

ACTION OF ATROPINE AND ATROPINE-LIKE SUBSTANCES
BEFORE AND AFTER ANAPHYLACTIC CONTRACTION
OF SMOOTH-MUSCLE ORGANS

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Acetylcholine and choline-like substances have been found to play an important role in the mechanism of the anaphylactic reaction of the smooth-muscle organs, with their rich cholinergic innervation [1, 3, 4, 5]. The further study of this problem must provide a better idea of the role of these substances in the development of anaphylaxis, and of their interaction with cholinesterase and atropine. In its pharmacological properties atropine is classed as a cholinergic drug [2]. There is reason to suppose that acetylcholine and atropine, by their pharmacological action on the tissues, compete for attachment to the same cholinergic receptor groups [8]. In previous studies we confirmed Undritsov's opinion [5] that atropine does not depress, but increases the tone of the loop of guinea pig's intestine after an anaphylactic contraction. We have also observed this inverted reaction to atropine in the uterus of guinea pigs and rats [4].

In the present research we continued the study of the mechanism of this phenomenon. Our object was to reproduce this inverted reaction to atropine in the smooth muscles of the bronchi of guinea pigs, and also to test the action of atropine-like substances (scopolamine, platyphyllin) before and after the anaphylactic reaction of smooth-muscle organs.

Reproduction of the Phenomenon in the Smooth Muscles of the Bronchi of the Isolated Lungs of Sensitized Guinea Pigs

Experiments were carried out on 30 female guinea pigs weighing 300-400 g, of which 8 were normal and 22 sensitized. The animals were sensitized by triple subcutaneous injections of 0.5 ml horse serum on alternate days. The animals took part in the experiments 18-30 days after the first sensitizing injection.



Fig. 1. A) Anaphylactic bronchospasm of the isolated lung of a guinea pig sensitized with horse serum on November 28, 29, and 30, 1962. Arrow of injection of antigen in a dilution of 1 : 100; time 20 sec. B) Action of atropine on the bronchi of the same guinea pig after anaphylactic bronchospasm. The arrow points to the time of injection of atropine in a dilution of 10^{-4} .

TABLE 1. Anaphylactic Bronchospasm of Isolated Lungs of Guinea Pigs and Inverted Reactions of Lungs to Subsequent Injection of Atropine

Date of experiment	Reaction to injection of antigen 1 : 100-1 : 500	Inverted reaction of smooth muscles of lungs to injection of atropine 10^{-4}
26/X 1962	Complete spasm	Complete spasm
27/X	" "	" "
28/X	" "	" "
28/X	" "	" "
29/X	" "	Incomplete spasm
5/II 1963	" "	" "
6/II	" "	Complete spasm
7/II	No spasm	No spasm
8/II	Complete spasm	Complete spasm
10/II	" "	" "
13/II	" "	" "
16/II	" "	Incomplete spasm
18/II	Incomplete spasm	" "
23/II	Complete spasm	Complete spasm
22/XI 1962	" "	" "

The technique of perfusion of the isolated lungs was that described by Alberty and Bhattacharya [6, 7]. The preparation of the isolated lungs was placed in a hermetically closed chamber. The viability of the lung tissues was maintained by perfusion with nutrient fluid consisting of Tyrode solution (2/3) and polyglucin solution (1/3) through the pulmonary artery. Movements of the lungs were produced by alternately creating a positive and negative atmospheric pressure in the chamber. The oscillation of air in the lungs was recorded on the drum of a rotating electrokymograph by means of a Marey's capsule connected to the trachea. The kymograph rotated at the rate of 0.5 mm/sec.

In the first series of experiments, conducted on 8 normal guinea pigs, the injection of horse serum in dilutions of 1 : 10 and 1 : 500 into the perfusion fluid did not cause bronchospasm. Administration of atropine in a concentration of 10^{-4} and 10^{-5} before and after the antigen also produced hardly any change in the lung movements. At the end of each experiment, to test the sensitivity of the muscles of the bronchi, histamine was injected in concentrations of 10^{-4} and 10^{-5} , as a result of which bronchospasm developed and continued for 5-8 min; the lung movements were gradually restored after 7-9 min.

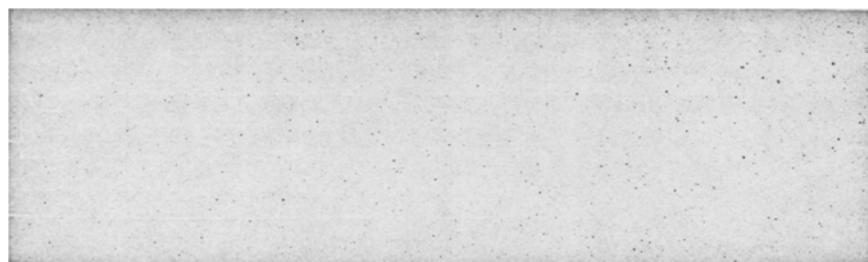


Fig. 2. Uterine cornu of a guinea pig sensitized with horse serum on November 15, 17, and 19, 1962. 1st arrow (on the left) injection of histamine (10^{-5}); 2nd and 6th arrows) injection of platyphylline (10^{-5}); 3rd and 7th arrows) injection of atropine (10^{-5}); 4th and 8th arrows) injection of scopolamine (10^{-5}); 5th arrow) injection of antigen (1 : 100). Time 30 sec.

The second series of experiments was carried out on 22 sensitized guinea pigs. At first the normal movement of the lungs was recorded. Next, the sensitivity of the isolated lungs to atropine in concentrations of 10^{-4} and 10^{-5} was tested, and in these concentrations the drug caused no changes. Injection of 3-4 ml of antigen (horse serum) in dilutions of 1 : 100 and 1 : 500 led to complete and prolonged (up to 12-18 min) spasm of the bronchi. In some experiments antigen in this dilution caused such severe bronchospasm that the lung movements could not be restored or had very low amplitude later in the experiments. In most experiments, therefore, antigen was used in a dilution of 1 : 500, which was sufficient to cause bronchospasm to develop 30-60 sec after injection of the reacting dose, and to last for 10-16 min on the average. The lung movements were fully restored after 15-30 min. In some experiments bronchospasm of a considerable duration was observed (22-35 min).

The subsequent injection of atropine in a dilution of 10^{-6} rapidly (on the average after 5-10 sec) caused spasm of the bronchi: in 12 experiments the spasm of the bronchi disappeared after 1-2 min, in 4 experiments after 6-8 min, and in 4 experiments after 16-25 min (Fig. 1). The results of this series of experiments are shown in Table 1.

Action of Atropine-like Substances before and after Anaphylactic Contraction of Smooth Muscles

The question arises whether atropine-like substances, like atropine, may cause an inverted reaction of the smooth-muscle organs after an anaphylactic contraction. Two atropine-like substances were investigated - scopolamine and platyphylline. Experiments were conducted on the uterine cornua of 16 sensitized guinea pigs (Fig. 2). The animals took part in the experiment 20-30 days after the first sensitizing injection.

The uterine contractions were recorded by the method of Schultz and Dale [9, 10]. The experimental conditions were described in a previous paper [4]. In all the experiments a uterine cornu measuring 1.0-1.5 cm in length was used. The experiment began with testing the sensitivity of the uterus to histamine in dilutions of 10^{-6} and 10^{-7} , atropine 10^{-5} and 10^{-6} , scopolamine 10^{-5} and 10^{-6} , and platyphylline in dilutions of 10^{-5} and 10^{-6} .

To produce an anaphylactic reaction, antigen was added to the bath in a concentration of 1 : 100. At the end of the reaction atropine or atropine-like substances (scopolamine, platyphylline) were again injected, after which a uterine contraction was observed (inverted reaction). The sensitivity of the uterus to histamine was then tested again to verify its viability.

Histamine in a concentration of 10^{-6} and 10^{-7} caused a uterine contraction the mean amplitude of which was 3-5 cm. After injection of atropine and atropine-like substances (10^{-5} , 10^{-6}) before the anaphylactic contracture a slight decrease in the tone of the organ or complete absence of changes was observed. On the addition of antigen (1 : 100) the uterus reacted with a strong contraction, its mean amplitude being 4-6 cm. The subsequent injection of atropine and atropine-like substances caused a marked contracture in 14 of the 16 experiments, appearing after 50-70 sec and reaching a maximum between the 2nd and 3rd minute; subsequent relaxation took place after 3-5 min. The results of this series of experiments are shown in Table 2.

Hence, the smooth-muscle organs of sensitized guinea pigs gave an inverted reaction to atropine and atropine-like substances after an anaphylactic contraction. The problem of the mechanism of this reaction during anaphylaxis requires further investigation.

TABLE 2. Anaphylactic Reaction of the Uterus of Guinea Pigs and Its Inverted Reaction to Subsequent Injection of Atropine and Atropine-Like Substances

Date of experiment (1962)	Anaphylactic reaction of uterus to antigen 1:100	Reaction of uterus to injection of		
		atropine	platyphylline	scopolamine
6/XI	+	—	±	±
7/XI	++			++
8/XI	+++			+++
9/XI	+++			+++
10/XI	+++			+++
11/XI	+++			+++
12/XI	+++		+++	
12/XI	++		++	
13/XI	++		++	
14/XI	+++		++	
16/XI	+++	++	++	+
18/XI	++	+	++	++
19/XI	+++	+++	++	+++
20/XI	+++	+++	++	+++
23/XI	+	+	±	±

Note. + Positive reaction; ++ marked reaction; +++ strong reaction; ± doubtful reaction.

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All abbreviations of periodicals in the above bibliography are letter-by-letter transliterations of the abbreviations as given in the original Russian journal. *Some or all of this periodical literature may well be available in English translation.* A complete list of the cover-to-cover English translations appears at the back of this issue.
