

LITERATURE CITED

- [1] V. M. Afanas'eva, Arkh. Patol. No. 4, 52-61 (1949).
- [2] A. D. Braun and M. F. Ivanov, Arkh. Anat., Gistol. i Embriol. 12, 1, 3 (1933).
- [3] V. K. Butkevich, Vestnik Leningrad. Gos. Univ. No. 1, 124 (1948).
- [4] S. M. Vereshchagin, Biull. Eksptl. Biol. i Med. 27, 291-294 (1949).
- [5] N. N. Gritsman, Arkh. Patol. 14, 4, 70-79 (1952).
- [6] V. S. Dmitrieva, Arkh. Patol. 10, 4, 69-77 (1948).
- [7] I. E. Kamnev, Recollections of A. A. Zavarzin* (Moscow-Leningrad, 1948), pp. 493-507.
- [8] T. D. Kan, Tuberculosis and the Heart* (Moscow-Leningrad, 1931).
- [9] M. B. Kiro, Izvest. Akad. Nauk SSSR, Ser. Biol. No. 4, 419 (1948).
- [10] N. M. Mul'tanovskii, Primary Tuberculosis of Muscle, Dissertation* (St. Petersburg, 1911).
- [11] D. N. Nasonov and K. S. Ravdonik, Fiziol. Zhur. SSSR 33, 5, 569-580 (1947).
- [12] A. T. Petriaeva, Pediatria No. 4, 40-49 (1950).
- [13] S. N. Romanov, Doklady Akad. Nauk SSSR 66, 2 (1949).
- [14] A. I. Strukov, Arkh. Patol. 8, 101-109 (1946).
- [15] I. P. Suzdal'skaia, Vestnik Leningrad. Gos. Univ. No. 7, 37 (1952).

THE SELECTIVE EFFECT OF SOME CHEMICAL STIMULANTS ON THE REFLEXES FROM CHEMORECEPTORS

COMMUNICATION VIII. THE EFFECT OF STREPTOMYCIN ON REFLEXES FROM THE CHEMORECEPTORS AND MECHANORECEPTORS OF THE PERICARDIUM

G. S. Kan

The Laboratory of Experimental Pathology and Therapy (Head — Candidate of Medical Sciences,

G. S. Kan) of the Leningrad A. Ia. Shternberg Institute of Tuberculosis

(Head — Prof. A. D. Semenov)

(Received December 28, 1956. Presented by Active Member Acad. Med. Sci. USSR, V. N. Chernigovskii)

In previous reports [1, 3, 4, 5] it has been shown that the parenteral injection of streptomycin depresses reflexes from the chemoreceptors of the small intestine, spleen, kidneys and the tissues of the hind limb.

According to reports in the literature, the conducting pathways from the chemoreceptors of the zones mentioned above pass through the spinal cord [2, 8, 9, 11]. In this connection it is important to ascertain the character of the effect of streptomycin on the reflexes from those reflexogenic zones from which the conducting path-

* In Russian.

ways lead mainly direct to the medulla oblongata, missing the spinal cord. A zone of this sort, in particular, is the interoceptive zone of the pericardium. As shown by a number of workers [2, 6, 7, 8], the main bulk of afferent impulses from the receptors of the pericardium reach the central nervous system by the aortic and vagus nerves, missing the spinal cord.

EXPERIMENTAL METHOD

Experiments were performed on cats under urethan anesthesia. The level of the arterial pressure and the respiratory movements were recorded by the usual methods.

In order to study the reflexes from the receptors in the pericardium, Drinker's method was used [10].

As a stimulant of the pericardial chemoreceptors we used nicotine in a dilution of 10^{-9} to 10^{-3} , which was injected in a volume of 0.3-0.5 ml into the pericardial cavity, and then washed out with warm physiological saline. In each experiment several dilutions of nicotine were used. The mechanoreceptors of the pericardium were stimulated by a stream of warm physiological saline directed at the pericardial membranes always in the same force and volume. Reflexes from the chemo- and mechanoreceptors of the pericardium were in most cases shown in the form of depression of the arterial pressure, increase in the rate of respiration and in its amplitude. Less commonly there was an increase in the level of the blood pressure.

In some of the experiments the threshold of excitability of the tibial nerve to stimulation with an electric current was determined in addition. Streptomycin (sulfate or calcium chloride complex) was in most cases injected intravenously in a dose of 70,000-127,000 units, but in some cases was injected intramuscularly in a dose of 250,000-400,000 units. After 5-20 min, and then after each 10-20 min repeated examinations were made of the excitability of the receptors of the pericardium to chemical and mechanical stimuli under the influence of the antibiotic.

EXPERIMENTAL RESULTS

The effect of streptomycin on the reflexes from the receptors of the pericardium was studied in 12 experiments.

In 2 experiments the effect of the antibiotic (400,000 units intramuscularly) was studied on the reflexes from the chemoreceptors of the pericardium to nicotine in a dilution of $1:10^{-9}$. In both cases the magnitude of the original reflex (depressor) gradually diminished, and one-and-a-half hours after the injection of streptomycin the reflex to nicotine was found to be completely suppressed (Fig. 1).

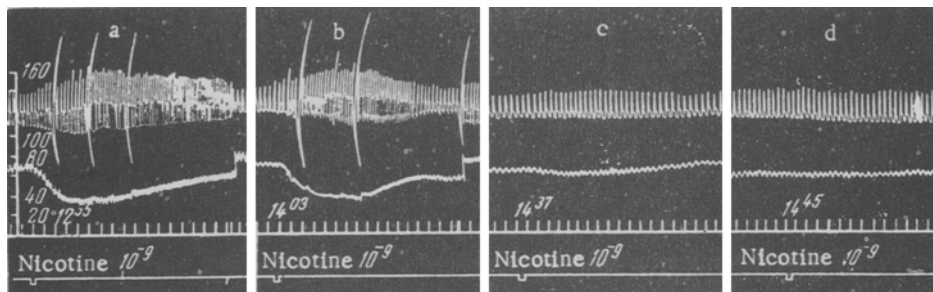


Fig. 1. The effect of streptomycin on reflexes from the chemoreceptors of the pericardium caused by nicotine. a) Original reflex; b, c, d) gradual development of complete suppression of the reflex as a result of streptomycin injected intramuscularly in 13 hrs in a dose of 400,000 units. Interpretation of the curves (from above downwards): respiration, arterial pressure, time marker (5 sec), stimulation marker.

In 3 experiments the effect of streptomycin was studied on the reflexes from the chemoreceptors of the pericardium caused by nicotine in a dilution of $1:10^{-8}$. One hour after the intravenous injection of streptomycin the reflex was distorted. In 2 experiments after injection of the preparation intramuscularly the reaction to nicotine diminished to 60 and 63% (after one-and-a-half hours).

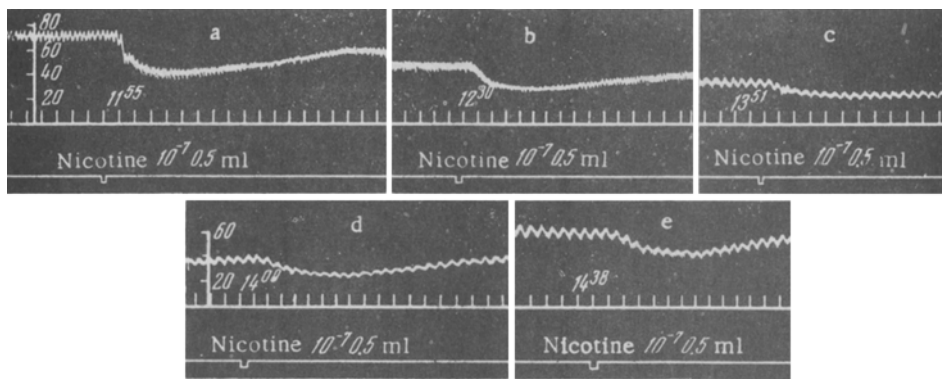


Fig. 2. The effect of streptomycin on reflexes from the chemoreceptors of the pericardium caused by injection of nicotine in a dilution of $1:10^{-7}$ (0.5 ml). a) Original reflex; b, c, d, e) suppression and subsequent partial restoration of the reflex after administration of streptomycin (injected intravenously in 12 hrs 14 min in a dose of 100,000 units). Interpretation of the curves (from above downwards): blood pressure, time marker (5 sec), stimulation marker.

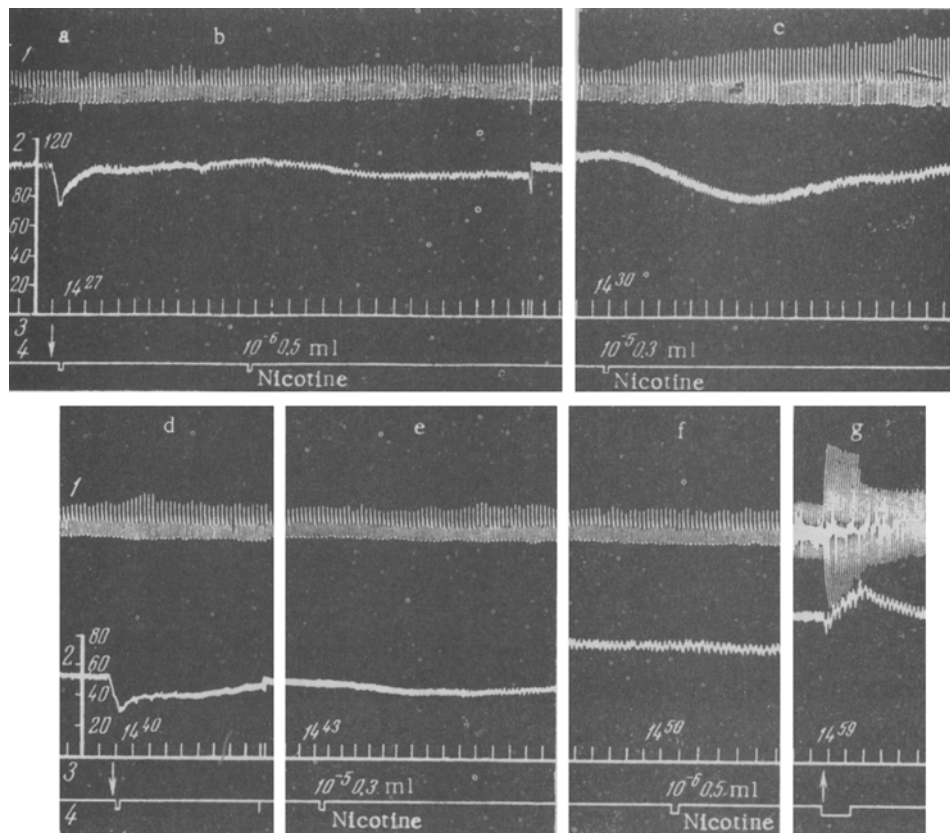


Fig. 3. The effect of streptomycin on reflexes caused by stimulation of the mechano- and chemoreceptors of the pericardium. a) Reflex caused by stimulation of the mechano-receptors; b) weak reflex caused by stimulation of the chemoreceptors (nicotine $1:10^{-6}$, 0.5 ml); c) clearly marked reflex caused by stimulation of the chemoreceptors (nicotine, $1:10^{-5}$, 0.3 ml). Tracings a, b and c were made before the injection of streptomycin. The next tracings d, e and f were made after the injection of streptomycin. The reflex caused by stimulation of the mechanoreceptors (d) was preserved. The reflexes caused by nicotine are absent; g) reflex caused by stimulation (\uparrow) of the peroneal nerve by an electric current. Interpretation of the curves as in Fig. 1.

In 7 experiments the effect of injection of streptomycin was studied on the reflex caused by nicotine in a dilution of $1:10^{-7}$. After the administration of the antibiotic the reflex to nicotine was completely suppressed in 2 experiments, and in 4 cases the reflex was considerably weakened (Fig. 2).

In 7 experiments the effect of streptomycin was studied on the reflex caused by nicotine in a dilution of $1:10^{-6}$. Under the influence of streptomycin the original reflex completely disappeared or was distorted (became pressor instead of depressor) in 4 cases, and in the remaining experiments it was considerably reduced. The maximum suppression of the reaction to nicotine was observed in 4 experiments at the beginning of the test — from 10–20 min after injection of the antibiotic. In the remaining experiments this effect began somewhat later — after 40–60 min.

In 4 experiments the effect of streptomycin was studied on the depressor reflex caused by nicotine in a dilution of $1:10^{-5}$. After intravenous injection of the antibiotic the original reaction was reduced in every case, although to a lesser degree than after administration of nicotine in higher dilutions.

In 9 experiments the effect of streptomycin was studied at the same time on the reflexes from the chemoreceptors (the results of these observations have been given above) and from the mechanoreceptors of the pericardium.

The original reflexes from the mechanoreceptors of the pericardium were depressor in every case. Under the influence of streptomycin in 6 experiments the reflexes from the mechanoreceptors of the pericardium diminished slightly, while in 3 experiments they increased. Thus in the majority of cases streptomycin has no obvious suppressive effect on the reflexes from the mechanoreceptors of the pericardium. At the same time the reflexes from the chemoreceptors were severely suppressed (Fig. 3). The different resistance to streptomycin of the reflexes from the chemo- and mechanoreceptors will be even more obvious if we follow the progress of the changes in the reflexes from the mechanoreceptors of the pericardium during the period of action of the antibiotic. In the majority of cases suppression of the reflexes from the mechanoreceptors of the pericardium was transient, and the reflex quickly regained its original magnitude or even exceeded it.

The different effects shown by streptomycin on the reflexes from the chemoreceptors and mechanoreceptors of the pericardium did not depend on differences in the magnitude of the original reflexes. Thus in the experiments in which the reflex fall in pressure on stimulation of the mechanoreceptors of the pericardium was from 6–9 mm Hg, under the influence of the antibiotic it either increased or briefly and insignificantly diminished. In contrast to this, the reflexes from the chemoreceptors to nicotine, which were far more pronounced, were suppressed completely or reduced by streptomycin.

In order to discover the nature of the suppressive influence of streptomycin on the reflexes from the chemoreceptors of the pericardium, in some of the experiments at the moment of greatest suppression of these reactions the threshold of excitability of a peripheral somatic sensory nerve (the tibial) to stimulation with an electric current was determined.

It was established that at the period when the excitability of the vasomotor center to impulses from the chemoreceptors of the pericardium was shown to be considerably suppressed by the effect of the antibiotic, its excitability to impulses from the tibial nerve still remained sufficiently high (Fig. 3,g).

In experiments in which the chemo- and mechanoreceptors of the pericardium were stimulated, not only vasomotor reflexes but respiratory reactions were also observed, and in most cases these took the form of increased amplitude and rate of the respiratory movements. Under the influence of streptomycin the reflexes acting on respiration were changed most commonly parallel with the reflexes acting on the blood pressure. In some cases it could be seen that the reflexes from the chemoreceptors on respiration were suppressed more quickly and intensively than those acting on the blood pressure.

The results of the observations carried out prove that streptomycin injected parenterally exhibits a marked suppressive action on the reflexes from the chemoreceptors and a much less pronounced action on the mechanoreceptors of the pericardium. From the results obtained it follows that streptomycin suppresses the reflexes from the chemoreceptors also in the case where the afferent pathways pass mainly direct to the medulla oblongata, missing the spinal cord.

The observations quoted in the present paper confirm yet again the hypothesis which we put forward previously that streptomycin suppresses reflexes from the chemoreceptors as a result of the effect which it exerts on the afferent part of the reflex arc in the central nervous system, commencing with the chemoreceptors.

SUMMARY

Short-term experiments were performed on cats under urethan anesthesia. The effect of streptomycin administered parenterally on the reflexes from the pericardial chemoreceptors and mechanoreceptors was studied. Intravenous injection of streptomycin in the dose of 250,000-400,000 units and in intramuscular injection of 70,000-127,000 units completely depresses or considerably inhibits the reflexes from the pericardial chemoreceptors caused by nicotine. However, in the majority of experiments no depression of reflexes appearing in stimulation of pericardial mechanoreceptors was noted in similar experimental conditions. At times only an insignificant decrease of these reflexes was revealed.

LITERATURE CITED

- [1] I. E. Gaber and G. S. Kan, *Biull. Eksptl. Biol. i Med.* No. 9, 48-53 (1953).
- [2] A. M. Grinshtein, *Pathways and Centers of the Nervous System** (Moscow, 1946).
- [3] G. S. Kan, *Proceedings of the 2nd All-Union Conference of Pathophysiologists** (Kiev, 1956), pp. 154-156.
- [4] G. S. Kan, *Biull. Eksptl. Biol. i Med.* No. 5, 40-43 (1956).**
- [5] G. S. Kan, *Biull. Eksptl. Biol. i Med.* No. 6, 40-44 (1957).**
- [6] B. S. Kulaev, *The Role of the Chemoreceptors of the Pericardium in the Regulation of the Circulation of the Blood and the Respiration, Author's Abstract of Dissertation** (Moscow, 1954).
- [7] V. I. Popov, *Transactions of the Sverdlovsk Medical Institute and the Research Institutes of the Sverdlovsk Region Public Health Department** (Sverdlovsk, 1941), 15, pp. 145-279.
- [8] V. N. Chernigovskii, *Afferent Systems of Internal Organs** (Kirov, 1943).
- [9] V. N. Chernigovskii, *Trudy Voen-morsk. med. akad., Leningrad*, 1949, vol. 17, pp. 395-442.
- [10] C. K. Drinker, *J. Exptl. Med.* 33, 675-676 (1921).
- [11] J. T. Irwing, B. A. McSwiney, and S. F. Suffolk, *J. Physiol.* 89, 407-420 (1937).

* In Russian.

** Original Russian pagination. See C. B. translation.