or relatively pure drugs that may be used therapeutically not on the basis of results in the animal, but rather on the basis of response actually seen in the human uterus. Secondly, such observations may provide a fairly reliable index for clinicians in their use of mixed estrogens. It becomes apparent that such drugs may have a wide range of biologic potency milligram for milligram depending entirely upon content of the more active estrogenic substances. In addition, a rational basis is provided for establishing therapeutically effective dosage levels of the various estrogenic preparations and the modification of these levels under certain circumstances, depending upon whether one is dealing with recently or remotely stimulated uteri.

*Summary.* Estradiol benzoate (as a standard), alpha estradiol, estrone, and beta estradiol preparations were bioassayed using withdrawal bleeding from previously stimulated uteri of postmenopausal women as an assay end point. Alpha estradiol and estrone were equally effective in causing withdrawal bleeding, and each was about two-thirds as potent as estradiol benzoate. Beta estradiol was found to be altogether ineffective in a total dosage of 45 mg given over a 3 week period.

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## Effect of Antrum Transplantation on Gastric Secretion in Experimental Animals.* (17784)

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In previous studies from this laboratory, the profound reduction in gastric secretion of Pavlov pouch dogs produced by removal of the antrum of the stomach has been recorded(1). In the present experiments, quantitative collections of gastric juice from Pavlov and Heidenhain pouch dogs and from animals with totally isolated stomach preparations have been made for control periods lasting several weeks. The antrum of the stomach has then been separated from the fundus, using great care not to interfere with its blood supply, and subsequently transplanted as a diverticulum into the duodenum and into the colon. The results have demonstrated quite conclusively that when the antrum is excluded from the gastro-intestinal tract so that it does not come in contact with food, it exerts little or no effect on gastric secretion. When it is transplanted into the duodenum, a very profound augmentation in gastric secretion results, and this is even more marked when the antrum is transplanted into the colon.

(1) *The Effect of Exteriorization of the Antrum of the Stomach on Gastric Secretion in Pavlov Pouch Dogs.* Pavlov pouches were prepared in 3 normal dogs and quantitative collections of the gastric secretion from the isolated pouches were made for control periods of several weeks by means of the tight-fitting nylon plastic cannulas previously described (2). The antrum of the stomach was then carefully separated from the fundus and the pylorus transected. The fundus was anastomosed to the side of the second portion of the duodenum. The proximal end of the antrum was infolded and closed and the pyloric portion brought to the surface as a fistula. Care

* This work was aided by a grant from the Division of Research Grants and Fellowships of the National Institutes of Health, United States Public Health Service.

1. Woodward, E. R., Bigelow, R. R., and Dragstedt, L. R., PROC. SOC. EXP. BIOL. AND MED., 1948, v68, 473.

2. Dragstedt, L. R., Haymond, H. E., and Ellis, J. C. *Surg., Gynec., and Obst.*, 1933, v56, 799.

was taken not to interfere with the blood supply to the antrum. In all three animals, exteriorization of the antrum in this fashion produced a marked reduction in the secretion of gastric juice from the Pavlov pouch comparable to that secured by antrum resection. In Dog 1, the average 24 hour output of hydrochloric acid decreased from 22 to 15 milliequivalents; in Dog 2 from 73 to 17 milliequivalents; and in Dog 3 from 51 to 18 milliequivalents in a 24-hour period.

(2) *Effect of Transplantation of the Antrum into the Duodenum on Gastric Secretion in Dogs Provided with A Vagus Denervated Total Isolated Stomach.* Total isolated stomach pouches with the vagus nerves divided after the method of Lim and Ivy(3) were prepared in 4 dogs. Quantitative collections of gastric juice from the isolated stomach were secured for control periods of 2 to 3 weeks. The antrum was then excised from the isolated stomach and transplanted as a diverticulum into the side of the duodenum, taking care not to interfere with its blood supply. In all cases, the transplantation of the antrum into the duodenum produced a marked augmentation of gastric secretion by the isolated fundus. In Dog 1, the average 24 hour output of hydrochloric acid by the isolated stomach increased from 2 to 77 milliequivalents; in Dog 2 from 5 to 51 milliequivalents; in Dog 3 from 7 to 120 milliequivalents; and in Dog 4 from 9 to 45 milliequivalents. It is thus evident that the antrum has little or no effect on gastric secretion when it is present in the isolated stomach and is subjected only to the contact with gastric juice. On the other hand, marked augmentation of secretion was produced when this antral mucosa came in contact with the duodenal content.

(3) *Effect of Transplantation of the Antrum of the Stomach into the Colon on Gastric Secretion in Pavlov Pouch Dogs.* In 3 animals Pavlov pouches were prepared and the control secretion determined. The antrum was then exteriorized as in the experiments described in paragraph one. After a control period, the exteriorized antrum was then transplanted into the middle of the transverse colon as a diverticulum and its effect on gastric secretion determined. In Dog 1, the average 24 hour output of hydrochloric acid from the Pavlov pouch under control conditions was 22 milliequivalents per 24 hours. With the antrum exteriorized, the average output fell to 15 milliequivalents per day. When the antrum was transplanted into the colon, the output of hydrochloric acid by the Pavlov pouch increased to 56 milliequivalents per day. In Dog 2, the average output of hydrochloric acid from the Pavlov pouch during the control period was 73 milliequivalents per day. When the antrum was exteriorized, the output fell to 17 milliequivalents per day. When the antrum was transplanted into the colon, the average secretion increased to 96 milliequivalents per day. In Dog 3, the average 24 hour output of hydrochloric acid from the Pavlov pouch during the control period was 51 milliequivalents per day. When the antrum was exteriorized, this fell to 18 milliequivalents, and when the antrum was subsequently transplanted into the colon, it increased to 120 milliequivalents.

(4) *Effect of Transplantation of the Antrum of the Stomach into the Colon on Gastric Secretion in Total Pouch Dogs.* Four dogs were prepared with totally isolated stomach pouches with the vagus nerves divided. After a control period of collection of gastric secretion, the antrum was separated from the isolated pouch and transplanted into the middle of the transverse colon as a diverticulum. In Dog 1, the average 24 hour output of hydrochloric acid from the isolated stomach during the control period was 20 milliequivalents, and this increased to 135 milliequivalents when the antrum was transplanted into the colon. In Dog 2, the average output of hydrochloric acid during the control period was 5 milliequivalents per day, and this increased to 75 milliequivalents when the antrum was transplanted into the colon. In Dog 3, the average output of hydrochloric acid during the control period was 13 milliequivalents per day, and this increased to 143 milliequivalents when the antrum was transplanted into the colon. In Dog 4, the average output of hydrochloric acid during the control period was 75

3. Lim, R. K. S., Ivy, A. C. and McCarthy, J. E. *Quart. J. Exp. Physiol.*, 1925, v15, 13.

milliequivalents per day, and this decreased to 19 milliequivalents when the antrum was exteriorized. When subsequently the antrum was transplanted into the duodenum, the average output of hydrochloric acid increased to 65 milliequivalents per day.

*Conclusions.* 1. Exteriorization of the antrum of the stomach produces a marked decrease in the secretion of Pavlov pouch dogs comparable to that secured by excision of the antrum. When this exteriorized antrum is subsequently transplanted into the duodenum or into the colon, a marked stimulation of gastric secretion is produced.

2. Transplantation of the antrum of dogs with totally isolated stomach pouches into the duodenum or into the colon produces a marked increase in gastric secretion. These findings support the view that the antrum mucosa is a specific internal secreting organ distinct in function from the mucous membrane of the stomach or duodenum.

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## Effect of Cortisone* on Experimental Fractures in the Rabbit.† (17785)

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It has been observed that wounds of patients treated with adrenocorticotrophic hormone (ACTH) fail at times to heal normally(1). These observations prompted an experimental evaluation of the action of cortisone on standard skin defects induced in rabbits' ears. It was established that cortisone caused a striking depression of all elements of connective tissue, including formation of new blood vessels, and produced evidence of hyperadrenalism as manifested by depression of circulating eosinophiles and mild hyperglycemia(2). In the light of these studies, it seemed of interest to observe the effect of this adrenal steroid on other mesenchymal tissues. Consequently the effect of cortisone on callus formation was investigated and the results are reported in the following experiments.

*Methods. Animals.* Healthy adult laboratory rabbits of mixed breeds and sexes weighing between 2.6 and 3.2 kg were used.

*Method of Fracture.* Under nembutal and ether anesthesia the right femur was fractured by a sharp blow with a mallet in the midshaft without breaking the skin.

*Methods of Pathological Study.* Animals were sacrificed with nembutal or the intracardiac injection of air. The injured extremities were removed *in toto,* frozen, and then split through the fracture site with a band-saw. Both longitudinal and transverse sections were taken through comparable areas of the fracture site. Sections of liver and adrenals were also made. Tissues were fixed in 80% alcohol, chilled acetone and alcohol-formalin, and were imbedded in paraffin. Sections of the fracture site were stained with the following technics: Hematoxylin and chlorazol fast pink B; Tol-

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2. Ragan, C., Howes, E. L., Plotz, C. M., Meyer, K. and Blunt, J. W., PROC. SOC. EXP. BIOL. AND MED., 1949, v72, 718.