acetylcholine liberated at the preganglionic endings. In support of that hypothesis they find that perfusion of the superior cervical ganglion with Locke's fluid containing eserine, which protects acetylcholine against cholinesterase, increases the contraction of the nictitating membrane elicited by a submaximal preganglionic stimulus. In order to test this theory of synaptic transmission by a different method we have injected eserine intravenously in amounts such that the concentration in the blood circulating through the ganglion was from 1:1,000,000 to 1:10,000. Throughout the experiments the preganglionic nerves were stimulated at a low frequency and the action potentials in the postganglionic fibers were recorded. We never observed any effect with the low concentrations of eserine and only a block of synaptic transmission with high concentrations.

It is to be emphasized, however, that our experiments need not be considered as opposed to those of Feldberg and Vartianen. They perfused the ganglion with Locke's fluid containing eserine while in our work the ganglion was circulated with blood. Our negative results may be due to the fact that with blood circulating through the ganglion so much eserine is needed that the ganglion is inactivated before the concentration of eserine is sufficient to protect the acetylcholine.

Bathing the ganglion with acetylcholine causes a marked discharge of postganglionic impulses.

8219 P

Response of a Sympathetic Ganglion to High Frequency Stimulation.*

D. W. BRONK AND R. J. PUMPHREY.

From the Eldridge Reeves Johnson Foundation for Medical Physics, University of Pennsylvania.

If a preganglionic mammalian nerve is stimulated at a low frequency, each volley of impulses initiates a fairly well synchronized discharge in the postganglionic nerve.[1] When the rate of stimulation is increased to 30 or 40 per second there is a progressive de-

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1 Bronk, D. W., Tower, S. S., and Solandt, D. Y., PROC. SOC. EXP. BIOL. AND MED., 1935, **32**, 1659.

crease in the height of the postganglionic spike potential. This apparent failure in the capacity of the ganglion to transmit impulses at a high frequency is a property of the synapse which must be taken into consideration in the formulation of any theory which attempts to explain the mechanism of synaptic transmission.

All of our experiments were performed on cats in a room maintained at close to body temperature. The pregaglionic fibers in the third or fourth thoracic root were stimulated by means of a thyratron stimulator and the impulse discharge from the stellate ganglion was recorded in the inferior cardiac nerve.

The effect which we are considering can be demonstrated by stimulating the preganglionic nerve at a frequency of about 60 per second. The successive postganglionic spike potentials rapidly decrease in height and after a variable number of stimuli they can no longer be detected at ordinary amplifications. There is no such rapid failure at these frequencies of the spike potential in either the pre- or postganglionic nerves when they are stimulated directly. This suggests that the ganglion blocks the transmission of impulses at high frequencies.

Two observations argue against such a conclusion. In the first place we have found that stimulation of the preganglionic fibers at frequencies as high as 120 per second produces cardiac acceleration throughout long periods of stimulation. In the second place, the electrical record of postganglionic activity during such stimulation frequently shows a negative displacement of the base line which continues until the end of the stimulus. It would appear therefore that there is continued activity in the postganglionic fibers despite the absence of the usual spike potential.

These several observations can be explained by assuming that the impulses become so scattered or temporally dispersed in the many postganglionic fibers that they no longer reveal themselves as synchronized spike potentials. We have shown that this is indeed the case by cutting down the postganglionic trunk to a few fibers and recording the activity in those fibres during high frequency preganglionic stimulation. We thus found that the initial preganglionic volleys set up well synchronized volleys of postganglionic impulses but that the synchronization becomes rapidly less until there is a completely random discharge in the various fibers. At certain frequencies of stimulation there is at first a synchronized response of the postganglionic fibers to every second or third or fourth preganglionic volley following which the discharge becomes more and more asynchronous.

This altered property of the ganglion develops more rapidly at high frequencies of stimulation than at low and persists for many seconds following the end of the stimulus. After various intervals of rest following a period of high frequency stimulation we have tested the transmission through the ganglion by repeating the high frequency stimulation. The initial postganglionic spike is again maximal after a recovery period of less than a second but a minute or more may be required before the tenth or twentieth impulse is again as large as it was in the initial series. At low temperatures the progressive decrease in height of the synchronized spike potential is more rapid and the recovery of the capacity for synchronized activity is much delayed.

We suggest that these results may be due to an increase in the refractory period of the ganglion cells which is different for the various cells. Or one may assume 2 types of synaptic transmission, the one which is responsible for the grouped discharge failing more rapidly than that which produces the asynchronous firing. But these are speculations which must be tested by additional experiments.

8220 P

Improvement in Female Sex Hormone Blood Test in Cyclical Menstruating Women and in Pregnancy Blood.

ROBERT T. FRANK AND MORRIS A. GOLDBERGER.

From the Gynecological Service and the Laboratories, Mount Sinai Hospital, New York City.

Advance in the chemistry of the female sex hormone or estrogenic factor—theelin, oestrin, etc.—has shown that some of the estrogenic compounds are ether insoluble. In consequence, we have returned to a modification of our earliest technic in which alcohol extraction was used.[1] By desiccating the venous blood specimen as heretofore with anhydrous sodium sulphate and then extracting with 95% alcohol, instead of ether, a great increase in estrogenic activity of the extract was noted.

The technic permits the accurate assay of a single specimen, the amount of extract employed in each animal depending upon the time of the cycle. By the old method[2] 40 cc. of blood give a negative

1 Frank. R. T., and Goldberger, M. A., *J. A. M. A.*, 1926, **87**, 1719.

2 Frank, R. T., and Goldberger, M. A., *J. A. M. A.*, 1928, **90**, 376.