

The phenomenon described above took place in animals of both groups. No reaction product was found in the lysosomes, biliary tubules, or bile ducts during examination of control preparations.

The results thus indicate that during involution of cirrhosis exocytosis of lysosomal enzymes by hepatocytes into the bile takes place in the liver. Since the process described above was observed 5 days after the last injection of  $\text{CCl}_4$ , when most fibrous tissue had already undergone resorption and the liver structure was largely restored, there is every reason to suppose that exocytosis of lysosomal enzymes by hepatocytes into the bile is not the result of the pathological process in the liver, but is a mechanism of bile secretion. This hypothesis is supported by the discovery of lysosomal enzymes in the bile of intact animals in a number of biochemical investigations [1, 2, 4-7, 10].

The physiological role of lysosomal "unloading" of hepatocytes into the bile is unknown. Some workers consider that it is responsible for removing indigestible particles from hepatocytes, through their accumulation in secondary lysosomes [1, 2]. It has also been suggested that some substances from hepatocytes, especially those transported by vesicles, can be associated with primary lysosomes before they are secreted into the bile by exocytosis. Lysosomal enzymes can degrade, or metabolize somehow or other, certain substances for their excretion into the bile [5].

#### LITERATURE CITED

1. C. De Duve, Ciba Foundation Symposium on Lysosomes, A. V. S. De Reuck and M. P. Cameron (eds.), Boston (1963), p. 1.
2. C. De Duve and G. R. Wattiaux, *Annu. Rev. Physiol.*, **28**, 435 (1966).
3. J. L. E. Ericsson and B. F. Trump, *Histochemie*, **4**, 470 (1965).
4. G. Holdsworth and R. Coleman, *Biochim. Biophys. Acta*, **389**, 47 (1975).
5. A. L. Jones, D. L. Schmucker, R. H. Renston, and T. Murakami, *Dig. Dis. Sci.*, **25**, 609 (1980).
6. N. F. La Russo and S. Fowler, *J. Clin. Invest.*, **64**, 948 (1979).
7. G. D. Le Sage, L. J. Kost, S. S. Barham, and N. F. La Russo, *J. Clin. Invest.*, **77**, 90 (1986).
8. A. B. Novikoff, *Proc. Natl. Acad. Sci. USA*, **73**, 2781 (1976).
9. P. M. Novikoff and A. Yam, *J. Cell Biol.*, **76**, 1 (1978).
10. S. Toyoda, Y. Eto, and K. Aoki, *Clin. Chim. Acta*, **79**, 291 (1977).

#### SPECIFIC FEATURES OF HEALING OF VENTRAL SKIN WOUNDS IN RATS

E. A. Efimov and T. V. Bukina

UDC 616.5-001.4-031:  
611.95]-003.9-092.9

KEY WORDS: skin wounds, wound contraction, completeness of repair, regeneration.

Most experimental studies of skin wounds have been undertaken on the dorsal region of rats and mice [1, 2]. Meanwhile no investigations of the healing of skin wounds on the ventral aspect of the trunk of laboratory animals could be found in the literature. The skin on the ventral aspect is thinner than in the dorsal region, it has a well-developed elastic skeleton, and contains fewer hairs. These differences suggested that the healing of wound defects on the ventral aspect of the trunk in animals would have certain characteristic distinguishing features.

The aim of this investigation was to compare the healing of full-thickness skin wounds on the ventral and dorsal aspects of the trunk in rats. During analysis of the results attention was concentrated on contraction of the wounds and completeness of repair of the skin.

Laboratory of Growth and Development, Institute of Human Morphology, Academy of Medical Sciences of the USSR, Moscow. (Presented by Academician of the Academy of Medical Sciences of the USSR P. A. Avtsyn.) Translated from *Byulleten' Éksperimental'noi Biologii i Meditsiny*, Vol. 104, No. 12, pp. 750-752, December, 1987. Original article submitted November 12, 1986.

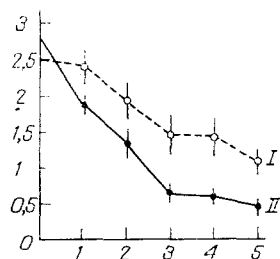


Fig. 1. Graph of wound contraction. Abscissa, area of wound (in cm<sup>2</sup>); ordinate, time after operation (in days). I) Dorsal wound. II) ventral wound.

#### EXPERIMENTAL METHOD

Experiments were carried out on 67 noninbred male albino rats weighing 130-150 g. A square wound measuring 1.5 × 1.5 cm was inflicted on 35 animals in the middle part of the abdominal wall and on 32 animals in the interscapular region. All operations were performed under ether anesthesia. To compare the time course of contraction, the area of the wounds was measured at successive times during healing. Tissue from the region of the defect and the adjacent skin was fixed in Carnoy's fluid on the 3rd, 7th, 12th, 20th, and 30th days after the operation, embedded in paraffin wax, and sections were cut from it to a thickness of 8-10 μ. The sections were stained with hematoxylin and eosin and with orcein.

#### EXPERIMENTAL RESULTS

Full-thickness wounds on the ventral aspect of the trunk closed much more rapidly than wounds of the same size on the dorsal aspect. Only 24 h after the operation, the area of the ventral wound was reduced by one-third, to an average value of  $1.8 \pm 0.15$  cm<sup>2</sup>. This state of affairs is attributed to contraction of the underlying muscles, which help to bring the intact skin into the zone of the defect in the early stages of healing, where it is firmly fixed by a fibrin clot. As a result of this mechanism, closing the defect, the wound edges are approximated and wound healing takes place virtually by first intention. The area of the wound on the dorsal aspect remained almost unchanged during the first day after the operation (Fig. 1). Complete epithelization of the wound on the ventral aspect occurred on the 5th-6th day after the operation, but on the dorsal aspect, not until the 8th-10th day. Epithelization of a wound on the dorsal aspect of seven animals did not take place until the 15th-22nd day. As a result of regeneration of the skin in the center of the original defect on the ventral aspect of the trunk, an epithelized strip 1-1.5 mm wide and 18-20 mm long, arranged perpendicularly to the long axis of the trunk, was found on the rats. The area of regeneration amounted to only 4-5% of the total initial area of the defect.

Histological investigation of the material showed that in the early stages of skin repair (7-12 days) a provisional zone of regeneration formed in the wound defect on the ventral aspect of the trunk, consisting of a closely interwoven network of fibers (Fig. 2a). Later this was transformed into a focus of regeneration of dermal type, in which the interweaving of the fibers resembled their arrangement in the intact dermis. Characteristic skin folds and elastic fibers were formed in it (Fig. 2b). Solitary hair follicles were found in the peripheral areas of the regenerating skin in three animals (Fig. 3).

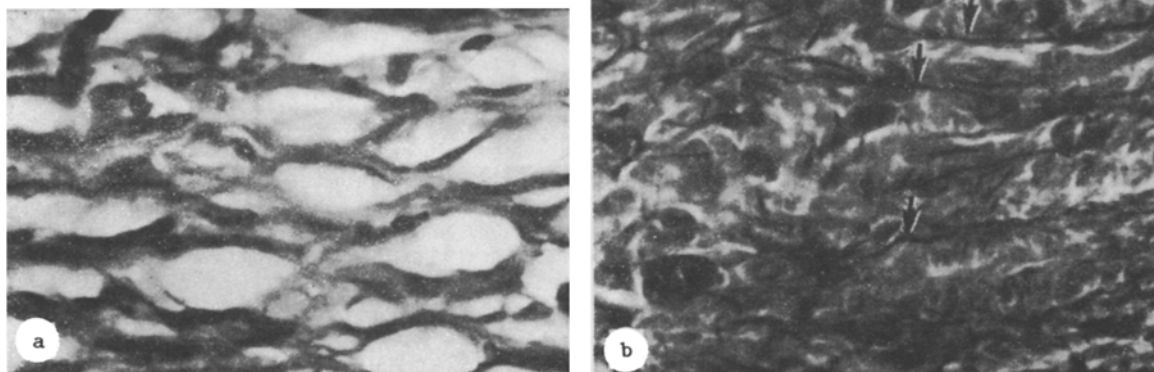


Fig. 2. Structure of regenerating skin. a) Region of regeneration on ventral aspect 7 days after operation. Hematoxylin-eosin. 200 ×; b) elastic fibers (arrows) in regenerating skin on ventral aspect 20 days after operation. Orcein. 600 ×.

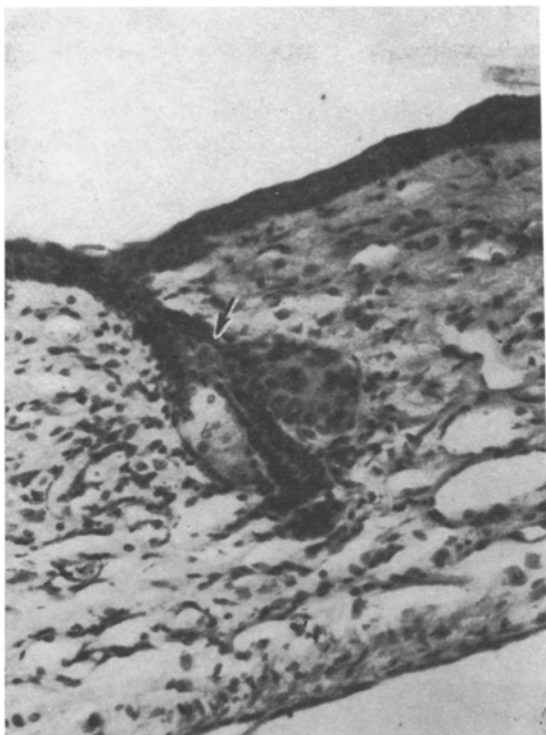


Fig. 3. Hair follicle in regenerating skin on ventral aspect of trunk (arrow) 12 days after operation. Hematoxylin-eosin. 200  $\times$ .

In those few cases when suppurative inflammation developed in the wound (four animals) healing ended with the formation of a linear, epithelized connective-tissue scar. In three animals in whose wound small local foci of suppurative inflammation were observed, regeneration was mosaic in pattern. In regenerating foci of this kind regions of fibrous tissue alternated with regions of dermis characteristic of ventral skin.

The regenerating skin on the dorsal aspect of the trunk always consisted of a star-shaped epithelized scar, the area of which was 9-11% of the area of the original wound. At no time of investigation were elastic fibers, air follicles, or sebaceous glands found in the scar. It consisted of coarse, densely packed collagen fibers, oriented mainly parallel to the surface of the defect. Solitary elongated fibrocytes were found between the fibers. The scar was covered with hypertrophied epidermis.

In our opinion the rapid and sound healing of skin wounds on the ventral aspect of the trunk has been formed in the course of evolution of animals, for the thin skin of this region is exposed more often to mechanical trauma than the dorsal skin.

#### LITERATURE CITED

1. E. A. Efimov, Post-Traumatic Regeneration of Skin [in Russian], Moscow (1975).
2. E. A. Efimov, Cellular Basis of Regeneration in Mammals [in Russian], Moscow (1984), pp. 78-86.