References of consensus 1 on Thyroid Hormone Therapy of Hypothyroidism

I) The view that hypothyroidism would be better treated by thyroxine alone is not based on solid scientific evidence

Arguments for treatment with T4 alone:

Guidelines on T4 recommendation

4. Roti E, Braverman LE. Thyroid hormone therapy: when to use it, when to avoid it. Drug Therapy. 1994; 24(4):2-35.

Arguments for treatment with either T4 alone, either T4 and T3

T3-T4 treatments work as well as T4 alone, but not better


Arguments pro treatment with T4 and T3 combinations

T3-T4 (and T3) treatments work better than T4


T3-T4 treatment: adding T3 to T4 results in greater improvement of clinical symptoms and signs in hypothyroid patients


When T3 and T4 are both supplemented to the food simultaneously with goitrogens, a much better prevention of goiter is obtained than when solely T4 is added, even if T4 is given at doses 7 times higher those of T3-T4 treatments

In humans, T4-T3 treatments reduce serum cholesterol and increase the speed of the Achilles tendon reflexes better than T4 treatments alone.


A study in rats rendered hypothyroid shows that cellular euthyroidism is only obtained in the target organs of hypothyroid rats if T3 is added to the classic T4 medication.


Medications with T4 alone do not succeed in achieving complete cellular euthyroidism in the target organs, probably because T3 is really the active hormone.


T3 is much more potent than T4.


Conditions that reduce the conversion of T4 to T3 such as aging, obesity, disease, stress, exercise, malnutrition, etc., may reduce the efficacy of a T4 alone treatment. In these conditions addition of T3 to T4 in the treatment may increase the efficacy of thyroid treatment.


26. Croxson MS and Ibbertson HK. Low serum triiodothyronine (T3) and hypothyroidism in anorexia nervosa. J Clin Endocrinol Metab. 1977;44: 167-73

27. Hams ARC, Fang SH, Vagenakis AG, and Braverman LE. Effect of starvation, nutriment replacement, and hypothyroidism on in vitro hepatic T4 to T3 conversion in the rat. Metabolism. 1978;27(11):1680-90


Toxic substances such as phenols, cadmium, mercury, etc, and medications such as propranolol, amiodarone and several others may interfere by stimulating or inhibiting the T4 to T3 conversion.


Deficiencies in hormones (T3 itself, TSH, growth hormone, insulin, melatonin, etc) and trace elements (selenium, iron, zinc, cupper, etc) partially block this essential step for thyroid function.


37. Erickson VJ, Cavalieri RR, Rosenberg LL. Thyroxine-5’-dioiodinase of rat thyroid, but not that of liver, is dependent on thyrotropin. Endocrinology. 1982;111:434-40


On the other hand, excesses in hormones (glucocorticoids, ACTH, estrogens,…) and trace elements (iodine, lithium, …) may slow down this conversion.


49. Scammell JG, Shiverick KT, Fregly MJ. Effect of chronic treatment with estrogen and thyroxine, alone and combined, on the rate of deiodination of L-Thyroxine to 3,5,3’-triiodothyronine in vitro. Pharmacology. 1986;33: 52-7


The absorption of oral T4 can be variable (50 to 73%[40,41], contrasting with that of T3 that is more constant and efficient (95%)


Defects in the commercial T4 preparation[43,44]


Corrective Thyroid Therapy

Thyroid medications

Alley RA, Danowski TS, Robbins TJ, Weir TF, Sabe G, Moses CL. Indices during administration of T4 and T3 to euthyroid adults. Metabolism. 1968 Feb;17(2):97-104 (equivalencies between T4, T3, T3 + T4, desiccated thyroid preparations)

Thyroxine

71. Oppenheimer JH, Braverman LE, Toft A, Jackson, IM, Ladenson, PW. Thyroid hormone treatment when and what? J Clin Endocrinol Metab. 1995;80:2873-83


73. Rolf E, Minelli R, Gardini E, Braverman LE. The use of misuse of thyroid hormone. Endocrine Rev. 1993;14:401-23


75. USP Dispensing Information: Volume 1- Drug Information for Health Care Professionals. The United States Pharmacopeial Convention, Rockville, MD, 1997

Thyroxine-triiodothyronine associations

81. Hertoghe T. Many conditions related to age reduce the conversion of thyroxine to triiodothyronine - a rationale for prescribing preferentially a combined T3 + T4 preparation in hypothyroid adults. Anti-Aging Medical Therapeutics 2000; IV: 138-53

Frequency of use of thyroid hormone treatment

83. 100. Sawin CT, Geller A, Hershman JM, Castelli W, Bacharach P. The aging thyroid: the use of thyroid hormone in older persons. JAMA 1989;261:2653-5

Thyroid treatment: thyroid hormone absorption and malabsorption

84. Hays MT, Nielsen KRK. Human thyroxine absorption: age effects and methodological analyses. Thyroid. 1994;4:55-64
91. Amin KB, Refetoff S, Fein HG, Weintraub BD. Pseudomalabsorption of levothyroxine. JAMA 1991;266:2118-20

Thyroid treatment: side effects, complications

105. Magner J, Gerber P. Urticaria due to blue dye in synthroid tablets. Thyroid. 1994 Fall;4(3):341

Some patients with low or borderline low cortisol levels may poorly tolerate any type of thyroid medication, and in particular thyroxin-triiodothyronine combinations.
Studies that show that the conversion of T4 into T3 and serum T3 is increased in cortisol deficiency, reducing the serum level of T4 while increasing that of T3


Studies that show that glucocorticoids reduce the conversion of T4 to T3


Studies that show reduced T3 nuclear receptors in adrenal deficiency