A METHOD OF FORMATION OF EXPERIMENTAL GASTRIC ULCER IN CATS

M. Kh. Yuldasheva

UDC 616.33-002.44-092.9

Many methods of producing experimental gastric ulcer in various animals have been described in the Soviet and Western literature [2, 6, 8, 9]. Each of these methods is based on a definite conception of the mechanism of development of peptic ulcer (peptic, traumatic, vascular factors, etc.) without taking into account the role of the central nervous system.

The author has devised a method of producing gastric ulcer in cats which can be used to verify the action of the peptic factor against the background of experimental neurosis, i.e., to examine the parts played by both the nervous and the peptic components in the genesis of the disease.

EXPERIMENTAL METHOD AND RESULTS

The experimental material was obtained in three series of experiments with appropriate controls (70 animals).

In series I the effect of the combined action of functional traumatization of the higher levels of the central nervous system and irrigation of the mucous membrane of the stomach with 0.5% solution of gastric juice on the stomach was studied. These experiments showed that the combined action causes the development of gastric ulcer in 93.7% of animals.

In series II the action of irrigation of the gastric mucous membrane (0.5% solution) alone was investigated. As a result, changes in the gastric mucous membrane appeared in 50% of the cats. The question arose why, as a result of the experiments of series II (the action of the peptic factor alone), was a gastric ulcer obtained in 50% of cases. The probable explanation of this was a slightly increased concentration of the irrigating solution. The acidity of the gastric juice in cats averaged 0.25-0.3% HCl. In control experiments in which the mucous membrane was irrigated with a 0.25% solution of gastric juice, destructive changes of the mucous membrane of the stomach were not observed.

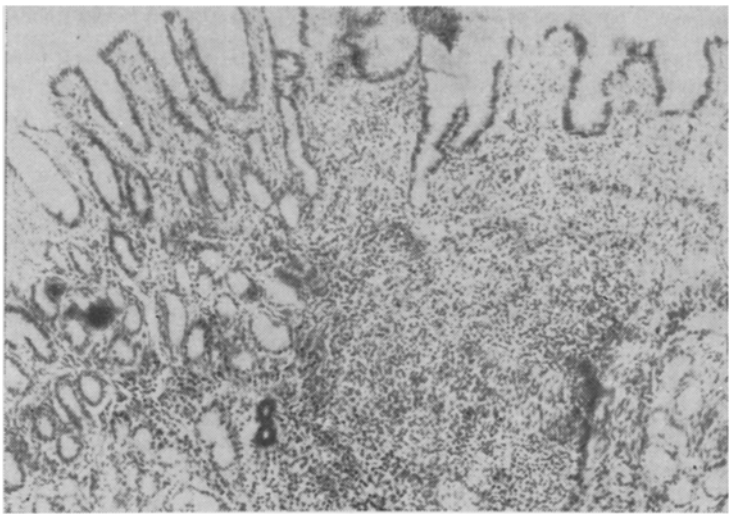
In the experiments of series III the effect of a 0.25% solution of gastric juice on the stomach was studied against the background of neurosis. As a result, a pre-ulcer state developed in 100% of the animals, followed by well marked ulcers. The results of control experiments in which the effect of an electric current and neurosis on the trophic state of the gastric mucous membrane was studied showed that neither an electric current (5-8V) nor conflict between the food and defensive reactions provided conditions for the development of peptic ulcer.

The starting point of these experiments was the assumption that during functional traumatization of the higher levels of the central nervous system the functional state both of the cortical cells of the brain and of the corresponding subcortical centers would be changed and that the cortical correcting mechanism would be disturbed. As a result, a dysfunction of the secretory apparatus would develop, accompanied by contractions of the muscles of the walls and blood vessels of the stomach. This, in turn, would lead to disturbance of the trophic state of the cells and tissues, as a result of which the resistance of the mucous membrane would be lowered and the additional action of the peptic factor would accelerate subsequent digestion of the mucous membrane, leading to the formation of an experimental ulcer.

The results obtained showed conclusively that functional trauma of the central nervous structures plays a predominant role in the mechanism of development of experimental ulcer.

The experiments were carried out on cats in chronic conditions. All the experimental animals had a Basow gastric fistula. From 2 to 2.5 weeks after the operation the secretory activity of the cats' stomach was investigated

Laboratory of Cortico-Visceral Physiology and Pathology, I. P. Pavlov Institute of Physiology, Academy of Sciences of the USSR, Leningrad (Presented by Academician V. V. Parin). Translated from Byulleten' Éksperimental'noi Biologii i Meditsiny, Vol. 62, No. 11, pp. 122-124, November, 1966. Original article submitted December 22, 1964.



Microscopic picture of an experimental ulcer of the pyloric division of the stomach. Hematoxylin-eosin. Objective 20 x, ocular 5x.

by the "sham feeding" method (100 ml of milk, temperature 38°). The milk which was drunk was withdrawn through a rubber tube introduced into the fistula, and brought out through an opening in the bottom of the box. The dynamics of the secretion of juice was then studied for 1 h. The volume of gastric juice was measured every 30 min. The acidity and digestive power (enzyme activity) were studied in hourly samples.

The gastric secretion was investigated in order to discover secretory disorders arising in the process of development of gastric ulcers. In most cases the changes in secretion which were observed were of a hyper- and hyposecretory character. The qualitative composition of the gastric juice was modified in all the animals. This was evidently due to a disturbance of the activity of the glandular apparatus producing the total volume of juice, acid, pepsin, and mucus, demonstrating a selective injury to the glandular cells.

After establishment of a background of secretion, a neurosis was produced by Kurtsin's modification of Kryazhev's method, and at the same time the gastric mucous membrane was irrigated. The animal was placed in a specially built box, the bottom of which was fitted with a hole for the fistula tube through which the irrigating fluid was introduced into the stomach, and in the center of which was a thin-walled rubber balloon for stretching the walls of the stomach. For this purpose, after it had been introduced into the stomach, the balloon was filled with 30-40 ml air. Irrigation was provided by means of a glass ampule (diameter 0.5 cm) with numerous holes the size of a pin-head. The holes in the ampule made it possible to irrigate all surfaces of the gastric mucous membrane simultaneously. The free end of the irrigating ampule was connected to a funnel with two stems. One of these (the inlet) was connected to an ultrathermostat, on a stand 50-60 cm above the animal, filled with irrigating fluid. In this way liquid could be introduced at a definite speed and temperature (37-38°), verified by a thermometer. The other end of the funnel, the outlet, was connected to a receiver into which the irrigating fluid escaped from the stomach.

As the receiver filled with fluid, fresh fluid was poured into the ultrathermostat. In this way, over a period of 2 h the gastric mucous membrane was irrigated with 25 liters of fluid. The irrigation stopped after formation of an ulcer. The total duration of the irrigations on the average was 22 h (10-12 days). The appearance of a gastric ulcer was accompanied in the animals by a worsening of the general condition, refusal to eat, vomiting, and emaciation. In the gastric juice of some animals, traces of blood and mucus appeared. Ulcer formation was accompanied by histological and morphological changes in the neurovascular and neuroglandular apparatuses.

The microscopic picture of the changes (see figure) in the initial stage took the place of increased infiltration with lymphocytes, enlargement of the lymphoid follicles, and marked dilatation of the blood vessels. These were followed by an increase in the lymphocytic infiltration, desquamation of the superficial epithelial cells, disintegration of the lymphoid elements, swelling and edema of the tissues, and exposure of the musclar layer, with obliteration and gaping of the pyloric glands, i.e., the formation of an ulcer. As the distance from the ulcer increased, the destructive changes in the glandular elements diminished. Similar results have been reported by other authors [5]. In these circumstances the nerve bundles were in a state of increased argentophilia and varicosity, and

individual fibers were fragmented, although it was noted that the morphological changes in the nerves of the stomach affected by peptic ulcer were not diffuse but localized in character. At the places of ulcer formation the pathological changes in the nerve fibers were more marked than those some distance away. Similar changes have been described by other authors [3, 4, 7].

By comparison with earlier methods, the one described in this paper thus combines the nervous and peptic factors and is closer to the mechanisms characteristic of the genesis of peptic ulcer in man.

LITERATURE CITED

1. K. M. Bykov and I. T. Kurtsin, The Cortico-Visceral Theory of the Pathogensis of Peptic Ulcer [in Russian], Moscow (1952).
2. I. S. Zavodskaya, Byull. éksp. Biol., 37, No. 1, 26 (1954).
3. A. N. Kartavenko, The Role of the Neurogenic Factor in the Pathogenesis and Clinical Picture of Gastric and Duodenal Ulcer. Author's Abstract of Doctorate Dissertation. Smolensk (1955).
4. A. N. Kartavenko, Terap. Arkh., No. 3, 13 (1959).
5. I. V. Malkiman, M. A. Vasilevskii, and E. A. Rudik, Byull. éksp. Biol., No. 10, 32 (1952).
6. Ya. M. Romanov, Proceedings of a Scientific Conference on the Physiology and Pathology of Digestion, in memory of Academician K. M. Bykov [in Russian], Ivanova (1960), p. 704.
7. B. A. Sennikov, Pathohistological Changes in the Intramural Nervous Apparatus of the Stomach in Peptic Ulcer and their Clinical Significance. Author's Abstract of Candidate Dissertation. Orenburg (1961).
8. F. C. Mann and C. S. Williamson, Ann. Surg., Vol. 77 (1923), p. 409.
9. J. A. Roth and A. C. Ivy, Gastroenterology, Vol. 2 (1944), p. 274.