

vents ATP from hydrolyzing and thus deprives the arterial tissue of the energy which is released from the high energy phosphate bond. If through the decomposition of ATP by its enzyme ATPase, tonus and constriction of the artery are maintained, it is possible that a drug which acutely relaxes the artery may do so by interfering with the ATPase activity of the tissue. Studies aimed at clarifying this postulate are in progress.

**Summary.** The ATPase activity of the vascular system of the dog has been studied. It has been shown that the enzyme content of the different arteries enjoys wide variation. The venous system does not contain the enzyme. ATPase activity of the aorta of the rat was not influenced by age or captivity. The aortic ATPase activity of various species of animals is presented.

1. DuBois, K. P., and Potter, V. R., *J. Biol. Chem.*, 1943, v150, 185.
2. Krantz, John C., Jr., Carr, C. Jelleff, and Bryant, Harold H., *J. Pharm. Exp. Therap.*, 1951, v102, 16.
3. Bell, Frederick K., Carr, C. Jelleff, and Krantz, John C., Jr., *Anal. Chem.*, in press.
4. Griswold, B. L., Humoller, F. L., and McIntyre, A. R., *Anal. Chem.*, 1951, v23, 192.
5. Lowry, O. H., and Lopez, J. A., *J. Biol. Chem.*, 1946, v162, 421.
6. Swanson, M. A., *J. Biol. Chem.*, 1951, v191, 577.
7. Kováts, J., *Nature*, 1949, v163, 606.
8. Csaspo, A., *Am. J. Physio.*, 1950, v160, 46.
9. Baló, J., Banga, I., and Josepovits, Gy., *Z. f. Vitamin-, Hormon- und Fermentforschung*, 1948-49, v2, 1.

Received May 26, 1952. P.S.E.B.M., 1952, v80.

### Gastric Secretion in Heidenhain Pouches Following Section of Vagus Nerves to Main Stomach. (19612)

E. H. STORER, E. J. SCHMITZ, L. R. SAUVAGE, E. A. KANAR, C. H. DIESSNER, AND H. N. HARKINS.

*From the Department of Surgery, University of Washington School of Medicine, and Veterans Administration Hospital, Seattle, Wash.*

The cephalic phase of gastric secretion is nervous in origin and is mediated via the vagus nerves to the stomach. Apparently the gastric phase is humoral in origin and is mediated by "gastrin" which is elaborated by the mucosa of the gastric antrum. A Heidenhain pouch is a separated, vagally denervated, greater curvature, gastric pouch. Thus, the exocrine secretion from this pouch is stimulated, probably exclusively, by the humoral phases of secretion, *i.e.*, antral and intestinal phases. Any observed change in Heidenhain pouch secretion produced by sectioning the vagi to the main stomach may be presumed to reflect a proportional change in the circulating chemical substances (hormone(s) and secretagogues) which are responsible for the chemical phases of secretion.

Although it is well known that the cephalic and gastric secretory mechanisms can function independently of the other, it is not yet es-

tablished whether the normal function of either is impaired by the absence of the physiological activity of the other. Grossman(1) recently stated "... that vagal stimuli and gastrin can act together in stimulating gastric secretion is certainly in accord with observations, in the sense that any two different stimuli can act together additively. However, the view that either of these two mechanisms for secretion regularly participates in producing a response to the other is open to serious question." Evidence is accumulating(2-4) that the gastric secretory response to vagal stimulation is decreased when the antral mucosa is defunctionalized by cocaineization, vascular impairment, or excision. The conclusion has been advanced that the cephalic phase is actually neurohumoral and not solely neural as formerly held. There is much less evidence of participation of the vagi in the gastrin mechanism. To our knowledge, no quantita-

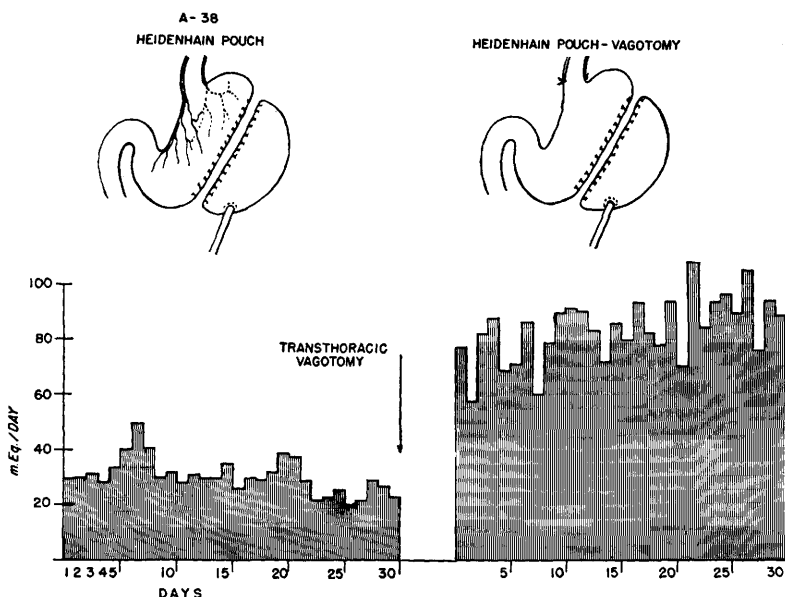


FIG. 1. Graphic representation of 30-day control period (on left) of free hydrochloric acid collection (expressed in mEq.) from Heidenhain pouch of Dog A-38 as compared to similar period (on right) after sectioning the vagus nerves to the main stomach.

tive studies have been done which shed much light on the relationship of the vagi to the physiological function of the antral mucosa. However, Harkins and Sauvage(5) showed that Banthine in doses which completely inhibited the gastric secretory response to sham feeding did not significantly change the total 24 hour secretion from Heidenhain pouches. This investigation determines only the total change in Heidenhain pouch acid secretion produced by sectioning the vagi to the main stomach and does not permit an analysis of the factors involved.

**Methods.** Large Heidenhain pouches, drained by a water-tight nylon cannula into football bladders for collection purposes, were made in the usual manner. After full recovery from surgery (usually two weeks) quantitative 24 hour pouch secretion collections were begun. These collections were considered as valid only if the animal maintained the following conditions: (1) constant body weight, (2) normal serum chlorides, (3) constant daily food intake. After at least 28 days of valid collections as a standard Heidenhain pouch, a transthoracic bilateral vagus section was done. After a recovery period, collections were resumed and 28 or more valid days of secretion collected according to the criteria

of the control period. Barium radiographic studies of the gastric emptying time were made before and after vagus section.

**Results.** The accompanying illustrated graph (Fig. 1) and Table I summarize the quantitative effect of section of the vagus nerves to the main stomach on the acid secretion from Heidenhain pouches. There was a definite increase in the secretion of free hydrochloric acid as expressed in milli-equivalents per 24 hours following the vagus section. This increase in secretion was maintained throughout the 28 day test period of collection of total 24 hour samples of pouch secretion. The x-ray studies showed that the passage of barium through the stomach was markedly delayed by vagus section.

**Discussion.** If the vagi to the gastric antrum are important in the release of gastrin, similar to the direct effect of these nerves on the parietal cells, one would expect section of the vagus nerves to decrease such gastrin release. This possible depressant role has been overshadowed in our experiment so that section of the vagus nerves has produced the opposite effect, *i.e.*, an increase in the chemical phase of acid secretion. Following the vagus section, the time required for animals to empty a barium meal from the stomach is prolonged

TABLE I. Effect of Transthoracic Vagotomy on the Quantitative Acid Secretion from Heidenhain Pouches.

|      | Before,<br>mEq. | After,<br>mEq. | %<br>increase |
|------|-----------------|----------------|---------------|
| A-38 | 46              | 88             | 92            |
| A-69 | 14              | 47             | 236           |
| A-71 | 20              | 105            | 425           |
| Avg  | 27              | 80             | 196           |

significantly. Thus, if food remains in contact with the gastric antrum for a longer period after vagus section than before, it is reasonable to assume that the antral phase of gastric secretion may be increased.

*Conclusions.* In the dog, section of the

vagus nerves to the main stomach causes a marked increase in the quantitative 24 hour acid secretion from Heidenhain pouches.

1. Grossman, M. I., *Physiol. Rev.*, 1950, v30, 33.
2. Uvnas, B., *Acta physiol. scandinav.*, 1942, v4, suppl. 13.
3. Linde, S., *Acta physiol. scandinav.*, 1950, v21, suppl. 74.
4. Lim, R. K. S., and Mozer, P., *Fed. Proc.*, 1951, v10, No. 1, 84.
5. Harkins, H. N., and Sauvage, L. R., *Surgical Forum: Clinical Congress of Am. Coll. of Surgeons* 1951, Philadelphia, W. B. Saunders Co. 1952, pp. 48-53.

Received February 26, 1952. P.S.E.B.M., 1952, v80.

### Intrapleurally Injected Colloidal Au<sup>198</sup> and Growth and Implantation of Free Tumor Cells in Pleural Exudate.\* (19613)

HORACE GOLDIE, HAROLD D. WEST, BARBARA R. JEFFRIES, AND CHARLES H. BUTLER.

*From the Cancer Research Laboratories, Meharry Medical College, Nashville, Tenn.*

Several authors(1) have reported clinical trials with intrapleurally injected colloidal Au<sup>198</sup> in the treatment of malignant pleural effusions and thoracic neoplasms. However, to the best of our knowledge, no attempt has been made to treat similar conditions in experimental animals. Previously(2,3) we have described a method of testing the effect of radioisotopes on free tumor cells in the peritoneal fluid and on their implants in the abdominal wall. A similar method provided a tool for assaying the effect of intrapleurally injected colloidal Au<sup>198</sup> on free tumor cells in pleural cavity. The results of this assay are reported below.

*Material and methods. A. Technic of tumor cell inoculation.* Requisite numbers (1 to 15 millions) of tumor cells (Sarcoma 37 in CFW mice, carcinoma in C3H and melanoma in dba)<sup>†</sup> were inoculated (in a volume of 0.2

to 0.5 ml) into the right phrenico-costal sinus (see details in (4)). Colloidal Au<sup>198</sup> was injected in the same area a few days later. *B. Treatment.* Colloidal Au<sup>198†</sup> was diluted with 0.85% NaCl solution to the concentration of 0.4 mc per cc, and doses of 0.5 ml of this solution were used. For each tumor, 3 series each of 20 mice were inoculated with tumor cell suspensions. On the 5th or 6th day after inoculation, 10 mice of each series were injected intrapleurally with 0.2 mc of Au<sup>198</sup>, while 10 mice were kept untreated as controls. Three or four days later the pleural exudate was withdrawn from at least 5 mice of each group and assayed as described below. On account of slow growth of melanoma cells, mice inoculated with such tumor cells were treated on the 10th day and sacrificed on the 20th day. *D. Assay of the results.* Stained specimens of the pleural exudate from treated mice and from controls were examined for morphological characteristics of tumor cells and for percentage of their mitoses. In a few animals of each group this microscopic assay of tumor cells was supplemented by biological assay: failure of inoculation of pleural exudate (0.1 ml) from treated mice to induce tumors

\* This work was carried out under Contract with the Division of Biology and Medicine, U. S. A. E. C.

† CFW mice obtained from Carworth Farms, New City, N. Y. C3H and dba obtained from Roscoe Jackson Memorial Laboratory, Bar Harbor, Me.

‡ Colloidal Au<sup>198</sup> obtained from Dr. D. L. Tabern, Abbott Laboratories, N. Chicago, Ill.