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EDITORIAL

The Battle-field of Subclinical Hypothyroidism

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Introduction

To treat or not to treat subclinical hypothyroidism is a question, which internationally creates much discussion and writing. Subclinical hypothyroidism is biochemically defined by a serum TSH above the upper reference limit, whereas serum T_4 estimates are within the reference range. This pattern of biochemistry indicates a slightly failing thyroid gland. Both subclinical and overt hypothyroidism show large differences in epidemiology between populations, probably caused by a combination of environmental and genetic factors. Whereas there has been consensus on the benefits of thyroid hormone replacement therapy of overt hypothyroidism for more than 100 years, opinions on how to deal with subclinical hypothyroidism are far from unanimous.

One controversy concerns delineation of upper normal serum TSH. Thyroid autoimmunity is very common in the population, and any random sample of adults would include people with some degree of autoimmune affection of the thyroid gland. Accordingly, a reference population that is not rigorously sorted may include many people with some abnormality of thyroid function. Because the risk of future thyroid failure increases with a serum TSH in the upper normal range it has been suggested that the "true" upper normal TSH is around 2.5 miu/L.[1] However, in a population study where all participants were carefully examined with family history, measurement of thyroid antibodies and thyroid ultrasonography, upper 97.5 per centile of serum TSH in participants with no risk factors was 3.6 miu/L.[2] This suggests that the upper normal value of around 4 miu/l used for most TSH assays is reasonable. As individual variation of serum TSH occurs within a more narrow range than between individual differences in the healthy population used for creating the reference range, there will always be a risk that a high normal TSH is slightly elevated for the individual in question.[3]

Even if consensus is obtained regarding upper normal serum TSH being around 4 miu/L, considerable disagreement exists on therapy in patients having a serum TSH above this level. Using a strictly evidence based medicine approach an international group lead by Surks[4] reviewed scientific evidence and published in 2004 that the consequences of subclinical hypothyroidism with a serum TSH below 10 miu/L are minimal and that routine treatment is not indicated. This

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year (2005) another group of experts[5] appointed by a number of scientific societies expanded on the issue and challenged the 2004 conclusions on several points. Their major point was that subclinical hypothyroidism with serum TSH below 10 miu/L is a milder disease, but clearly an abnormal state of health, and that no one would recommend patients treated for overt hypothyroidism to be left with an elevated TSH. They argued that a careful evaluation of individual patients should be the basis for offering therapy in case of persistently elevated serum TSH.

More evidence for or against the beneficial effects of therapy would be most welcome. We support the suggestion that an individual approach including focus on the opinion of the informed patient is necessary,[6] and that therapy should clearly be given to subgroups of patients, such as pregnant women.

Massive high quality intervention studies involving pharmaceutical products are normally financed by the pharmaceutical companies holding licenses. This approach is not realistic when new indications, such as therapy of subclinical hypothyroidism, appear for an old medication, such as L-Thyroxine. Hopefully, non-commercial funding will, in the future, allow the necessary large scale studies to firmly establish the consequences of observation vs. replacement therapy in the many patients with subclinical hypothyroidism.

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