

APPENDIX 46



The International Hormone Society'S Consensus Group of Experts on Hormone Therapies Consensus # 1 on "Thyroid Hormone Therapy of Hypothyroidism" of September 29, 2005

After having reviewed the scientific literature and exchanged experiences between physicians from all over the world who are competent in hormone therapies, we, members of the Consensus Group of Experts of the International Hormone Society, think the time is ripe to reconsider current concepts on thyroid treatment of hypothyroidism.

The view that hypothyroidism is best treated by thyroxin alone is not based on solid scientific evidence. The studies comparing the efficacy of thyroxin alone versus that of combination thyroxin and triiodothyronine medications have in general **not shown superiority of thyroxin alone** above the combination of thyroxin with a smaller dose of triiodothyronine. On the contrary, **a few studies** have shown a **significantly greater efficacy of combined thyroxin-triiodothyronine medications** compared to the use of thyroxin alone in humans on such divergent parameters as serum cholesterol, mental and physical symptoms, and in animals on goitre formation and intracellular triiodothyronine(T3)-euthyroidism, just to name some of the greater benefits. The facts that T3 is the major intracellular thyroid hormone, and that a low serum level of T3 is more often than a low serum T4 (thyroxin) or a high TSH, the critical parameter in mortality studies, especially cardiovascular, and that the absorption of T3 is much more efficient and stable than that of T4, give credibility to the view that a combination of thyroxin with triiodothyronine may be better for the hypothyroid patient.

The evidence is sufficient to guarantee the physician a **freedom of choice in thyroid medication: either thyroxin alone or thyroxin and triiodothyronine.**

As hypothyroidism has serious adverse consequences on the quality of life and health of patients, we recommend that physicians, in light of the solid evidence here collected, should **first** try to treat hypothyroid patients with **a combined thyroxin and triiodothyronine preparation.**

As the combination treatment contains the immediately active triiodothyronine, we recommend that physicians **follow some safety guidelines**, in addition to the obvious one of avoiding overdoses when they administer thyroxin and triiodothyronine medications. Following the measures listed below increases the safety and tolerance of the treatment:

1. The **first** guideline is to start the treatment at very low doses and then to slowly and gradually increase the dose until clinical eu-thyroidism is reached.
2. The **second** guideline is to tell the patient to avoid all caffeinated and similar stimulating drinks that may increase the orthosympathic activity.
3. The **third** guideline is to regularly follow-up the patient with a good clinical interview and examination and laboratory tests every two to twelve months depending on the patient's needs.
4. The **fourth** guideline is to carefully screen for adrenal deficiency in hypothyroid patients, as some patients with low or borderline low cortisol levels may poorly tolerate any type of thyroid medication, and in particular thyroxin-triiodothyronine combinations. The intolerance may come from over-activity of the orthosympathic nervous system that often accompanies states of low cortisol, and an excessive and rapid conversion of thyroxin to triiodothyronine that puts these patients easily into a state of excess T3 and thus hyperthyroidism, and further increases the orthosympathic activity. In patients with cortisol deficiency, we recommend the physician to treat the low cortisol state prior to or simultaneously with the thyroid treatment. If not, thyroxin alone may be the better treatment of hypothyroidism in the presence of an untreated cortisol deficiency. In most other instances, thyroxin and triiodothyronine remains the first, but not exclusive, choice for treatment of hypothyroidism for the International Hormone Society's Consensus Group.

Concerning the debate about which combination treatment works best: **synthetic T3-T4 or desiccated thyroid**, the Consensus Group states the following:

Reports of patients feeling better on desiccated thyroid may have scientific evidence as these preparations contain along with T3 and T4 a number of other substances that may have some thyroid activity as diiodo- and monoiodo-thyronines. In addition, the binding of much of the thyroid hormones to the bigger thyroglobulin molecule allows a slower intestinal absorption and, later, once arrived in the bloodstream, a slower release of thyroid hormones in the blood, thereby insuring a more persistent action and a better tolerance by spreading the action over a longer period of time. Thus, desiccated thyroid may work better.

The view that the potency of thyroid preparations of animal origin may have more fluctuations has arguments. For this reason, preference is given to preparations that are officially registered and well-controlled. It must be said that the frequent FDA-recalls of poorly reliable, less potent than announced thyroxin preparations of various pharmaceutical firms in the USA, makes thyroxin not a better alternative. In the light of the Mad Cow's Disease, the International Hormone Society does not recommend the use of desiccated thyroid of beef origin. For these reasons, the position adopted by the Consensus Group members of The International Hormone Society is that both type of T3 -T4 preparations have their pros and cons, and the freedom of choice between these two should be left over to the physician."