



## L-T<sub>4</sub> Treatment of Patients With Subclinical Hypothyroidism Can Partially Restore Cardiac Flow Reserve

### Conclusions

In 9 patients with slightly to substantially elevated TSH values, analysis of <sup>13</sup>N-ammonia uptake indicated that several parameters of coronary micro-

vascular function were significantly below control levels. In the 8 patients given 6 months of treatment with L-T<sub>4</sub>, the mean corrected coronary blood flow improved but was not normalized.

### ANALYSIS AND COMMENTARY ● ● ● ● ●

It is somewhat surprising that there was no analysis of pretreatment and posttreatment data for individual patients, since they would have served as their own controls. Nonetheless, the findings seem consistent with recent echocardiographic studies on myocardial microvascular function, and they raise the possibility that myocardial, smooth muscle, endothelial, neural, or stromal changes, rather than major vessel dysfunction, may be present in some patients. Hashimoto's thyroiditis is the commonest cause of subclinical hypothyroidism, but other possible causes include advanced age, obesity, polymorphisms in genes such as phosphodiesterase-8, and TSH-receptor blocking antibodies. An increased TSH level also can occur—usually transiently—after taking certain foods or drugs, or during recovery from subacute, painless or postpartum thyroiditis, or from nonspecific illness. Some of these diagnoses are difficult to confirm, but a positive TPOAb titer does not prove that Hashimoto's thyroiditis caused a patient's subclinical hypothyroidism: for example, in the patient who required 500 μg of L-T<sub>4</sub> for 6 months to normalize the TSH, a more obscure diagnosis (or noncompliance) might be possible. Furthermore, the wide range of TSH levels and the small number of subjects makes it difficult to know what to do with these results.

However, over the past 10 years or so, an upper limit of 10 μU/ml TSH for “watchful waiting” in subclinical hypothyroidism has become widely accepted. Patients whose TSH is consistently above 10 μU/ml are known to be much more likely to advance to overt hypothyroidism, and a recent analysis of 11 prospective studies indicates that such patients are at increased risk of coronary heart disease and death (3). In a patient who has symptoms consistent with hypothyroidism, which cannot be otherwise unexplained, and whose TSH is slightly above normal but below 10, it seems reasonable to try a “therapeutic trial” of L-T<sub>4</sub>, recognizing that a favorable response does not prove that hypothyroidism was the cause. However, there are two clinical situations that require the physician's special attention when considering treatment of mild subclinical hypothyroidism. 1) In the pregnant patient, there is a clear consensus for giving L-T<sub>4</sub>. 2) In contrast, L-T<sub>4</sub> treatment of elderly patients with mild subclinical hypothyroidism must be closely monitored. TSH levels increase with age regardless of anti-TPO positivity, and some studies have found that slightly elevated TSH levels are associated with increased survival to great age. The dose of L-T<sub>4</sub> given to elderly patients is of special concern, since a recent study found that over 40% of patients aged 65 were receiving overreplacement, and this group is especially at risk for cardiovascular and skeletal side effects (4).

— Stephen W. Spaulding, MD


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