A GASTRIC ULCER IN RATS OF VARIOUS AGES

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It has been shown that the vasomotor component of the inflammatory reaction does not occur at an early age [1-5, 7, 8]. A closely related fact is that trophic ulcers fail to develop in young animals [6, 11, 12].

K. A. Meshcherskaya [17] induced gastric ulcers in adult rats by the injection of caffeine and arsenous acid, and interpreted the abscess formation as a dystrophic process which occurred in all cases. We have observed the same effect in adult nonpregnant rats [19].

The object of the present work has been to investigate experimentally the possibility of the formation of gastric ulcers in young rats at early stages of their development.

EXPERIMENTAL METHOD

We used a slight variation of K. A. Meshcherskaya's method [16] which we also applied to adult animals. In the morning, by means of a special tube attached to a cylinder, we introduced into the stomach first 5 mg/100 g caffeine, and then, 30 min later, 1 mg/100 g arsenous acid. To compare the results with those we obtained previously on adult control rats, we also used a dose of caffeine equal to twice the amount recommended by K. A. Meshcherskaya in her article. In one set of experiments the dose was increased to 10 mg/100 g. Because of the small solubility of arsenous acid, 100 mg of sodium bicarbonate was added to 100 ml of the aqueous solution. In two sets of experiments the dose of arsenous acid was increased to 1.1-1.2 mg/100 g. Caffeine was given as a 1% solution, and arsenous acid as a 0.2% solution. Altogether we carried out seven sets of experiments. In the first five we used five litters of rats which had received the preparations from the 5-9th day daily for 14-21 days. In these experiments we used 42 young rats. Two sets of experiments were carried out on rats of an intermediate age who received the preparations after the 18th day (sixth series), and after the 24th day (seventh series); they were given 22 doses in the course of 25 days. They were then killed with ether, and the stomach was opened and photographed to show the mucous membrane.

EXPERIMENTAL RESULTS

In the first set of experiments 9 rats from a single litter were used. Caffeine (5 mg/100 g) and arsenous acid (1 mg/100 g) was given from the 9th day onwards. The animals received 17 injections over a period of 20 days. On the 29th day they were killed. Dissection showed that the mucosa of the antral and pyloric parts of the stomach was normal and there were no signs of gastric ulcer. As we showed in our previous investigation, in adult control rats the ulcers formed in the antral part of the stomach. During the 20 days of the experiment the weight increased to 30-35 g, i.e., almost as much as that of the controls.

In the next set of experiments we tried to induce ulcer formation by increasing the dose of arsenous acid: 8 rats aged 8 days received 5 mg/100 g of caffeine and the dose of arsenous acid was increased to 1.3 mg/100 g. This dose was found to be toxic, and the animals died on the 2nd and 4th day. No ulcers were found post mortem. In the work on adult rats an increase of the dose of arsenous acid to 1.5 mg/100 g did not cause death.

Because of the toxic effect of arsenous acid on young rats, on the 3rd day of the experiment 5 animals received a dose which was increased to 1.1 mg/100 g. The caffeine dose was increased to 5 mg/100 g. Treatment was started on the 8th day and continued for 16 days. The rats were killed on the 24th day. Post mortem examination revealed no trace of gastric ulcer. On the 24th day the weight ranged from 30 to 35 g.

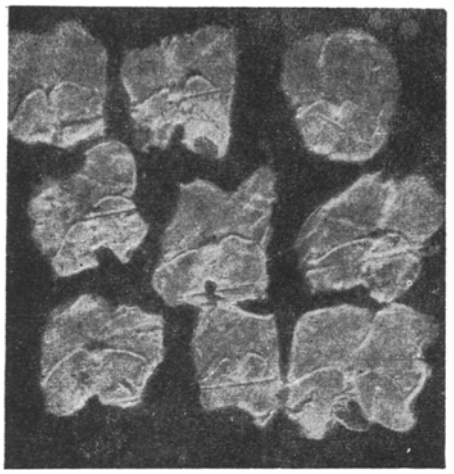

Fig. 1

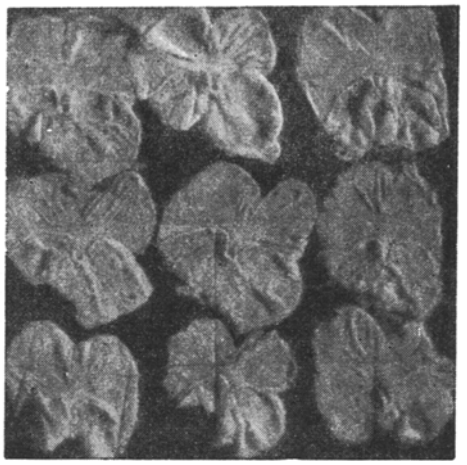

Fig. 2

Fig. 1. Fifth set of experiments: gastric mucosas from 9 rats who received 18 doses of 10 mg/100 g caffeine and 1 mg/ 100 g arsenous acid for 21 days, starting on the fifth day of life.

Fig. 2. Sixth set of experiments: mucosas of 9 rats which received 22 doses of 5 mg/100 g caffeine and 1 mg/100 g arsenous acid for 18 days, starting at the 25th day of life.

In the fourth set of experiments on eleven 9-day-old rats we made a small increase in the caffeine and arsenous acid doses. The animals received 5.5 mg/100 g of caffeine, and 1.2 mg/100 g of arsenous acid, and the substances were given 12 times over a period of 14 days. The duration of the experiment was reduced because a death occurred on the 5th, 7th, and on the 14th day, and the remaining 8 animals showed signs of poisoning: they were emaciated, exhausted, and there was no milk in their stomachs. A state of collapse developed. By the 23rd day the weight increased only to 18-20 g, and developmentally the animals were far behind the controls. On this account, by the 23rd day administration of the preparations was ceased and the rats were killed. Dissection of the stomach showed that the mucosa of both the antral and pyloric parts was normal and there were no signs of gastric ulcer. Therefore an increase of the amount of arsenous acid and caffeine in young rats did not lead to gastric ulcer formation. However a small increase in the dose of arsenous acid, up to 1.2 mg/100 g, was toxic.

In the fifth set of experiments on 9 rats we investigated the influence of larger doses of caffeine (up to 10 mg per 100 g) while the amount of arsenous acid was kept to the same at 1 mg/100 g. The substances were given from five days onwards as 18 doses over a period of 21 days. During this time there were no signs of toxic effects. The animals increased in weight to 30-35 g, and were killed on the 22nd day. Dissection of the stomach showed no signs of gastric ulcer despite the increased caffeine dose and the younger age at which the experiment was started. As can be seen from Fig. 1, the upper thin antral part of the stomach is very distinct from the lower pyloric portion. The esophagus does not enter the antral portion but connects at a ridge separating the pyloric and antral regions. There were no signs of gastric ulcer in the antral portion of the stomachs of any of the 9 rats.

Thus in the experiments on 42 blind young rats which had received the preparation for 22-29 days from the 5th to 9th days onwards there was no indication of gastric ulcer, whereas in the control adult rats the condition developed in every case. An increase of the preparations in young rats again failed to induce an ulcer.

In the next two sets of experiments the caffeine and arsenous acid were given from the 18th to 24th days to older animals which were not fed by the mother.

In the sixth set of experiments 9 rats from a single litter weighing 20-22 g received 5 mg/100 g caffeine and 1 mg/100 g arsenous acid; the treatment was started on the 18th day and given on 22 occasions over a period of 25 days During the first 10 days the rats gained 15-20 g weight. They were killed when 43 days old. Dissection of the stomach showed that in most there were no signs of gastric ulcer on the mucosa (Fig. 2). Only in 3 animals (see Fig. 2, right-hand stomach of upper row, and middle stomach of second and bottom rows), in the antral part of their stomach on the left, was there some thickening of the mucosa to 0.2-0.3 mm, presenting the appearance of a pinhead.

Fig. 3. Seventh set of experiments: mucosa of rat No. 7 which received 22 doses of 5 mg/100 g caffeine and 1 mg/100 g arsenous acid for 25 days, starting on the 24th day.

This structure could not be seen from the side of the serous membrane. From our previous observations on adult rats [19], such thickenings represent the initial appearance of ulcer formation. However in adult animals they are larger and form a ridge having a dip in the center; furthermore they are more numerous; they finally merge with each other and involve the deeper layers of the stomach wall, forming large abscesses which can be seen from the side of the serous membrane. Subsequently, protrusions can be seen from outside the stomach, and the process frequently terminates in perforation.

In the seventh set of experiments 7 young rats weighing from 31 to 37 g received 5 mg/100 g of caffeine and 1 mg/100 g of arsenous acid; these substances were given 22 times starting on the 24th day of life. For 25 days there were no noticeable differences, most of the animals increased in weight to 81-90 g, and rat No. 7 alone reached only 75 g. At the age of 49 days, they were killed. Post mortem examination revealed signs of gastric ulcer in 5 out of the 7 animals. In rat No. 6 in the antral part of the stomach there were three not very clearly defined thickenings of up to 0.2-0.4 mm. In the antral part of the stomach of rat No. 7, in which there were still more superficial ulcers, there was a large ulcer formed from the fusion of several superficial ones; it was close to the junction between the pyloric and antral portions near the entrance of the esophagus (Fig. 3).

It can be seen, therefore, that the first signs of gastric ulcer may appear after the 18th day, and large ulcers may develop from the 24th day onwards. However, the number of abscesses developed at this time is very small in comparison with the incidence in adult rats. The degree of damage is also very much less, particularly in the 18-day-old animals.

According to published reports gastric ulcers are found only exceptionally in young children. Z. D. Khakhina, [21] in a study of 7,000 post mortem examinations of children less than one year old, found only two cases of erosion and one of duodenal ulcer Other authors [9, 20] have reported similar findings. It has frequently been stated that in children above 10 years of age the incidence of gastric ulcer is somewhat greater than in the younger age groups; gastric ulcers occurring before the age of 10 comprise only 1% of the total cases [10, 13, 14, 15, 18].

Our results indicate that methods of inducing gastric ulcer which are effective in adult rats do not produce ulcers in young rats still fed by the mother.

In experiments in which caffeine and arsenous acid was given to rats aged 18-24 days, gastric ulcers were induced, but only exceptionally.

SUMMARY

A study was made of gastric ulcer development in young rats; it was related to the absence in young animals of the vasomotor component of the inflammatory reaction, and on the failure of trophic ulcers to develop. We used a modification of K. A. Meshcherskaya's method in which caffeine and arsenous acid were given by mouth; ulcers were induced in 90-100% of adult rats [16, 19]. In young rats which received the preparation for 14-21 days, starting at the 5th-9th day after birth, no gastric ulcers formed. When these substances were given to rats from the 18-24th day after birth onwards gastric ulcers developed occasionally. However the incidence was very low.

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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.
