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This Week's Citation Classic

Jacobs L S, Snyder P J, Wilber J F, Utiger R D & Daughaday W H. Increased serum prolactin after administration of synthetic thyrotropin releasing hormone (TRH) in man. J. *Clin. Endocrinol. Metab.* **33:**996-8, 1971.
[Endocrine Divs., Depts. Med., Washington Univ. Sch. Med., St. Louis, MO, Northwestern Univ. Sch. Med., Evanston, IL, and Univ. Pennsylvania Sch. Med., Philadelphia, PA]

Intravenous thyrotropin-releasing hormone (TRH) caused a prompt rise in serum prolactin in normal subjects, and slight fasting hyperprolactinemia was shown to occur in primary hypothyroidism. TRH or a structurally similar molecule was suggested as the mediator of hypothalamic stimulation of prolactin secretion. [The *SCI*® indicates that this paper has been cited over 295 times since 1971.]

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"Many investigators were convinced, by 1970, that human prolactin must exist despite the inability to isolate it biochemically at that time. A series of elegant biosynthetic and immunologic experiments then underway led to the development of a radioimmunoassay for human prolactin in Friesen's laboratory.[1] At that time, I was a postdoctoral fellow in Daughaday's lab; he had been working at the prolactin problem using a rodent mammary bioassay. I decided to attempt the measurement of human prolactin with combinations of animal prolactins and their antisera, and was lucky to obtain a satisfactory result with one of the early experiments. The cited paper grew out *of* a convergence of this work with the early clinical experiments with TRH, the first of the hypothalamic peptides to be isolated and tested in man. TRH has been shown to release only TSH in normal subjects, and total specificity of action was assumed.

When we and Friesen became able to measure human prolactin by radioimmunoassay, roughly simultaneously, one of the first questions we asked related to possible effects of TRH on prolactin. Tashjian's lab[2] had shown that TRH stimulated prolactin synthesis by cultured rat pituitary tumor cells. Our paper, demonstrating the potent prolactin releasing effect of TRH, was published essentially simultaneously with one from Friesen's laboratory showing similar results, in late 1971 [3] The full description of our heterologous assay system was not published until six months later.[4]

"Peter Snyder, Jack Wilber, and Bob Utiger, with whom we collaborated, had saved every possible scrap of serum from their TRH-TSH study. This laudable pack-rat behavior, so common in clinical investigation, made possible the 'freezer' study we then performed. Wilber and Utiger, who also had served as fellows in Daughaday's lab, have gone on to head endocrine-metabolism units of their own, and all of us have remained actively engaged in both clinical and bench research in neuroendocrinology.

"A number of factors undoubtedly contribute to the frequent citation of our paper, including the explosive growth of the neuro-sciences and especially clinical neuroendo-crinology during the past decade. In addition, prolactin pathophysiology has touched upon many areas; pituitary tumors, dopa-minergic neuro-regulation of the pituitary, thyroid disease, hypogonadism and reproductive endocrinology, hormonal control of breast function, and biochemical effects of neuroleptics are some of these areas. The extent and intensity of fundamental bench and clinical investigations on prolactin which were rapidly undertaken can be appreciated by noting that three major international symposia devoted to prolactin had already taken place by the summer of 1973. It was a red-hot area then, and remains quite warm today."

1. Hwang P, Guyda H & Friesen H. *Proc. Nat. Acad. Sci. US* **68:**1902-6, 1971.
2. Tashjian A H, Barowsky J & Jensen D K. *Biochem. Biophys. Res. Commun.* **43:**516-23, 1971.
3. Bowers C Y, Friesen H G, Hwang P, Guy da H J & Folkers K. *Biochem. Biophys. Res. Commun.* **45:**1033-41, 1971.
4. Jacobs L S, Mark I K & Daughaday W H. J. *Clin. Endocrinol. Metab.* **34:**484-90, 1972.