

This Week's Citation Classic

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Yalow R S & Berson S A. Radioimmunoassay of gastrin.

Gastroenterology 58:1-14, 1970.

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Elevated plasma gastrin was noted in five patients with Zollinger-Ellison syndrome (ZE) and 17 pernicious anemia (PA) patients using a highly specific homologous porcine gastrin radioimmunoassay. Oral administration of HCl to PA patients produced an acute fall in plasma gastrin with a disappearance half-time of about seven minutes. [The *SCI*[®] indicates that this paper has been cited in over 620 publications since 1970.]

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"In 1967, we had completed our studies on the immunochemical heterogeneity of plasma parathyroid hormone¹ and our detailed paper on the radioimmunoassay (RIA) of plasma ACTH.² RIA was already extensively employed by endocrinologists. It seemed an appropriate time for us to apply RIA to another field, gastroenterology. McGuigan had developed an RIA for gastrin³ using antibodies to the carboxyl-terminal tetrapeptide of gastrin (G4) and ³H-labeled G4 as tracer, but this was too insensitive to measure plasma gastrin. Since purified pork gastrin or synthetic human gastrin was in short supply and/or expensive, we used for immunization two crude porcine gastrin preparations (one only ~0.5 per-

cent pure and the other only ~10 percent pure) kindly provided by Wilson Laboratories in May 1968. By September 1968, we had produced antisera suitable for assay of plasma gastrin using these preparations. Morton Grossman, who had stimulated our interest in this area, provided us with 50µg each of purified porcine gastrin (G17) with sulfated and non-sulfated tyrosines that he had obtained from Rodney Gregory.

"During the next year we validated the assay, applied it to the diagnosis of gastrin secreting tumors, and noted the elevated gastrin levels in pernicious anemia and the rapid suppression by oral HCl in the latter condition. We also suggested that in older patients with an increased incidence of achlorhydria, there might be a modest elevation of basal gastrin. By the time we submitted this paper in September 1969, we had preliminary evidence that there was immunoreactive gastrin in plasma that differed from G17 and we were careful to note that 'the form in which endogenous human plasma gastrin circulates is not known.' We subsequently reported the discovery of 'big gastrin,'⁴ now known to be a 34 amino acid peptide.

"I believe this paper has become a *Citation Classic* because of its unequivocal demonstration that immunization with a very low purity antigen is practical for RIA procedures and because it was the first to establish the low levels of gastrin in normal fasting serum. It has served as a model for gastroenterologists as to the need for careful validation of RIAs for gastrointestinal hormones."

1. Berson S A & Yalow R S. Immunochemical heterogeneity of parathyroid hormone. *J. Clin. Endocrinol Metab* 28:1037-47. 1968.

2.----- Radioimmunoassay of ACTH in plasma. *J. Clin Invest* 47:2725-51. 1968.

3. McGuigan J E. Antibodies to the carboxyl-terminal tetrapeptide of gastrin. *Gastroenterology* 53:697-705. 1967.

4. Yalow R S & Berson S A. Size and charge distinctions between endogenous human plasma gastrin in peripheral blood and heptadecapeptide gastrins. *Gastroenterology* 58:609-15. 1970.