

titities of ACTH were released from the kidney of the stressed dog. In fact, in 5 of 6 dogs, there was more activity in arterial than in renal venous blood. It therefore seems unlikely that any significant renal release of ACTH occurred following surgical stress or hemorrhage.

Summary. The amount of ACTH that could be extracted from kidneys of surgically stressed normal dogs was 0 and 4 mU/kidney in 2 lots tested. Seventy-two percent of the ACTH added to half of one batch of kidneys was recovered by the extraction technic used. On injection into hypophysectomized dogs, renal venous plasma from surgically stressed or hemorrhaged dogs had no more adrenal cortical stimulating activity than peripheral arterial plasma collected at the same time. These findings do not support the hypothesis that significant amounts of ACTH are released from the kidneys into the circulation during surgical stress or hemorrhage.

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Response of Rats with Gastric Fistulas to Injection of Gastrin.* (28123)

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This study was done to determine whether rats with gastric fistulas would secrete acid in response to injection of extracts containing gastrin. It was found that they did respond and a comparison was made between gastrin and histamine as secretory stimulants.

Methods. Gastrin free of histamine was prepared from the mucosa of the pyloric gland area of the stomachs of hogs by a method previously described(1). Doses of gastrin are expressed as grams of mucosa from which the extract was derived. The protein plus polypeptide content of the gastrin extract was 1.1 mg per gram wet weight of mucosa. A single pooled sample of gastrin was used for all the studies reported here.

Ampules containing 1 mg histamine phosphate per ml were used. Doses of histamine are expressed as mg of this salt.

Injections of gastrin or histamine were given subcutaneously.

Gastric fistulas were prepared by the method of Lane *et al.*(2) in 8 male rats of the Long-Evans strain weighing between 336 and 452 g. Rats were first used for testing 1 week after surgery.

Before each test the rats were fasted for 18 hours by placing them in a restraining cage (3). Water was allowed during this period but was removed during testing. The rats remained in the restraining cages during the tests. Hypodermic needles (22 gauge) were inserted under the skin at the beginning of the test and were left in place until injections had been given. The cannulas were opened; the stomach was flushed repeatedly with water

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and allowed to drain for 1 hour; 2 30-minute basal collections were made; the test substance was injected subcutaneously; and collections were continued at 30-minute intervals for 4 hours. A rubber tube led from the cannula to the graduated test tube collecting the juice. A hypodermic needle inserted into the rubber tube served as an air vent and allowed flushing with air to clear the tube.

The volume of each sample was measured and the concentration of acid determined by titrating a measured portion with 0.2 N NaOH using phenol red indicator. Mixing during titration was accomplished by bubbling nitrogen through the sample. Acid output was expressed as μeq per 30 minutes. The peak rate of secretion was taken as the highest output of acid during any 30-minute period after injection.

An interval of at least 2 days elapsed between tests on any one rat. Each rat had 2 tests with each dose of gastrin or histamine and 3 tests in which 1 ml 0.9% sodium chloride solution was injected subcutaneously to serve as a control.

Results. Graded doses of gastrin ranging from 1.25 to 10 g gave graded responses (Fig. 1 and 2). Both peak rate and duration of secretion increased as dose was increased. Graded doses of histamine phosphate ranging from 0.5 to 4 mg also gave graded responses but at a lower level than those obtained with gastrin (Fig. 2 and 3). In confirmation of Lane *et al.*(2) we found that maximal peak rates were attained with 2 mg histamine phosphate; 4 mg did not produce higher mean responses. The maximal mean peak rate for histamine (149 $\mu\text{eq}/30\text{ min}$) was significantly lower ($p < 0.01$) than the mean peak rate for the lowest dose of gastrin used, 1.25 g, (207 $\mu\text{eq}/30\text{ min}$) and was less than one-half the mean peak rate for the highest dose of gastrin, 10 g, (304 $\mu\text{eq}/30\text{ min}$).

Discussion. Gastrin extracts have been shown to be capable of stimulating gastric secretion in man(4), dogs(4) and cats(5). We have found no previous report of studies of the action of gastrin in rats.

In dogs with Heidenhain pouches we(1) found that maximal secretory response to histamine was almost twice as great as the maxi-

mal secretory response to gastrin. In subsequent unpublished studies we have found that in dogs with gastric fistulas (vagal innervated) the maximal responses to histamine and gastrin are equal. The present study shows that in rats with gastric fistulas the maximal secretory response to gastrin is con-

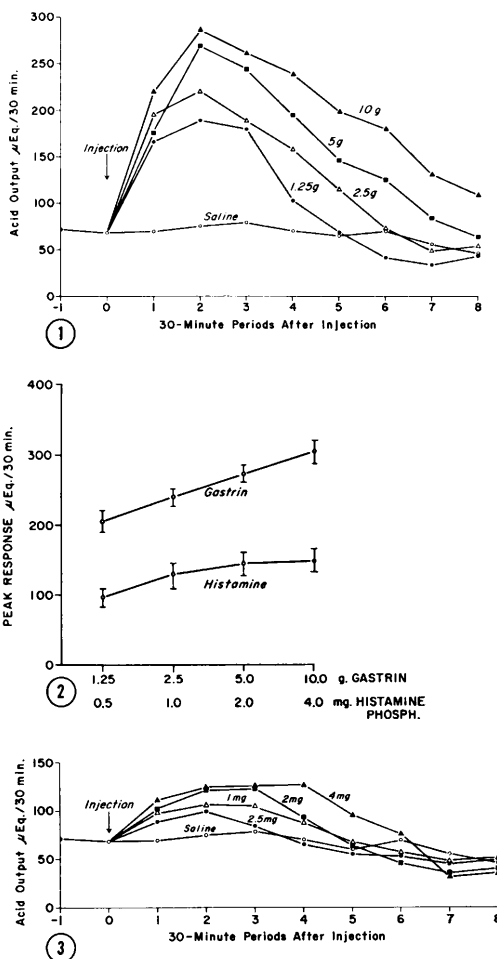


FIG. 1. Mean acid output during 30-min periods before and after injection of various doses of gastrin or of a control injection of saline. For gastrin each point is the mean of 16 tests on 8 rats; for saline, 24 tests on 8 rats.

FIG. 2. Means and standard errors of peak rates of secretion in response to various doses of gastrin or of histamine. The peak occurred in the first to third 30-min period after histamine; median, second 30-min period. The peak occurred in the first to fourth 30-min period after gastrin; median, second 30-min period.

FIG. 3. Mean acid output during 30-min periods before and after injection of various doses of histamine phosphate or of control injection of saline. For histamine each point is mean of 16 tests on 8 rats; for saline, 24 tests on 8 rats.

siderably higher than to histamine. The relation between maximal response to gastrin and to histamine thus varies both with species and type of gastric preparation studied. The large discrepancies between maximal response to gastrin and to histamine in some of these test objects are difficult to reconcile with the hypothesis that histamine is the final common mediator for stimulation of gastric secretion(6).

Both basal and histamine-stimulated secretion were higher in the present study than in that reported by Lane *et al.*(2), probably because of the higher body weights of our rats. The mean basal rate was 140 μ eq per hour in the present study and 58 μ eq per hour in the study of Lane *et al.* Similarly, the output of acid during the first hour after subcutaneous injection of 2 mg histamine phosphate was 221 μ eq per hour in the present study and 187 μ eq per hour in the study of Lane *et al.* The higher secretory rate in the present study could be accounted for almost entirely by

higher volume rates. The concentration of acid was not significantly different from that reported by Lane *et al.*

Summary. Gastrin prepared from the stomach of hogs stimulated secretion of acid when injected subcutaneously into rats with gastric fistulas. The highest rate of secretion attained with gastrin was more than double the maximal rate in response to histamine.

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Retention of Strontium, Calcium, and Phosphorus in Human Infants. (28124)

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Radioactive strontium produced by tests of nuclear weapons reaches the human population primarily by contamination of the diet. The level of long-lived strontium 90 to be attained in the population depends mainly on 2 factors: the strontium 90 to calcium ratio of the total diet, and the comparative retention of the two substances in the body.

The differential behavior of strontium and calcium in biological systems has been expressed quantitatively by Comar *et al.*(1) as the Observed Ratio (OR):

$$\text{OR}_{\text{sample / precursor}} = \frac{\text{Sr/Ca of sample}}{\text{Sr/Ca of precursor}}.$$

OR_{body / diet} values for adults of most mammalian species including man have been determined by a variety of experimental meth-

ods to range from 0.2 to 0.5 with most values falling near 0.25(2). For example, extensive analyses of human bones and diets for stable strontium and calcium have given an average population value of OR_{body / diet} = 0.25 in the United Kingdom(3); Spencer *et al.*(4) in studies with 16 adult cancer patients using radiostrontium and radiocalcium as double tracers found a mean OR_{body / diet} of 0.29. Thus, there is consistently in adults about a 4-fold discrimination against strontium in favor of calcium in the passage of these 2 elements from the diet to bone.

Early studies of factors that might affect the differential behavior of strontium and calcium indicated that substances which increased gastrointestinal absorption of alkaline earths tended to decrease the discrimination