

## Hypothyroidism #2 – Treatment Considerations

Patients with hypothyroidism (low thyroid hormone levels) need to be treated with oral thyroid hormone supplements. In principal, this should be a straightforward process. One might think that one could adjust the dose of a thyroid hormone supplement until one obtains a "good level" and all should be well. However, the situation is more complicated than that. Here are some of the reasons why:

1. The thyroid gland makes not one, but two variants of thyroid hormone: thyroxine (or tetraiodothyronine, T4) and triiodothyronine (T3). Most experts consider T4 to be a "prohormone" because it has little or no intrinsic biological activity. The primary function of T4 is to serve as the precursor for T3, the biologically active hormone.
2. The production of T3 from T4 is accomplished by two different enzymes (Type I and Type II T4-5'-deiodinase) that occur in varying amounts in different parts of the body. The Type I enzyme is primarily in the liver, kidney, and thyroid gland and makes about 35% of circulating T3. The Type II enzyme is primarily in muscle, brain, pituitary, and skin tissue, and makes about 65% of circulating T3.
3. The thyroid gland of an average healthy person makes about 90 mcg of T4 daily and about 7 mcg of T3 daily. Each day, a total of approximately 30 mcg of T3 is made in various tissues by conversion from T4.
4. There is variation from person to person in the efficiency of the conversion of T4 to T3. In part, this is because there are common variants of the genes that code for the deiodinase enzymes amongst healthy people.
5. The conversion of T4 to T3 is a regulated process in normal individuals. Variation of conversion efficiency occurs depending on current health and nutrition status. These variations help us to better survive malnutrition and various types of illness.
6. The reference ranges for T4 and T3 vary widely amongst healthy people. Levels that may be good for one person may not be good for another.
7. Thyroid hormone supplements are available as purified T4 preparations, purified T3 preparations, and mixtures of the two. A T4 preparation is broken down by the body slowly; half of an administered dose is still circulating after 1 week. But T3 is broken down much faster; half of an administered dose is broken down in 10 to 36 hours. Time-release T3 supplements are currently not available. The T3/T4 mixtures were originally derived from extracts of pig thyroid glands. These products are good for pigs – but not people!

With such complexity, how can treatment for hypothyroidism be optimized? Measurement of the thyroid stimulating hormone (TSH, made by the pituitary gland) provides an important clue. If T4 and T3 levels are too low, the TSH level will rise. Conversely, if T4 and T3 levels are too high, the TSH level will fall. But the reference range for TSH in the normal population is also very broad (spans a 10-fold range) and varies with age. A TSH level that is optimal for one person is not necessarily good for another person. Also T3 is 3-4 times more potent at suppressing the TSH level than is T4. Finally, most of the T3 and T4 hormones are bound to proteins, but only the non-bound fractions can carry out hormone functions. So, to achieve optimal thyroid hormone treatment, multiple factors must be considered, including levels of the nonbound T3 and T4 hormones, the TSH hormone level, the patient's symptoms, other concurrent medical/biological issues, and physical exam findings.

After all is said and done, most people with hypothyroidism (perhaps 80-90%) can achieve excellent results with a once daily carefully adjusted dose of a purified T4 medication. If optimal results are not achieved with this approach, combination therapy with purified T3 and T4 medications may be required. You need an experienced endocrinologist to guide you through this process.