

# ON THE MECHANISM OF ACTION OF GANGLIOPLEGICS ON PERIPHERAL VISCERO-VISCERAL REFLEXES

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Our previous investigations [1] have shown that ganglionic blocking substances — tetraethylammonium (TEA), Pentamine (pentamethyldiethylenetriamine dibromide), and hexamethonium — are able following total destruction of the central nervous system, to depress viscerovisceral reflexes, in particular those from the distal portion of the ileum to the proximal ileum and the jejunum, and from the urinary bladder to the colon, ileum, and jejunum. On the basis of these facts, and also in view of the fact that after the corresponding sympathetic ganglia are removed these reflexes are not observed, we advanced the interpretation that in this case ganglioplegic substances suppress local viscerovisceral reflexes. But the design of our experiments did not completely exclude the possibility that the observed phenomena develop on the basis of axon reflexes with preganglionic fibers participating.

To define this question more precisely we undertook new investigations in which the effect of ganglionic blocking agents on reflexes from the urinary bladder to the colon, ileum, and jejunum was studied following preliminary section of all preganglionic fibers of the inferior mesenteric ganglia. By this means degeneration of these fibers was produced, and consequently, the possibility of bringing about axon reflexes with the participation of preganglionic axons was eliminated.

## METHODS AND EXPERIMENTAL RESULTS

The experiments were carried out on cats in which all the nerve fibers going to the inferior mesenteric ganglia from the sympathetic chain and the solar plexus were first (3-30 days previously) sectioned. This operation was carried out under ether anesthesia and aseptic conditions. Before the experiment the animals were anesthetized with ether, and the entire central nervous system was then destroyed. The animals' breathing was maintained artificially. The urinary bladder was stimulated by distending a rubber balloon which was inflated with air, usually under a pressure of 80 mm Hg. The pressure in the balloon was measured with a mercury manometer. The response of the colon, ileum, or jeju-

num was recorded with a water-air system which consisted of a rubber balloon, inserted into the lumen of the given segment of intestine, filled with water, and connected with a Marie capsule which recorded the contractions of the intestine on a kymograph. When the urinary bladder was distended, inhibition of the contractions of the colon, ileum, or jejunum occurred.

After degeneration of the preganglionic fibers of the inferior mesenteric ganglia, ganglionic blocking agents — TEA (1 mg/kg), Pentamine (2 mg/kg), and hexamethonium (1 mg/kg) — injected intravenously suppress reflexes from the urinary bladder to the colon, ileum, and jejunum (Fig. 1). These ganglioplegics produce this effect in doses at which they suppress the same reflexes without section of the preganglionic fibers, and also with the central nervous system intact. Thus the question of the possibility that the ganglioplegics suppress the indicated viscerovisceral reflexes with the participation of preganglionic fibers was settled by us in the negative.

In view of the fact that ganglionic blocking agents interfere with impulse transmission in ganglionic synapses, we could not assume that the excitation is transmitted from the urinary bladder to the colon, ileum, and jejunum in the manner of a postganglionic axon reflex. This would require that ganglionic blocking agents be able to exert an effect on the conduction of impulses along axons, for which there is no foundation.

To clarify the question of the effect of ganglioplegic substances on the peripheral component of local reflexes, we made a separate check of the transmission of excitation from postganglionic fibers to effector organs. In several experiments, we tested the state of impulse transmission from postganglionic fibers of the inferior mesenteric ganglion to the colon under the influence of ganglionic blocking agents. The postganglionic fibers of the inferior mesenteric ganglion were sectioned at the time of experiment, and were subjected to repetitive electrical stimulation (at a frequency of 30 cps) from an electronic generator. These experiments showed that TEA, Pentamine, and

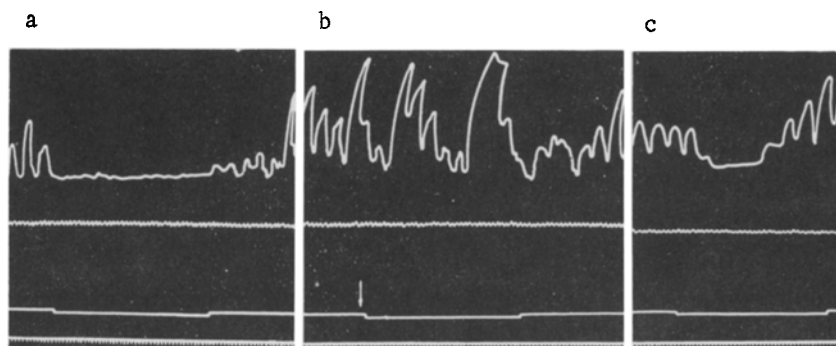


Fig. 1. Experiment 19 days after section of preganglionic fibers of the inferior mesenteric ganglion. Effect of Pentamine on reflex inhibition of contractions of small intestine following distention of urinary bladder. Interpretation of curves (top to bottom): contractions of intestine, cardiac contractions, stimulus marker, time marker (1 sec); a) before administration of Pentamine; b) 10 minutes after intravenous injection of 2 mg/kg Pentamine ( $\downarrow$ ); c) the same, after 1 hour and 45 minutes.

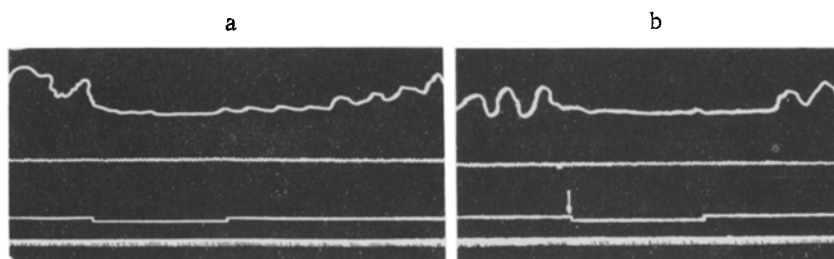


Fig. 2. Effect of hexamethonium on impulse transmission from postganglionic fibers of the inferior mesenteric ganglion to colon. Curves (top to bottom): contractions of intestine, cardiac contractions, stimulus marker, time marker (1 sec); a) before administration of hexamethonium b) 15 minutes after intravenous injection of 2 mg/kg of hexamethonium ( $\downarrow$ ).

hexamethonium injected intravenously in doses at which local viscerovisceral reflexes are suppressed have no effect on the transmission of excitation from postganglionic fibers of the inferior mesenteric ganglion to the colon (Fig. 2). Consequently, the suppression of viscerovisceral reflexes by ganglionic blocking agents, observed by us, does not depend on any changes in impulse transmission in the peripheral component of these reflexes.

Thus ganglioplegic substances suppress the transmission of excitation from the urinary bladder to the intestine by interfering with synaptic transmission of impulses from afferent pathways to efferent ones — in the inferior mesenteric ganglia. In this case, "afferent pathways" must be understood to mean Dogiel's cells of the second type.

By way of developing this concept we carried out investigations of still another type. The effect of ganglioplegic substances on local reflexes was studied in experiments according to the classical scheme of N. M. Sokovnin [3] as modified by I. P. Razenkov [2], i.e., the effect of these substances on reflex contractions of the urinary bladder in response to stimulation of the central end of a sectioned hypogastric nerve was studied after preliminary section of

all preganglionic fibers of the inferior mesenteric ganglia.

The experiments of this series, like the previous ones, were carried out on cats. From 1 to 30 days before the experiment, all fibers going to the inferior mesenteric ganglia from the sympathetic chain and the solar plexus were sectioned under aseptic conditions with the animals under nembutal anesthesia. By this means, degeneration of the preganglionic fibers of the inferior mesenteric ganglia was brought about.

Before the experiment, the animals were anesthetized with urethane or ether. After the vagus nerves were sectioned in the neck, the entire central nervous system was destroyed. The animal's breathing was maintained artificially. The abdominal cavity was then opened, and one of the hypogastric nerves was sectioned.

The central end of this nerve was repetitively stimulated with sinusoidal stimuli (frequency 20 cps, amplitude 0.5–2 V) from an electronic generator.

The response to stimulation of the central end of the hypogastric nerve appeared as a contraction of the urinary bladder. These contractions were recorded on a kymograph by a mechanographic air–water system consisting of a rubber balloon filled with water

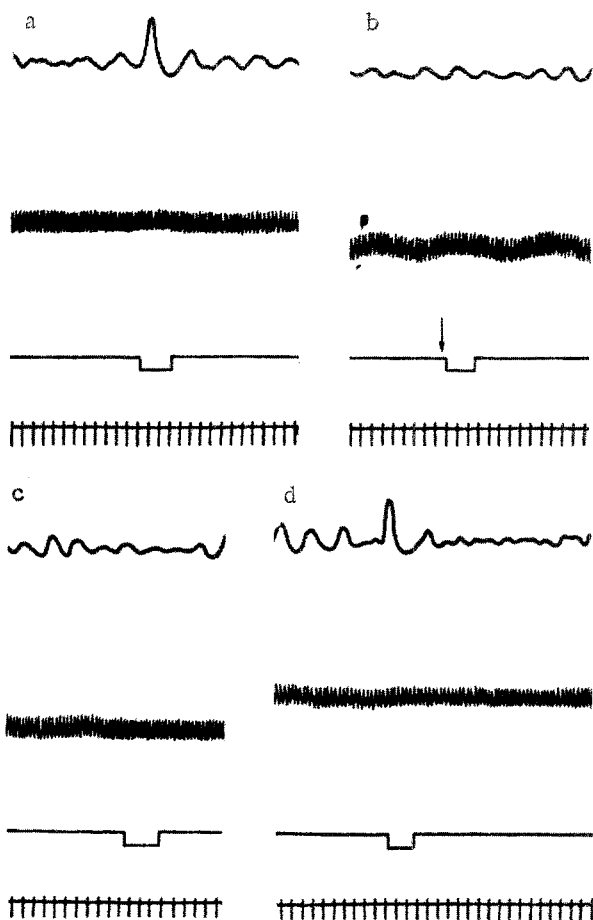


Fig. 3. Experiment 12 days after section of preganglionic fibers of the inferior mesenteric ganglion. Effect of hexamethonium on reflex contraction of urinary bladder upon stimulation of central end of sectioned hypogastric nerve. Interpretation of curves (top to bottom): contractions of urinary bladder, cardiac contractions, stimulus marker, time marker (1 sec); a) before administration of hexamethonium; b) 5 minutes after intravenous injection of 2 mg/kg hexamethonium ( $\downarrow$ ); c) the same, after 20 minutes; d) the same, after 2 hours.

and inserted into the urinary bladder through an incision in the apex, or a catheter inserted through the urethra,

It was found that even after degeneration of the preganglionic fibers of the inferior mesenteric ganglia, TEA (1–2 mg/kg), Pentamine (2–3 mg/kg), and hexamethonium (1.5–2 mg/kg) injected intravenously suppress contractions of the urinary bladder in response to stimulation of the central end of the sectioned hypogastric nerve (Fig. 3). Thus ganglioplegic substances suppress many peripheral viscerovisceral reflexes after degeneration of preganglionic fibers. When we consider that these substances have no effect on the transmission of excitation from postganglionic fibers to effector organs, we can only conclude that ganglionic blocking agents suppress the transmission of excitation from afferent to efferent pathways in the autonomic ganglia.

#### SUMMARY

The authors investigated the effect of tetraethylammonium, Pentamine, and hexamethonium on reflexes from the urinary bladder to the colon, ileum, and jejunum, and on the reflex contractions of the urinary bladder following stimulation of the central end of the sectioned hypogastric nerve, after preliminary section (3–30 days previously) of all the preganglionic fibers of the inferior mesenteric ganglion. This was done to ascertain the mechanism of action of the ganglioplegics on peripheral viscerovisceral reflexes. It was found that these substances continued to depress the reflexes mentioned after degeneration of the preganglionic axons of the inferior mesenteric ganglia.

Thus the data obtained demonstrate that the ganglionic blocking agents depress local reflexes, thus inhibiting the transmission of excitation in autonomic ganglia from afferent to efferent neurons.

#### LITERATURE CITED

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