

Breakthrough Discovery: Need For T3 Could Be Genetic by Dr Gary Pepper

Do you wonder if you need t3 (Cytomel, triiodothyronine, liothyronine) added to your thyroid hormone treatment to feel normal again? The answer could be in your genes.

Recent discoveries reviewed by Antonio C. Bianco, M.D., Ph.D. at the recent American Thyroid Association meeting, reveal how genetic differences influence the effectiveness of thyroid hormone replacement. Dr. Bianco's lecture focused on studies pinpointing inborn differences in the way people metabolism thyroid hormone to explain why t3 treatment of hypothyroidism is probably required by some to restore normal functioning of their brain, muscle and heart.

The most frustrating problem for people with hypothyroidism is being unable to convince their doctor that treatment with Synthroid, Levoxyl or similar pure t4 product, isn't working. Continued symptoms of fatigue, weakness, inability to concentrate or think clearly, and inability to lose weight despite really trying, result in tension between the doctor and the "complainer". When assessing the adequacy of thyroid hormone replacement therapy most doctors rely on the blood tests known as the Thyroid Function Panel. Typically this includes a measurement of t4, t3, t3RU, and TSH. Some panels may also include free t4 or free t3 measurements. If the hormone levels on these tests are "within normal limits" the doctor will often insist that the treatment is a success but it is the patient who fails to recognize this. A minority of endocrinologists know many of these "failures" can be turned into success by the addition of t3, the less utilized but much more powerful form of thyroid hormone.

Most of the biological effects of thyroid hormone in the body are due to the action of t3. The most common forms of thyroid hormone replacement however, involve giving t4 in the form of Synthroid, Levoxyl, levothyroxine etc. The t3 required by our tissues is produced by specific enzymes which convert t4 to t3 in the cells of the liver, kidney, brain, muscle, heart etc. These converting enzymes are known as deiodinases and under normal conditions they are responsible for about 80% of the body's t3. The process by which t3 is produced from t4 is known as peripheral conversion.

It has long been the contention of the leaders in thyroid disorders that based on their arithmetic, t4 replacement is sufficient to provide all the t3 the body needs via peripheral conversion and giving t3 supplementation doesn't make good medical sense. Now, based on the new information provided by researchers like Dr. Bianco, the "arithmetic guys" will, in my opinion, need to revise their thinking finally allowing the way for acceptance of t3 replacement approaches.

I will continue the explanation of the new breakthrough in genetic control of thyroid hormone replacement treatment in Part 2 of this post.

Breakthrough Discovery in Thyroid Hormone Therapy: Part 2

Treatment of hypothyroidism (low thyroid function) is accomplished by administering thyroid hormone by mouth in sufficient amounts to restore levels back to normal. At first glance this might seem like a simple goal to achieve. The truth is hormone replacement therapy is complex because there exists two very different thyroid hormones and because levels of thyroid hormone in the blood do not always reflect the amount of thyroid hormone within the cells where the hormone exerts its effects. In Part One of this blog I began to discuss how genetic differences among individuals could explain why some people need a complex mix of thyroid hormones to adequately treat hypothyroidism. In Part 2, I want to explain the nature of the differences between individuals and how it determines what sort of thyroid hormone therapy may be needed.

In May 2009 a group of researchers (Panicker, V. et al) in the UK published the WATTS study, the largest and most comprehensive study to date, of hypothyroid patients treated with combination t4 and t3. The goal of the study was to discover whether genetic differences in the population of hypothyroid patients accounts for some individuals needing t3 in addition to traditional t4 therapy. The researchers looked at 697 hypothyroid individuals and analyzed their DNA for differences in the portions controlling crucial enzymes which process thyroid hormones known as deiodinases. These enzymes are found widely distributed in the body including the thyroid, brain, muscle, liver, kidney and pituitary gland. As explained above, deiodinases convert t4 to the much stronger form of thyroid hormone, t3. At the same time the researchers measured patients' mood and sense of well being on t4 alone and when t3 was added to the therapy.

Key findings of the WATTS study are that there is a substantial difference among individuals in the genes that make the deiodinases. In other words, due to genetic differences (mutations), there are differences in the way individuals make t3 out of t4. In a group of people, mutations in the genes that make a particular protein (in this case, the deiodinase), are called polymorphisms. The researchers discovered that a certain mutation in the deiodinase gene is associated with a poor sense of well being on t4 only therapy, and in the presence of this mutation a significantly better response to adding t3 can be found compared to those without this mutation. Of the group of hypothyroid patients studied in the UK about 16% possessed the faulty deiodinase gene. In other groups in other countries the percentage of people with this mutation could be higher or lower.

The traditional treatment of hypothyroidism is to administer t4 (Synthroid, Levothyroxine, Levoxyl etc.). It is the conventional wisdom that inactive t4 is converted in the body to the

active thyroid hormone t3 by “peripheral conversion” in sufficient amounts to restore normal thyroid balance. The recent breakthrough discoveries described in the WATTS study reveal for the first time that individuals differ in how their bodies process (metabolize) thyroid hormone. While some may convert enough t4 to t3 in the cells of the body to restore normal function, due to genetic differences some individuals will not be able to make enough t3 leaving them with persistent hypothyroid symptoms. Since the problem is a deficiency of t3 within the cells of the body, measuring thyroid hormone levels in the blood cannot adequately reveal the problem. T4 replacement treatment alone can result in thyroid levels that appear normal on blood tests so doctors conclude that persistent hypothyroid symptoms are not related to the hormone therapy.

Based on my personal experience and the documented experience of many of the members of Metabolism.com it is clear that endocrinologists and other physicians are often reluctant to consider combination therapy for hypothyroidism, either by using Armour thyroid or adding t3 (Cytomel, liothyronine) to t4 only therapy. With this new research in hand, hypothyroid individuals and their advocates can finally state with confidence that: Yes! There is a firm scientific foundation for combination t4/t3 therapy and; No! We are not just chronic complainers or kooks. If I had hypothyroidism and was going to request a change in my thyroid treatment I would say something like, “Due to polymorphism of the deiodinase gene I probably possess a defective D2 deiodinase and therefore my peripheral conversion of t4 to t3 is impaired. I need t3 added to t4 to compensate for reduced intracellular t3 levels which cannot be detected on blood tests. Without t3 I continue to suffer with cellular hypothyroidism which is the likely cause of my persistent symptoms.”

If you try this approach and your doctor looks bewildered hand them a copy of the study by Panicker et al in the Journal of Clinical Endocrinology and Metabolism, 2009, 94(5): 1623-1629.

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<http://www.metabolism.com/2009/11/07/breakthrough-discovery-thyroid-hormone-therapy-part-2/>

To see Panicker et al Abstract go to:

<http://jcem.endojournals.org/cgi/content/abstract/94/5/1623>

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