Local Hypersensitiveness of the Rabbit Stomach.* (19270)

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A local state of hypersensitiveness restricted to the organ which was the site of the primary injection, was obtained in the eye with exogenous antigens by Seegal and Seegal(1); in the eye, cerebrum and lung with exogenous and autogenous antigens by Jahiel *et al.*(2-5) and in the cerebrum with exogenous antigens by Davidoff *et al.*(6). These experimental studies were performed chiefly in rabbits, and following the intravenous shock injection lesions were noted in the organ which had received the primary sensitization.

The present series of experiments were made to determine whether the rabbit's stomach is capable of becoming actively and locally hypersensitive and to study the nature of the lesions obtained.

Material and methods. Horse serum was used as an antigen. Fifty rabbits were sensitized locally, after ether anesthesia and laparotomy, with .05-.8 cc horse serum injected with a 27-gauge needle subserosally in the stomach wall; after a free interval varying from 9 days to 9 weeks, they were tested with 1 to 5 cc of the same antigen injected intravenously. Twenty-one control rabbits received only the sensitizing injection. Thirteen other controls received only the intravenous injection. The rabbits were killed or died at various intervals after injection. Their stomachs were compared with those of a series of 70 untreated animals. All animals came from the same source for each series of experiments and their controls. They weighed approximately 3 lb when purchased and remained in the laboratory for at least one week before use. During that period and postoperatively they were fed uniformly.

Results. Normal untreated rabbits revealed in our laboratory 8% of localized spontaneous gastric lesions or ulcerations. Twenty-six of the 50 experimental animals had gastric lesions or ulcerations representing an incidence of 52%. Four of the 34 controls had gastric lesions representing an incidence of 12%. Thus the incidence of lesions in the group of rabbits locally sensitized and tested afterwards by intravenous injection was significantly greater than those in either series of controls, indicating that a phenomenon of local hypersensitiveness can be obtained in the rabbit's stomach.

The lesions varied in intensity in the experimental animals. The most discrete ones consisted of a localized area of mucosal and submucosal edema with moderate infiltration with lymphocytes, plasma cells, and a few eosinophilic cells. Less discrete ones showed localized hemorrhagic foci in the lowermost part of the mucosa. When the process was more extensive, the hemorrhagic and exudative lesions extended throughout the mucosa with minute areas of necrosis and erosions. In the most extensive lesions there was an actively bleeding ulceration extending to the muscularis mucosae with inflammatory reactions in the underlying submucosa but no erosion through the muscularis mucosa. In a few cases these varied lesions were seen in the same animal.

The factors common to these lesions were: (1) the predominance of the vascular features, namely, edema, hemorrhage, endothelial reaction, perivascular infiltration particularly around minute vessels; no lesions in the vessel wall were encountered however; (2) the constant involvement of the lowermost part of the mucosa. The lesions appeared within 2 hours after the shock injection. In the animals killed within the first 24 hours active edema and hemorrhage were present and necrosis and cellular infiltration were already observed. In the animals killed after 24 hours, the edema was much decreased or absent; there were no fresh hemorrhage, and necrotic areas infiltrated with polymorphonuclears were the most noteworthy features.

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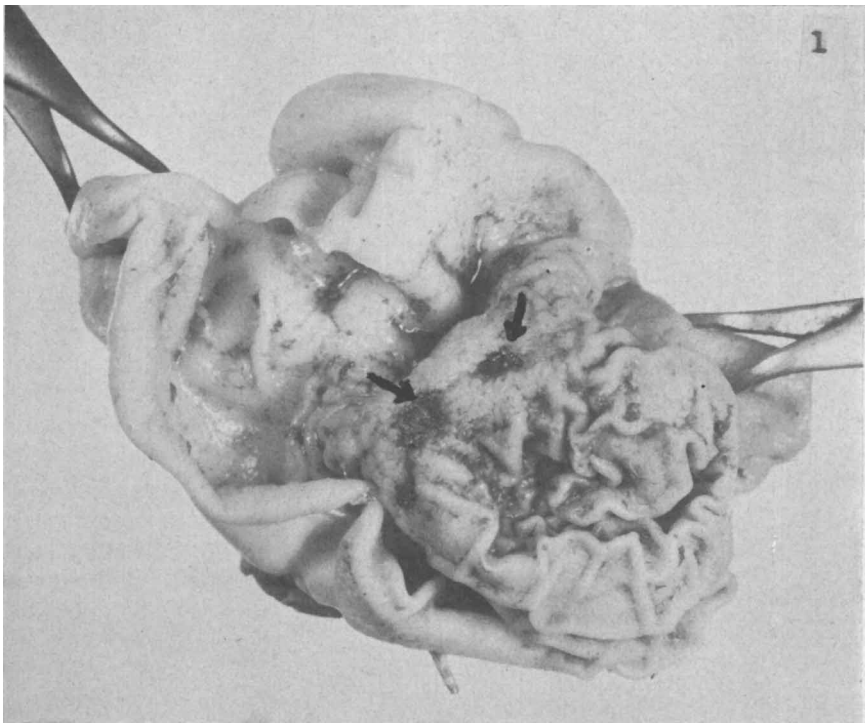

FIG. 1. Rabbit 27. Sensitized after laparotomy, with .2 cc horse serum. Shocked 21 days later with 2 cc horse serum intrav. Killed 3½ hr after injection. Hemorrhagic ulcerations in supracardiac region.

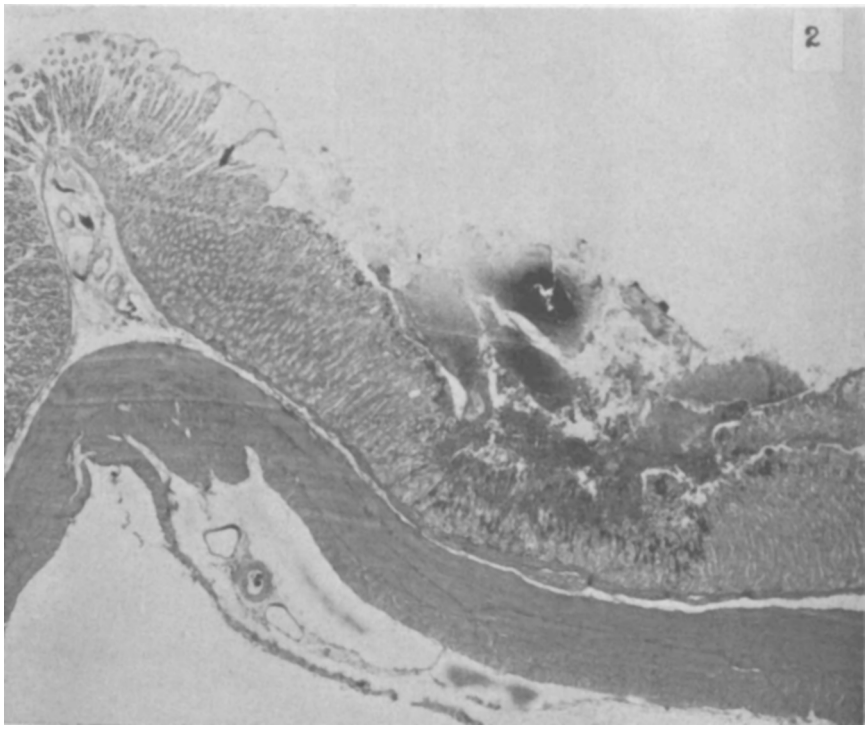

FIG. 2. Rabbit 27. Hemorrhagic crater, × 30.

The location and number of lesions varied. They were found near the cardia, in the lesser curvature, at the pyloro duodenal junction, or in the anterior and posterior wall near the cardia. They were not found along the greater curvature. The lesions were not at the exact site of the sensitizing injection but were within a wider area of the stomach mucosa. We interpret this fact as due to variations in diffusion of antigen at the time of the sensitizing injection. The lesions occurred as either single or 2 or 3 separate erosions or ulcerations with areas of edema in between them. The incidence and severity of the lesions were not significantly affected by variations in the doses or the time interval between the two injections within the range used in these experiments.

No apparent lesions were found in other organs of the experimental animal. When spontaneous lesions were observed or when lesions were seen in the control animals, they were similar to the ones observed in the experimental animals, namely, edematous, hemorrhagic or ulcerative lesions (except for an occasional infection).

Comment. Anaphylactic reactions of the Arthus type were described in the stomach of generally sensitized animals by various observers (Shapiro and Ivy(7), Alessio(8), de Gara and Angevine(9).) Cytotoxins were used by Bolton(10), and Myagawa(11). Anaphylactic reactions in the passively sensitized stomachs of dogs and monkeys were produced following intravenous injection of antigen by Walzer(12) and Friesen(13). To our knowledge, no attempt was made until now to obtain a local active hypersensitiveness of the stomach. This organ responds to the phenomenon of local organ hypersensitiveness with lesions variable in number and intensity. Organs other than the stomach have not shown lesions following primary sensitization of this organ.

Compared to peptic ulcer in man, the lesions obtained represent in most of the cases, erosions rather than ulcers according to Ivy's classification(14). They may resemble lesions seen early in the disease. Bernard described recently(15) scattered "intramural" lesions in the stomachs of patients with ulcers. These lesions were detected only by serial sections of specimens of gastrectomy; they were sometimes located at a certain distance from the ulcer crater; they did not reach the surface of the mucosa, hence they were not visible in the gross specimen. Although such a study, by serial histological sections, was not performed on our experimental specimens, some of our slides showed lesions of the lowermost part of the mucosa resembling the intramural aspects observed in human stomach by Bernard.

Summary. (1) A phenomenon of local organ hypersensitiveness, using an exogenous antigen (horse serum) was produced in the rabbit stomach. (2) The stomach wall, at the time of laparotomy was the site of primary sensitization. After an interval of several days to several weeks, the shock injection was given intravenously. (3) The lesions obtained were single or multiple. In a number of animals actively bleeding lesions with crater formation surrounded by edema were produced. (4) The stomach was the sole organ grossly involved.

1. Seegal, D., and Seegal, B. C., PROC. SOC. EXP. BIOL. AND MED., 1930, v27, 390.

2. Jahiel, R., and Nectoux, R., *Compt. Rend. Soc. de Biol.*, 1938, v129, 1073.

3. Gosset, A., Jahiel, R., and Delauney, S., *Compt. Rend. Acad. des Sc.*, 1939, v208, 140.

4. Jahiel, R., Rosen, M., and Morel, R., *Compt. Rend. Soc. de Biol.*, 1939, v130, 1005.

5. Jahiel, R., and Jahiel, R., *J. Allergy*, 1950, v21, 102.

6. Davidoff, L., Kopeloff, L. M., and Kopeloff, N., *J. Lab. and Clin. Med.*, 1935, v20, 1238.

7. Shapiro, P. F., and Ivy, A. C., *Arch. Int. Med.*, 1926, v38, 237.

8. Alessio, F., *Pathologica*, 1928, v20, 302.

9. de Gara, P. F., and Angevine, D. M., *J. Exp. Med.*, 1943, v78, 135.

10. Bolton, C., *Lancet*, 1908, v1, 1330.

11. Myagawa, Y., *J. Path. Bact.*, 1920, v23, 462.

12. Walzer, M., Gray, I., Strauss, H. W., and Livingston, S. J., *Immunol.*, 1938, v34, 91.

13. Friesen, S. R., State, D., Jasper, D. E., Finn, M., and Wangensteen, O. H., *Surgery*, 1948, v23, 167.

14. Ivy, A. C., Grossman, M. I., and Bachrach, W. H., *Peptic Ulcer*, Blakiston Ed., 1950, 17.

15. Bernard, A., *J. Dig. Diseases*, 1951, v18, 197.

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