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Production of Experimental Jejunal Ulcer.

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The following method has been devised for the production of experimental jejunal ulcer. The abdomen of a cat, under Nembutal anaesthesia, is opened and 3 adjacent segments, each 6-8 cm long, are cut from the first loop of the jejunum distal to the ligament of Treitz. A mesenteric pedicle of adequate size is chosen to ensure a good blood supply to each segment. L-shaped cannulae with rounded tips are tied into the ends of each segment. The sections of intestine are then replaced in the abdominal cavity, care being taken to avoid strangulation. The open ends of the cannulae are brought through stab incisions in the abdominal wall, which is then closed.

The solutions to be perfused through the segments are pre-heated to 37-38° C. and are introduced via the distal cannulae to be drained proximally. A constant pressure of about 20 mm Hg is maintained

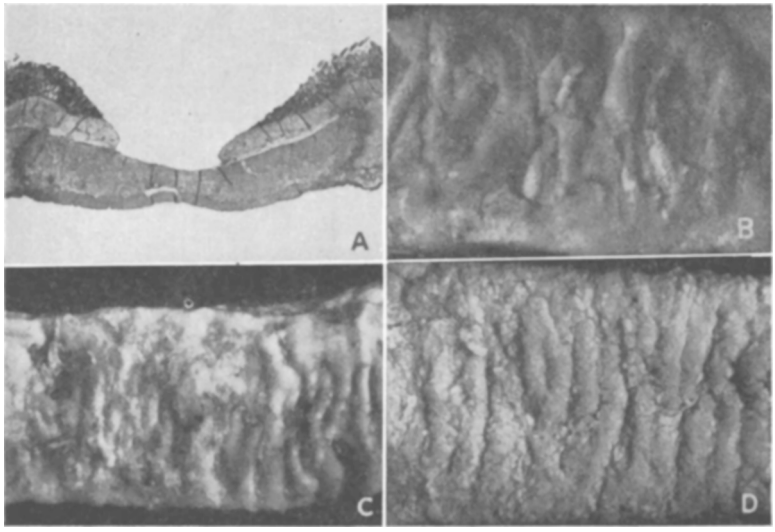

FIG. 1.

(a) Perfusion of jejunum with acid-pepsin (described in text). (b) Perfusion with 0.1 N HCl: little destruction of villi and some inflammatory changes. (c) Perfusion with acid-pepsin solution: upper left quadrant, perforation; lower right quadrant, ulceration through circular muscle; lower center, ulceration through mucous membrane; multiple ulceration marked by small blood clots throughout. (d) Perfusion with acid-pepsin and colloidal aluminum hydroxide: coating of aluminum hydroxide; no pathological changes. *Note:* b, c, and d are adjacent segments of jejunum from one animal and were each perfused for 12 hours.

by filling and inverting a 200-cc burette over a funnel leading to the heating jacket. The solutions used were (a) 0.1 N HCl, pH 1.2; (b) 3% pepsin (Parke, Davis & Co., 1:3,000) in 0.1 N HCl, pH 1.2; (c) 1 part colloidal aluminum hydroxide in 10 parts solution "b", pH 3.5; (d) 1 part aluminum phosphate gel in 10 parts solution "b", pH 2.0. The solutions are introduced at a rate of 1-2 cc per minute. After 12 hours, the sections of intestine are removed, examined grossly, and then fixed for histological study.

The experimental data are shown in Table I. In all but one instance, blood appeared in the acid-pepsin perfusate during the first 2 hours. Perforation occurred 3 times as a result of perfusion with acid-pepsin. This solution always caused ulceration, which usually consisted of 2 large areas of ulceration at the points of contact of the intestinal mucosa and the tips of the cannulae. There were moreover multiple small ulcers throughout the rest of the intestinal segment. Hydrochloric acid alone caused some destruction of the villi, but ulceration was never observed. The addition of either aluminum hydroxide or aluminum phosphate to the acid-pepsin mixture protected the intestine from damage.

The typical microscopic picture after 12 hours' perfusion with acid-pepsin is shown in Figure 1(a). Not only are the mucous membrane and the sub-mucosa destroyed, but part of the circular muscle as well. Both colloidal aluminum hydroxide and aluminum phosphate form a protective coating over the surface of the intestine and prevent ulceration. This is to be expected, since it has been shown in this laboratory that both compounds precipitate pepsin.[1, 2] This is in addition to their buffering action.

TABLE I.
Perfusion of Jejunal Segments.

Date, 1940	Sol. "a" 0.1 N HCl pH 1.2 cc/hr	Sol. "b" 3% pepsin in 0.1 N HCl pH 1.2 cc/hr	Sol. "c" 1 $Al(OH)_3$ in 10 sol. "b" pH 3.5 cc/hr	Sol. "d" 1 $AlPO_4$ in 10 sol. "b" pH 2.0 cc/hr	Duration hrs
August 28	81	82			10½
" 30	91	89	84		12
Sept. 2	85	88	89		12
" 3	120	120	111		10
" 4	96	96		96	5¼
" 5	108	105*		96	12
" 6	123	120		115	10
" 9	118	113		117	12
" 10	112	101*	92		7¾
" 24	96	96*	104		12

*Perforation of loop perfused with acid-pepsin solution.

1 Komarov, S. A., and Komarov, O., *Am. J. Dig. Dis.*, 1940, **7**, 166.

2 Schiffrin, M. J., and Komarov, S. A., to be published.

This method of producing ulceration is similar to some described by other workers, but to the best of the writer's knowledge no acute experiments of this type have been extended over a period of 12 hours and no ulceration or perforation was previously observed. The extremely important rôle of pepsin in the etiology of ulcer is indicated. The mechanism by which aluminum hydroxide and aluminum phosphate protect the intestinal mucosa may be studied *in vivo* by this technic.

We intend to apply the same method of perfusion to other parts of the gastro-intestinal tract.

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Comparative Activity of Naturally Occurring Estrogens on the Infantile Rat Uterus and Vagina.* †

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In a previous report it was shown that there is a distinct difference between estrone and estriol in their respective abilities to cause hypertrophy of the infantile rat uterus and vaginal introitus.[1] These observations have been confirmed and extended by other workers to include estradiol.[2, 3] In this communication we have further extended these comparative studies to include, in addition to estrone, α-estradiol, and estriol, the benzoates of estrone and estradiol and also equilen and equilenin.

The estrogens employed in this study were dissolved in olive oil so that the daily amount administered was always contained in 0.2 cc of oil. Twenty-five-day old female rats were injected subcutaneously once daily for 5 days. Twenty-four hours after the last injection, the animals were sacrificed. Body weight, uterine weight, and vaginal

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1 Dorfman, Ralph I., Gallagher, T. F., and Koch, F. C., *Endocrinology*, 1935, **19**, 33.

2 Marlow, H. W., *Science*, 1936, **84**, 377.

3 Lauson, H. D., Heller, C. G., Golden, J. B., and Sevringhaus, E. L., *Endocrinology*, 1939, **24**, 35.