ministration of estrogen. Injections of estrogen extending over long periods increases the amount of fibrous-hyaline material which is deposited in the stroma; this increase is the greater, the larger the amounts of estrogen injected at each period and the longer it is continued. If very large doses of estrogen (100 or more rat units in oil) are injected weekly, large amounts of a hyaline substance are deposited, which act as foreign bodies and cause the formation of epithelioid and giant cells and an ingrowth of connective tissue. Thus an organization of this substance is attempted, which is interrupted, however, by renewed deposition of this hyaline material. In certain places solution processes seem to be associated with the hyalinization of the connective tissue and non-striated muscle layers. No definite statement can be made at present as to the chemical nature of this substance and its possible relation to a plasma constituent, except that it is not amyloid.

A hormone, estrogen, may affect therefore the stroma of various organs in two opposite directions: By inducing growth processes in the epithelial structures and perhaps also by definite changes in the circulation it may cause an activation of the stroma and a diminution in the amount of fibrous-hyaline material in various tissues; this seems to occur also in uterus and vagina under certain conditions. But if very large doses of this hormone are administered over long periods of time, the opposite effect may be obtained, namely, a very intense fibrosis and hyalinization of the stroma which may induce abnormal reactions in the surrounding tissue. In this way it seems to be possible to accelerate and intensify very much some of the old age changes in certain organs.

LEO LOEB
V. SUNTZEFF
E. L. BURNS

LABORATORY OF RESEARCH PATHOLOGY,
OSCAR JOHNSON INSTITUTE,
WASHINGTON UNIVERSITY
SCHOOL OF MEDICINE,
ST. LOUIS

THE EFFECTS OF AGE AND HORMONES ON THE STROMA OF THYROID AND MAMMARY GLAND IN THE GUINEA PIG[1]

IT is assumed that one of the changes characteristic of old age in higher organisms consists in an increase and condensation of the collagen in the stroma of various organs and that such changes may reduce the metabolic activities of sensitive tissues. We have begun, therefore, a study of the changes which take place in the stroma at different age periods, as well as of the effect of various hormones on this tissue.

(1) In the thyroid gland of guinea pigs at about the time of birth the amount and density of the stroma are relatively slight. From then on a constant increase in the amount of fibrous tissue takes place, especially around the arteries, but less about the veins and least around the lymph vessels. This increase is already considerable in young, sexually immature female guinea pigs weighing about 180 grams; it increases still more in older guinea pigs, although in individual cases certain variations occur in this respect. Growth and functional stimulation of the thyroid gland by the stimulating hormone of the anterior pituitary gland causes a partial loosening of the stroma, owing to increased transudation from the blood vessels. However this does not, as a rule, cause a noticeable loosening of the dense fibrous tissue directly surrounding the arteries.

(2) In the mammary gland and in the surrounding fat tissue changes occur similar to those observed in the thyroid gland of young and adult guinea pigs; but here much dense fibrous tissue develops, not only around the blood vessels, but also around the larger ducts. There is less fibrous tissue around the end ducts and acini, which function and grow actively; however, a complete parallelism between the amount and density of the stroma in thyroid and mammary gland does not exist because of the differences in functional and growth changes and other more accidental factors in these organs.

In the mammary gland a transformation of the dense fibrous-hyaline into loose fibroblastic, fibrillar stroma can be readily accomplished under the influence of hormones which stimulate the growth of the mammary gland tissue. Implantations of pieces of cattle anterior pituitary gland previously treated with formalin or with urea and glycerin are very efficient for this purpose; they cause maturation of ovarian follicles and the discharge of oestrogen into the circulation. Accompanying the growth processes in the epithelium of the mammary gland a marked stimulation of the surrounding stroma occurs, leading to mitotic proliferation and amoeboid movement of fibroblasts. They readily change the dense fibrous tissue around the ducts into a loose and much more permeable fibrillar, cellular stroma. These effects begin around the glandular structures, but they may extend from there with gradually diminishing intensity also to the adjoining fibrous-hyaline material around arteries and to the fibrous-hyaline bands in the fat tissue. This condition suggests the action of hormone-like contact substances which are given off by the active gland structures and which then diffuse for a certain distance into the neighboring stroma. Such a conception would agree with our earlier conclusion that contact substances might be responsible for growth and move-

[1] These investigations were carried out with the aid of grants from the International Cancer Research Foundation and from the Committee on Research in Endocrinology of the National Research Council.

ments of previously resting cells surrounding active cells or tissues. While in the mammary gland hormones in all probability affect the stroma only indirectly by way of the glandular structures, a hormone given off by the corpus luteum is able to exert a direct growth-stimulating effect on the uterine stroma.

We may then conclude that an increase in amount and density of stroma elements in certain organs begins very early in life and progresses steadily from then on, and that hormones may counteract this effect by loosening the stroma in three different ways, namely: (1) by their effect on the circulation; (2) by their stimulating action on epithelial parenchyma and (3) by a direct effect on the stroma. These observations suggest that the fibrosis and hyalinization of the stroma which occurs with advancing age may perhaps be reversible under the influence of hormones, at least in certain instances.

LEO LOEB
R. M. SIMPSON
LABORATORY OF RESEARCH PATHOLOGY,
OSCAR JOHNSON INSTITUTE,
WASHINGTON UNIVERSITY
SCHOOL OF MEDICINE,
ST. LOUIS

AN ADRENALINE-LIKE SUBSTANCE IN POSTGANGLIONIC SYMPATHETIC FIBERS

BY using bicarbonate-free Ringer's solution containing physostigmine (1: 50,000) extracts were made from different nerves of the cat, dog, rabbit and frog. The extracts were dialyzed against physostigmine-Ringer's solution by the method of Loewi.[1] After four hours the dialysate was tested on isolated hearts of frogs, according to the method of Straub. Control experiments were made with the other acetylcholine extraction methods (acid alcohol, trichloracetic acid and heating) and were tested on the frog heart, rectus abdominis of the frog and the back muscle of the leech.

Extracts of various nerves (vagus and sympathetic of the neck, sciatic, phrenic, optic, thoracic sympathetic chain and superior cervical ganglion) contain different amounts of acetylcholine.

Preganglionically denervated superior cervical ganglia (with the postganglionic fibers) of the cat and rabbit, one to two weeks after operation, no longer contain acetylcholine, but an adrenaline-like substance having positive inotropic and chronotropic effects on the frog heart. In cats and dogs the ventral esophageal branches of the vagi were cut below the diaphragm. After two weeks the postganglionic sympathetic fibers along the superior mesenteric artery were extracted and were found to contain no acetylcholine but an adrenaline-like substance.

[1] O. Loewi, *Pflüger's Arch.*, 227: 504, 1936.

If extracts of mixed nerves were made with bicarbonate-free Ringer's solution without physostigmine, acetylcholine was totally eliminated and only the adrenaline-like substance was present.

These experiments showed that from all the nerves examined which contain postganglionic sympathetic fibers an adrenaline-like substance can be extracted. The vagus fibers of the dog, but not of the cat, contain this substance. Evidence of its presence was found in extracts from the cervical sympathetic ganglia and their fibers, from the sciatic, from the superior mesenteric plexus and ganglion, but not from the phrenic nerve.

This adrenaline-like substance passes easily through a dialysis membrane (Cellophane), is oxidizable and is destroyed by ashing or simple heating to near the boiling point for a few minutes. It has positive inotropic and chronotropic effects on a hypodynamic frog heart, which are abolished by ergotoxine. The substance has a positive action on the blood pressure of the cat (adrenals ligated). The substance has properties similar to sympathin and adrenaline. On the assumption that it is sympathin the highest content was found in the superior mesenteric plexus of the cat (about 4 to 6 γ per gram of nerve). The amount from the superior mesenteric plexus of one cat is enough to cause, when intravenously injected, a rise of 20 mm Hg. in the blood pressure of another cat. This action on the cat's blood pressure provides the possibility of studying the properties of sympathin more completely in further experiments.

K. LISSÁK,
Fellow of the Rockefeller Foundation
DEPARTMENT OF PHYSIOLOGY,
HARVARD MEDICAL SCHOOL

BOOKS RECEIVED

Catalogue des Manuscrits Éthiopiens de la Collection Griaule, Première Partie, Sections I–VI; Travaus et Memoires de L'Institut D'Ethnologie, XXIX. Pp. ix + 320. 8 plates. Institut D'Ethnologie, University of Paris. 125 fr.

The Collected Works of George Abram Miller; Vol. II. Pp. xi + 537. University of Illinois. $7.50.

HOFFMANN, RALPH. *Birds of the Pacific States.* Pp. xix + 353. Illustrated. Houghton Mifflin. $3.50.

ROBERTS, W. R. WESTROPP. *Elliptic and Hyperelliptic Integrals and Allied Theory.* Pp. viii + 311. Cambridge University Press, Macmillan. $3.75.

ROJANSKY, VLADIMIR. *Introductory Quantum Mechanics.* Pp. x + 544. Prentice-Hall. $5.50.

The Snellius-Expedition in the Eastern Part of the Netherlands East-Indies, 1929–1930, under the Leadership of P. M. Van Riel; Vol. I, Voyage. Pp. viii + 177. Illustrated. 20 guilders. *Vol. II, Part 4, Oceanographic Results; Surface-Observations, Temperature, Salinity, Density; by Dr. S. W. Visser.* Pp. 62. 5 guilders. E. J. Brill, Leiden, Holland.

STRONG, JOHN and others. *Procedures in Experimental Physics.* Pp. x + 642. Illustrated. Prentice-Hall. $5.00.