The Anti-Clinical ATA/AACE 2012 Hypothyroidism Guidelines

Clinical medicine used to mean that we physicians listened to and examined patients and adjusted their treatment to alleviate their suffering and restore their health and vitality. However, in the 2012 guidelines for the diagnosis and treatment of hypothyroidism from the American Thyroid Association and American Association of Clinical Endocrinologists, we are told that "clinical" now means "laboratory", and specifically just "TSH level". We are told that the TSH is the "best test" of a persons thyroid status and we should ignore our patients' signs and symptoms. But can we, rationally and ethically, rely on the TSH, or even the FT4 and their broad ranges and ignore symptoms? To base our practices on the evidence is a good thing, but we must be certain that the assumptions used to gather and interpret the evidence are logically and physiologically sound. The ATA/AACE guidelines and most of the research quoted contain these unstated, illogical and unscientific assumptions:

1. Laboratory reference ranges define optimal levels for human health.
2. Hypothyroidism is low thyroid-gland output as evidenced by a below-range FT4 level.
3. The TSH level can be used as the "best test" of thyroid hormone status, unless the physician knows that there is damage to the hypothalamic-pituitary (H-P) system.
4. TSH secretion and all tissues in the body respond to once-daily T4 therapy exactly as they do to endogenous thyroid gland output. A normal TSH guarantees optimal treatment.
5. "Euthyroidism" is having a TSH and free T4 within the reference ranges; regardless of symptoms or of the actual FT4 level (i.e. whether it's near the top or the bottom of the range).
6. The level of T3, that active thyroid hormone, can be ignored in both diagnosis and treatment. The physician does not need to test for, or to prescribe the active hormone.

None of these assumptions stands up to scrutiny:

1. Laboratory reference ranges for thyroid values are not based upon any research into what is ideal for health, as are ranges for glucose, cholesterol, vitamin D, and HgbA1C. They are just raw 95% population reference ranges (2 standard deviations from the mean). They arbitrarily define only the top and bottom 2.5% of the tested population as "abnormal". And it gets worse. (See below.)
2. Euthyroidism must be defined physiologically and clinically—as sufficient T3-effect indicated by the absence hypothyroid signs, symptoms, and test results. That is what we really mean, right?
3. Thyroid stimulating hormone (TSH) is not a thyroid hormone The TSH is an indirect and fallible reflection of T4/T3 levels and effects in the body. TSH secretion is not immaculate. Hyposecretion of TSH is just as likely as hyposecretion of any other pituitary hormone (LH, FSH, ACTH). Dysfunctional TSH secretion (partial central hypothyroidism) may be more common than primary hypothyroidism..
4. Even if a patient's TSH secretion is perfect, it is improbable that it and all other tissues respond to once-daily oral T4 exactly as they respond to endogenous thyroid production. Indeed, studies show that TSH-normalizing T4 therapy does not restore quality of life or health.[1,2,3] FT3 levels are lower in T4-treated patients than in controls.[4,5]

T3 is the active thyroid hormone and FT3 levels matter. However, most T3 in the body is produce by the conversion of T4-to-T3 within the cells of the body. So in an untreated patient, the most important test is the FT4 level. What free T4 level is sufficient or optimal? What do the laboratory ranges mean?

In order to produce a reference range, the manufacturer of a FT4 test kit samples 200 or so "apparently healthy" adults, based on their availability (friends, family, etc.). The subjects are not screened for symptoms of hypothyroidism. The individual laboratories that use the kit must "validate" the range for their use in their facility, with their patient-population. However, they do not spend the time and money to screen and test 200 adults; they instead modify the kit's unscreened population range using their FT4 results from physician-ordered thyroid panels--on treated and untreated patients.[6] There persons may have symptomatic hypothyroidism. Labs assume that if the TSH is normal, the FT4 must be "normal" too (TSH-thyroidology is a self-perpetuating myth). The labs thus produce very broad FT4 ranges with lower limits of 0.6 to 0.82 ng/dL and upper limits of 1.7 to 2.0 ng/dL. In contrast, when relatively healthy non-patients have been studied with similar kits, again without screening for symptoms, the 95%-inclusive FT4 range has been found to be 1.0 to 1.6ng/dL.[7,8,9,10] The lower limit is much higher than the laboratories' limit. This indicates that the labs' ranges are indeed including TSH-normal symptomatic patients; persons with partial central hypothyroidism. The labs' upper ranges are also higher due to inclusion of T4-treated patients. Consider that if labs were to report a lower limit of 1.0ng/dL instead of 0.8ng/dL, vastly greater numbers of symptomatic persons would be diagnosed as hypothyroid. Yet even 1.0ng/dL is not a diagnostic level; it's just the lowest 2.5 percent of unscreened adults. It is likely that many persons in the lower 1/3rd of the population range may have suboptimal levels and resultant symptoms.

Relying on the TSH is even worse than relying on the FT4 sick-patient ranges. The TSH level is wholly irrelevant to either diagnosis or treatment; it is useful only to determine the cause of hypo- or hyperthyroidism. The relevant tests for diagnosis are the FT4 and FT3. Their reference ranges should be based upon carefully-screened populations and upon all other medical knowledge about optimal thyroid levels/effects. However, some persons may have genetic abnormalities affecting T4-to-T3 conversion or sensitivity to T3. So ultimately, the physician must practice clinical thyroidology—he/she must diagnose and treat hypothyroidism according to signs and symptoms first and the FT4/FT3 levels second. He/she should adjust T4/T3 replacement therapy to achieve the best clinical effect, while avoiding signs or symptoms of thyrotoxicosis. This is the only true clinical thyroidology.

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Tunkhannock, Pennsylvania, Updated August 10, 2016

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[1] Saravanan P et al. Psychological well-being in patients on 'adequate' doses of l-thyroxine: results of a large, controlled community-based questionnaire study. Clin Endocrinol (Oxf) 2002:57:577-85.

[2] Wekking EM et al, Cognitive functioning and well-being in euthyroid patients on thyroxine replacement therapy for primary hypothyroidism. Eur J Endocrinol. 2005: Dec;153(6):747-53.

[3] Samuels MH et al. Health status, psychological symptoms, mood, and cognition in L-thyroxine-treated hypothyroid subjects. Thyroid 2007 17:249-58.

[4] Woeber KA. Levothyroxine therapy and serum free thyroxine and free triiodothyronine concentrations. J Endocrinol Invest 2002 25:106-9.

[5] Mortoglou A, Candiloros H The serum triiodothyronine to thyroxine (T3/T4) ratio in various thyroid disorders and after Levothyroxine replacement therapy. Hormones 2004: 3:120-6.

[6] Personal communication with directors of national and local laboratories

[7] Kratzsch J et al. New reference intervals for thyrotropin and thyroid hormones based on National Academy of Clinical Biochemistry criteria and regular ultrasonography of the thyroid. Clin Chem. 2005: Aug;51(8):1480-6.

[8] Takeda K et al. Evaluated reference intervals for serum free thyroxine and thyrotropin using the conventional outliner rejection test without regard to presence of thyroid antibodies and prevalence of thyroid dysfunction in Japanese subjects. Endocr J. 2009;56(9):1059-66.

[9] González-Sagrado M et al. Population-specific reference values for thyroid hormones on the Abbott Architect i2000 analyzer. Clin Chem Lab Med. 2004 May;42(5):540-2. (range found 0.84-1.42ng/dl, shifted downard by 0.2ng/dl with different kit.)

[10] Walter Reed Army Medical Center, 2009, based on 120 healthy soldiers