

# EFFECT OF ADRENOCORTICAL HORMONES ON DEGENERATION AND REGENERATION OF AN INJURED NERVE

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Intramuscular injection of hydrocortisone in a dose of 1.5 mg/kg daily for 10 days after suture of the divided sciatic nerve in rabbits leads to the formation of a less dense scar and to more active growth of young nerve fibers. Administration of hydrocortisone in the same dose for 30 days after nerve suture worsens the general state of the animals during the period of healing of postoperative wounds, intensifies trophic disorders in the operated limb, and retards Wallerian degeneration.

The beneficial effect of hydrocorticoids in inflammatory diseases and traumatic injuries of the nervous system has frequently been described [4-6]. However, relatively few experimental investigations have been made to compare clinical results with morphological data, and such conclusions as have been drawn are contradictory.

There is likewise no general agreement regarding the optimal dose and the best time of administration of the hormones.

Degeneration and regeneration in an injured nerve was studied in rabbits during administration of hydrocortisone.

## EXPERIMENTAL METHOD

The animals (26 rabbits) were divided into 3 groups. In the 10 rabbits of group 1 the sciatic nerve was divided and then sutured, and hydrocortisone was injected intramuscularly for 10 days in a dose of 1.5 mg/kg body weight daily. Because of published data indicating that adrenocortical hormones depress antibody formation and activate bacterial infections [1, 2], in the period of administration of hydrocortisone benzathine penicillin was injected intramuscularly in a dose of 100,000 units once every 5 days. Antibiotics, notably penicillin, given to animals have no direct effect on the growth of young nerve fibers, as investigations have shown [3], but they prevent the development of bacterial infections, including wound infections. The 6 animals of group 2 received hydrocortisone and benzathine penicillin in the doses indicated above for 30 days after division and suture of the nerve. The 10 rabbits of group 3 acted as controls. In the animals of this group the sciatic nerve was divided and sutured only, and neither hydrocortisone nor benzathine penicillin were given. The rabbits were sacrificed after 5, 10, 30, 90, and 180 days.

The whole peripheral segment of the nerve, with the muscles and skin supplied by it, the central segment, and also the corresponding segments of the spinal cord and the adrenals were examined histologically. The material was stained by the methods of Nissl, Van Gieson, Cajal-Favorskii, Marchi, and Weigert.

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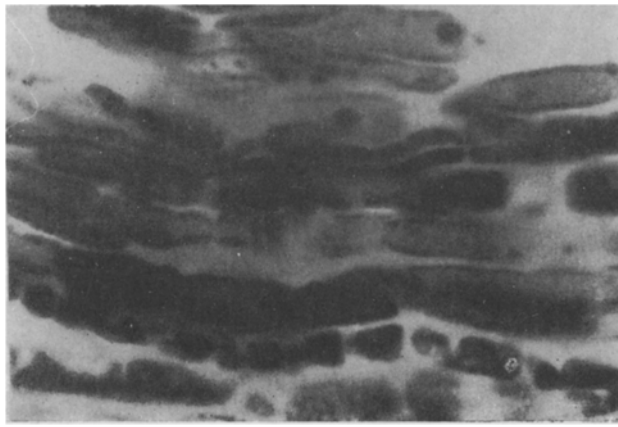


Fig. 1. Sciatic nerve of control rabbit 5 days after operation. Part of nerve distal to point of division. Destruction of medullated fibers clearly visible. Weigert, 280 $\times$ .

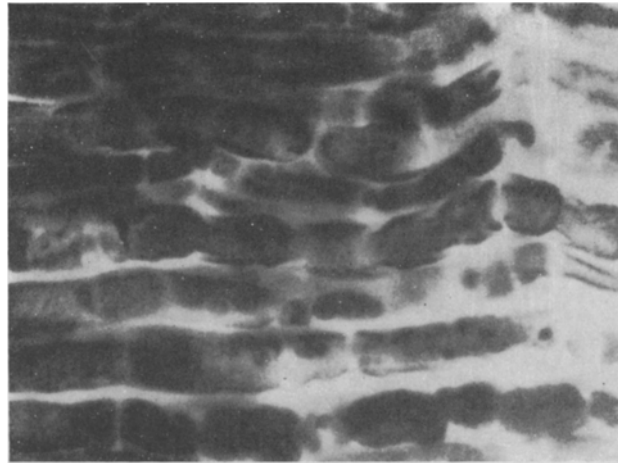


Fig. 2. Sciatic nerve of rabbit treated with hydrocortisone, 5 days after operation. Segment of nerve distal to point of division. Destruction of medullated fibers less marked than in control rabbit, structural elements of myelin sheath better preserved. Weigert, 280 $\times$ .

## EXPERIMENTAL RESULTS

The general condition of the control rabbits and the animals receiving hydrocortisone for 10 days remained perfectly satisfactory at all times of observation. In most of the rabbits receiving the hormone for 30 days, on the other hand, the general condition definitely deteriorated toward the end of its administration. In cases where the sutures separated and the postoperative wounds gaped in animals receiving hydrocortisone, healing did not take place until administration of hormone ceased, although no suppuration was observed; the wound began to epithelize after discontinuation of the hormone and it healed on the 6th-7th day.

The first signs of recovery of muscle tone, movement, and sensation in the denervated limb were observed at approximately the same times in the rabbits of groups 1 and 3, and somewhat later in the animals of group 2 receiving the hormone for 30 days.

Trophic disorders in the denervated limb were slight in degree in the animals living 5 and 10 days after the operation. Of the 6 animals surviving 30 days after the operation, marked trophic changes of the soft tissues, with an ulcer on the dorsum of the foot, were observed in only 1 of the group treated with

hydrocortisone for 30 days. In most rabbits surviving 90 and 180 days after the operation, trophic disorders were observed in the denervated limb, and were expressed by falling out of the hair, edema of the tissues, the development of ulcers on the foot, and changes in the bones of the foot (osteoporosis, fractures, destruction of the joints). The trophic disorders were severe in only 2 of the 4 rabbits of the control group, in 3 of the 4 rabbits receiving hydrocortisone for 10 days, but in all 4 animals receiving the hormone for 30 days. In the rabbits receiving the hormone for 10 days, the trophic disorders had become less severe or had disappeared completely 3-4 months after the operation. In the rabbits receiving hydrocortisone for 30 days, on the other hand, they were more severe and lasting, for a normal state of tissue nutrition was not restored even at the latest times of observation.

From 5 to 10 days after the operation the first signs of formation of a connective-tissue scar and of growth of young nerve fibers into it from the central end of the divided nerve toward the periphery could be seen at the site of nerve suture. In the rabbits receiving hydrocortisone, there were fewer cells between the ends of the divided nerve than in the control animals, the growing young nerve fibers were straighter in their course, and they penetrated further into the scar from the central end.

In the peripheral end of the nerve at this time, Wallerian degeneration had begun and absorption of the breakdown products had started. This integration of axons and myelin sheaths took place more slowly in the rabbits receiving hydrocortisone than in the controls, as was confirmed by the larger size of the fragments of the disintegrating nerve fibers, the better state of preservation of the structures of the myelin sheath (nodes of Ranvier, incisures of Lantermann); the thin nerve fibers remained undestroyed for a longer time (Figs. 1 and 2). Disappearance of the breakdown products also took place more actively in these animals than in the controls.

In the central end of the divided nerve, in the immediate proximity of the point of division slight periaxonal changes were observed. In the sheaths of the central end of the nerve in some rabbits of the control group small foci of infiltration could be seen. Changes in the cells of the spinal ganglia and anterior horns of the gray matter of the spinal cord, with displacement of chromatophilic material toward the center of the cell, swelling of the cell, and displacement of the nucleus to the periphery (signs of primary irritation) were more clearly marked in the control animals. Later after the operation (30, 90, and 180 days), a neuroma formed at the site of suture, the scar between the ends of the nerve became denser, and connective-tissue capsules were formed around the sutures. In animals receiving hydrocortisone, fewer cells were present in the scar between the ends of the divided nerve, and they were mainly fibroblasts, and the young nerve fibers were growing more actively through the scar than in the control animals, they were straighter in their course, more of them reached the peripheral end of the nerve, and their myelin sheath was more mature. These differences were particularly clear in rabbits sacrificed 30 days after nerve suture. Destruction of the nerve fibers and disappearance of the breakdown products in the peripheral end of the divided nerve took place more slowly in the rabbits receiving hydrocortisone for 30 days.

Regression of the manifestations of primary irritation in the cells of the spinal ganglia and gray matter of the anterior horns of the spinal cord in the animals receiving hydrocortisone for 30 days was delayed by comparison with the animals of the other two groups.

Histological examination of the adrenals of the rabbits receiving hydrocortisone showed the changes which have been described many times previously. These consisted of atrophy of the adrenal cortex, especially of the zona fasciculata, and they were most clearly observed in rabbits receiving hydrocortisone for 30 days.

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