# The Role of Radioimmunoassay in the Management of Thyroid Disease

**Ian B. Hales**

*Department of Nuclear Medicine and Endocrinology,*
*The Royal North Shore Hospital of Sydney, NSW AUSTRALIA.*

## INTRODUCTION

Radioimmunossay has a continuing role in diagnosis, prognosis, therapy and research of thyroid disease and is unlikely to be replaced by alternate immunoassays in the immediate future.

## DIAGNOSIS

Although there is a tendency to rely entirely on invitro radioimmunoassays, particularly to diagnose thyroid metabolic state, there remains a place of invivo isotope studies, this is even more apparent in attempting to make pathological diagnosis.

Metabolic State (Table 1)

1. Hyperthyroidism – at present no single test can be relied upon entirely. Assays which measures triiodothyronine (T3) and thyroxine (T4) either as the free T3 and free T4 or total T3 or T4 corrected for thyroxine binding globin (TBG) are the most useful tests. The current free T3 and T4 kit methods have certain inherent problems and could obscure problems related to binding protein abnormalities. Theoretically a very sensitive thyroid stimulating hormone (TSH) assay could be useful in demonstrating suppressed pituitary secretion of TSH, and consequently the detection of a measurable level of TSH should exclude the diagnosis of hyperthyroidism.
2. Hypothyroidism – A low free T4 or corrected total T4 plus an elevated TSH should be found in all cases of primary hypothyroidism a low TSH may suggest a pituitary of hypothalamic defect. In neonatal thyroid screening TSH assay is the test of choice.
3. Sick euthyroid state causes considerable difficulty and may have either high or low T4, and usually low T3 values. TSH is usually low normal and it may be necessary to measure TBG, reverse T3 (rT3) and other binding proteins. Demonstration of a normal pituitary response to hypothalamic thyrotrophin releasing hormone (TRH) may be needed to confirm the diagnosis.

Table 1. The Role of RIA in the Diagnosis of Metabolic Thyroid Disease.

| Metabolic State | RIA's of Value | Other Tests Required |
|---|---|---|
| Hyperthyroid | * Corrected Total T3 | |
| | * Corrected Total T4 | |
| | FT3 FT4 TSH | |
| Hypothyroid | Corrected Total T4 | |
| | FT4 TSH | |
| Sick Euthyroid | Total T3 Total T4 | TRH TEST |
| | TSH TBG | |

* Corrected Values are Those Corrected for TBG or T3 Resin Uptake.

Pathological Diagnosis (Table 2)

Radioimmunoassays are a useful adjunct to making a pathological diagnosis.

1. Thyroid autonomy exists in both Graves' disease and autonomous functioning nodules. A positive elevation of TSH following TRH injection excludes such autonomy. To confirm autonomy invivo isotope uptake tests may be needed. Measurement of thyroid stimulating immunoglobulin (TSI) or thyrotrophin binding inhibiting immunoglobulins (TBII) may be helpful in difficult cases, e.g., ophthalmic Graves' disease.
2. Subacute thyroiditis – The hyperthyroid state can be differentiated from iatrogenic hyperthyroidism by measuring circulating thyroglobulin (Tg), in subacute thyroiditis there is gross release of thyroglobulin into the circulation due to thyroid gland destruction, while in patients receiving thyroixine therapy thyroglobulin is almost always undetectable.
3. Hashimoto's disease – Antibodies either microsomal or thyroglobulin are usually present in high titres.
4. Thyroid cancer – Tg is often grossly elevated but this can also be the case in many other thyroid conditions, particularly hyperthyroidism.
5. Dyshormonogenetic goitre – TSH, T3, rT3, diiodothyronine (T2), monoiodothyronine (T1) may all be useful to assess the type of defect.
6. Iodine deficient goitre – T3/T4 ratio is increased.

## PROGNOSIS

The changes in TBII, TSI and Tg have all been reported to be of prognostic value in assessing the outcome of antithyroid drug therapy in Graves' disease – this is still to be proven. Also the presence of antibodies (microsomal or thyroglobulin) may suggest the possibilities of the develop-

Table 2. The Role of RIA in the Diagnosis of Thyroid Pathology.

| Pathological Condition | RIA's of Value | Other Tests Required |
|---|---|---|
| A. Hyperthyroid States | | |
| 1. Graves' Disease | TSI TBII | 131I Uptake<br>T3 Suppression |
| 2. Autonomous Nodule | | SCAN |
| 3. Subacute Thyroiditis | TG | 131I/Uptake F.N.A. |
| B. Hypothyroid States | | |
| 1. Primary Hypothyroid | TSH | |
| 2. Secondary Hypothyroid | TSH | TRH Response Absent or Blunted |
| C. Euthyroid States | | |
| 1. Hashimoto's Disease | Antibodies | SCAN, KCL04 Discharge |
| | TSH | F.N.A. |
| 2. Cancer | TG | Scan U/Sound F.N.A. |
| 3. Iodine Deficient | T3/T4 Ratio | 131I Uptake |
| 4. Dyshormonogenetic | T3, T4, RT3 | 131I KCL04 Discharge |
| Goitre | T1, T2 | Peripheral Deiodination |

ment of spontaneous hypothyroidism. The presence of TBII and TSI during pregnancy alert one to the possibility of neonatal hyperthyroidism and blocking antibodies may lead to neonatal hypothyroidism.

## THERAPY

T4, T3, TSH are used to monitor treatment of both hyper and hypothyroidism. Tg is useful to indicate residual tissue or metastases in the follow-up of patients with thyroid cancer but this is not 100% reliable as inferred by some authors. The disappearance of TSI and or TBII may indicate no further treatment is required in Graves' disease but this has still to be proven. TRH responsiveness has also been similarly interpreted. Labelled antibody studies have already been introduced to identify residual thyroid metastases in vivo and may supplement other tests for studying response to therapy of thyroid cancer.

## RESEARCH

New assays are being developed. At present we have assays available for most analogues of thyroxine including some non-iodinated compounds such as DIMIT. The latter is a most interesting compound with significant possible clinical applications. TRH assays are available and may be useful in physiological studies. The labelling of thyroglobulin antibodies with radioiostope for therapeutic purposes is being investigated but problems arise with radiation damage of the antibody when high specific activity is required for therapeutic purposes.