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Redefining Hypothyroidism—A Paradigm Shift

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In the clinical investigation of patients with suspected thyroid disease, TSH is an established first-line test. A spontaneous low value raises the possibility of hyperthyroidism. A high TSH is considered to signify hypothyroidism. So far, things look straightforward.

In industrialised societies, most cases of hypothyroidism are the result of an autoimmune attack on the gland. So far, there is also general consensus.

Since the introduction of the TSH analysis, this test has become the most trusted single measure of the condition of the thyroid. The importance bestowed on the TSH necessitates a clearly defined reference range. Over the years, the lower range has undergone relatively small adjustments. What is regarded as a "high" value has, however, been subject to repeated downward shifts. Also, there are considerable inter-laboratory differences as to the upper limit of "normal." It is very unfortunate that today, there is no clear and universally accepted upper limit of "normal" for this crucially important test.

As autoimmunity is the leading cause of thyroid disease, it is important to document thyroid autoimmune activity. *Indirectly*, thyroid autoantibodies such as antibodies to thyroid peroxidase and thyroglobulin, and TSH receptor antibodies serve as evidence of thyroid autoimmunity.

A *direct* approach to demonstrate thyroid autoimmunity is to examine the gland by means of fine-needle aspiration cytology (FNA). For many years, this has been a routine procedure in our centre in Stockholm, Sweden. The diagnostic and therapeutic potential of FNA as a complement to conventional first-line tests is remarkable.[1][2] In summary, we found that no less than 40% of unselected patients with chronic fatigue (90% women) had definite evidence of lymphocytic invasion of the thyroid—the gold standard criterion of thyroid autoimmunity.

What about TSH in patients with FNA-documented evidence of thyroid autoimmunity? We found that TSH values were scattered, ranging from less than 1 mU/L to over 30; the median TSH value was 3.8.[1] (These were baseline values, and none of the patients were on thyroid medication.) In patients with cytologically-demonstrated thyroid autoimmunity, the clinical response to thyroid medication was equally favourable, regardless of the presenting TSH value.

Applying this experience to our everyday clinical practice, in patients with suspected thyroid imbalance, we must not rely on a "normal" TSH. Investigation should focus on thyroid autoimmunity, including analysis of thyroid autoantibodies, and, most desirably, FNA. This statement is not of mere academic interest; if the patient is a victim of overlooked thyroid autoimmunity/hypothyroidism, she (or he) will be condemned to continue a poor quality of life.

How, then, should we define hypothyroidism? It is obvious from the morphological findings that symptomatic autoimmune thyroid disease is far more common than revealed by biochemical assessment alone. In addition to conventional biochemical criteria (probably having a high diagnostic specificity), including morphological evidence of thyroid autoimmunity would substantially widen the scope to encompass more patients in need of thyroid medication. In my—and, above all, in the patients'—opinion, this is a welcome paradigm shift representing true progress.

References

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