may be sufficient for inactivation of blood ACTH.

The experimental results reported here are not strictly comparable with those reported by Gemzell *et al.*(3) since the latter analyzed blood from the inferior vena cava. Blood from the abdominal aorta was employed in the present studies. We have confirmed Gemzell *et al.*(3) that blood of the adrenalectomized rat has a greater concentration of ACTH than normal. However, these investigators were unable to detect activity in 448 ml of plasma from intact rats, whereas our data indicate that 12 ml of blood from these animals induce a definite depletion of adrenal ascorbic acid.

*Summary.* 1. The oxycellulose technic for isolation of ACTH from pituitary has been successfully employed to concentrate and quantitatively to measure blood ACTH. The method a) appears to be specific for ACTH since hypophysectomized rat blood induces no adrenal ascorbic acid depletion in the assay animal, b) almost completely recovers ACTH added to hypophysectomized rat blood, c) almost completely recovers endogenous ACTH, d) yields concentrates which are not toxic to the assay animal and e) is reproducible. 2. It is estimated that rat blood, obtained by acute exsanguination of intact animals, contains 2 to 3 mu ACTH per 100 ml, whereas blood obtained under similar conditions from rats bilaterally adrenalectomized for one week contains 10 to 12 mu ACTH per 100 ml.

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## A New Operative Preparation for Production of Peptic Ulcer in the Dog.* (19404)

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Many data have been obtained by previous investigators concerning experimentally induced acid-peptic ulceration of the stomach and juxtapositioned parts of the alimentary canal. However, the methods employed to produce the ulceration are open to serious question. The procedure of duodenal drainage (Mann and Williamson)(1), causes severe nutritional difficulties in the dog leading to inanition. In addition, it has been shown (Storer, Oberhelman, Woodward, and Dragstedt)(2), that gastric secretion is greatly increased by this procedure. We feel that these objections have been satisfactorily overcome by our preparations to be described below. In the human and in the dog most of the secretion of the parietal cells occurs in response to neurogenic (vagal) or hormonal stimulation, the latter arising mainly from the antral mucosa and to a lesser extent from the small intestine. Accordingly, it is not physiologic to evaluate experimentally vagotomy or antrum resection in the dog when an exogenous stimulus to the parietal cells, as histamine, is employed.

We have devised an alternate method of producing experimental peptic ulceration in

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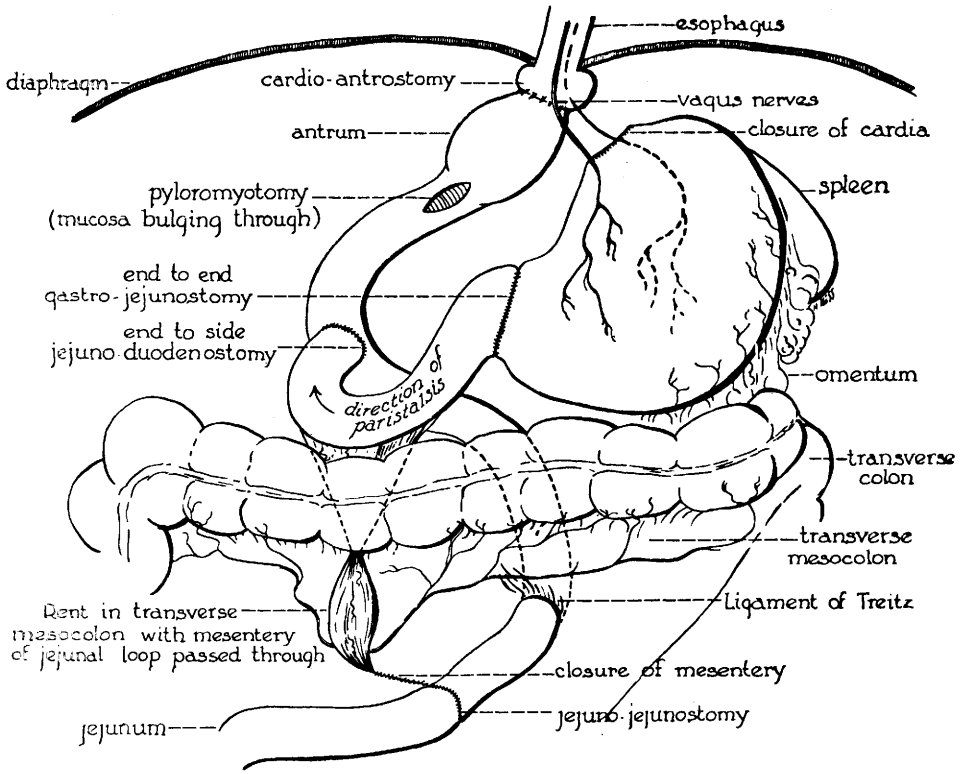


FIG. 1. A 3-phase total parietal cell pouch drained by a peristaltic jejunal fistula into the duodenum. Each of the 3 phases of gastric secretion (vagal, antral, and intestinal) are operating upon the pouch.

the dog and have studied the incidence of ulceration and average survival time in our animals. This method satisfies the following criteria for an acceptable ulcer producing preparation: 1. It must be a method by which ulcers can be produced (preferably rapidly) that will parallel as closely as possible peptic ulceration in man without requiring complicated post-operative care or artificial stimulation in the test animals. 2. It must permit evaluation of therapeutic methods as to their effectiveness in preventing peptic ulcers in these preparations. 3. When ulcer formation has been prevented (by some test procedure), the experimental animal must survive in good condition for prolonged periods of time.

*Experimental methods.* This preparation consists of a total parietal cell pouch drained by an iso-peristaltic jejunal fistula into the second portion of the duodenum. The procedure has been performed on healthy adult mongrel dogs through a left subcostal incision with the dog under nembutal anesthesia. The pouch is formed by dividing the stomach 1 cm distal to the esophagogastric junction and again at the upper border of the antrum. The proximal end of the pouch is closed with a running serosal suture. A jejunal fistula 15 cm in length is procured by transecting the jejunum at 5 and 20 cm distal to the ligament of Treitz. Jejunal continuity is reestablished by end-to-end anastomosis. The fistula is then made ante-colic or retro-colic and anastomosed end-to-end to the distal pouch and end-to-side to the duodenum. In the 3-phase total parietal cell pouch the vagi are preserved to the pouch and the antrum is anastomosed to the remnant of the cardia attached to the esophagus (Fig. 1). In the antral-intestinal phase pouch the vagi are divided and the antrum anastomosed to the cardia as in the 3-phase pouch. In the cephalic-intestinal phase

TABLE I. Influence of Vagotomy, of Antrumectomy, and the Two Combined upon Development of Ulcers in the Dog with a Total Parietal Cell Pouch Drained by a Peristaltic Jejunal Fistula into the Duodenum.

| | 3-phase pouch (cephalic, antral, intestinal) | | | 2-phase pouch (antral, intestinal) | | | 2-phase pouch (cephalic, intestinal) | | | 1-phase pouch (intestinal) | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | No. | % of total | Avg survival, days | No. | % of total | Avg survival, days | No. | % of total | Avg survival, days | No. | % of total | Avg survival, days |
| Total dogs | 16 | 100 | | 10 | 100 | | 9 | 100 | | 11 | 100 | |
| Dogs still living* | 1 | 6 | 136 | 2 | 20 | 82 | 5 | 56 | 56 | 5 | 45 | 87 |
| Dogs dead without ulcer† | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 11 | 106 | 5 | 45 | 37 |
| Dogs dead with ulcer | | | | | | | | | | | | |
| Gastric | 3 | 19 | 9 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 9 | 33 |
| Jejunal | 9 | 56 | 26 | 8 | 80 | 32 | 3 | 33 | 34 | 0 | 0 | 0 |
| Gastric and jejunal | 3 | 19 | 21 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| Total dogs dead with ulcer | 15 | 94 | 21 | 8 | 80 | 32 | 3 | 33 | 34 | 1 | 9 | 33 |

* Includes dogs living 4 weeks or more after operation.
† " " dying " " " " " " " " without ulcer.

pouch the vagi are preserved, but the antrum is excised and the cardia anastomosed end-to-end to the first portion of the duodenum. In the one-phase pouch the antrum is excised and the vagi divided; the cardia is anastomosed to the duodenum as in the cephalic-intestinal phase pouch. The esophagogastric sphincteric mechanism is preserved by leaving a small segment of cardia (usually less than 1 cm) attached to the esophagus. Animals in whom this was not done frequently suffered from continuous post-operative vomiting. Likewise in those dogs with the antrum in continuity pyloromyotomy greatly reduced post-operative vomiting. Retention of food was enhanced by an operative approach via the abdomen rather than through the chest. The division of diaphragmatic fibers about the lower esophagus apparently destroyed at least a part of the normal sphincteric mechanism. Post-operative care of these animals has consisted of subcutaneous fluids on the day of operation, penicillin for 3 days after operation, water as desired, milk on the 3rd day, soft food on the 4th day, and then general kennel rations as tolerated.

*Results.* Vomiting has not been a serious problem after the dogs have become adjusted to eating slowly. The 5 one-phase dogs that are still living an average of 87 days after the operation have lost an average of 10% of body weight. Their stools appear quite normal. Most of our dogs dying of causes other than ulcer have died of intestinal obstruction due to herniation of the small bowel behind the mesentery of the jejunal fistula that was placed in an ante-colic position. We now make all fistulas retro-colic.

Both fistulous and pouch ulcers have been observed, occasionally multiple and in some instances both types in the same animal. The jejunal ulcers typically have occurred just distal to the gastrojejunostomy and have varied in size from discrete ulcers 1 cm in diameter to large ulcerations extending the entire length of the fistula. Death usually resulted from generalized peritonitis subsequent to ulcer perforation. These ulcers have been of an acute nature on the basis of gross pathologic examination when the animal survived only a few days and of a more chronic nature when the animal survived for longer periods. The incidence of ulceration and the average survival times of the dogs in the 4 groups are shown in Table I.

*Discussion.* It appears that dogs are less severely impaired nutritionally by this procedure than by the Mann-Williamson procedure. That the 3-phase pouch is a potent ulcerogenic preparation is attested to by the fact that 94% of these dogs died with ulcer an average of 21 days after operation. Our preliminary results would seem to indicate that antrumectomy in the dog affords greater pro-

tection against the development of ulceration than does vagotomy. Antrumectomy and vagotomy combined appear to give the dog a considerable measure of protection against the development of ulceration. This method of producing peptic ulceration in the dog may have certain advantages over the standard methods that will render it useful for further experimental study of the ulcer problem.

*Summary.* 1. A method for production of experimental peptic ulcer in dogs is presented. Its advantages are reliability, simplicity of post-operative care, rapidity of ulcer development, and survival of animals in good nutritional condition, thus allowing prolonged study in protected animals. The ulcers are produced without extraneous stimulation. 2. Four groups of animals were studied. The effect of vagotomy alone, antrumectomy alone, and vagotomy combined with antrumectomy are evaluated as to incidence of ulcer and period of survival (an indication of the time required for development of ulcer).

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## Cation Adsorption by Alginic Acid in Humans.* (19405)

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The removal of exogenous sodium from the intestinal tract and prevention of its absorption into the body by means of cation exchange resins has offered a new therapeutic approach to the management of the edematous state. In clinical practice, however, the use of these agents has been attended by several undesirable effects(1), including unpalatibility, anorexia, fullness, vomiting, constipation and the potential hazard of sodium depletion and acidosis. The search for substances with similar clinical promise, but without the limitations and disadvantages of the resins has led to the investigation of alginic acid. It is the purpose of this report to describe initial experiences and record laboratory data on the cation adsorbing ability of this agent in humans.

Alginic acid† is a water-insoluble amorphous solid with marked hydrophilic properties which is widely used in the food and pharmaceutical industry as a stabilizing, emulsifying and thickening agent. Chemically the substance is a polymer of anhydro-B-D-mannuronic acid. It is extracted from giant kelp (*Macrocystis pyrifera*) and is closely related to cellulose and pectic acid. Each anhydromannuronic acid residue contains one free carboxyl group which is responsible for its theoretical cation adsorption capacity of 5.7 meq. per g. *In vitro* studies(2) have shown that sodium adsorption by alginic acid is primarily dependent on hydrogen ion concentration of the medium. In unbuffered solutions of sodium chloride, alginic acid combined with less than 1 meq. sodium/g and this was not appreciably influenced by changes in sodium concentration. During the adsorption process liberation of hydrogen ion lowered the pH of the medium from neutrality to approximately 3. However, when equilibrated with sodium ion in solutions buffered to approximately physiological pH of 7.6 the sodium adsorption per gram of alginic acid rose to 4.2 meq. These *in vitro* studies suggested that alginic acid had cation adsorption capacities similar to synthetic resins. Feeding experiments in ani-

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