

<https://chriskresser.com/low-t3-syndrome-i-its-not-about-the-thyroid/>
Basic thyroid physiology

In order to understand Low T3 Syndrome, you'll need a basic understanding of thyroid physiology. Regulation of thyroid metabolism can be broken down into the following five steps:

1. The hypothalamus (a pea-sized gland in the brain) monitors the levels of thyroid hormone in the body and produces thyrotropin releasing hormone (TRH).
2. TRH acts on the anterior pituitary (directly below the hypothalamus, but outside of the blood-brain barrier) to produce thyrotropin, a.k.a. thyroid stimulating hormone (TSH).
3. TSH acts on the thyroid gland, which produces thyroxine (T4) and triiodothyronine (T3), the primary circulating thyroid hormones. The thyroid produces T4 in significantly greater quantities (**in a ratio of 17:1**) than T3, which is approximately 5x more biologically active than T4.
4. T4 is converted into the more active T3 by the deiodinase system (D1, D2, D3) in multiple tissues and organs, but especially in the liver, gut, skeletal muscle, brain and the thyroid gland itself. D3 converts T3 into an inactive form of thyroid hormone in the liver.
5. Transport proteins produced by the liver – thyroid binding globulin (TBG), transthyretin and albumin – carry T4 and T3 to the tissues, where they are cleaved from their protein-carriers to become free T4 and free T3 and bind to thyroid hormone receptors (THR) and exert their metabolic effect.

Mechanisms of Low T3 Syndrome

As you can see, the production, distribution and activation of thyroid hormone is complex and involves several other organs and tissues other than the thyroid gland itself.

Hypothyroidism is a defect in step #3, because it typically involves a dysfunction of the thyroid gland itself – most often caused by autoimmune disease (Hashimoto's, Ord's, Graves') and/or iodine deficiency.

However, in Low T3 Syndrome, the problem generally occurs in steps #1, #2, #4 and #5. None of those steps are directly related to the function of the thyroid gland itself.

More specifically, Low T3 Syndrome can include the **following mechanisms**:

- Modifications to the hypothalamic-pituitary axis
- Altered binding of thyroid hormone to carrier proteins

- Modified entry of thyroid hormone into tissue
- Changes in thyroid hormone metabolism due to modified expression of the deiodinases
- Changes in thyroid hormone receptor (THR) expression or function

Low T3 Syndrome in acute and chronic illness

Most of the studies on Low T3 Syndrome have been done on people suffering from acute, life-threatening illness. In the intensive care unit, the prevalence of abnormal thyroid function tests is remarkably high. More than **70% of patients show low T3 and around 50% have low T4**.

Many of these studies have indicated a **direct relationship between Low T3 Syndrome the severity and both short- and long-term outcome of disease**. The lower the T3 level in critically ill patients, the worse the outcome tends to be.

However, studies examining thyroid hormone replacement in these situations have shown mixed results. In most cases – with the exception of cardiovascular disease –**taking thyroid hormone did not improve outcomes**. We'll discuss this in more detail later.

Recently, more attention has been given to Low T3 Syndrome in non-critical, chronic illness. Specifically, the question on everyone's mind (including mine) is whether thyroid hormone replacement is useful in this situation, or if – as some have suggested – it could even be harmful.

In emotional, psychological or physiological stress, the body will convert excess T4 to reverse T3 (rT3) as a means of conserving energy for healing and repair. It is at least possible, therefore, that replacing thyroid hormone in these cases may not be beneficial.

On the other hand, in those suffering from long-term chronic illness, Low T3 Syndrome may be more reflective of pathology than adaptation, and this group may benefit from T4 or T3 supplementation.

We'll explore all of these questions in more detail in the articles to follow, and I'll also share some of my observations from my clinical practice. Stay tuned!