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DETECTION OF RECEPTOR ANTIBODIES BY USING RADIORECEPTOR ASSAY.

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Radioreceptor assay is now widely used for the detection of receptor antibodies which inhibit the binding of ligands to receptor sites. Clinical usefulness and limitation of the assay was studied by using a currently available kit for the detection of TSH-binding inhibitor immunoglobulins (TBII).

The sensitivity of the assay was found to be significantly improved by a longer preincubation of the receptors with sample sera (120 min. instead of 15 min.). By using a longer preincubation period, incidences of TBII in 20 untreated patients with Graves' disease, 40 patients treated with antithyroid drugs, and 19 patients with "euthyroid Graves' disease" were 90, 40 and 42 %, respectively. Two out of 12 patients with primary hypothyroidism were positive for TBII. All the TBII-positive IgGs in Graves' patients stimulated cyclic AMP increase in thyroid cells, while those in hypothyroid patients blocked thyroid stimulation induced by TSH. Thus, the assay of TBII was useful for the diagnosis of both borderline cases of Graves' disease and "euthyroid Graves' disease" and also for the diagnosis of hypothyroidism due to the blocking type of receptor antibodies.

High TBII activities in mothers were significantly associated with the

occurrence of neonatal Graves' disease, or hypothyroidism in their offsprings. The finding not only supports the pathogenetic role of TBII, but also indicates the clinical usefulness of the measurement of TBII for the prediction of these complications.

Thyroid uptake was nonsuppressible by T_3 in 81 % of the TBII-positive patients of the maintenance dose of antithyroid drugs, while that in 42 % of TBII-negative patients were suppressible. Thus, TBII appeared to serve as a marker of disease activity during antithyroid drug treatment of Graves' disease.

On the other hand, it must be kept in mind that TBII activity does not represent biological activity. Furthermore, the assay can be interfered by the presence of anti-TSH antibodies, and can not detect receptor antibodies which react to antigens other than binding sites.

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COMPARISON OF RADIOIMMUNOASSAY WITH NON-ISOTOPIIC IMMUNOASSAYS. Y.Endo, N.Hata and K.Miyai. Department of Laboratory Medicine, Osaka University Medical School, Fukushima-ku, Osaka.

Radioimmunoassay (RIA) is a sensitive and specific method and has wide applications, but requires special facilities for its use and for radioisotope disposal. Usually, physical separation of bound and free form is necessary and the labeled substances have a short half-life. Consequently, efforts have been made to develop non-isotopic immunoassays (non-RIA) that does not require a radioisotope. We have developed several enzyme immunoassays (EIA) for the measurements of hormones and proteins in human circulation. Our EIA system for thyrotropin (TSH) is successfully used for a mass screening of congenital hypothyroidism in newborns. Recently, we have developed a new EIA for free thyroxine based on a favorable situation that enzyme-labeled thyroxine is bound to anti-thyroxine antibody but not to thyroxine-binding proteins. Generally, however, labeling and assay procedures in EIA are rather complicated. Furthermore, EIA is sometimes insensitive because the affinity of antigen-antibody interaction is frequently reduced by labeling with high molecular weight enzyme and some unknown factors in serum sample interfere non-specifically in antigen-antibody interaction. Thus, there are yet several essential problems to be solved in EIA.

The sensitivities and specificities of RIA and non-RIA depend to a great extent on the quality of antibodies used in the assays. Recently, we designed a new method for separation of antibodies with high affinity or high specificity from polyclonal antiserum. It is based on the difference in the isoelectric points of individual clonotype antibodies. Using clonotype antibodies separated by this method, we could construct a highly specific RIA for TSH, and highly sensitive RIA and non-RIA for thyroxine.

It is concluded that RIA and non-RIA have some different characteristics, and that they should be made good use to display their advantages in the methodology and clinical usefulness.