EFFECT OF THYROID-STIMULATING HORMONE ON REGENERATION AND METABOLISM OF SKIN

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The effect of adenohypophyseal thyroid-stimulating hormone on the level of metabolism and intensity of regeneration of skin was studied in relation to the topography of injury. Under the influence of this hormone the metabolic rate rises with the result that conditions favorable to more rapid woundhealing are created. Stimulation of repair is manifested most clearly in the early periods of regeneration. The stimulating effect was independent of the topography of injury but was more clearly marked in animals with wounds on the lateral surface of the body.

KEY WORDS: thyroid stimulating hormone; skin wounds; tissue respiration.

In present-day medical practice it is necessary not only to know the conditions that lead to effective regeneration but also to seek methods of speeding the course of regeneration in various tissues. As the result of advances in hormone therapy, the study of the effect of hormones of the endocrine glands on repair processes in the skin is particularly important [1-6, 9-11]. Among the various hormones, one which attracts attention is the thyrotrophic hormone of the adenohypophysis, for its effect on posttraumatic regeneration of the skin has not previously been studied.

Accordingly, in the investigation described below, the character and dynamics of repair in the skin were studied in animals receiving thyroid-stimulating hormone (TSH) after injury to different parts of the body.

EXPERIMENTAL METHOD

Experiments were carried out on 128 albino rats (mean weight 176 g). The animals were divided into four series. In the rats of series I a piece of skin with an area of 225 mm^2 was removed from the lateral surface of the body. A similar wound was inflicted on the animals of series II and TSH was given to these animals in a dose of 5 mg daily. In the rats of series III a similar piece of skin was removed from the back. A piece of skin was removed from the back of the animals of series IV and they were given TSH in a dose of 5 mg. Administration of the hormone began 3 days before the operation and continued for 20 days, with an interval of 10 days. The intensity of tissue respiration and of anaerobic glycolysis was determined manometrically in a Warburg apparatus before and 5, 10, and 15 days after the operation. The quantity of O_2 absorbed and CO_2 excreted was expressed in $mm^3/h/mg$ dry weight of skin. Healing of the wounds was judged from the results of a study of the cytological composition of the wound exudate and biopsy material taken from the edges of the wound at different times after the operation. Besides the usual histological methods, certain histochemical methods also were used.

EXPERIMENTAL RESULTS

Wounding and subsequent repair in the skin of the control animals were accompanied by increased tissue respiration. High values of oxidative metabolism coincided with dedifferentiation and growth, proliferation, and differentiation of the tissue structures. During administration of TSH the intensity of tissue

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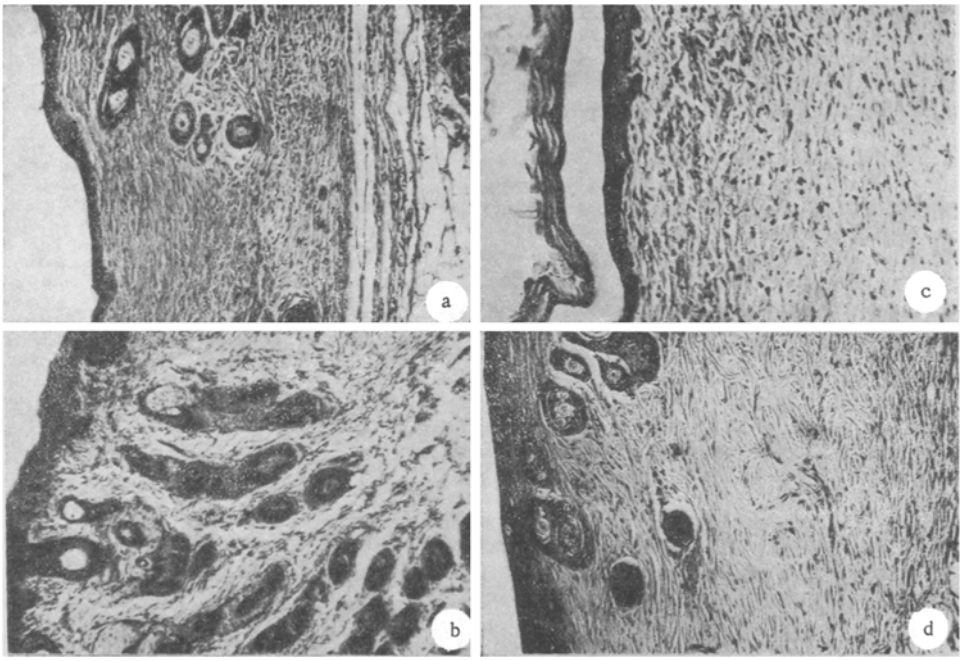

Fig. 1. Morphogenetic processes in the skin (60 days after operation): a) control (flank); b) TSH (flank); c) control (back); d) TSH (back). Hematoxylin–eosin, 120×.

respiration rose considerably to reach a maximum after 15 days. Parallel with the increase in endogenous respiration, in animals of all the series mentioned anaerobic glycolysis was increased during healing.

Changes in the level and character of metabolism were reflected sufficiently objectively in the course of regeneration of the skin. Differences between the experimental series were revealed by the study of the inflammatory process. In the period of inflammation, a typical response of emigration of neutrophils was seen in the wound exudate of the animals of the control series (wound on the side). The cells contained a moderate amount of glycogen and RNP. Administration of TSH to the animals activated the emigration of neutrophils and polyblasts, which were transformed into macrophages. These increased in size, their nuclei became irregular in shape, and vacuoles appeared in their cytoplasm. Under these conditions not only were changes in the composition of the cells of the wound exudate observed, but their content of glycogen and RNP also increased.

After wounding on the back, emigration of the cells was slower. The histochemical reactions were weak. Under the influence of TSH, the response of the blood and connective tissue cells under these conditions was more marked. Polyblasts were seen much more frequently than in the control. In squash preparations cells with an average glycogen content predominated. Small quantities of RNP were found.

On histological study of biopsy material the differences mentioned above were seen more clearly. In the control animals (wound on the flank) the granulation tissue contained chiefly fibroblasts, arranged parallel to the wound surface; the granulations were traversed by vertical capillaries. As a rule the epithelial wedge contained five or six layers with distinct boundaries. The basal surface formed small projections into the underlying tissue, from which specific derivatives were formed in the late stages of healing (Fig. 1a). Newly formed hairs and glands were distributed chiefly at the boundary between the scar tissue and uninjured skin.

Injection of TSH into the animals had a favorable action on the healing process. In connection with its action on proliferation processes, the stimulating effect was seen most clearly in the first half of the healing process. Granulation tissue formed under these conditions was distinguished by its great thickness and consisted of cells of hematogenous and connective-tissue origin. The boundary zone of the newly formed epithelium formed projections into the underlying tissue, from which the derivatives of the skin – glands and hair – were formed. Numerous hair follicles were situated in the thickness of the dermis at the boundary with the small area of scar tissue in the center of the former defect (Fig. 1b). Isolated derivatives were formed in the center of the regenerating focus.

In the rats of series III (wound on the back) features of a sluggish inflammatory reaction persisted for some time in the region of injury. Granulation tissue developed slowly. Preferential development in it was shown by the layer of vertical vessels. The epithelium grew slowly. Some special features were noted in the formation of the structures in the late stages of regeneration. The newly formed fibrous tissue covered a wide area. No specific skin derivatives could be seen to be formed in the scar. Outwardly the regenerating focus was covered by a smooth layer of epithelium which did not form projections (Fig. 1c).

In the animals of series IV, through the influence of TSH the granulation tissue contained many cells of both hematogenous and tissue origin. Proliferation of the epithelium was well marked. In the late stages of healing, skin derivatives were formed in the regenerating focus, mainly at the periphery; these derivatives were formed from projections of the epithelium and they penetrated deep into the corium (Fig. 1d).

The results of these experiments show that administration of TSH leads to a considerable increase in the intensity of tissue respiration and anaerobic glycolysis, and in that way the hormone influences the rate and character of regeneration. The positive effect of TSH was most clearly manifested in the first half of the repair process. The granulation tissue formed a well-developed layer as a result of accumulation of cells of varied genesis. The young epithelium was of considerable extent and its inner surface formed projections from which the specific derivatives developed. The stimulating effect of the hormone was exhibited regardless of the position of the injury, but it was more marked in animals with wounds on the flank. This fact can evidently be explained by the restricted mobility of the skin on the back. its relatively poor blood supply, and the arrangement of the Langer's lines [12].

The writers suggest that the beneficial effect of TSH on the repair process in the skin can be linked with activation of thyroid hormone production. Under the influence of TSH, features of hyperthyroidism develop [7, 8]. In the thyroid gland proteolysis of thyroglobulin takes place, with the liberation of thyroxine and triiodothyronine, and the secretion into the blood stream. The concentration of thyroid hormones rises gradually as they are secreted from the gland. Under these conditions the cells of the macrophage system are activated, granulation tissue forms rapidly, and the experimental injuries subsequently undergo epithelization.

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