

This Week's Citation Classic

Vaitukaitis J L, Braunstein G D & Ross G T. A radioimmunoassay which specifically measures human chorionic gonadotropin in the presence of human luteinizing hormone. *Amer. J. Obstet. Gynecol.* 113:751-8, 1972.
[Reproduction Research Branch, Natl. Inst. Child Health and Human Development, Natl. Insts. Health, Bethesda, MD]

This paper presents the first radioimmunoassay capable of selectively measuring low levels of human chorionic gonadotropin (hCG) in blood samples containing luteinizing hormone (LH), hCG, or both hormones. [The SCI® indicates that this paper has been cited in over 555 publications since 1972.]

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"Luteinizing hormone (LH) and human chorionic gonadotropin (hCG) share extensive sequence homology which had precluded generating relatively specific antibody to selectively measure low levels of hCG in blood samples containing physiologic concentrations of LH. In the early-1970s, in the course of carrying out studies designed to define the immunologic differences and similarities between the two subunits, alpha and beta, of hCG and the other glycoprotein hormones, we observed that some hCG β antisera recognized relatively marked immunologic differences between highly purified pituitary LH and hCG, suggesting structural differences between their beta subunits.¹ Human CG and LH share indistinguishable biologic activities and only with insensitive, cumbersome chromatographic techniques could one distinguish between those two glycoprotein hormones.

"Since the amount of highly purified hCG subunits available was limited, we used an

intradermal immunization technique we devised to overcome limitations of immunogen availability.² Interestingly, the description of that technique has also become a *Citation Classic*. The first animal (SB6) immunized with 50 μ g hCG β produced the best antisera for clinical measurement of hCG in blood. Unfortunately, this assay has been labeled the 'beta subunit assay,' misleading clinicians into thinking that only hCG β and not the entire hCG molecule is detected. The initial assay technique has been modified to further enhance its specificity and sensitivity for measuring hCG.³

"To validate the specific hCG assay, serum samples from several different patients with high physiologic LH concentrations were assayed. Several samples from one of those patients repeatedly yielded high hCG concentrations which we initially thought reflected LH cross-reactivity. At that point, we almost gave up developing the assay. Fortunately, on reviewing the patient's chart, we found that the patient had received hCG injections for the several days his blood samples contained significant hCG levels.

"We realized the hCG was far more sensitive than any other technique. Since the specific hCG assay was sufficiently sensitive to detect hCG in the blood of women several days before onset of expected menses in a menstrual cycle in which they conceived, we chose to publish the technique in an obstetrical journal. Although we initially knew that the assay was an invaluable adjunct to monitor women with gestational trophoblastic neoplasms, we had not anticipated how important the assay would become in monitoring men with germinal cell testicular tumors. This paper became a *Citation Classic* because of its wide clinical applicability to monitoring patients with some hCG-secreting tumors and for the early detection of normal and abnormal pregnancies."

1. Vaitukaitis J L & Ross G T. Antigenic similarities among the human glycoprotein hormones and their subunits. (Saxena B, Gandy H & Beling C, eds.) *Gonadotropins*. New York: Wiley, 1972. p. 435-47.
2. Vaitukaitis J L, Robbins J B, Nieschlag E & Ross G T. A method for producing specific antisera with small doses of immunogen. *J. Clin. Endocrinol. Metab.* 33:988-91, 1971.
[Citation Classic. *Current Contents/Life Sciences* 23(33):12, 18 August 1980.]
3. Vaitukaitis J L. Specific human chorionic gonadotropin assay. (Jaffee B M & Behrman H R, eds.) *Methods of hormone radioimmunoassay*. New York: Academic Press, 1979. p. 817-29.