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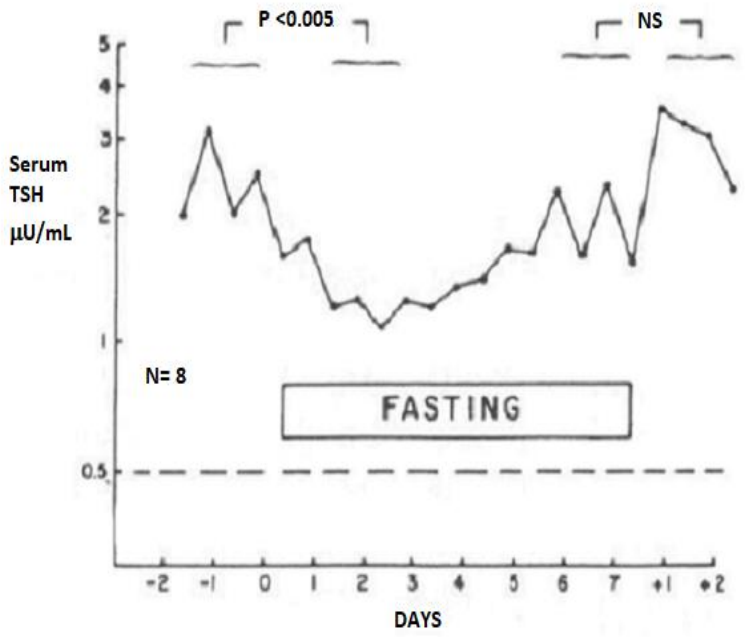
July 2018

Letter to Providers regarding how I evaluate and treat famine state hypothyroidism

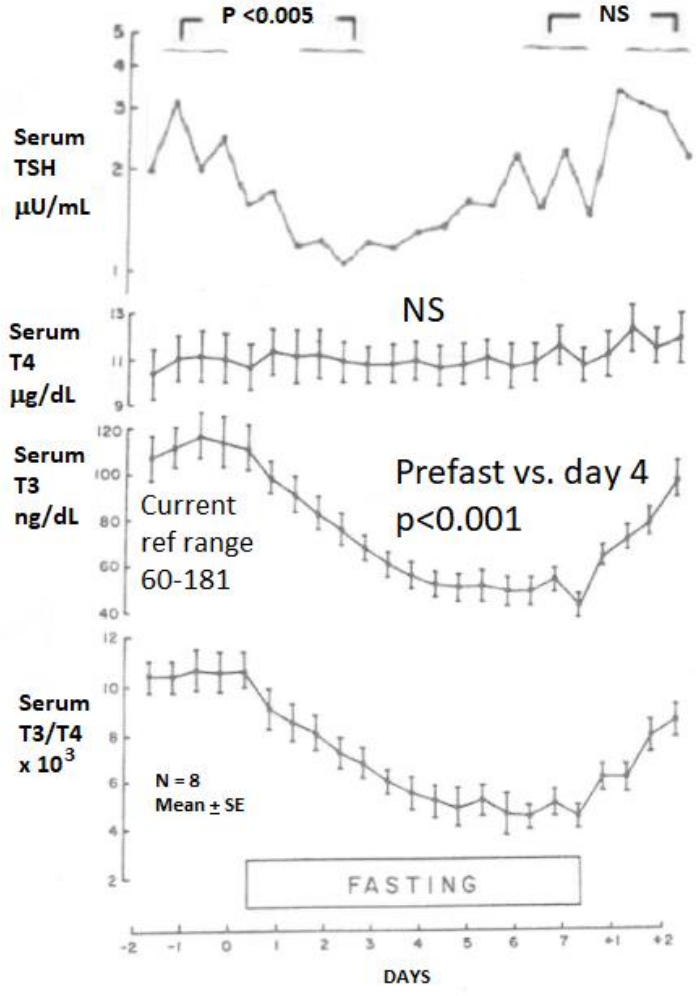
When you see a suppressed TSH, of course it looks like hyperthyroidism. From my background as a PhD evolutionary/ecological physiologist, I've gained a different understanding of this highly evolved system. Having worked in weight management for 15 years, I am convinced that standard evaluation and treatment of hypothyroidism is inappropriate for those trying to lose weight.

We were all taught that the gold standard for evaluating thyroid levels is TSH and that treatment should be with T_4 without valuing both symptoms and thyroid hormone levels (T_3 and reverse T_3). The medical community assumes that homeostasis is being maintained with a stable setpoint for body temperature/metabolism. But during weight loss attempts, about 90% of people decrease that setpoint, presumably to survive famine. Considerable literature from 1950 to the present supports this statement. Normal TSH values really mean that the thermostat and furnace are working together to maintain a setpoint. But it doesn't tell us what the setpoint is. While earlier studies such as the one shown here were done with fasting or extremely hypocaloric diets, even moderate caloric reduction causes the same results.

I argue that this narrow view of a stable setpoint for thyroid regulation is incorrect and harms patients trying to lose weight, helping to fuel the obesity epidemic.



In a study of fasting men with obesity, Croxson et al. (1977. *J Clin Endocrinol Metabol*. 45:560), clearly showed that conventional dogma is incorrect. (The following graphics are adapted from the Croxson study.) Two days into the fast, assessing only TSH levels lead you to assume that both thyroid hormones and metabolism *increased*. Then over the next several days, TSH increases, such that on the last two days of the fast, TSH has returned to approximately its pre-fast levels. You would assume this means that thyroid hormone levels *decreased* before the fast ended.



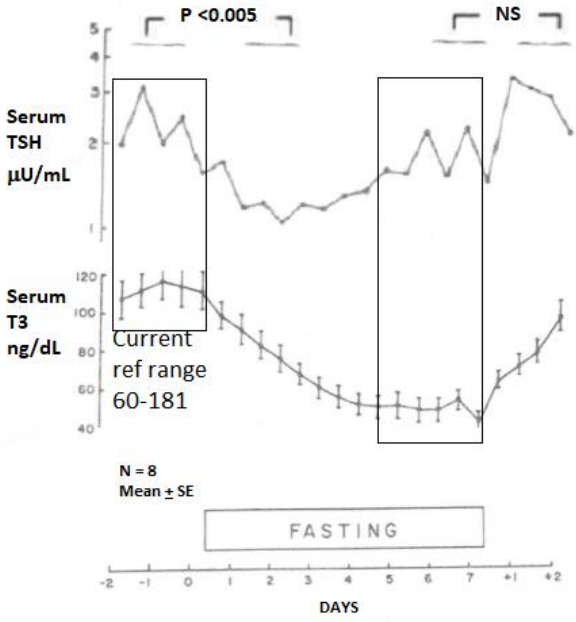
Now if we add the other hormones measured in Croxson's study, the picture changes.

If we look at TT_4, you will see no change. Other studies report stable, increased, or decreased TT_4 and FT_4. Thus, it's unclear what exactly is going on with T_4. But T_4 is a prohormone which must be converted to T_3, the active thyroid hormone. So, we really need to understand what's happening with T_3.

By looking at TT_3 values, you now see that the relationship between TSH and serum T_3 shows a decrease in T_3 during the fast. More recent studies show that the same applies for FT_3. Conventional interpretation does not explain this. The ratio of T_3/T_4 shows the same pattern.

This is all hard to understand if you don't recognize a broader view. In nature, both predictable and unpredictable environmental changes can cause lifesaving changes in setpoints for hormonal feedback systems.

Two years after Croxson's study was published, Gardner *et al.* proved the mechanism for the change in hypothalamic setpoint for thyroid in the famine response (*NEJM* 300:579). Now look at just the relationship between TSH and T_3 in Croxson,. The first box to the left shows that prefamine, there is a stable relationship between TSH and T_3. TT_3 is being regulated at approximately 120 ng/dL, which is the middle of the current reference range (60-181). (Croxson did not report reference ranges.) When the famine begins, TSH dips slightly and loses its circadian rhythmicity, then returns to normal in the second box, *while the famine is still ongoing*. At the beginning of the famine T_3 dips, but unlike the TSH, it stays down, resulting in a new relationship between TSH and T_3 levels. A lower level of T_3 is being accepted by the hypothalamus as the "correct" level for current conditions. Note that TT_3 is slightly below the low end of normal for the current reference range. This change in relationship between TSH and serum T_3 is both the demonstration and proof of a change in setpoint.

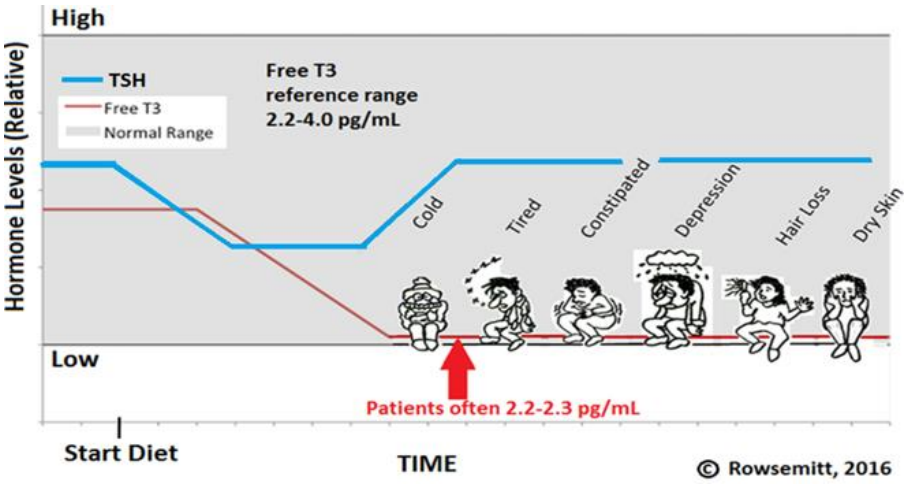


One need not be fasting to see this response. Overweight women fed 1000 Kcal/day with exercise and controlled behavior decreased 24-hr energy expenditure on day 1 and resting energy expenditure on day 2. So, the power to slow metabolism in the face of decreased food supply occurs quickly.

When a patient comes to you struggling to lose weight (whether on thyroid or not), if you look more closely you'll find typical dieting patients have symptoms of low thyroid, many swear they are eating as advised for weight loss, and the TSH is perfectly normal. T_3, the active hormone, as either TT_3 or FT_3, is often at the very low end of normal. If you decided to alleviate the hypothyroid symptoms with T_4, no improvement would occur because very little T_4 is converted to T_3 during the famine response. If you decided to treat with T_3 to

attain euthyroid symptomatology, you would find that T_3 would be in the upper level of normal values yet TSH would be suppressed. But why is the TSH suppressed? It only makes sense if you understand that the hypothalamic thermostat has been lowered to allow for decreased metabolism to defend against death from famine. The patient now is euthyroid symptomatically, able to lose weight when doing the right behaviors, and the **only** signal telling us that the patient is hyperthyroid is the TSH.

The enclosed poster (presented at the Obesity Medicine Association conference in September 2016) provides more detail. [Poster is attached; If you wish to receive a printed copy, please contact me and I will mail one.] The phenomenon is similar to nonthyroidal illness syndrome (NTIS). When I treat to normalize T_3 levels and eliminate hypothyroid symptoms, TSH is suppressed because of this protective setpoint change.



The study by Croxson in 1977 did not report symptoms. But if you look at my cartoon graphic, you'll see that my patients (3 weeks on low carb diet, not fasting) often are at the low end of normal free T_3 and usually display some of the hypothyroid symptoms shown. They also may have plateaued while continuing the good behaviors that previously caused weight loss.

While the famine response (increased appetite and decreased metabolism) has been studied for over 50 years, its ramifications on weight loss attempts are not generally recognized. In recent years, Kevin Hall, PhD, a physicist at NIH, has shown that the metabolic dip experienced by extreme dieters lasts at least 6 years regardless of whether the patients maintain the loss or regain weight. Even a small decrease in food intake can decrease metabolism. A minority of people can successfully lose weight and keep it off simply with behavior changes; these outliers make it easy to think that everyone can succeed on their own. In fact, Hall and others show that a minority of individuals do not develop the decreased metabolism of the famine response.

Most people have trouble picturing what's going on here. But my patients understand it when I tell them: *"We're having an argument with the thermostat in your brain that regulates metabolism. Your brain recognizes that your decreased food intake threatens survival. It's trying to save your life in this famine by bringing you as close to hibernation as a person can get. This gives you a better chance of surviving the famine. But* **we** *know that you are not in danger of dying of starvation. And* **we** *know that the goal is for you to lose weight and that dropping your metabolism is counterproductive. This is why I prescribe a form of* T_3*.* ***The brain finds normal circulating*** T_3 ***level with insufficient food and concludes that you're going to die of starvation, so it attempts to decrease thyroid hormone production by sending TSH to zero****."* If I were to lower the T_3 to a level that results in normal TSH, weight loss is almost impossible because I would be agreeing with the brain that the patient **should** have low metabolism.

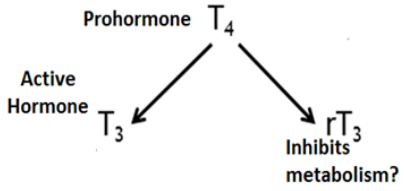
Obviously, this is not conventional medicine. The enclosed abstract from *Annals of Internal Medicine* (Elizabeth McAninch and Antonio Bianco [an author of the 2014 American Thyroid Association Guidelines for the Treatment of Hypothyroidism]) shows that recognized experts are rethinking evaluation and treatment of hypothyroidism. (In a personal discussion with Dr. McAninch, I found that she clearly understands the issues associated with the famine response although that is not her primary research direction.)

As a nurse practitioner, I specialize in weight loss and the decreased metabolism frequently associated with dieting. From 2003 until his retirement from practice in 2010, I worked with Dr. Thomas Najarian (inventor of the weight loss drug Qsymia) in his private practice. He and I continue to collaborate on issues of hypothyroidism during weight loss attempts, which I now call "famine response hypothyroidism."

Dr. Najarian and I treated thyroid with these concepts over a decade ago in his weight loss practice. While double-blind studies on this treatment are lacking, I believe there is compelling intellectual justification in the published literature for treating with some form of T_3 for certain weight loss patients. The alternative of not

treating patients with famine response hypothyroidism is to leave them fighting a battle which is extremely difficult with their decreased metabolism.

Earlier published studies using T_3 were quite different from what we have done. Studies were performed with specific doses and sometimes with insufficient dietary protein. Our approach only treats patients who are symptomatic of low thyroid and have either free T_3 less than mid-range or a low ratio of FT_3/rT_3. I never give people thyroid hormones to force weight loss; I give thyroid hormones to eliminate low thyroid symptoms while keeping the patient's FT_3 within normal limits. This allows the patient to lose weight when they are doing the typically advised types of diet and exercise, so that the 3500 Kcal rule will work for them. [The ratio of FT_3/rT_3 is considered because in some patients, rT_3 increases via decreased plasma clearance as it does in NTIS. Its significance is under debate, but for those patients whose rT_3 increases, it appears to correlate with symptoms, even if we are uncertain of its mechanism.]



In the past few years, I have given a series of peer-reviewed presentations on this topic: a CME webinar for the Obesity Medicine Association (formerly American Society of Bariatric Physicians) in January 2016; both a talk and the attached poster at their conference in September, 2016; and coauthored a poster with Dr. Najarian and a group from Stanford examining the value of T_3, rT_3, and symptoms in predicting weight loss in bariatric surgery patients (Obesity Week 2016; combined meetings of The Obesity Society and American Society for Metabolic and Bariatric Surgery). Dr. Najarian and I also published two papers in the online journal Thyroid Science.

http://www.thyroidscience.com/editorials/editorials/rowsemett.najarian.7.25.11.htm

http://www.thyroidscience.com/hypotheses/rowsemitt.najarian.H.6.11/rowsemitt.najarian.6.11.htm

http://www.thyroidscience.com/cases/najarian.rowsemitt.6.2011/najarian.rowsemitt.6.11.htm

So, by conventional wisdom, you see an obese or overweight patient who claims to be doing all the right things but is unable to lose weight. The thyroid looks fine by TSH and free T_4. It's easy to think she/he is cheating on the diet (harder to think conventional wisdom is wrong and that TSH is leading us to misjudge the situation). And, when treated my way, the TSH plummets, making most providers conclude that I'm overtreating thyroid. Yet when you understand that this is a classic example of a highly adaptive eco-physiological change in feedback setpoint, you understand that using the TSH signal with a conventional view misinterprets this condition. My patients rarely suffer adverse effects of treatment. (I can prove literature supporting this view.)

One can also envision that these thoughts may prove useful for patients who are hypothyroid and normal weight, but do not feel well-treated on T_4. I have numerous patients who feel I've given them their lives back by basing treatment on FT_3, FT_3/rT_3, and symptoms, while ignoring TSH. McAninch's work focusses on genetic abnormalities in the main enzyme which converts T_4 to T_3. This may apply to approximately 10% of hypothyroid patients.

I can be reached at (805) 748-6752 or by email rosey805@gmail.com. I'd be happy to come visit with you to discuss these ideas if you are interested.

Sincerely,

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Family Nurse Practitioner

Enclosures:
Abstract: McAninch and Bianco *Annals of Internal Medicine* 2017
Poster, Rowsemitt and Najarian Obesity Medicine Association 2016

Ann Intern Med. 2016 Jan 5;164(1):50-6. doi: 10.7326/M15-1799.

The History and Future of Treatment of Hypothyroidism.

McAninch EA, Bianco AC.

Erratum in

- Correction: History and Future of Treatment of Hypothyroidism. [Ann Intern Med. 2016]

Abstract

Thyroid hormone replacement has been used for more than a century to treat hypothyroidism. Natural thyroid preparations (thyroid extract, desiccated thyroid, or thyroglobulin), which contain both thyroxine (T4) and triiodothyronine (T3), were the first pharmacologic treatments available and dominated the market for the better part of the 20th century. Dosages were adjusted to resolve symptoms and to normalize the basal metabolic rate and/or serum protein-bound iodine level, but thyrotoxic adverse effects were not uncommon. Two major developments in the 1970s led to a transition in clinical practice: 1) The development of the serum thyroid-stimulating hormone (TSH) radioimmunoassay led to the discovery that many patients were overtreated, resulting in a dramatic reduction in thyroid hormone replacement dosage, and 2) the identification of peripheral deiodinase-mediated T4-to-T3 conversion provided a physiologic means to justify l-thyroxine monotherapy, obviating concerns about inconsistencies with desiccated thyroid. Thereafter, l-thyroxine monotherapy at doses to normalize the serum TSH became the standard of care. Since then, a subgroup of thyroid hormone-treated patients with residual symptoms of hypothyroidism despite normalization of the serum TSH has been identified. This has brought into question the inability of l-thyroxine monotherapy to universally normalize serum T3 levels. New research suggests mechanisms for the inadequacies of l-thyroxine monotherapy and highlights the possible role for personalized medicine based on deiodinase polymorphisms. Understanding the historical events that affected clinical practice trends provides invaluable insight into formulation of an approach to help all patients achieve clinical and biochemical euthyroidism.

PMID:26747302

PMCID:PMC4980994

DOI:10.7326/M15-1799

Thyroid Treatment in Weight Loss Patients: Ecological Physiology Provides a New Paradigm

Carol N. Rowsemitt, PhD, RN, FNP-C & Thomas Najarian, MD

CNR: Comprehensive Weight Management, A Nursing Corp., Templeton, CA; TN: Incline Village, NV (OMA 9/16)

ABSTRACT

Chronic decreased metabolism occurs in weight loss. Current thought on thyroid fails to understand this condition. Evaluation is primarily with thyroid stimulating hormone (TSH); treatment is with levothyroxine (T_4). We explain why both are wrong for most weight loss patients. Viewing the hypothalamic-pituitary-thyroid axis as having a stable set point is a mistake.

Eco-physiological studies inform us that animals evolved to adjust to environmental changes. Feedback loop set points change to achieve these adaptations. Most studied is seasonal breeding: e.g., adult male hamsters basically undergo puberty every spring, and reverse the process every fall. Higher levels of testosterone are needed to suppress gonadotropin secretion in summer than in winter, proving a set point change. In humans, dieting lowers the set point for the active thyroid hormone, liothyronine (T_3), so the hypothalamus redefines the range of normal free T_3 to be at a lower level than when well-fed.

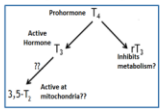
When a patient presents with symptoms of low thyroid and a weight-loss plateau despite appropriate behaviors, but has normal TSH, most clinicians conclude the thyroid is fine. But free T_3 is often at the low end of normal or the ratio of free T_3/reverse T_3 is low. (Reverse T_3 either decreases metabolism or is a marker for decreased metabolism.) In either case, treatment with a source of T_3 returns T_3 to mid- or high-normal. Hypothyroid symptoms resolve, and weight loss restarts. Yet TSH is zero due to the decreased set point.

The patient is hyperthyroid in one measure only: TSH. Most providers would conclude the patient is hyperthyroid and discontinue T_3, resulting in recurrence of hypothyroid symptoms and plateau. Treating with T_4 will fail, as T_4 does not increase T_3 in the famine state. Understanding this framework leads us to focus on symptoms and thyroid hormone levels.

While many questions remain, failure to recognize the eco-physiological changes in the famine response may be dooming many patients to only a 10% weight loss with possible regain even while continuing a low calorie diet.

Basic & Ecological Physiology

Thyroid Pathways



Negative Feedback Loops

Maintain Homeostasis.

- But set points can change (e.g., puberty)

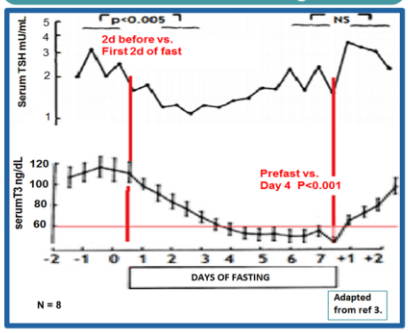
Seasonal breeders:

- **In breeding season, males have a high set point for testosterone feedback on gonadotropin secretion.**
- **In non-breeding season, males revert to a low set point.[1]**

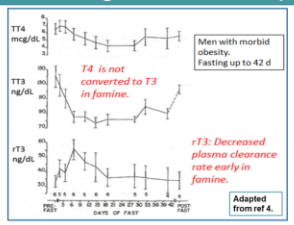
***Dieters* experience a decrease in set point for both total T3[2] and free T3.**

CNR contact info: rosey805@gmail.com

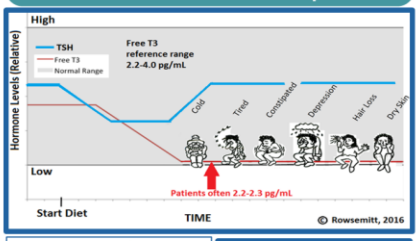
T3/TSH Set Point Changes

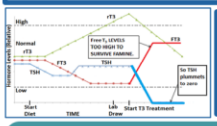


Reverse T3 Changes in Famine Response



Our Patients in Famine Response





Maladaptive Hypothyroidism: [5,6]

- **Low T_3 or low ratio FT_3/rT_3 [7]**
- **Low thyroid symptoms**
- **Prevents weight loss while on diet**

Treat with T_3

- **Symptoms resolve.[6]**

CONCLUSIONS

In Famine Response:

- ***TSH is the wrong signal* for assessing thyroid before and during treatment.**
- ***T4 is the wrong treatment.***
- ***Compounded sustained release T3* is often the best treatment for resumption of weight loss and elimination of hypothyroid symptoms.**

REFERENCES

1. Turek. (1977). *Endocrinology* 101:1210.
2. Gardner et al. (1979). *N Engl J Med.* 300:579.
3. Croxson, et al. (1977). *J Clin Endocrinol Metab.*45:560.
4. Carlson *et al.*(1977). *J Clin Endo Metab.* 45:707
5. Rowsemitt and Najarian. (2011). *Thyroid Science.* 6(4):H1.
6. Najarian and Rowsemitt. (2011). *Thyroid Science.* 6(6):CR1.
7. Holtorf. (2014). *J Restorative Med* 3:53.
Modified to correct references 4/16/18