SOME DATA ON INTESTINAL PARESIS IN EXPERIMENTAL PERITONITIS

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Until now investigators have held divergent opinions in regard to the reasons for intestinal paresis in peritonitis. A number of authors connect the drop in the tonus of the intestinal musculature, which is seen in this disease process, with a disturbance of the activity of the vegetative nervous system, innervating the intestine [1, 8, 11, 12]. However, in the opinion of some investigators, the parasympathetic innervation is depressed [1, 11], while others believe the reason for disruption of the intestinal motor activity lies in excitation of the sympathetic nervous system [6], or, on the contrary, in its depression [8, 10, 12].

In view of this, we decided to investigate the influence of the vegetative nervous system on the motor activity of the intestine, and to determine the effect of stimulating the posterior spinal roots at different intervals in the development of experimental peritonitis. In order to judge the degree and character of the disturbance in activity of the vegetative innervation, we also determined the concentration of neuromediators (acetylcholine, adrenalin) in the blood, and the serum cholinesterase activity, since it is known from the works of D. E. Al'pern [2] and other authors [3, 7], that the concentration of neurohumoral factors in the blood reflects the level of synthesis of chemical mediators in the organism, and thus, the functional state of different divisions of the vegetative nervous system.

EXPERIMENTAL METHOD

The experiments were carried out on dogs. For acetylcholine determinations we drew 5 ml of blood from the v. saphena into a syringe containing 5 ml of a proserine solution in a concentration of 5×10^{-4}. The blood was defibrinated. The concentration of acetylcholine in the blood was determined according to the method of Corsten [11], on an isolated frog lung, whose contraction occurs at a dilution of acetylcholine of 1×10^{-20}. Determination of the serum cholinesterase activity was performed by the titration method of T. V. Pravdich-Neminskaya [7]. To determine the amount of adrenalin in the blood we used the method of luminescence analysis, following the modification described by K. V. Lebedev and S. V. Senkevich [5]. The adrenalin was determined in the blood plasma, where it is contained in a greater quantity than in the serum. Blood for this determination was also drawn from the v. saphena, this time collecting 3 ml into a syringe containing 1 ml of a 2% sodium citrate solution. To bring out the fluorescence of the adrenalin, the plasma obtained from the citrated blood was radiated with a mercury-quartz lamp. The fluorescing intensity of the plasma was photometrically compared to the luminescence of a standard solution of pharmacological adrenalin (5 micrograms/ml).

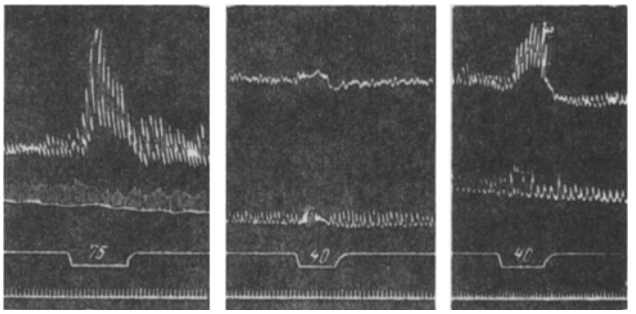
Peritonitis was induced in the dogs by injecting 0.4-0.6 ml of feces (30% dilution) per kg of body weight into the peritoneal cavity.

Examination of the blood for acetylcholine, cholinesterase, and adrenalin was carried out before injection of the feces, and again 2 hours after its injection, and on the following 1-12 days if the animal survived.

In a series of experiments at different intervals in the development of the peritonitis, we recorded the motor activity of the intestine under morphine-hexanol narcosis by inserting a rubber balloon into the lumen of the ileum and connecting it to a recording system (water manometer, Marey capsule). The respiratory movements were simultaneously registered. The cervical portion of the vagus, the II-III spinal roots, and the splanchnic nerves were dissected out. Stimulation of the nerves was performed with an induction current from a sliding coil, fed by a storage cell (2.5 v).

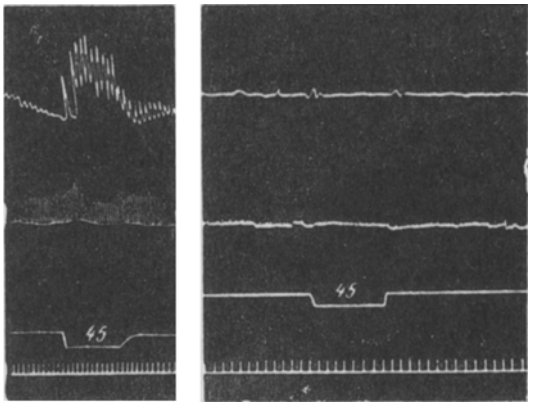
Changes in the Concentration of Mediators in the Blood During Experimental Peritonitis (Mean Indices)

Index	Before injection of irritant (control)	After injection									
		after 2 hours	after 24 hours	on the 2nd day	on the 3rd day	on the 4th day	on the 5th day	on the 6th day	on the 7th day	on the 9th day	on the 10th day	on the 12th day
Concentration of adrenalin (micrograms/ml)	1,4	2,6	1,9	2,3	2,0	2,3	1,9	1,8	1,6	1,5	1,4	—
Concentration of acetylcholine	$2 \cdot 10^{-5}$	$2 \cdot 10^{-10}$	$2 \cdot 10^{-7}$	$2 \cdot 10^{-12}$	$2 \cdot 10^{-11}$	$2 \cdot 10^{-11}$	$2 \cdot 10^{-9}$	$2 \cdot 10^{-8}$	$2 \cdot 10^{-7}$	—	$2 \cdot 10^{-6}$	$2 \cdot 10^{-5}$



a b c

Fig. 1. The effect of stimulating the right vagus on the motor activity of the intestine. a) In a healthy dog (DC 75 mm); b) on the 3rd day of development of the peritonitis (DC 40 mm); c) on the 3rd day of development of the peritonitis after compensatory injection of acetylcholine (DC 40 mm). Meaning of the curves (from above downward): tracing of the intestinal motor activity; tracing of the respiratory movements; stimulus marking; time markings (5 seconds).



a b

Fig. 2. The effect of stimulating the II posterior spinal root on the motor activity of the intestine. a) In a healthy dog (DC 45 mm); b) on the 2nd day of development of the peritonitis (DC 45 mm). Meaning of the curve is the same as in Fig. 1.

EXPERIMENTAL RESULTS

The level of acetylcholine in the experimental dogs ranged from 2×10^{-4} – 2×10^{-6} and the concentration of serum cholinesterase was an average of 25.8%, ranging from 18.2 - 34.5%. The concentration of adrenalin in the blood was an average of 1.4 micrograms, ranging from 0.85 to 2.7 micrograms/ml.

Injection of the peritoneal irritant into the dogs caused an extremely marked excitation within 5-10 minutes, accompanied by violent movements and screaming. Then the animals became constrained, laid down, stood unwillingly, and moved slowly and carefully. Vomiting occured in the majority of them. Respiration quickened and became more superficial; the pulse also increased in rate, and was less full. The abdomen was found to be markedly tense and tender to palpation. In the following days the dogs remained in a depressed state, and they accepted little food, doing so relunctantly. The

stool was retained, and then diarrhea ensued.

In the blood taken from the dogs for investigation 2 hours after injection of the peritoneal irritant, we observed a significant reduction in the level of acetylcholine (to $2 \times 10^{-9} - 2 \times 10^{-11}$) and marked depression of the cholinesterate activity (by 54%). After 24 hours the amount of acetylcholine increased, but did not reach the original figure and the level of cholinesterase also rose, but fell short of the original level by 10%. Beginning with the 2nd day there again occurred a marked depression in the cholinergic reaction of the blood. The level of acetylcholine fell to $2 \times 10^{-13} - 2 \times 10^{-15}$. Cholinesterase activity decreased by 19% in comparison with the original level. Changes in the cholinergic reaction of the blood were also considerable by the 4th day, when we noted an appreciable reduction in the cholinesterase activity (by 52.7% of the original figure), and the level of acetylcholine ranged from $2 \times 10^{-9} - 2 \times 10^{-13}$. Subsequently, a rather rapid elevation occurred in the level of acetylcholine and the cholinesterase activity, with approximation of the original values by the 10-12th days after injection of the peritoneal irritant. When the course of the peritonitis was more serious, the depression of the cholinergic reaction of the blood was even clearer and lasted longer. Determination of the adrenalin in the blood 2 hours after injection of the peritoneal irritant showed marked elevation of its concentration: the mean figure was 2.6 micrograms/ml, exceeding the original level by 85.7%. At the end of the first 24 hours the concentration of adrenalin exceeded the normal by 36%, i.e., the hyperadrenalinemia was less manifest than in the first 2 hours. On the 2nd and 4th days the level of adrenalin again rose, exceeding the original by 64.4%. On the 5th day a new reduction occurred in the concentration of adrenalin, and its level returned to the original on the 9-10th days (see table). The most significant and clear hyperadrenalinemia took place during a serious course of peritonitis, accompanied by more impressive morphological changes in the peritoneal cavity. In extremely severe cases of the disease process the concentration of adrenalin fell sharply.

From the presented data, it is obvious that stimulation of the powerful receptor apparatus in the peritoneum by injection of a pathogenic agent leads to a considerable increase in the output of adrenalin into the blood, especially by the 2nd hour after application of the irritant. Then the level of adrenalin falls, but from the 2nd to the 4th days it again rises, with subsequent gradual lowering. On the other hand, the acetylcholine - cholinesterase system is observed to be markedly depressed on the first day. Only starting with the 5th day does there occur an elevation in the level of acetylcholine in the blood, and a rise in the serum cholinesterase activity.

While prior to the development of experimental peritonitis stimulation of the vagal nerves (coil distance (DC) 70 mm) caused an elevation of the tonus and a strengthening of the peristaltic waves in the intestine, after injection of the peritoneal irritant, beginning with the first 24 hours, we noted a marked depression in the automatic activity of the intestine, and, in the majority of the experiments, stimulation of the vagal nerves (DC 40-0mm) did not cause any strengthening of the intestinal motor activity (Fig. 1b). Similar results were obtained on the 4th day after beginning of the development of peritonitis, i.e. at the time when the manifest hyperadrenalinemia and the marked depression in the cholinergic reaction of the blood took place. In experiments performed on these days, stimulation of the corresponding posterior roots (Fig. 2b) produced a stimulatory effect on the intestinal motor activity which was also incomplete or markedly attenuated. The splanchnic nerves, in the period from the 2nd to the 4th days of development of the peritonitis, retained their inhibitory influence on the contracting activity of the intestinal musculature. Inasmuch as automatic activity of the intestine was almost completely absent, the inhibitory influence of the sympathetic nervous system on the contracting activity of the intestine was more apparent with transection of the splanchnic nerves. In this setting, it was possible, in a series of experiments, to observe a motor effect from stimulating the vagus nerves, which was normally absent if the splanchnic nerves were intact. In the period when the effect of the cholinergic nerves on the intestine was markedly weakened, a compensatory effect could be obtained by injecting pharmacological acetylcholine (1 ml in a concentration of $1 \times 10^{-3} - 1 \times 10^{-4}$) before or during the trial: in this case a certain strengthening of intestinal peristalsis took place, and stimulation of the vagus nerves in the series of experiments caused an appreciable motor effect (Fig. 1c).

Thus, the results obtained show that on the 1st day [4] of development of experimental peritonitis there occurs a marked depression of the cholinergic reaction of the blood, which indicates a significant disturbance in the acetylcholine metabolism within the organism. As a result of this, apparently, there is a depression in the automatic activity of the intestine, observed by us at these periods, with marked weakening, down to complete elimination, of the stimulatory influence exerted on the intestinal motor activity by the vagus nerve and the posterior roots of the spinal cord. Out conclusion is supported by the investigation of M. A. Karlin [4], who observed analogous changes in the automatic activity of the intestine and its neural regulation associated with experimental disruption of acetylcholine synthesis by means of partial depancreatization. From here it may be concluded that intestinal paresis in

experimental peritonitis is caused by depression of the cholinergic system, which leads to weakening of the contracting activity of the intestine and elimination of the stimulatory activity from the parasympathetic innervation. In this setting, preservation of the inhibitory influence of the sympathetic nerves on the motor activity of the intestine only aggravates the pathological disturbance in the contracting activity of the latter.

SUMMARY

Disturbances of the vegetative system control of the small intestine motor activity were studied in dogs with a parallel investigation of the blood neuromediators in conditions of expermental fecal peritonitis. The following was established: a reduction of the acetylcholine level, of the cholinesterase activity and a rise of adrenalin content from the 2nd to the 4th day with a gradual normalization by the 10th-12th day. The period of the greatest acetylcholine metabolism disturbance coincided with the loss of the effect produced by the vagus nerves and by the posterior spinal cord roots on the intestinal motor function. This effect is partially restored by administration of pharmacological acetylcholine. The inhibitory effect of the splanchnic nerves is retained at these periods of peritonitis development. Thus disturbed vegetative control of the intestinal motor function in conditions of peritonitis plays an important role in the development of the intestinal wall paresis.

LITERATURE CITED

1. M. I. Avdeev, and D. N. Vyropaev, Arkh. Pat. Anat. 2, No. 2 (1936), p. 109.
2. D. E. Al'pern, Inflammation [in Russian]. (Moscow, 1959).
3. I. N. Volkova, and O. S. Kochnev, Byull. Éksper. Biol. i Med., No. 4 (1960), p.41.
4. M. A. Karlin, in the book: On the Physiological Role of Mediators [in Russian]. (Kazan, 1959), p. 157.
5. K. V. Lebedev, and S. V. Senkevich, in the book: On the Physiological Role of Mediators [in Russian]. (Kazan, 1959), p. 82.
6. T. A. Malyugina, Éksper. Khir. No. 4 (1959), p. 45.
7. T. V. Pravdich-Neminskaya, Doklady Akad. Nauk SSSR 65, No. 3 (1949), p. 405.
8. B. G. Rubinshtein, Vrach. Delo. No. 6 (1936), p. 481.
9. M. D. Shmagina, Changes in the Autonomic Nervous System in the Intestine, the Mesentery, the Solar Plexus, and the Peritoneum Associated with Generalized Peritonitis. Cand. Diss. [in Russian] (Kazan, 1946).
10. G. M. Shpolyanskii, in the book: Collection of Works by Members of the Leningrad Obstetrics and Gynecology Society During the War and the Blockade [in Russian] 2 (1945), p. 101.
11. M. Corsten, Pflüg. Arch. Ges. Physiol. 244 (1940), p. 281.
12. A. Labori, and P. Gyugenar, Hibernotherapy in Medical Practice [in Russian] (Moscow, 1956).
