

Experimental Exophthalmos in the Guinea Pig.

DONALD L. PAULSON. (Introduced by C. M. Jackson.)

From the Department of Anatomy, University of Minnesota.

Smelser¹ described a stainable infiltrate occurring between the fat cells, muscle fibers, the lobules of the lacrimal gland, and in the connective tissue of the orbit in thyroidectomized guinea pigs injected with thyrotropic hormone. This infiltrate was said to consist of granules and droplets, presumably lipid, as well as many lymphocytes scattered throughout the tissue. He reported that human biopsy specimens of muscles, orbital connective tissue and fat obtained at operation from 2 low B. M. R. exophthalmos cases showed an infiltration indistinguishable from that obtained experimentally.

In the present study 12 immature guinea pigs whose weights ranged between 232 and 320 gm. were used. In 6 animals a thyroidectomy was done. One intact and one thyroidectomized animal were used as controls. Five intact and 5 thyroidectomized animals were given daily intraperitoneal injections of 25 to 40 guinea pig units of Antuitrin "T",* a potent anterior pituitary gland extract containing the thyrotropic factor separated from the other hormones of the hypophysis. Biopsy of the thyroid gland in 2 instances after 5 injections of the extract revealed a marked hyperplasia. The animals were sacrificed at intervals, after from 10 to 55 daily injections of the hormone. The control animals were sacrificed after 55 days, at the end of the experiment. At autopsy, the orbital contents were removed as one piece of tissue and specimens of skeletal muscle from various parts of the body were taken.

Exophthalmos was judged as having developed in 4 of 5 intact and in 4 of 5 thyroidectomized animals from the seventh to the tenth days of injection. The apparent proptosis was more definite early in the experiment and appeared to be of the same degree in both sets of animals.

Histologically, definite changes in the lacrimal gland were found in all animals injected with the thyrotropic hormone. While the lacrimal glands of the control animals occasionally contain isolated areas of excessive vacuolization of the alveolar cells, this is marked in the animals given thyrotropic hormone. The alveoli are abnor-

¹ Smelser, G. K., *PROC. SOC. EXP. BIOL. AND MED.*, 1936, **35**, 128.

* Antuitrin "T" was provided for this experiment by Dr. E. A. Sharp, Director, Department of Experimental Medicine, Parke, Davis and Co. Each cc. contains 50 guinea pig units of the thyrotropic factor.

mally dilated, and there are numerous large areas of apparent degeneration. The glandular cells contain large vacuoles and pyknotic nuclei. In some cells the cytoplasm is entirely gone. The connective tissue stroma is apparently increased and fibroblasts are present. In some areas this connective tissue preserves the outlines of the alveoli; in others the architecture of the gland is completely lacking. Collections of lymphocytes are only occasionally seen. These changes are most marked in the Harderian lacrimal gland (the extensive gland occupying a large part of the orbit in the guinea pig), but are seen also to a lesser degree in the intraorbital lacrimal gland (occupying the posterior angle of the orbit).

These findings are evident in the lacrimal gland of one animal sacrificed after receiving 10 injections of the extract, and are most marked in an intact animal with exophthalmos sacrificed after receiving 18 injections. In all other instances, these changes are present but to less extent, despite the fact that these animals received from 30 to 55 injections of the hormone. This fact appears to be correlated with the observation that the exophthalmos was most marked early in the experiment.

With respect to the extra-ocular muscles, in some instances a definite degeneration and interstitial edema are present. The muscle fibers are broken at intervals, have a granular appearance, and a loss of striations and substance is evident. The fibers are widely separated, and the connective tissue is edematous but not increased in amount. These findings are not consistent in the extra-ocular muscles of all animals, nor are they consistent in those muscles of the same animal. They were observed in 4 animals, 2 of which were thyroidectomized, and were most marked in a thyroidectomized animal sacrificed after 47 injections of the hormone.

No changes were found in the other skeletal muscles except for the *orbicularis oculi*, where in a few instances degeneration of muscle fibers is evident.

Reese² described degeneration, fibrosis and lymphocytic collections in the lacrimal glands of 2 human cases of progressive exophthalmos. It is possible that in man and the guinea pig these changes are the result of hyperfunction of the gland.

The pathology in the extra-ocular muscles appears to be similar to that accompanying progressive exophthalmos in man described by Burch³ and Naffziger.⁴

² Reese, A., *Arch. Ophthalm.*, 1935, **13**, 855.

³ Burch, F. E., *Minn. Med.*, 1929, **12**, 668.

⁴ Naffziger, H. C., *Ann. Surg.*, 1931, **94**, 582.