Thyroid Function Tests in the UK

Geoff Beckett, Tony Toft, *Maurice O'Kane,

Clinical Biochemistry, The Royal Infirmary of Edinburgh, 51 Little France Crescent, Little France, Edinburgh,EH16 4SA and *Clinical Chemistry, Altnagelvin Hospital, Londonderry, N Ireland, BT 47 6SB

Comments to G.J.Beckett@ed.ac.uk

Background

Thyroid disorders and thyroid function testing are common resulting in 10 million requests each year in the UK at an estimated cost of at least £30 million. Thyroid function tests include thyroid stimulating hormone (TSH), free or total thyroxine (FT4; TT4), and free or total tri-iodothyronine (FT3; TT3); various combinations of these analytes have been advocated as providing the most cost-effective means of diagnosing thyroid dysfunction. Virtually all thyroid function testing currently takes place in hospital laboratories in departments of Clinical Biochemistry.

The purpose of this paper is to provide recommendations for what combination of thyroid function tests are considered to be both cost-effect and deliver optimal patient care. These recommendations are based largely on the recent "UK Guidelines for the use of thyroid function tests" that were developed by a group comprising representatives from the Association of Clinical Biochemistry, British Thyroid Association and the British Thyroid Foundation [1]

UK Practice Regarding the Selective Use of Thyroid Function Tests

Total or free thyroid hormones?

Current views relating to the mechanism of action of thyroid hormones consider that it is only the unbound (free fraction) of thyroid hormone that can enter the cell and confer biological activity. Physiology thus dictates that free hormones and not total homes should be measured for assessing thyroid status. This needs to be balanced, however, with the known methodological shortcomings of routine free hormone measurement and the absence of an accepted reference method that is accurately calibrated. The majority of UK laboratories now offer free hormone measurements. The use of total hormone measurements is acceptable but laboratories must have available free hormone measurements for situations where abnormal TBG concentrations may give rise to misleading results for total thyroid hormones (e.g. pregnancy, oestrogen-containing oral contraceptives, liver disease). Total and free hormone methods usually have similar costs if workload is similar.

For the purposes of this document we will use the abbreviations T4 and T3 to indicate that free or total hormone measurements are appropriate. FT4 and FT3 will be used when we consider that free hormones are essential.

Current strategies in UK for thyroid function testing
The two most common strategies for thyroid function testing in the UK are:-

First line TSH – (cascading to thyroid hormone measurements when TSH is abnormal)
This strategy is attractive since it has the potential to offer the most cost effective means of diagnosing thyroid disorders. This strategy is acceptable when the hypothalamic-pituitary-thyroid axis is intact and stable. A normal TSH then usually excludes primary thyroid dysfunction. A low TSH should lead to measurement of T4 and T3 whilst a raised TSH should usually initiate only a measure of T4.
TSH first- line is considered sub-optimal in a number of clinical situations. To ensure appropriate test requesting it is essential that communication channels between clinicians and the laboratory are sufficient to identify, on an individual patient basis, cases where TSH –first line is inappropriate.
If clinical details are not available then it may be prudent for laboratories to measure serum TSH and T4 on all specimens rather than embark on a first-line serum TSH testing strategy

Appropriate use of first-line TSH (Hypothalamic – pituitary- thyroid axis Intact)

- Screening at risk groups, such as type 1 diabetes, dyslipidaemia, osteoporosis, sub-fertility, atrial fibrillation, post neck irradiation, Down's syndrome, Turner's syndrome, lithium or amiodarone therapy.
- Monitoring thyroxine therapy in patients previously optimised for therapy.

Inappropriate use of TSH-firstline (Hypothalamic- pituitary – thyroid axis may not be intact)

- Testing new patients presenting with symptoms suggestive of thyroid dysfunction
- Optimising thyroxine replacement therapy in the early months of treatment for primary hypothyroidism
- Diagnosing and monitoring thyroid disorders in pregnancy (For pregnancy FT4 not TT4 must be used).
- Monitoring patients with hyperthyroidism in the early months after treatment.
- Diagnosis and monitoring treatment for central hypothyroidism.
- Identifying patients with end-organ thyroid hormone resistance or TSH-secreting pituitary adenomas

First line TSH and T4 (cascading to T3 if TSH is low)
Initial measurement of both TSH and T4 together provides the most satisfactory method of assessing thyroid status. However, it is essential to understand and appreciate the factors that can affect the results of thyroid function tests for correct interpretation.

Adjunct T3 Measurements
In both the above strategies, T3 measurements will need to be performed in patients that have an undetectable TSH in order to

- Define the severity of hyperthyroidism
- Monitor treatment for hyperthyroidism during the early months of treatment.
- Identify patients with low TSH due to non-thyroidal illness.

Measurement of T3 need not be performed in patients taking T4 replacement therapy except where, for clinical reasons, it has been decided to keep TSH at <0.1mU/L. In such patients T3 must not be allowed to remain above the upper reference limit.

Other strategies employed to a lesser extent in UK

First line TSH, T4 and T3
This strategy provides all the information required for diagnosing and monitoring thyroid disorders. However it is not regarded as being cost-effective since a large number of T3 measurements will be performed that are unnecessary.

First-Line TSH with T3 (cascading to T4 if TSH is abnormal)
This is performed by few laboratories and has no advantage over and above the use of TSH with T4 first-line.

Conclusion
Laboratories that are able to identify samples that are inappropriate for first-line TSH (as defined above) may choose to offer TSH first-line and TSH with T4 as appropriate. Laboratories where clinical communication is lacking should employ a TSH with T4 approach for all samples. Measurement of T3 need only be offered in specific situations such as when TSH is < 0.1 mU/L or in the first 6 months following treatment for hyperthyroidism. Free hormone measurements must be available for situations where TT3 and TT4 may give misleading results.

References
Association of Clinical Biochemistry, British Thyroid Association, British Thyroid Foundation 2006 UK guidelines for the use of thyroid function tests
http://acb.org.uk/docs/tftguidelinefinal.pdf