ALTERATIONS IN GASTRIC FUNCTION PRODUCED BY THE ACTION OF THE ANTIGEN OF THE DYSENTERY BACILLUS UPON THE INTESTINAL MUCOUS MEMBRANE

E.A. Brodskaia

From the Laboratory of Pathological Physiology (Chief – Active Member Acad. Med. Sci. USSR N.N. Sirotinin) of the Institute of Infectious Diseases (Director – Corresponding Member Acad. Med. Sci. USSR I.L. Bogdanov) Acad. Med. Sci. USSR, Kiev

(Received June 20, 1957. Presented by Active Member Acad. Med. Sci. USSR N.N. Sirotinin)

Dysentery produces prolonged and diverse functional alterations of the gastrointestinal tract, particularly of the stomach [3, 6, 8] with pronounced morphological changes [11] which have a great influence upon the course of the disease.

The goal of the present investigation was an examination of the alterations produced experimentally in the gastric functions of dogs when both the large and small intestines are subjected to long-term irritation with the complete antigen of the Flexner bacillus. Moreover, we wished to clarify the mechanism of these changes.

It is known that when dysentery bacilli of their antigens are introduced into dogs or puppies functional disturbances occur in the animals [1] as well as separate elements of the dysenteric process [5, 12, 13, 14, 15]. K.M. Bykov and V.N. Chernigovskii applied the exotoxin of the Grigor'eva Shiga bacilli or the Flexner endotoxin to the interoceptors of dog small intestine and produced a prolonged, if slight, rise in the blood pressure and also a deepening and increased rate of respiration. In view of the results obtained by these workers we also employed dogs as our experimental animals.

EXPERIMENTAL METHOD

The studies were conducted on 21 dogs with Basov fistulae and intestinal loops isolated by the Pavlov or Thiry-Vella method; two dogs had a Pavlov pouch, and three had Klementsevich-Heidenhain pouches in addition to an isolated intestinal loop. The experiments were all long-term in type. Throughout the study the general condition of the dogs was noted and their blood picture examined. The experiments were begun while the gastric glands were in a state of "rest." Gastric secretion in the dogs was stimulated by means of sham feedings lasting 10 minutes, so that the animals with the Pavlov or Heidenhain pouches swallowed 100-200 g of meat. The functions of the stomach were studied for secretory activity (amount and acidity of gastric juice), excretory activity (urea in the gastric juice and chromatoscopic findings) and motor activity (rate of passage from stomach to intestine of a 2% solution of starch).

EXPERIMENTAL RESULTS

After recording the normal gastric activity in the experimental animals, we introduced the antigen of the Flexner bacillus into the isolated intestinal segments. In some of the experiments we used antigen tagged with radioactive phosphorus according to the method of M.Ia. Korn.

Either immediately at the conclusion of the sham feeding or 1-2 minutes before its conclusion, we introduced into the segment of the intestine isolated by the Pavlov method a solution of the complete antigen and the fistula was then closed with a plug. While the condition and behavior of the animals remained within normal limits, the gastric functions became altered: there was observed a moderate hyposecretion with decreased acidity, a rise in urea concentration in the gastric juice, a slowing of the removal of neutral red and a delay in evacuation. The indicated functions were restored at varying time intervals; the motor activity lagged behind the secretory-excretory. These findings agree with the material obtained by K.M. Loban [8] who studied dysenteric patients. A repetition of the antigen introduced 16-17 days later produced alterations in the general condition of the animals such as restlessness, vomiting, temperature elevation, some leucocytosis, etc., as well as more pronounced and prolonged gastric functional disturbances in the direction of hyposecretion, decrease of acidity, rise in urea concentration, slowing in the removal of neutral red and delay in evacuation.

We conducted analogous experiments using proteus antigen and found that this neither altered the general state of the animals nor changed their gastric functions. Later, we attempted to analyze the individual elements of the upset gastric functions produced by the dysentery antigen applied to the intestinal mucosa since this problem is still in dispute [4, 9, 10].

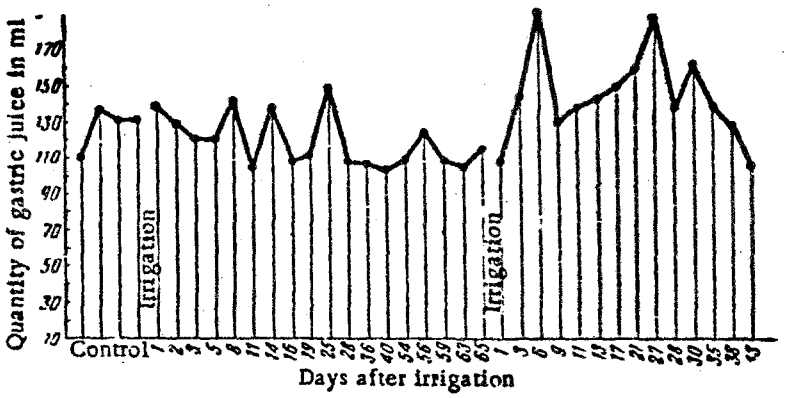

Fig. 1. Quantity of gastric juice secreted by dog Damka after the isolated segment of the small intestine had been irrigated with Flexner antigen.

The antigen in these experiments was permitted to remain in the isolated intestinal segments for an hour during which time it not only acted upon the receptor apparatus but also became absorbed partially. In order to exclude, as far as possible, any toxic effect of the antigen, the isolated intestinal segment with both its ends just under the skin was irrigated with antigen and then rinsed with physiological saline. This irrigation did not affect the general state of the animals nor did it alter in any substantial manner the gastric functions (Figure 1). Repetition of the irrigation was accompanied by persisting gastric juice hypersecretion (Figure 1 – right side of graph) lasting for 37 days; acidity fluctuations at the upper limits of normal and often exceeding them. The concentration of the urea was within normal limits while gastric emptying of starch solution was hastened. Thus, the antigen irrigation of the small intestinal segment produced irritation of nerve receptors and was accompanied by disturbances of gastric functions; the character of these disturbances was different from those produced by the antigen when it was introduced for one hour and had the opportunity to become absorbed.

Analogous experiments were conducted on dogs with isolated loops of the large intestine. When the bacterial antigen was placed into this loop for an hour, there was no visible change in the normal behavior of the animals even though the gastric functions underwent a few alterations (rise in urea concentration of the gastric juice, more rapid evacuation, etc.). The second and third introductions of the antigen (after 11-15-70-80 days) was accompanied by rise of the body temperatures of the animals, great restlessness and retching movements. The amount of 3-hour gastric secretion reached 25-40 ml, while before the antigen had been introduced it totaled 75-100 ml. The free and combined hydrochloric acidity diminished sharply; the speed of removal of neutral red decreased; the urea concentration of the gastric juice remained elevated (Figure 2) and returned to base levels only occasionally. These deviations were observed to persist for the 60-78 days of observation without a tendency

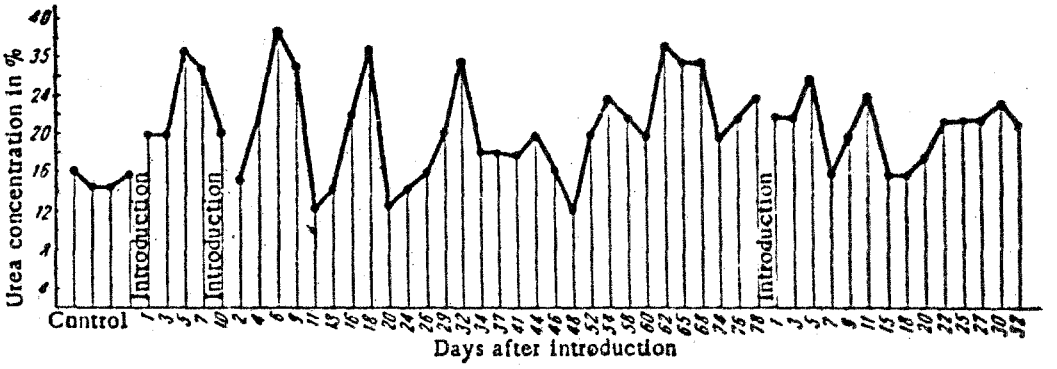

Fig. 2. Urea concentration in the gastric juice of dog Belka after Flexner antigen had been introduced into an isolated segment of the large intestine.

to normalization. Our experimental material has clinical confirmation [6, 8].

Introduction of the antigen into the isolated segments of the large and small intestines did not always produce identical disturbances in gastric function; this is understandable if one stops to consider the peculiarities of the anatomic structure and innervation of the different portions of the gastrointestinal tract.

One must note that irrigation with dysentery antigen of the isolated segments of the large intestine did not affect the behavior of the animals but did result in some alterations of gastric activity: the second and third irrigation with antigen (after 22-60 days) led to analogous but more pronounced and prolonged gastric functional disturbances: there was hypersecretion of gastric juice (Figure 3), moderate increase in acidity, slowed removal of neutral red; urea concentration on some days exceeded base levels. Gastric motor activity was unchanged on some days but, more frequently, it would slow from 20-30 to 40-60 minutes.

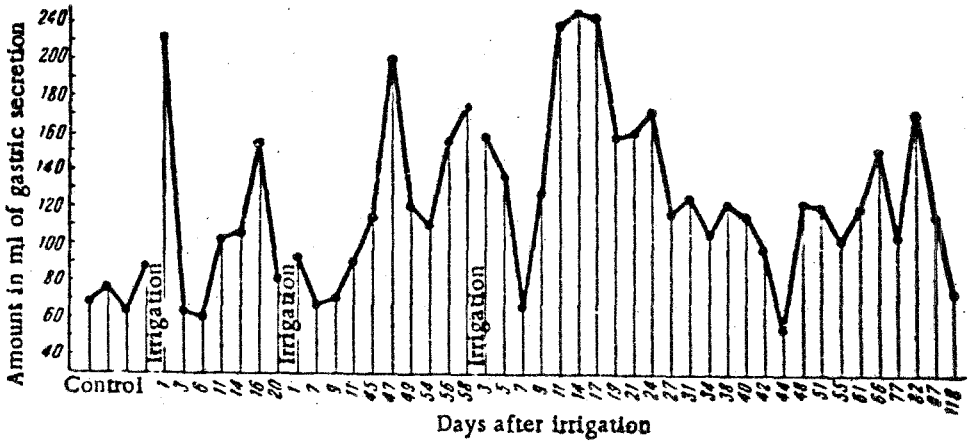

Fig. 3. Quantity of gastric secretion in dog Naida after an isolated segment of the large intestine had been irrigated with Flexner antigen.

When dysentery antigen was used to irrigate isolated intestinal segments, i.e., stimulate the first link of the reflex arc from the receptor field, gastric function was disturbed, this being taken as proof of the reflex nature of these disturbances. This hypothesis was supported by us in experiments in which we employed tagged antigen (activity of 643-780 impulses per minute) in the irrigation of isolated intestinal loops. During the entire time of irrigation and for the next 48 hours the use of counter B failed to show any trace of the antigen in the blood. We must suppose, then, that the observed alterations were reflex in nature. When, however, the antigen was allowed to stay within the loop for an hour, there was not only reflex irritation but also some absorption.

Therefore, the gastric disturbances were not analogous since there had been absorbtion of the antigen and the gastric alterations were no longer purely reflex in nature.

To clarify the role of the receptor apparatus in the transmission to the stomach of intestinal impulses, we irrigated the isolated loops with a 2% novocain solution before introducing the antigen. In these cases we also obtained disturbances of gastric function but differing somewhat from those seen in animals having an intact receptor field. Functional gastric disturbances occurring in dogs whose intestinal mucosa had been anesthesized to exclude receptors prove that the mechanism of transmission includes other than purely nervous paths.

To rule out the vagus nerve in the transmission of interoceptive impulses, we performed experiments on dogs having isolated Heidenhain pouches. After a series of control studies had established the chemical composition of the gastric juice, we irrigated isolated intestinal loops with solutions of the total antigen, this being accompanied by hypersecretion, rise in gastric acidity and rise of urea concentration. Repetition of antigen introduction caused analogous functional disturbances of the stomach. When we compared the gastric disturbances produced after antigen introduction into isolated loop segments of the intestine of dogs with intact and excluded vagi, it became quite evident that dogs with undisturbed gastric innervations returned to normal much more quickly than dogs with Heidenhain pouches. Besides, the character of the disturbances is different: in dogs with an intact innervation, introduction of the antigen led to hyposecretion and decrease in acidity while in dogs with excluded vagi there was hypersecretion and hyperacidity; the gastric urea level rose in both groups.

We believe that in dogs with Heidenhain pouches the sympathetic innervation is preserved and that gastric functional disturbances after dysentery antigen introduction are due to the sympathetic stimulation of the suprarenals and the hypophysis (pituitrin), etc. Thus, the transmission of interoceptive stimuli from the intestine to the stomach takes the reflex pathway with the aid of humoral factors.

SUMMARY

Pronounced and prolonged disfunction of the stomach results from the introduction of the dysentery bacillus antigen into isolated (by Pavlov's method) portions of the small and large intestine. This is due to the fact that the antigen not only stimulates the nervous apparatus of the intestine, but is also absorbed. Irrigation of isolated portions of the intestine by the Thiry-Vella method, which prevents absorption of the antigen (this was proved by experiments with labeled antigen) is also associated with disturbed function of the stomach, which, however, differs qualitatively. It was demonstrated on animals deprived of parasympathetic innervation of the stomach that the function is disturbed when the antigen is introduced into the isolated portions of intestines. This shows that the sympathetic innervation of the stomach and certain humoral factors take part in the influence of the intestine on the gastric function. Therefore, both the neuroflex mechanism and the humoral factors participate in interoceptive transmission from the intestine to the stomach.

LITERATURE CITED

[1] A.D. Ado, in the book: Antigens as Special Stimulants of the Nervous System* (Moscow, 1952).

[2] K.M. Bykov, Cerebral Cortex and Internal Organs* (Moscow-Leningrad, 1952).

[3] L.F. Volkov, Zhur. Voenno-Med. 12, 29-34 (1954).

[4] Z.M. Volynskii, Sovet. Vrachebni Zhur. 5, 349-355 (1941).

[5] I.S. Dergachev, Pediatriia 4, 14-20 (1954).

[6] E.I. Zverev and A.D. Belova, Problems of Epidemiology, Prophylaxis, and Clinical Care of Intestinal Infections* 229-269 (1954).

[7] M.Ia. Korn, Studies on the Use of Radioactive Isotopes in Medicine* (Moscow, 1953).

[8] K.M. Loban, Arch. Terap. 26, section 5, 41-47 (1954).

[9] P.N. Stepanov, Chronic Dysentery* (Sverdlovsk, 1946).

[10] P.S. Chulkov, Trudy Voenno-Med. Akad. Leningrad, 4, 279-303 (1935).

*In Russian.

[11] V.P. Emaikina, Pediatrila 3, 44-50 (1952).

[12] Dold and Fisher, I Abt. Originale 85, 3, 198-206 (1921).

[13] H. Dold, Deutsche med. Wschr. 42, 811-813 (1916).

[14] R. Schiga, op. cit. 27, 741-744 (1901).

[15] Ibid, Zbt. für Bact. Parasitenkunde u. Infektionskrank. XXIV, 24, 913-918 (1898).