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Failure of Histamine and "Gastrin" to Provoke Gastric Secretion in Monkeys with Anacidity.

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In the course of gastric analysis upon healthy Rhesus monkeys, it was found that 3 of 12 monkeys failed to secrete free hydrochloric acid following a meal, an alcoholic test meal, and also subcutaneous injections of histamine in dosages up to one milligram.

Since these animals were not responsive to histamine, it was thought that they might respond to "gastrin" or an extract of pyloric mucosa; and if so, we would have proof that "gastrin" and histamine are not identical[1] and also that the anacidity of the 3 monkeys is due to the absence of the "gastrin" mechanism.

Gastric analysis was performed upon 12 healthy Rhesus monkeys *(Macaca mulatta)* which had been fasted for 24 hours. A Rehfuss tube (minus the olive) was passed into the stomach and the fasting contents were removed; the stomach was washed with distilled water and emptied. The monkeys then each received 0.5 mg. histamine (ergamine acid phosphate) subcutaneously. If free acid failed to appear in the gastric samples, the dosage of histamine was increased to 1.0 mg. Gastric samples were taken 45 to 60 minutes after each injection and analyzed for free acid (p-dimethylamino-azobenzene) and bile (naked eye). "Gastrin" extracts of pyloric mucosa (pig) were prepared after the method of Keeton and Koch.[2] The quantity of "gastrin" equivalent to one mg. of histamine was determined by subcutaneous injection in a dog with a pouch of the whole stomach.[3] The vaso-depressor activity of the "gastrin" as compared to histamine was determined by intravenous injection in the dog.

Hemoglobin, hematocrit and red blood cell determinations were made on all of the monkeys.

The viscid, mucoid fasting contents of the stomach were scanty, never contained free acid and but little total acid.

None of the monkeys secreted free acid in response to 7% alcohol or to a meal of farina gruel and boiled potatoes.

Six out of 12 monkeys failed to develop free acid in their gastric

[1] Sacks, Ivy, Burgess and Vandolah, *Am. J. Physiol.*, 1932, **101**, 331.

[2] Keeton and Koch, *Am. J. Physiol.*, 1915, **37**, 481.

[3] Lim, Ivy and McCarthy, *Quart. J. Exp. Physiol.*, 1925, **15**, 13.

juice 45 to 60 minutes after subcutaneous injections of 0.5 mg. histamine. Three out of 12 monkeys (Nos. 5, 10, 12) showed no free acid when the dosage of histamine was raised to 1.0 mg.

Two cc. of the "gastrin" solution given subcutaneously resulted in a stimulation of gastric secretion in the dog with a pouch of the whole stomach quantitatively similar to 1.0 mg. histamine. One cc. of the "gastrin" solution given intravenously had a vaso-depressor action in the dog quantitatively similar to 0.5 mg. histamine.

Five out of 12 monkeys failed to show free gastric HCl following 1.0 cc. of "gastrin" solution. The same 3 monkeys (Nos. 5, 10, 12) that failed to respond to 1.0 cc. histamine also failed to respond to 2.0 cc. of the "gastrin" solution.

In the monkeys showing anacidity the gastric secretions were scanty (2 cc.), thick and viscid, resembling the fasting secretion.

The blood studies showed that none of the monkeys were anemic at the time these studies were made.

If "gastrin" and histamine are different and if "gastrin" rather than histamine is the gastric secretory hormone, one might expect a stimulation of gastric secretion in the monkeys refractory to histamine. A positive response to "gastrin" and a negative response to histamine would have been very significant. Since a positive response to "gastrin" was not obtained, the parietal cells of the 3 anacid monkeys are refractory to all ordinary stimuli. These results add an indirect point of evidence supporting the conclusion of Sacks, Ivy, *et al.*,[1] that histamine is the sole gastric secretory excitant in acid extracts of pyloric mucosa.

Summary and Conclusions. 1. Six out of 12 Rhesus monkeys failed to secrete free acid in their gastric juice 45 to 60 minutes after subcutaneous injections of 0.5 mg. histamine while 5 out of 12 failed to respond to 1.0 cc. of a preparation of "gastrin". 2. Three out of 12 monkeys were refractory to 1.0 mg. of histamine and to 2.0 cc. of the "gastrin" preparation. 3. The "gastrin extracts" of hog's pyloric mucosa did not contain a substance capable of stimulating acid gastric secretion other than histamine, both in the normal and anacid monkeys. 4. None of the 12 monkeys secreted free acid in the gastric juice in response to 7% alcohol or to a meal of farina gruel and boiled potatoes.