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Baron J H. Studies of basal and peak acid output with an augmented histamine test. *Gut* 4:136-44, 1963.
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The most repeatable measure of aspirated titratable acid output of the stomach is the mean of those in the two highest consecutive collections (peak acid output) after the injection of a maximal stimulus to the parietal cells. [The *SCI*® indicates that this paper has been cited in over 270 publications.]

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I had been interested in gastric acid secretion since my undergraduate days. As a resident in 1959-1961, I studied hypersecretion. A.W. Kay[1] had just revolutionised gastric tests by measuring maximal secretion with his augmented (40 μg/kg) histamine test, preceded by an antihistamine to prevent side effects.

After a histamine injection, acid output increases and decreases within an hour. Some researchers use the whole 60-minute output to determine exocrine response, but this time frame includes periods of submaximal secretion surrounding the maximal. Kay used four 15-minute fractions and claimed that the two central ones 15-45 minutes after injection showed the maximum histamine response. I found the maximum value to be in any one of the four fractions, presumably because of variable rates of absorption from the histamine injection. Although this highest single fraction had been used before, it was abandoned because of variable gastric emptying. Could these errors in measuring acid output be minimised by adding consecutive fractions? The maximal half hour in my 250 tests occurred in the first (20 percent), middle (46 percent), or last (27 percent) fraction and was highly repeatable with a weighted mean coefficient of variation of only 7 percent. (In 7 percent of the tests, the maximal secretion could not be related to a specific time fraction.)

This peak acid output (PAO, in millimoles per hour [mmol/hr]) is still widely calculated as the sum of the two highest consecutive collection periods, whether 15-, 10-, or 5-minute fractions, following any single parenteral injection by any route (IM, SC, or IV). In animals PAO is identical to the plateau response to IV infusion of histamine.[2] PAO can be used for agonists that stimulate for over one hour: insulin, histalog, gastrin, and pentagastrin (now the preferred gastric stimulant).

In Mount Sinai, New York, C.V. Perrier, H.D. Janowitz, D.A. Drelling, and I stimulated the pancreas maximally with IV Vitrum secretin and produced peak bicarbonate output in the dog.[3] This maximal pancreatic alkaline capacity is a measure of pancreatic secretory mass, just as maximal acid output is a function of parietal cell mass.

Using PAO as my index, I suggested the now accepted pattern of an overlap between duodenal ulcer (DU) and the normal range. Some patients with DU had abnormally high PAO, but there was a lower level of PAO (15 mmol/hr) below which DUs were not found.[4] In Cox's postmortem count of oxyntic cells there was a comparable threshold of 10^9 parietal cells exceeded by every DU.[5]

I suppose that the popularity of my 1963 paper in *Gut* is due to the simplicity of its clear standardised test protocol, scarcely altered today.[6] The PAO concept is easily grasped, sufficiently precise, repeatable, and applicable to any exocrine response to a single injection of any agonist.[7] The pathophysiological threshold DU model (Baron's Law[8]) predicts that any acid-lowering drug or operation (gastrectomy or vagotomy) that reduces PAO and keeps it below 15 mmol/hr will allow a DU to heal and stay healed.

1. **Kay A W.** Effect of large doses of histamine on gastric secretion of HCl. *Brit. Med. J.* 2:77-80, 1953. (Cited 805 times since 1955.)
2. **Marks I N, Komarov S A & Shay H.** Maximal acid secretory response to histamine and its relation to parietal cell mass in the dog. *Amer. J. Physiol.* 199:579-88, 1960. (Cited 95 times.)
3. **Baron J H, Perrier C V, Janowitz H D & Drelling D A.** Maximal alkaline (bicarbonate) output of the dog pancreas. *Amer. J. Physiol.* 204:251-6, 1963. (Cited 65 times.)
4. **Baron J H.** An assessment of the augmented histamine test in the diagnosis of peptic ulcer. *Gut* 4:243-53, 1963. (Cited 140 times.)
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6. **Baron J H.** Gastric secretion. (Misiewicz J J, Pounder R E & Venables C W, eds.) *Diseases of the gut and pancreas.* Oxford: Blackwell, 1987. p. 229-38.
7. **Baron J H.** *Clinical tests of gastric secretion: history, methodology, and interpretation.* New York: Oxford University Press, 1979. 277 p. (Cited 75 times.)
8. **Koster K H.** Gastric acid secretion in patients with duodenal ulcer. *Scand. J. Gastroenterol.* 1:199-206, 1968.

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