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NORMAL TSH CONCENTRATIONS IN LOW  $T_3$  SYNDROME. F. Kakezono, U. Nagayama, T. Kiriya, N. Yokoyama, S. Morita, I. Kubo, S. Ohtakara, S. Okamoto, I. Morimoto, M. Izumi and S. Nagataki. The First Department of Internal Medicine Nagasaki University School of Medicine

It is well known that the concentrations of serum  $T_3$  (and  $T_4$ ) are often decreased in nonthyroidal illness and it is not known whether these decreases are due to decreased serum TSH concentration, because it had been difficult to measure accurately lower concentrations of serum TSH. This study was, therefore, undertaken to investigate the mechanism for these decreases in serum  $T_3$  (and  $T_4$ ) measuring TSH concentrations using the SUCROSEP of a high sensitive assay for TSH. A decrease in serum  $T_3$  concentration was found in 12 of 33 patients with nonthyroidal illness and a decrease in serum  $T_4$  concentration in 3/33. The concentration of serum free  $T_4$  and TBG was normal in all patients including 3 patients with low  $T_4$  syndrome. The concentration of serum TSH did not correlate with that of serum  $T_3$ ,  $T_4$  and free  $T_4$ . These results suggest that decreased serum  $T_3$  and  $T_4$  in these patients with nonthyroidal illness are not due to decreased TSH secretion but may be due to inhibition of binding of  $T_4$  and  $T_3$  to TBG.

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THE MEASUREMENT OF SERUM TSH IN NORMALS AND PATIENTS WITH THYROID DISEASES USING HIGH SENSITIVE ASSAY METHODS. T. Sakamoto, F. Kakezono, U. Nagayama, T. Kiriya, N. Yokoyama, S. Morita, I. Kubo, S. Ohtakara, S. Okamoto, I. Morimoto, M. Izumi and S. Nagataki. The First Department of Internal Medicine, Nagasaki University School of Medicine, Nagasaki.

The serum TSH concentrations were measured by high sensitive RIA, using DP-5061 kit (Daiichi Aisotop) RIA gnost hTSH kit (Hoechst) and SUCROSEP TSH IRMA Kit (Boots Celltech). The serum TSH concentrations measured by a polyclonal monoclonal sandwich method (DP-5061 Kit) is slightly but significantly increased compared to monoclonal monoclonal sandwich method (RIA gnost, and SUCROSEP) in normal subjects and no difference was found in TSH increased samples either of hypothyroid patients or of TRH test serum. This difference in normal subjects was found to be due to the method itself but not due to supposed molecular difference between TSH at basal state and TSH at stimulated state, since dilution curves of increased TSH serum showed a straight line in three assay methods. The concentrations of serum TSH in normal subject were clearly higher than those in patients with active Graves' disease, in these three assays. The measurement of TSH by high sensitive assays is clinically and pathophysiologically useful.

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FUNDAMENTAL AND CLINICAL EVALUATION ON A HIGH SENSITIVE RADIOIMMUNOASSAY FOR SERUM TSH:RIAgnost TSH IRMA kit. H. Hara, Y. Ban, H. Nagakura, K. Kushima, R. Sato and H. Niitani. Showa University, school of medicine, Tokyo.

We have reported fundamental and clinical evaluation on a high sensitive IRMA for serum TSH concentration. Serum was obtained from 95 healthy euthyroid subjects, 85 patients with Graves' disease, 43 patients with chronic thyroiditis and 318 pregnant women. This method could measure for 120 minutes at room temperature and the assay had an absolute sensitivity of 0.08 uU/ml. The coefficient of variation of intraassay and interassay were 4.79--18.58 and 3.42--13.68%, respectively. Using three kinds of serum, the mean recoveries were  $91.5 \pm 6.47$  (SD),  $102 \pm 4.27$ ,  $91.6 \pm 12.87\%$ , respectively. Serum TSH levels on diluted serum were shown linear to 4096 times. The crossreactivity between anti- $\beta$ -chain monoclonal antibody and LH, FSH, HCG,  $\beta$ -HCG was absent. This assay was never influenced by addition of albumin, olate and hemoglobin. The mean circulating TSH concentration was  $1.5 \pm 1.31$  (SD) in normal subjects,  $0.09 \pm 0.02$  in untreated patients with Graves' disease,  $5.08 \pm 12.33$  in patients with Graves' disease in remission,  $1.65 \pm 2.53$  in patients treated with antithyroid drugs. The normal range was 0.3--3.4 uU/ml by Hoffman's method. During pregnancy the level of TSH was slightly decreased but not so in non-pregnant women. Concluding these results, we have reported the utility and value for clinical usefulness.

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A CLINICAL STUDY ON SERUM TSH(hTSH) BY A SENSITIVE RADIOIMMUNOMETRIC ASSAY(RIMA) IN PATIENTS WITH THYROID DISEASE AND NONTHYROIDAL ILLNESS. H. Uchimura, N. Akimoto, T. Mitsuhashi, N. Sasaki, Y. Imai and F. Takaku. The Third Department of Internal Medicine, University of Tokyo, Tokyo

Very recently highly sensitive RIMA's for hTSH have been developed by several laboratories. Most of these methods employ specific monoclonal anti-hTSH antibodies. The present study was examined the clinical significance of measurements for hTSH by a highly sensitive RIMA with monoclonal mouse antibody. Sera were obtained from normal subjects (118), patients with thyroid disease (299) or nonthyroidal illness (134). Two hundred  $\mu$ l of serum was incubated with I-125-anti-hTSH antibody in antibody-coated tubes for 2h at 4C. Decantation was performed by aspiration. Normal value was  $1.25 \pm 0.71$  uU/ml (n=118, M $\pm$ SD). Minimal detectability was 0.01 uU/ml. Basal and TRH-induced TSH increase were detected in thyrotoxic patients with Graves' disease. Serum TSH was closely and inversely correlated with  $FT_4$  in patients with thyroid disease. In patients with nonthyroidal illness, no relation was found among TSH,  $T_4$ ,  $T_3$ , and  $FT_3$ . However, there was significant negative correlation between TSH and  $FT_4$ . These results suggest that TSH is secreted from the pituitary in thyrotoxic Graves' patients and the secretion of TSH might be directly or indirectly related to circulating  $FT_4$  in patients with thyroid disease or nonthyroidal illness.