsum of the rats by the arrangement of the hair structures and, in the case of defects of the tail skin, by the formation of hair follicles.

For the experimental study of processes taking place during regeneration of the skin in laboratory animals (rats, mice, rabbits), wounds are usually inflicted on the skin in the dorsal region. Most investigators consider that a connective-tissue scar is formed at the site of the defect and that it remains in this form without changing into skin with the typical structure [2, 5-7, 9]. However, other workers who have studied regeneration of the skin on the concha auriculae of rabbits and on the head in mice [1, 3, 4, 8] found an area of regenerating tissue at the site of the defect which resembled to some extent normal skin in its structure. Completeness of regeneration of the skin evidently depends on the site of the defect. It is therefore important to know whether differences exist in wound healing depending on the site of the defect in the animals most commonly used for experimental purposes, namely rats.

The object of the investigation described below was to compare the healing of skin wounds on the head and tail of rats.

EXPERIMENTAL METHOD

The experimental animals were 64 noninbred male albino rats weighing 150-180 g. Full-thickness square pieces of skin measuring 1 cm^2 were removed from the scalp over the vault of the skull of half of the animals (series I). Full-thickness square pieces of skin measuring 0.75 cm^2 were taken from the tail of the other half of the animals, 1 cm away from its base (series II). Before removal of the skin, the place of the future wound was marked with ink 0.5-1 mm away from its edge. All manipulations on the animals were carried out under ether anesthesia. The area of the wounds, and later the areas of the epithelized surfaces of the defects, were measured at successive times of healing. Pieces of tissue were taken for histological analysis from the region of the wound and adjacent areas of intact skin on the 6th, 11th, 20th, and 40th days and 5 months after the operation in the experiments with head wounds and on the 17th day and in the 2nd, 3rd, and 7th months after the operation in the experiments with tail wounds. The reason for the later times of investigation in the latter case was the slower rate of healing of the wounds by comparison with wounds of the scalp.

The pieces of tissue were taken through celloidin and embedded in paraffin wax. Sections, 7-9 μ in thickness, were stained with hematoxylin-eosin and orcein.

EXPERIMENTAL RESULTS

Healing of the scalp wounds took place under a thin scab. The concentric contraction of the wound margins was well marked. The mean area of the wound on the 6th day after the operation was 0.34 cm^2

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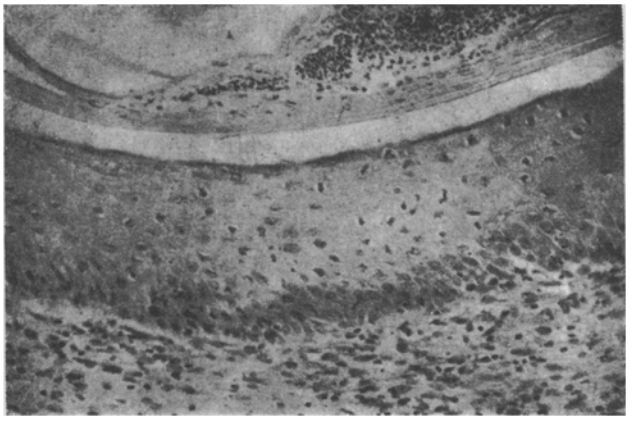

Fig. 1. Vertical section through defect of skin of the tail 17 days after operation. Hematoxylin-eosin, 200 ×.

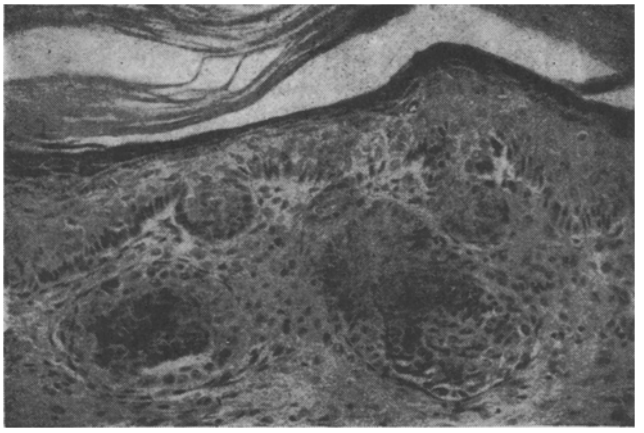

Fig. 2. Vertical section through central part of defect on skin of the tail 2 months after operation. Early stage of development of hair follicles, hematoxylin-eosin, 200 ×.

(original area of the wound 1.1 cm^2). Complete epithelization of the surface of the defect occurred 10-12 days after the operation. By the 12th day the mean area of the epithelized surface of the defect was 0.24 cm^2.

Later the area of the epithelized surface of the wound remained virtually unchanged. The epithelized surface was stretched along a line parallel to the long axis of the head. Ink marks were 1-1.5 mm away from the edge of the epithelized surface of the wound defect.

The wounds on the tail healed under a thick scab. Epithelization of the defect was complete by the 16th-18th day after the operation. The mean area of the epithelized surface at this time was 0.68 cm^2, i.e., there was virtually no contraction of the wound. However, by the 30th day after the operation, the epithelized surface of the wound defect had shrunk and its mean area was now 0.28 cm^2. The label was 1 mm away from the edge of the defect. In other words, contraction of the wound took place after complete epithelization of the defect. The mean area of the epithelized surface of the defect 3 months after the operation was 0.19 cm^2, and no further contraction took place. The epithelized surface was stretched perpendicularly to the long axis of the tail.

Histological study of the material showed that on the 11th day after wounding on the head the defect was filled with young loose connective tissue, consisting of cells, thin fibrils, and numerous dilated blood

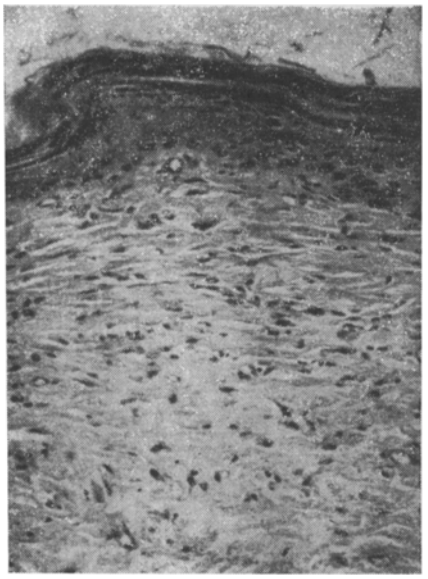

Fig. 3. Vertical section through defect in skin of the scalp 5 months after operation. Hematoxylin-eosin, 200 ×.

vessels. The mean thickness of the young connective tissue was 760 μ. The epithelium covering the young connective tissue consisted of 5-6 layers of cells; its mean thickness was 43 μ (thickness of intact epithelium 21 μ).

Similar pictures as regards the structure of the tissues filling the defect were observed in wounds on the tail 17 days after the operation. The epithelium covering the defect consisted of 12-13 layers of cells; its mean thickness was 175 μ (thickness of the intact epithelium 56 μ). The young connective tissue filling the defect also consisted of thin fibrils, cells, and dilated blood vessels (Fig. 1). The mean thickness of the young connective tissue was 680 μ.

On the 20th day after the operation, the young connective tissue in the skin defect on the head became condensed and consisted of fibrils arranged mainly parallel to the surface of the defect, and cells. The fibers formed intersections. The mean thickness of the young connective tissue was 410 μ.

The epithelium covering the defect consisted of 4 or 5 layers of cells; its mean thickness was 31 μ. Thickening and condensation of the fibrous structures in the zone of the defect, compared with the preceding period, were observed 40 days after the operation. In all layers of the defect the fibers were interwoven. The thickness of the epithelium and young connective tissue were virtually unchanged compared with the previous period.

In defects on the tail 2 months after the operation, the young connective tissue consisted of fibers and cells. Blood vessels arranged mainly vertically relative to the surface of the defect were visible in it.

The epithelium covering the defect consisted of 7 or 8 layers of cells and its mean thickness was 88 μ. Unlike the epithelium covering the defect on the head it formed projections into the underlying young connective tissue.

In 3 of the 7 animals sacrificed for histological investigation at this time specific epithelial downgrowths could be found at the center of the defect. In transverse sections the cells in these downgrowths were arranged in circles. Desquamated cells were visible inside these formations. The epithelial formations were surrounded by a thin outer membrane (Fig. 2). These downgrowths were regarded as early stages of development of hair follicles.

The young connective tissue in the skin defects on the head 5 months after the operation consisted of interweaving fibers and single cells (Fig. 3). In the deep layers of the defect, thin elastic fibrils were seen. The mean thickness of the young connective tissue was 650 μ (thickness of the intact dermis 810 μ). The epithelium covering the wound defect consisted of 4 or 5 layers of cells; its mean thickness was 29 μ (thickness of the intact epithelium 19 μ). No formation of hairs or glands was found in the regenerating tissue.

The epithelium covering the wound was still hypertrophied 3 and 7 months after formation of the defect of the tail. It consisted of 6 or 7 layers of cells and its mean thickness was 68 μ (thickness of the intact epithelium 54 μ). In some places short epithelial downgrowths into the underlying tissue were found (at all times marked deposition of keratin was observed above the epithelium).

The fibrous structures filling the defect were interwoven in the upper layers. However, in the deep layers of the wound defect the fibers were mainly arranged parallel to the surface of the defect. The mean thickness of the young connective tissue was 770 μ (thickness of the intact dermis 820 μ), i.e., it was similar in thickness to the normal dermis.

It follows from these experimental results that the healing of skin wounds on the head and tail of rats differs in certain of its features. Closure of the defect in the scalp took place more rapidly than closure of the defect in the skin of the tail, despite the fact that the defect on the scalp was larger. Contraction of the wound on the scalp ended when epithelization of the defect was complete; contraction of the wounds in the tail skin, on the other hand, began and continued for a long time after complete epithelization of the defect.

As the outcome of regeneration of the skin on the head and tail of the rats, areas of imperfectly regenerated skin were formed. At the same time, they differed from the typical scar formed at the site of a skin defect on the dorsum of rats in the arrangement of the hair structures and in the appearance of single hair follicles (in regenerating tail skin). Despite the long periods of observation on healing of comparatively small skin wounds on the tail and head of the rats, it is evident that the regenerative processes in the skin defects were not completely at an end.

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