This paper describes the application of a thyrotropin (TSH) radioimmunoassay (RIA) for differentiation of primary hypothyroidism from hypothyroidism due to pituitary disease. Synthetic thyrotropin-releasing hormone (TRH) was intravenously injected to increase serum TSH levels. We showed the clinical utility of the TSH measurement and studied the dynamic aspects of pituitary TSH secretion. 

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The first measurements of serum thyrotropin (TSH) by radioimmunoassay (RIA) were made by Robert Utiger and William Odell and their colleagues in 1965. Both investigators very kindly advised me about the art of RIA of TSH. Jim Pittman and I were both interested in clinical measurement of the hormone. Charles Baugh of our biochemistry department in Birmingham synthesized TRH so that we could test its effects in man before Abbott Laboratories had made it widely available. We had reported our preliminary work on clinical studies with TRH the previous year in a rapid publication format. We provided additional data indicating the suppression of TSH secretion in hyperthyroidism, and we showed the use of TRH for evaluation of TSH reserve in differential diagnosis of hypothyroidism. TRH given orally produced a smaller response than one-tenth the dose given intravenously, but the response to oral TRH was a superimposition of the pituitary response to oral TRH and the failing resistance of the TSH response to oral TRH. Pittman was a superb clinical investigator. He terminated his research career prematurely to accept the leadership of the VA research program in Washington and then the deanship of the University of Alabama School of Medicine. Subsequently, my colleagues at UCLA and I improved the TSH assay considerably so that we could define the normal range with precision. 

Our "highly sensitive" RIA has been joined in the last two years by a slew of commercial kits for ultrasensitive measurement of serum TSH levels. The basis for the interest in this field is the frequency of thyroid disease and the popularity of the TSH measurement.

I think that the paper is highly cited because it summarized three years of work in my laboratory and nowadays would probably be divided into several discrete reports. A recent review of control of TSH secretion is available.  

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