THE EFFECT OF STAPHYLOCOCCAL ENTEROTOXIN ON GASTRIC AND INTESTINAL MOTILITY

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In recent years, considerable success has been achieved in the study of staphylococcal enterotoxin. However, the mode of action of the toxin has been comparatively little investigated.

J. Lavergne, J. C. Burdin and J. Sommelet [4] concluded from experiments on two cats that there was no sympathotropic action.

M. Bayliss [3] suggested that the direct action of the toxin on the peripheral nervous system was of considerably greater importance in the etiology of vomiting than was any direct action on the vomiting center.

J. Richmond and C. Reed [5], in their experiments on isolated sections of rabbit intestine, concluded that the staphylococcal enterotoxin exerts a direct action on the smooth muscle of the intestine.

Our observations were made on cats, kittens, and puppies which were given filtered extracts of the toxin intravenously, per os, and intraperitoneally; this caused gastrointestinal disturbance (diarrhea and vomiting) as well as central nervous effects (staggering gait, tremor, convulsions).

These observations were our starting point in the investigation of the mode of action of enterotoxin filtrates. We therefore carried out several experiments on adult cats under urethane anesthesia and with no interference to the nervous connections. Altogether, we investigated 51 cats varying in weight from 2,200 to 4,000 grams.

Filtrates of the enterotoxin were taken from staphylococcal strains which were effective in producing the gastrointestinal syndrome in cats, kittens and puppies.

EXPERIMENTAL METHODS

The method of preparing the enterotoxin filtrate was as follows. A 24-hour agar culture of the staphylococcus, known to produce the enterotoxin, was transplanted to a nutrient medium and incubated in a thermostat for three days. An amount of CO_2 equal to 25-30% of the volume of the vessel was introduced daily. On the fourth day the culture was filtered through a sterile steatite filter. In order to destroy the thermolabile hemolysin, the lethal filtrate of the toxin was heated for 30 minutes in a bath of boiling water. In order to exclude any effect of the nutritive medium, we carried out a control experiment in each group, using uninfected medium.

In the first experiments, we studied the effects of the filtrates on the gastrointestinal motility of the cat in situ.

The experiments were carried out as follows (using the principle of N. P. Nikolaev as modified by the department of Pharmacology of the Lvov Medical Institute). A laparotomy was performed under urethane anesthesia. After we cut the omentum and placed ligatures on the greater curvature of the stomach, small, and large intestines, we introduced a glass cylinder (13 cm long and 7 cm in diameter, open at both ends) into the peritoneal cavity. The cylinder was held in a vertical position in a holder, and 100-150 ml of Ringer-Locke solution heated to 38-39°C was poured through its upper end into the peritoneal cavity. Each of the three ligatures from the stomach, small, and large intestine were brought to the outside and connected to the recording system. The contractions were recorded on ordinary paper by glass ink recorders attached to levers.

After recording the normal contractions of the stomach and intestines, 2 ml per 1 kg of the filtrate were given intravenously, but the amount was not allowed to exceed 6 ml.

EXPERIMENTAL RESULTS

Twenty-one experiments on the effect of staphylococcal enterotoxin filtrates on gastric and intestinal motility were carried out. A record was made of the changes in motility of the stomach and intestine as affected by the staphylococcal enterotoxin filtrate. Injection of the filtrate caused an increase in gastrointestinal activity.

Fig. 1. The effect of staphylococcal enterotoxin filtrate (strain No. 1594) on the motility of stomach and intestine in the cat. Shows increase in contractions and tone.

The effect on both tone and rate of contraction is shown in Fig. 1.

In six control experiments with filtrates from uninfected media and from nontoxic strains of staphylococcus, there was no effect on the motility of the stomach or small intestine. In the experiments on the effect of the medium, there was a reduction in tone of the large intestine, and in two experiments the gastric tone was also reduced.

Having established the effect of the filtrate on the motility of the gastrointestinal tract, we then studied its action on the stomach and intestine after their motility had already been reduced by other means. For this purpose we used adrenalin, atropine, and papaverine.

After the motility of the intestine had been reduced in this way, the enterotoxin filtrate was given intravenously. Altogether, 17 experiments were carried out.

In adrenalin-treated animals, intravenous injections of enterotoxin filtrate caused an increase in tone of all parts of the gastrointestinal tract. There was an increase in the motility of the small and large intestine. In animals which had been treated with papaverine, there was a small increase in tone of all parts after enterotoxin filtrate was given. After atropine administration, the effect of enterotoxin filtrate was much less marked. There was sometimes a small effect on the large intestine.

For a more complete investigation, we carried out experiments with enterotoxin filtrates on spinally transected animals. Seven of these experiments were performed.

These gave similar results. However, spinal section caused a considerable change in the rhythm of the contractions, there being a greater change in the actual contraction movement than in the relaxation.

Finally, we studied the effect of "pure" enterotoxin filtrates on isolated sections of cat and rabbit intestine both with and without preliminary treatment with adrenalin and gynergen, or with cholinergic substances such as atropine, pylocarpine, and carbocholine.

These experiments showed that the staphylococcal enterotoxin filtrate increases the motility of isolated gut sections, increasing the tone, amplitude, and frequency of the contraction. Thus, there was an increase in tone in 47 out of 58 experiments, an increase in amplitude in 42, and an increase in frequency in 27 experiments. The control experiments showed that the effect of the sterile medium is to reduce the tone as well as the amplitude and frequency of the contractions.

Filtrates of nontoxic staphylococcal cultures and filtrates of sterile media also reduced the motility of isolated sections of intestine (Figs. 2, 3).

Fourteen experiments were carried out to find the effect of enterotoxin filtrates on isolated sections of intestine which had been previously treated with adrenalin. After recording the normal contractions of a strip of cat intestine, 1-3 drops of 0.1% adrenalin in 100 grams of Tyrode solution were introduced. After 10-15 minutes, 3 ml of enterotoxin filtrate was added.

These experiments showed that the effect of the enterotoxin filtrate on a toneless loop of small intestine was to restore the tone and to increase the frequency and amplitude of the contractions.

In further experiments, adrenalin was added after the enterotoxin. When this was done the adrenalin failed to produce a complete relaxation.

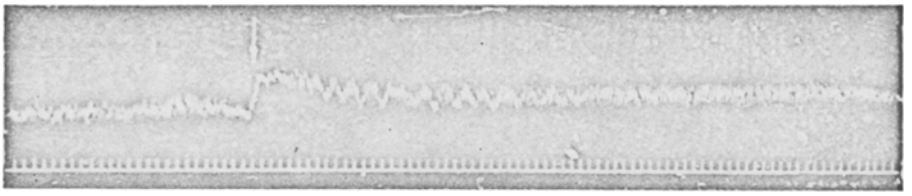

Fig. 2. Reaction of isolated strip of small intestine to staphylococcal enterotoxin filtrate (strain No. 1197), time intervals 20 seconds.

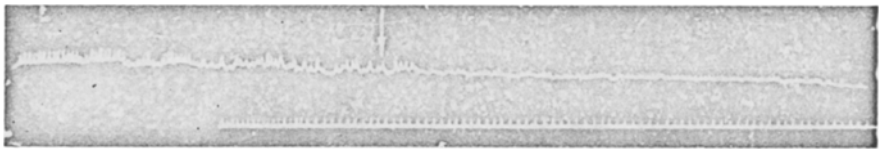

Fig. 3. Abolition of motility after the addition to a strip of small intestine of a non-enterotoxic staphylococcal filtrate (strain V4D-46), experiment No. 156. Time intervals, 20 seconds.

Nineteen experiments were arranged to investigate the action of staphylococcal enterotoxin filtrate on isolated strips of the small intestine of a cat already stimulated by gynergen. These experiments showed that the enterotoxin caused a further increase of tone and frequency of contraction over and above that caused by the gynergen.

In 18 experiments with atropine, it was shown that this drug considerably reduces the stimulant effect of the enterotoxin on isolated strips of small intestine. The addition of the enterotoxin after atropine reduced the tone, amplitude, and frequency of the contractions. In 14 experiments, after stimulating the motility of strips

of rabbit small intestine with the enterotoxin, we added three drops of a 0.1% solution of atropine. The atropine caused a considerable reduction in tone and in the amplitude of the contractions which had been increased by the action of the enterotoxin.

The following 43 experiments were carried out with pilocarpine and carbocholine. After the stimulant action of pilocarpine, the addition of enterotoxin filtrate had no clear effect, and in half of the experiments there was even some reduction in the amplitude of the contractions. Similar effects were noted with carbocholine. Thus in experiments the typical stimulant effect of the enterotoxin filtrate was not shown.

Our experiments showed, therefore, that the staphylococcal enterotoxin filtrate applied to cats in situ had a stimulant effect on gastrointestinal motility. The effect was shown most strongly in the large intestine, less strongly in the small intestine, and least of all in the stomach.

It was established that there was an increase in the tone of the smooth muscle of the gut in animals previously treated with adrenalin and papaverine. Some reduction in motility was found in animals treated with atropine. The increase in smooth muscle tone caused by the enterotoxin in adrenalin-treated animals shows that the adrenergic nerve fibres of the intestine play hardly any part in this action.

The absence of any increase in smooth muscle tone in animals receiving the enterotoxin after preliminary treatment with atropine, shows that the enterotoxin can stimulate the cholinergic nerves. The same conclusion applies in the case of the animals treated with papaverine.

The increase in the motility of stomach and intestine resulting from the enterotoxin applied to animals after spinal section, confirms the cholinergic nature of the action. Experiments with isolated strips of intestine show that the enterotoxin directly increases the motility. This effect is less clearly shown with atropine, and is reduced by subsequent application of the latter. Sympathotropic substances do not change the above reaction.

The effect is progressively less in the large intestine, small intestine, and stomach, respectively.

Thus sympathomimetic substances have no effect on the sensitivity of the animal to the staphylococcal enterotoxin.

The effect of the enterotoxin is mediated by cholinergic nerves, and is shown by an increase in the muscular tone of the intestine and by a reduction in this reaction in atropinized animals, as well as by a reduction in tone when atropine is given after the enterotoxin.

SUMMARY

It was established in experiments on cats in situ that enterotoxin excites the motor activity of organs of the gastrointestinal tract. The most pronounced reaction to staphylococcus enterotoxin occurred in the large intestine, then the small intestine and stomach respectively. Pharmacological substances which enhanced the sympathetic reactions had no effect on the sensitivity of the animal to staphylococcus enterotoxin. Experiments were carried out to study the effect of enterotoxic staphylococci on the motor activity of the isolated strips of small intestines of cats and rabbits. It was shown that enterotoxin excited the motor activity and increased the tonus, amplitude and frequency of contractions. On the basis of these experiments it may be suggested that staphylococcus enterotoxin possesses a cholinergic effect.

In Russian.

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