Thyroid hormones and the right tests to diagnose low thyroid.

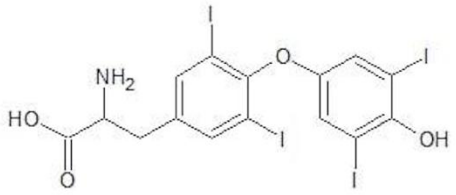
Thyroid produces 2 major *hormones* – T4 and T3. It also makes another hormone called Calcitonin, which is involved in calcium metabolism.

To make a thyroid hormone, you need to put together 2 molecules of an amino acid *tyrosine* plus 3 or 4 iodine atoms. An amino acid is a building block of protein, there are 20 different amino acids altogether.

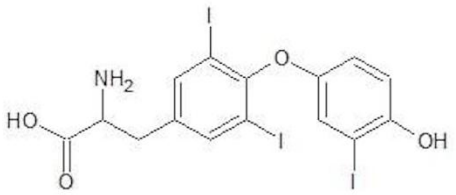
There is an enzyme that combines 2 tyrosines with 3-4 iodines, it is called thyroid peroxidase (TPO).

T4, also called *thyroxine*, has 4 atoms of iodine. T3 or *tri-iodo-thyronine* has 3 atoms of iodine. If you look at the chemical formula of T3 and T4, you will see 2 round looking structures, those are tyrosines. Iodine is represented by letter I. There are other letters in this picture. H means hydrogen, O means oxygen, N means nitrogen. There is once element that is not shown, but presupposed, it is Carbon, represented by letter C, but often not shown and just presumed to be where 2 or more straight lines meet to form an angle. So thyroid hormones contain lots of C, they are just not shown.

Thyroid Hormones



Thyroxine (T4)



Triiodothyronine (T3)

The active hormone is T3. It can be made directly by the thyroid gland, or by removing one of the iodines from T4. This is done by an enzyme called *deiodinase*. The iodine removed from T4 to make T3 must be a very specific one, the one in the right upper corner. If a different iodine is removed, the one in the upper left corner, the result is a *reverse T3*, a totally inactive substance without any effect.
Most of T4 and T3 are collected in the thyroglobulin (TG) and colloid inside the thyroid gland. We talked about colloid and thyroglobulin earlier. In other word, there are lots of thyroid hormones within the gland, already made and ready to be released as needed, and more can be made quicky from thyroglobulin.
A fraction of T4 and T3 go directly into the blood and are distributed throughout the body.

Now you know that T4 can turn into T3. But that's not the end of the story. T3 can turn into T2 if you remove one more iodine, and T2 can become T1. The function of T2 and T1 is not fully understood. There are suggestions that they also participate in metabolic regulation and may have antioxidant activity. They are not usually measured by thyroid blood tests.

The bulk of both T4 and T3 are attached to proteins, which carry them in the blood. These hormones are called "bound". Only a small fraction of T3 and T4 are not bound. They are called "free" and they are the ones doing the thyroid work. The bound hormones are inactive, but don't think of them as somehow imprisoned. They are released and become "free" when needed, so this is simply a way to have some hormones ready to go, on standby as it were, immediately available when needed.

The discussion of thyroid hormones would not be complete without mentioning TSH and TRH. I have a special report about them, feel free to download and read it.

Briefly, TSH stands for thyroid stimulating hormone also known as thyrotrophin. It stimulates the thyroid gland into making more T3 and T4. It's like a whip for a horse, makes it run faster. TSH is produced by a gland in the brain called pituitary. How much TSH is present depends on 2 factors. 1st, the level of thyroid hormones. This relationship is called "negative feedback" What it means is that the more thyroid hormones, the less TSH and vice versa, the less thyroid hormones you have, the higher the TSH will go to stimulate the thyroid into action.

Pituitary is itself regulated by another part of the brain called hypothalamus. It produces TRH (thyrotrophin releasing hormone), a hormone that stimulates the pituitary gland to produce TSH.

In short, there is a complex interaction of various substances produced by the brain and the thyroid gland, all carefully regulated to create the optimal levels of thyroid hormones.

There is another hormone that needs to be mentioned. Besides the cells that make T4 and T3, thyroid gland also has special cells, called C-cells, that make a hormone called Calcitonin. The job of Calcitonin is to make Calcium in the blood lower.

Calcium level in the blood is very important for normal heart and muscle function, so calcium is very tightly regulated. There are hormones that make it go up when necessary and there is **Calcitonin** that makes it go down. The goal is to keep calcium levels normal.

Blood tests to order to check for low thyroid

Most doctors just order TSH level. "Normal" level of TSH is 0.4-4.5. If your level is higher than 4.5, there is a suspicion that you may have low thyroid, but if it's not higher, then you are called normal. Some doctors also check T4. "Normal" T4 is 5 to 12. If your level is less than 5 then your doctor may consider that you may have low thyroid. But if it is more than 5, then you are normal, no matter how many symptoms you may have.

What I usually check in every patient are TSH, total T4 (free plus bound), free T4, total T3, and free T3. I often order reverse T3 as well. In some situations, I also order antibodies against thyroglobulin (anti TG antibodies) and antibodies against thyroid peroxidase (anti TPO antibodies).

The point is that most doctors do not do the right blood testing and as a result miss many cases of low thyroid. You need to work with an experienced doctor who can order all the right tests.