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CLINICAL INVESTIGATION¹

By Dr. GEORGE R. MINOT

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VISITING PHYSICIAN, BOSTON CITY HOSPITAL

WE are here to-day to celebrate the opening of the Squibb Institute for Medical Research, which stands as a fitting tribute to Edward Robinson Squibb, the founder of this distinguished pharmaceutical organization. Dr. Squibb was an eminent physician and chemist and his name has become synonymous with certain ideals in medicine and pharmacy. The scientist's love for truth, so marked in him, and the painstaking and conscientious care of every detail of his activities led him to never neglect research and general scientific work, which he recognized as essential. Dr. Squibb's services to the army and navy, especially during the Civil War, were most significant, for he supplied them with highly dependable medical supplies and particularly anesthetics. His master formula was honor. in-

tegrity and trustworthiness. His work was such that no contemporary had to consider writing such a book as Christopher Merrett wrote in 1669 with the title, "A Short View of the Frauds and Abuses committed by Apothecaries; as well in Relation to Patients, as Physicians: and the only Remedy thereof by Physicians making their own Medicines." Dr. Squibb's published investigative studies extended from 1855 to 1900, in which year he died at the age of eighty-one. The studies concern especially the production and preparation of therapeutic substances which the physician prescribes and which must in final analysis be tested on human beings for their exact action and value—a form of clinical investigation.

It is a physician who undertakes clinical investigation, and I plan to consider a few general aspects concerning this subject especially as referable to the physician and patient.

¹ Presented at the dedication exercises of the Squibb Institute for Medical Research, New Brunswick, N. J., on October 11, 1938.

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

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WASHINGTON UNIVERSITY
SCHOOL OF MEDICINE,
ST. LOUIS

AN ADRENALINE-LIKE SUBSTANCE IN POSTGANGLIONIC SYMPA- THETIC 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, trichloroacetic 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*; Travaux et Mémoires 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.

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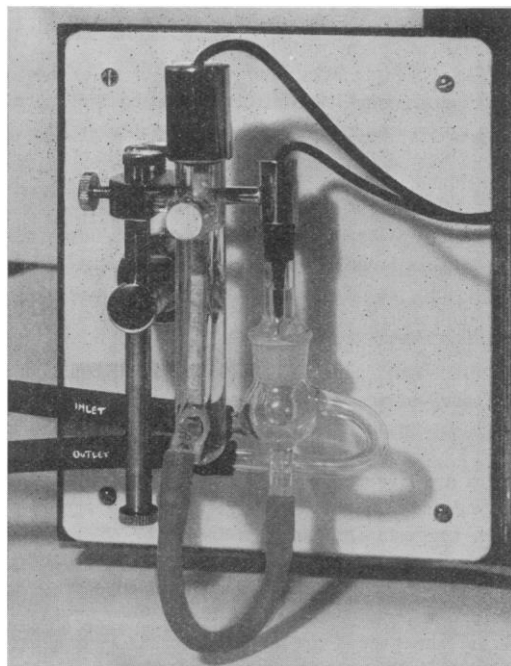
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