

Stadil F & Rehfeld J F. Determination of gastrin in serum: an evaluation of the reliability of a radioimmunoassay. *Scand. J. Gastroenterol.* 8:101-12, 1973.
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Unspecific factors that influence the accuracy of serum gastrin measurements were evaluated in detail. Careful control of these factors proved necessary not only to ensure reliable measurements, but also to explain the conflicting results of gastrin measurements reported previously. [The *SCI*® indicates that this paper has been cited in over 220 publications, making it the most-cited paper from this journal.]

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In spite of the fact that the concept of hormonal regulation was born in the gut,¹ gut endocrinology had long remained obscure in comparison with other disciplines of endocrinology. Therefore, gastroenterologists—clinical as well as physiological—became high-spirited in the late 1960s and early 1970s when reasonably pure gut hormones became available for development of radioimmunoassays. Such assays would for the first time allow insight into the hormonal control of digestion (the gut is the largest endocrine organ in the body). Moreover, the assays were expected to enhance the understanding of several digestive diseases and to improve their diagnosis. Gastrin was the first gut hormone for which assay development was attempted.

Since 1968 I had worked in the Department of Clinical Chemistry at Bispebjerg Hospital, trying to produce antibodies to isotope-label gastrin. In the beginning my success was limited. It helped significantly, however, when Flemming Stadil from Rigshospitalet energetically joined the effort in 1970, making resources from two hospitals available. Extensive immunizations² and development of a new

labelling technique³ soon led to sensitive and specific gastrin radioimmunoassays—the first on the European continent. Although ready for serum measurements, we realized that contemporary gastrin assays in the US, the UK, and Australia measured somewhat different concentrations. Having worked in clinical chemistry, we were aware that we had to examine factors that might influence the serum measurements. Thus, we simply studied the effects of salt, protein, temperature, pH, time, separation techniques, and the quality of reagents on the classical reliability parameters. We also collected serum samples from the hitherto largest groups of normal subjects as well as patients with relevant diseases and examined the influence of age, sex, and disease. The results explained quite reasonably the interlaboratory variations reported up to then. They also pinpointed unspecific factors that required particular consideration.

It is in some respects surprising that this work has been cited so frequently. The approach was not particularly original, nor were the results flabbergasting. Also, publication in a small Scandinavian journal should have limited the number of citations. On the other hand, it is possible to spot factors that might have contributed to the many citations. First, work like ours was probably badly needed in the early and mid-1970s because most of the gastrin assays were then performed by physiologists and clinical gastroenterologists, whose trade was not thorough critical evaluation of a biochemical analysis. In contrast, Stadil and I learned from our seniors in clinical chemistry. Thus, the fact that gastrin measurements were performed mainly at clinical and physiological departments may have made our study attractive as a reference work. Also, publication in a clinical rather than a methodological journal may have added some effect. Finally, we produced enough antiserum² to supply nearly 300 laboratories. This widespread use of our reagents may also have contributed to make the work a standard reference.

For the immunoassay work on gastrin and the related hormone cholecystokinin,⁴ I received the Mack-Foster Award from the European Society of Clinical Investigation in 1979 and the Jahre prize from the University of Oslo in 1980. Reliability problems for gut hormone assays have recently been reviewed.⁵

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2. Rehfeld J F, Stadil F & Rubin B. Production and evaluation of antibodies for the radioimmunoassay of gastrin. *Scand. J. Clin. Lab. Invest.* 30:221-32, 1972. (Cited 310 times.)
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