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Can My Lab Work Tell Me I Am Depressed?

For the next few weeks, I want to focus on different blood markers and their relationship to depression. For the first week, I want to talk about a few thyroid blood patterns and how they relate to signs/symptoms of depression. If a patient is suffering from depression, their labs can tell you a lot as to what area may be the problem. Remember, depression can have several origins. Taking an in-depth look at their lab values may help you locate a contributing area of cortical dysfunction.

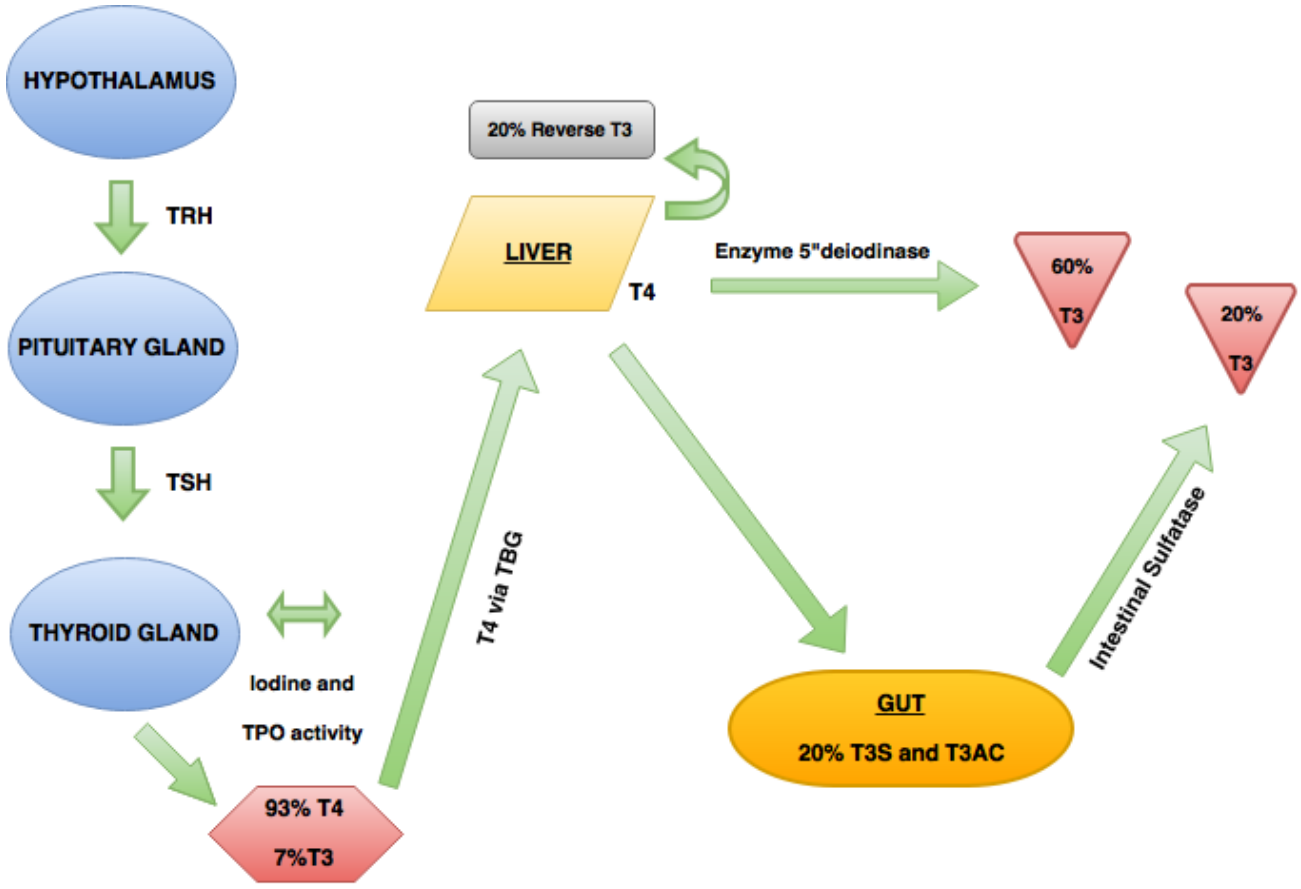
Lab work can be evaluated by using pathological or functional ranges. When a patient goes to his or her doctor and has labs drawn, the results are usually assessed within the pathological range. The pathological range is used to assess disease. If the patient's numbers fall above or below the pathological range, the patient has illness or disease. If the patient is within the pathological range, they are considered healthy. The functional range can be thought of as a tighter range. This is important because if a patient is within the pathological range but outside the functional range, it tells the provider that the patient is trending towards illness or disease. The patient may not be showing signs or symptoms of disease at the time of the first blood draw. If they continue to live the way they have been living, however, then the numbers that were once within the pathological range may soon fall outside the range and the patient will have disease.

An example of this is when assessing Thyroid Stimulating Hormone (TSH). The pathological range on most labs is 0.45-4.5 and the functional range is 1.8-3.0. So if the TSH is 3.5, from a pathological perspective, the patient is considered normal. From a functional range, they are considered to have a high TSH, which may be indicative of hypothyroidism. Let's dig deeper into what a basic thyroid panel should look like, a few thyroid patterns and their relationship with depression.

The literature shows that there is a direct relationship between the role of thyroid function and the pathophysiology of mood disorders. Subclinical thyroid dysfunction, more specifically autoimmune thyroiditis, has been associated with depression. Subclinical thyroid dysfunction is defined as an abnormal TSH (either too high as in hypothyroidism or too low as in hyperthyroidism) and normal free T4 levels. To understand why the TSH is high as in hypothyroidism or too low as in hyperthyroidism, we should look at the communication between the brain, thyroid, gut, liver and peripheral tissues.

The hypothalamus releases thyroid releasing hormone (TRH) to the anterior portion of the pituitary gland. The pituitary gland releases thyroid stimulating hormone (TSH) to the thyroid gland. When the thyroid gland is stimulated, it begins to create the thyroid hormones thyroxine (T4) and triiodothyronine (T3) by pulling iodine into the thyroid gland and stimulating thyroid peroxidase (TPO) activity. The important difference between these two thyroid hormones is that the thyroid creates around 93% of T4, which is an **inactive** hormone and around 7% of T3 which is an **active** hormone. Therefore, the majority of thyroid hormones initially produced are inactive. T4 must become active in order to fulfill it's duties as an important thyroid hormone. T4 travels to the liver by hopping a ride onto thyroid binding globulin (TBG). Once in the liver, 60% of T4 gets converted into T3 by the enzyme 5'deiodinase. Of the other 40%, 20% becomes inactive as reverse T3 and the other 20% goes to the gut as T3 sulfate (T3S) and triiodothyroacetic acid (T3AC) where they remain inactive until converted to T3 by intestinal sulfatase. See the diagram below for a summary of the physiology:

Thyroid Physiology



**concept retrieved from Dr. Datis Kharrazian

Just from the diagram, it is easy to tell that the thyroid and its metabolism are very complex. It incorporates several areas throughout the body. If there is a breakdown in communication between the brain and the pituitary, there may be thyroid-related issues. If there is a breakdown in communication between the pituitary and the thyroid gland, there may be issues. If there is liver or gut dysfunction, there may be thyroid issues. If the brain is unaware of thyroid activity in the peripheral tissues, there will be issues. I hope it is becoming evident of how important it is for several areas of the body to be working optimally in order for the thyroid to work optimally and how important it is for the thyroid to work well so other areas can work optimally.

Take Home Points:

-Pathological lab ranges look for disease.
-Functional lab ranges look for areas trending towards disease.
-Thyroid dysfunction can be a contributing factor to mood disorders and depression.
-There are several different areas where the thyroid can become dysfunctional.

Thyroid Stimulating Hormone (TSH) is the most frequently assessed hormone on a patient's blood work. Conventionally, if a TSH is high (usually greater than 4.5), the patient's doctor may tell them they have hypothyroidism. This usually leads to the patient being placed on thyroid replacement therapy. One of the most common medications prescribed in the United States every year that serves this purpose is Synthroid. Synthroid is a synthetic, chemically identical version of T4. This is convenient because the body's natural response is that when T4 levels drop, the hypothalamus will tell the pituitary gland to release TSH. So if more T4 is in the system, and the brain is able to identify this, then the pituitary gland will decrease its release of TSH, eventually lowering TSH levels. And voilà, hypothyroidism no longer exists, except it probably does.

Remember, just by looking at the diagram above, one can tell that if there is a change in the TSH, there can **at least** be five different things going on (there are many more ways TSH can be affected). The most common cause of hypothyroidism is Hashimoto's autoimmunity. Hashimoto's can not be determined by just a TSH level. If the TSH is outside the laboratory range, then Thyroid Peroxidase Antibodies (TPO) and Thyroglobulin Antibodies (Tg) must be assessed to determine if the patient has hypothyroidism due to an autoimmune disorder. A comprehensive physical exam is also warranted due to the fact that the TSH changes may be due to changes in iodine or related to a goiter. Getting a little more complex? This is just the beginning of thyroid dysfunction. Like I mentioned earlier, there are several areas outside the thyroid that warrant investigation when there are changes in thyroid lab markers.

Another important thing to remember is that blood work can be assessed from a pathological perspective or a functional perspective. The differences in common thyroid markers are listed in the table on the next page.

Thyroid Functional Ranges vs. Pathological Ranges

Thyroid Marker	Functional Range	Pathological Range
TSH	1.8-3.0 mIU/L	0.45-4.5 mIU/L
Total T4	6-12 ug/dL	4.5-12 ug/dL
Free T4	1-1.5 ng/dL	0.82-1.7 ng/dL
Total T3	100-180 ng/dL	71-180 ng/dL
Free T3	3.0-4.0 pg/mL	2.0-4.4 pg/mL
Reverse T3	25-30 ng/dL	9.2-24.1 ng/dL
T3 Uptake	28-38%	24-39%
Free Thyroxine Index (FTI)	1.2-4.9 mg/dL	1.2-4.9 mg/dL
Thyroid Peroxidase Antibodies (TPO)	Above Lab Range	0-34
Anti-Thyroglobulin Antibody	Above Lab Range	0-0.9
Thyroid Binding Globulin	18-27 ug/mL	10-24 ug/mL

When you compare the two ranges listed above, you can see that the numbers in the functional ranges are much closer together. This allows the practitioner and the patient to be able to identify thyroid markers that are not necessarily in a disease state, but may be trending that way. Let's look at a patient to see if he is suffering from thyroid dysfunction.

Tyler is a 35 year-old male who comes to your office seeking care. He heard about your office from his friend Ralph who had suffered a concussion from a car accident two years ago (Tyler was Ralph's passenger). Ralph suffered from several symptoms such as chronic fatigue, weight gain, constipation, bloating, short-term memory loss, chronic headaches and depression. Ralph's treatment consisted of mainly specific neurological rehabilitation exercises and minor dietary changes. He was very excited about his results and is continuing to do well.

Tyler states that he began developing very similar symptoms to Ralph three months after his accident. After performing a comprehensive physical exam on Tyler, you find inconsistencies in his neurological function that need attention. You also determine that it may be in his best interest to run a few labs on him, based off of some extra things he told you during the physical (in this scenario, we are only going to run thyroid markers). You get Tyler's thyroid panel back and compare the pathological ranges on the lab report to the functional ranges you use to assess your patients. His results are listed on the next page.

Tyler's Basic Thyroid Panel

Thyroid Marker	Value
TSH	3.5 mIU/L
Total T4	7.3 ug/dL
Free T4	1.6 ng/dL
Total T3	188 ng/dL
Free T3	4.1 pg/mL
Reverse T3	14.5 ng/dL
T3 Uptake	39%
Free Thyroxine Index (FTI)	2.1 mg/dL
Thyroid Peroxidase Antibodies (TPO)	Did not perform
Anti-Thyroglobulin Antibody	Did not perform
Thyroid Binding Globulin	17 ug/mL

Although a few of the hormones fall within the normal laboratory ranges, when compared to the functional ranges you see some inconsistencies. One thing you notice is that TSH is above the functional range which, when comparing to your history and physical exam, makes you think Tyler may be trending towards hypothyroidism. You already know that the most common form of hypothyroidism is autoimmune in nature, so you decide to run thyroid antibodies. Thyroid Peroxidase Antibodies come back and are 181 IU/mL.

Now it looks like Tyler is not only suffering from the effects of post-concussive symptoms, he is also autoimmune. This is an important point. The literature shows that patients who suffer from traumatic brain injury (TBI), mild traumatic brain injury (mTBI) and concussions can also be suffering from pituitary dysfunction. Since the pituitary gland plays a very important role in thyroid physiology, it may be in the patient's best interest to run labs to see if alterations in the patient's endocrine system are playing a role with their symptoms.

Take Home Points:

-The most common form of hypothyroidism is Hashimoto's autoimmunity.
-Patients suffering from a head injury may also be suffering from concomitant neuroendocrine effects.
-The neuroendocrine effects can be autoimmune in nature.
-A multidisciplinary approach may be in the patient's best interest to return to optimal health.

Depression is a common symptom associated with thyroid dysfunction. If the labs are only being assessed from a pathological perspective, preventative measures will not be incorporated to help fix the problem. This short paper is just a small example of how important looking at labs from a functional perspective can be for the patient's health. If you are interested in reading more on the topic of thyroid physiology and dysfunction, Dr. Datis Kharrazian wrote a great book on thyroid health.

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