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HIGH SENSITIVE IMMUNOMETRIC ASSAY FOR TSH--BASIC CONSIDERATIONS AND ITS CLINICAL APPLICATIONS. K.Ichihara,N.Amino and K.Miyai.Department of Laboratory Medicine, Osaka University School of Medicine, Osaka.

The conventional radioimmunoassay (RIA) using the principle of competitive inhibition is not sensitive enough to distinguish TSH value of normal individual from that of thyrotoxic patients. Recently reappraisal of immunoradiometric assay (IRMA), being facilitated by easy availability of monoclonal antibody against human TSH, lead to the development of many commercial assay kits with more than 10 fold increase in sensitivity (minimal detectable dose (MDD) of 0.2-0.05 μU/ml). The advantages of IRMA over conventional RIA include (1) shorter incubation time, (2) higher specificity, (3) simpler B/F separation. Meanwhile, only minor disadvantages are noticed. They inclde (1) larger intra- and interassay variation at the low concentration of TSH because of low radiation count attained at that dose level, and (2) the need of larger sample volume to obtain maximal sensitivity. Furthermore, although nonspecific serum effect in IRMA is much less than that in RIA, the distribution of TSH values among thyrotoxic patient seems to depend on the matrix used for zero dose standard. Our data suggest that if the matrix dose not contain globulin, the count bound for thyrotoxic serum tends to be less than that of zero dose.

Alternative immunonetric assay using enzyme (IEMA), fluorescence (IFMA) or chemiluminescent (ICMA) labeled antibody are also being developed. They are shown to have MDD ranging from 0.1 to 0.0002 μU/ml with use of less sample volume than that needed by IRMA. The better sensitivity is attributed to higher specific activity (signal per molecule) for the labeled antibody and to the availability of a measure to amplify the signal emitted from the original label.

There are a wide range of clinical applications of the new TSH measurements. Firstly, detailed analysis can be made on the physiological variations of TSH secretion in response to pregnancy, exercise and alteration in temperature, and also on the pharmacological effects of agents suppressing TSH secretions such as dopamine, and T3. We have examined TSH suppressive effect of a single oral dose (50 μg) of T3 in healthy individual and found its clinical use in assessing the patients with inappropriate secretion of TSH. Secondly, the high sensitive assay facilitates analyses of disorders with low or suppressed TSH level, making the conventional TRH test almost of no use except in special cases of hypothalamic disorders. The basal values of TSH were found normal in most cases of hypothalamaic hypothyroidism. The pathological significance of such TSH level is unknown. Thirdly, the assay is useful to determine optimal dosage for thyroid hormone replacement/suppression therapy as well as antithyroid drugs therapy. Fourthly, in our development of TSH IEMA for neonatal screening of cretin, the high sensitivitiy had an critical role in greatly reducing sample volume up to 5 μl of blood.

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CLINICAL USE OF A HIGHLY SENSITIVE IMMUNOASSAY OF GH IN PATIENTS WITH PITUITARY DISORDERS. Yuzuru Kato[1], Naoki Hattori[1], Yoshio Murakami[1], Seiichi Hashida[2], Eiji Ishikawa[2], Zen-ichi Mohri[3]. Second Medical Medical Clinic, Department of Medicine[1], Kyoto University Faculty of Medicine, Kyoto; Department of Biochemistry[2], Medical College of Miyazaki,Miyazaki;and Research Institute[3] Sumitomo Pharmaceutical Company,Takarazuka.

Using a highly sensitive and specific EIA (Clin. Chim. Acta 135:263, 1983), human GH was detectable as little as 3 pg/ml of serum and 0.4 pg/ml of urine. The minimum detectable quantity of GH was 50 pg/ml of serum in the revised RIA. Plasma GH values determined by EIA and RIA were well correlated. Basal plasma GH values in normal subjects were mostly less than 500 pg/ml, which were not determined by a conventional RIA of GH. Plasma GH levels in a number of patients with hypopituitarism were less than 50 pg/ml, which were only detectable by EIA. Plasma GH levels after insulin-induced hypoglycemia and GRF proved to be useful for differentiating primary pituitary dysfunction from hypothalamic disorders. Urine GH levels were well correlated to plasma GH changes. It was possible, therefore, that the pituitary function could be determined by measuring GH concentrations in the urine samples obtained after stimulation tests or for 24 hrs. It was also demonstrated that a very small amount of GH release was detectable in the superfusion system of the pituitary adenoma cells in vitro. It is concluded that a highly sensitive assay of GH is very valuable for clinical use.