Fasting Acid Output and Plasma Gastrin in Conscious Monkeys (36247)

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In a mixed group of human subjects, an inverse relationship has been demonstrated between serum gastrin concentration and both basal and histamine stimulated gastric acid output (1). These experiments were designed to examine the role of circulating gastrin in the fasting acid secretion of conscious monkeys. Similar to man, the rhesus monkey (*Macaca mulatta*) possesses a fasting acid scretion. Adaptation to chronic restraint in a primate chair permits repeated gastric secretory studies under reproducible conditions.

Methods. Five male macaques (4 to 7 kg) were equipped with a gastric cannula and an indwelling polyvinyl catheter in the vena cava. The monkeys were adapted to chronic restraint in primate chairs and housed within individual booths. Exepriments were begun 1 month after operation and placement in the primate chair.

Experiments were conducted after an overnight fast of at least 16 hr. Gastric juice was collected through a polyethylene catheter connected to pump suction at a negative pressure of 2 mm Hg. Acid concentration was determined by titration to pH 7.0 electrometrically. Five milliliter blood samples were collected in a heparinized syringe for the determination of plasma gastrin by the radioimmunoassay technique (2). Plasma gastrin levels have been shown to be similar to serum gastrin levels (3) and were used here so that the red cells could be returned to the monkey at the end of the experiment after suspension of the red cells in 0.9% saline. Fasting secretion was determined by discarding the first 15 min collection period to rid the stomach of overnight secretions, following which, the next two 30 min periods were collected; their sum represented the fasting acid output. The fasting plasma gastrin was collected at the end of the first 30 min collection ($n = 84$), while, on occasion, the plasma gastrin was obtained with the cannula closed ($n = 17$).

The maximal histamine response (MHR) was determined on different days by exploring the dose range of 0.02 to 0.08 mg/kg/hr of histamine infused intravenously (calculated in terms of histamine diphosphate). Histamine acid phosphate (Eli Lilly & Co., Indianapolis, IN) was diluted in 0.9% saline and was infused at the constant rate of 25 ml/hr by pump. The concentration of the solution was varied to deliver the appropriate dose. The first 15 min collection was discarded; and the following four 10 min periods were taken as the response to that dose of histamine. The dose was then doubled; and the process was repeated.

Results. Table I lists the data obtained in five monkeys. Fasting acid output varied from 0.25 ± 0.04 to 0.75 ± 0.14 mEq/hr (mean ± SE) while the maximal secretory response to histamine varied from 2.32 ± 0.13 to 9.39 ± 0.15 mEq/hr. The "F" test demonstrates a greater variation among monkeys than within each monkey, both in fasting acid secretory rates ($p < .001$) and maximal acid secretory rates ($p < .001$). Fasting acid secretion tended to increase with an increasing MHR, but this finding was not significant. Plasma gastrin levels varied from 66.18 ± 6.35 to 99.13 ± 8.93 pg/ml. Plasma gastrin levels among the group were similar except for monkey He, who demonstrated the highest fasting plasma gastrin (Table I). The levels of circulating gastrin are similar to those for other species, including man, which have been determined by the radioimmunoas-

TABLE I.[a]

	Fasting acid output (mEq/hr)	Maximal histamine response (mEq/hr)	Fasting gastrin (pg/ml)
He	0.250 ± 0.041 (38)	2.32 ± 0.13 (9)	99.13 ± 8.93 (23)
J	0.378 ± 0.048 (36)	3.33 ± 0.16 (9)	78.64 ± 5.93 (33)
G	0.424 ± 0.057 (21)	9.39 ± 0.15 (2)	66.18 ± 6.35 (22)
Ha	0.740 ± 0.063 (37)	5.20 ± 0.26 (11)	74.43 ± 7.48 (23)
F	0.755 ± 0.145 (20)	5.75 ± 0.19 (9)	

[a] Values represent mean ± SE (no. of expts.).

say technique in this laboratory (4).

Paired collections of fasting acid output and plasma gastrin concentrations were obtained in 84 tests in four monkeys. Plasma gastrin concentration was plotted against acid output and regression lines were fitted to the data for each monkey. No statistical correlation was demonstrated in three. Monkey He, however, showed a significant inverse relationship between plasma gastrin and fasting acid output (Table II).

In monkey He, acid secretory rates less than 0.3 mEq/hr were associated with a higher plasma gastrin compared to plasma gastrin levels with acid secretory rates greater than 0.3 mEq/hr ($p < .01$). The other three monkeys showed no statistical difference in plasma gastrin, when separated into these two ranges of acid output. At secretory rates > 0.3 mEq/hr, monkey He showed plasma gastrin levels in the range of the other monkeys (Table III).

Discussion. The level of circulating gastrin is not the prime determinant of fasting gastric acid secretion in this species. Despite the fact that this group of monkeys demonstrates significant differences in acid secretory capacity, both fasting and after maximal histamine stimulation, the fasting levels of circulating plasma gastrin are similar. Further, in paired collections of acid output and plasma gastrin, no correlation was demonstrated between fasting acid output and plasma gastrin levels in three of the four monkeys. These results differ from those reported in human subjects where an inverse relationship has been demonstrated between fasting acid secretion and fasting serum gastrin concentration (1). Several possibilities could explain this discrepancy. The differences could represent a species difference in gastrin dynamics and this possibility cannot be ruled out. A second possibility is that prolonged chronic restraint alters acid secretory and gastrin dynamics. However, analysis of both parameters showed no significant differences in acid secretion or gastrin concentrations during consecutive 30 day periods over the course of the experiment. Alternatively, the variance could be the result of the human population studied. That group represented a mixture of patients, some with gastric disease, some normal controls, and some with peptic ulcer. The most marked difference in serum gastrin was found in the group with the lowest fasting acid output and the lowest maximal histamine response. In this group, the highest serum gastrin levels were found, and it would appear that the inverse correlation was heavily dependent upon this group. Similarly, one of our monkeys demonstrated an inverse relationship between plasma gastrin concentration and fasting acid output, and this monkey

TABLE II. Regression Equations of the Form $Y = ax + b$, Where Y = Fasting Plasma Gastrin, and x = Fasting Acid Output.

Monkey	No. of expts.	Regression equation	Correlation coefficient	p value
G	21	$Y = 55.069 + 21.708x$	+0.276	>0.2
J	29	$Y = 61.735 + 35.231x$	+0.289	>0.1
Ha	17	$Y = 83.403 - 1.803x$	−0.017	>0.5
He	17	$Y = 154.593 - 169.875x$	−0.657	<0.01

TABLE III. Plasma Gastrin (pg/ml) with Different Rates of Acid Secretion.[a]

Monkey	Acid output	
	<0.3 mEq/hr	>0.3 mEq/hr
Monkey "He"	141 ± 14.7 (8)	71 ± 6.5 (9)
Other monkeys	67 ± 5.8 (21)	79 ± 5.6 (43)

[a] Values represent mean ± SE (no. of expts.).

also had the lowest fasting acid secretion and the lowest maximal histamine response. This particular monkey was the most immature of the group, judged by body size and weight and the lack of canine teeth. Whether the difference in gastrin dynamics in this immature animal is the result of chronic hypochlorhydria or of some developmental factor is unknown. In the mature macaque, however, which demonstrates higher rates of acid secretion, fasting acid output was clearly independent of the plasma level of gastrin. This suggests the possibility that the inverse relationship between serum gastrin concentration and fasting acid secretion reported in humans may be the result of the inclusion of chronic hypochlorhydric subjects in the test group. What will be required to resolve this discrepancy is an analysis of a group of normal and hypochlorhydric human subjects, or ideally, repeated studies in individual people over a period of time.

Summary. The level of circulating gastrin does not correlate with the fasting acid secretion in conscious monkeys. One young monkey demonstrated high plasma gastrin levels at very low levels of fasting acid secretion.

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