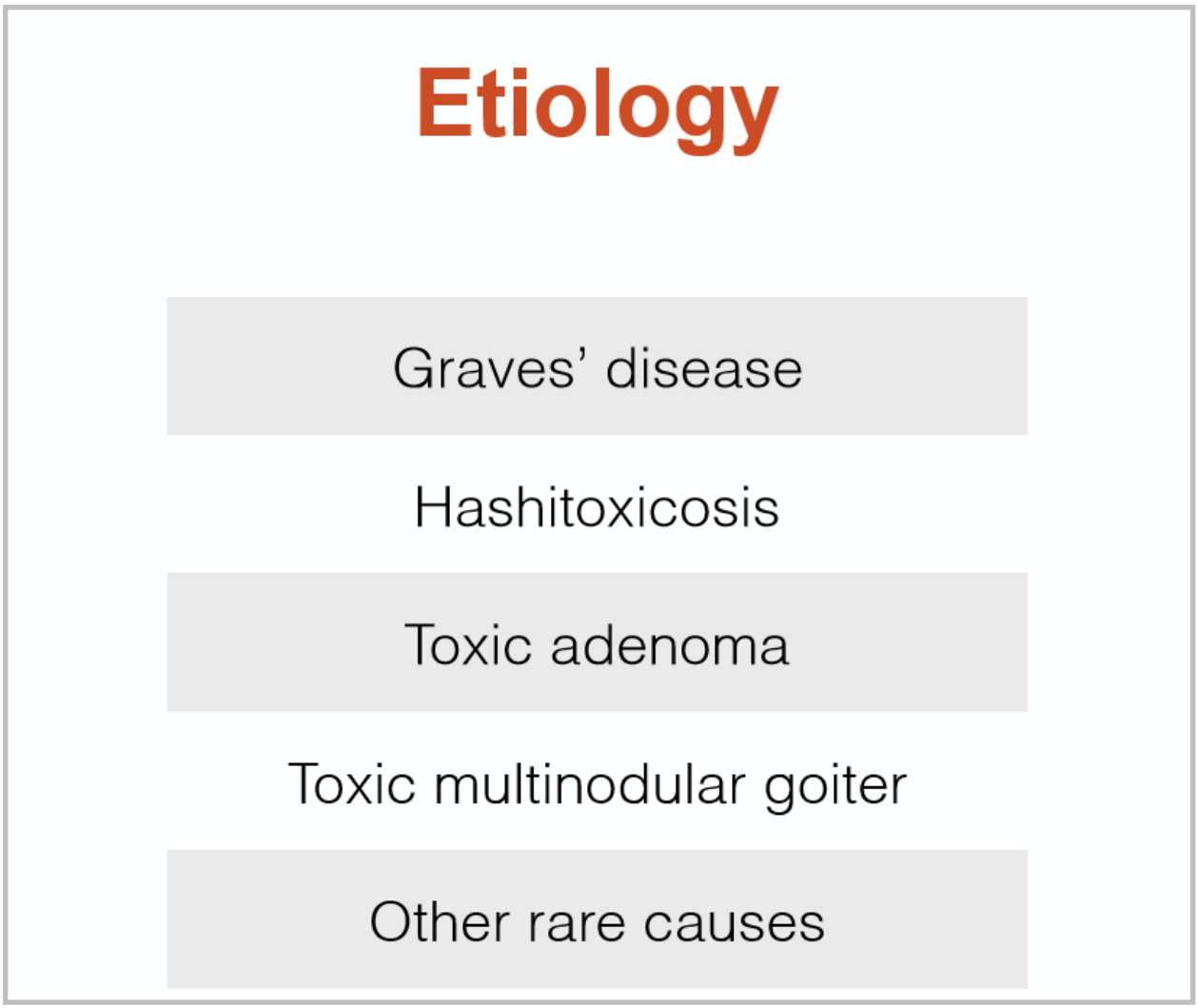
Thyroid Hyperfunction – Part One

Hey, everyone. In this presentation, I'm going to discuss hyperthyroidism. This is far less common than hypothyroidism, and you're less likely to see it in practice, though, of course, you will see some patients with this condition. I've had probably 10 patients over an eight-year period with frank hyperthyroidism or Graves' disease, so I won't have as many case studies for you as a result, but it is a subject I know a fair amount about because my wife was diagnosed several years ago with Graves' when we were trying to get pregnant with our daughter Sylvie. Although I don't believe she has it now, it was something we needed to address before she was able to get pregnant. I did a very deep dive into the scientific literature, spoke with many colleagues, and learned as much as I could about it because I had a very personal reason for that at the time. I'm going to cover the highlights of what I think you need to know in this presentation. Let's start with some background and basics, and then we'll dive right into cases.

There are two main forms of hyperthyroidism: overt and subclinical. Overt hyperthyroidism, which is sometimes referred to as primary hyperthyroidism, is when the patient has low TSH and high T4 and T3. This is the classic textbook presentation. Most patients with overt hyperthyroidism have Graves' disease, and in this case, they will have higher levels of T3 than T4, but a subset of patients will have high T4 and normal T3, and this is called T4 toxicosis. This is more common in patients with inflammatory diseases that reduce the conversion of T4 to T3.

Subclinical hyperthyroidism is when the patient has low TSH but normal T4 and T3 levels, so this is, of course, the opposite of subclinical hypothyroidism, where they have high TSH and normal T4 and T3.



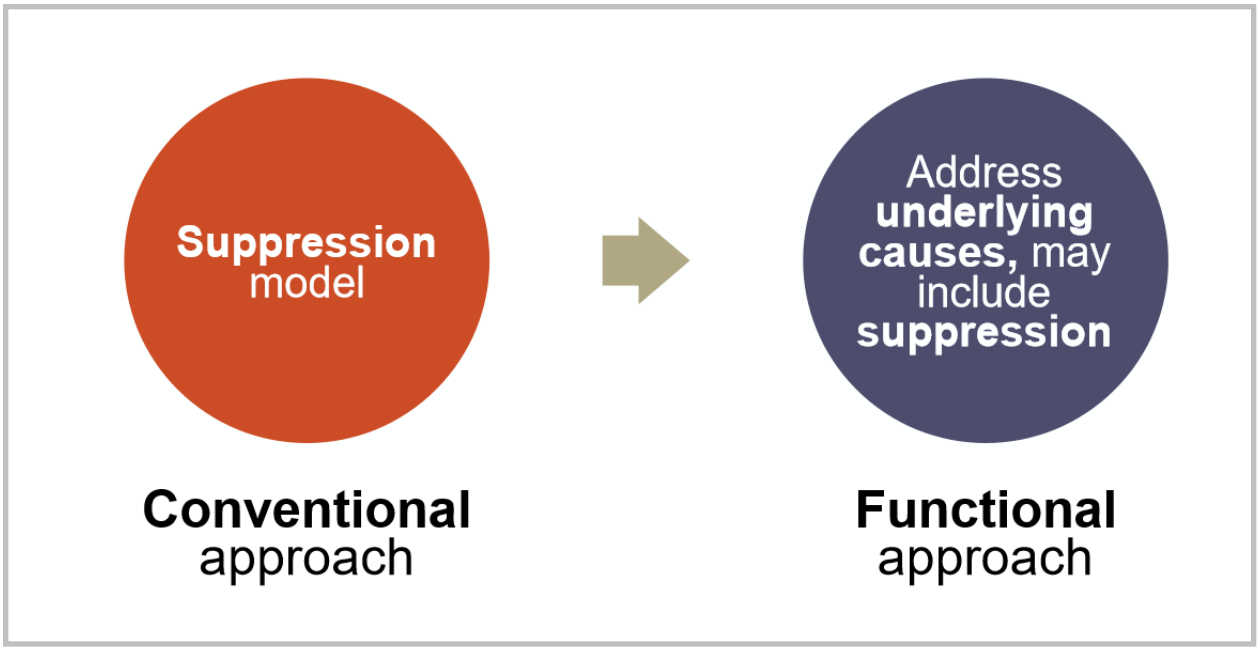
Once you figure out which form of hyperthyroidism is present, the next step is to determine the etiology. Again, there are several categories here. Graves' disease is the most common cause. This is an autoimmune disorder resulting in the production of TSH receptor antibodies, which stimulate thyroid growth and release thyroid hormone. Hashitoxicosis is another cause. This refers to patients with Hashimoto's who initially present with TSH receptor antibodies, high radioiodine uptake, and low TSH and high T4 or T3. Another cause is toxic adenoma and toxic multinodular goiter. These have a significant genetic component but are more common in areas with low iodine take, such as the developing world. There are a number of other causes that are pretty rare in clinical practice, such as iodine-induced hyperthyroidism, trophoblastic disease and germ cell tumors, and TSH-mediated hyperthyroidism. We're not going to talk about those because you probably won't see them. In this presentation, we're going to focus on Graves' disease, since it's the most common cause of hyperthyroidism in a functional medicine context.

Graves' disease affects between 1-4% of the U.S. population.

The prevalence of Graves' is still unknown, but estimates suggest it affects less than 1 percent of the U.S. population. However, some research suggests that up to 3 to 4 percent may have subclinical Graves' with elevated antibodies, low TSH, and normal T4 and T3. Graves' disease primarily affects women. It is seven times more prevalent in women than men. The onset is typically between 20 and 40 years old, although young children and the elderly are sometimes affected. For reasons that are not yet well understood, the symptoms of Graves' disease in men are often worse than in women, although they are less commonly affected, and men are more likely to develop muscle disorders as a secondary complication of Graves' disease.

Graves' is caused by the production of TSH receptor antibodies, as I mentioned before, and these are also known as thyroid-stimulating immunoglobulins, or TSI. TSI activate the TSH receptor in thyroid cells, which replicates the action of TSH and bypasses negative feedback inhibition and thus stimulates excess production of thyroid hormone. TSI also stimulate orbital cells, causing Graves' ophthalmopathy, and they stimulate dermal cells, causing pretibial myxoedema. Other signs and symptoms of Graves' include anxiety, nervousness, weariness, hair and nail changes, weight loss, increased heart rate, and increased systolic blood pressures, heat intolerance, tremors, change in libido, increased temperature, sweating, frequent bowel movements, headaches, hives, nausea and vomiting, muscle weakness, fatigue, swollen lymph nodes, and increased appetite. These all fall under the category of increased basal metabolism, which is, of course, the core deficit with Graves'.

If you think of the thyroid gland as the motor of the body, Graves' causes it to idle at a higher rpm, whereas hypothyroidism causes it to idle at a lower rpm.

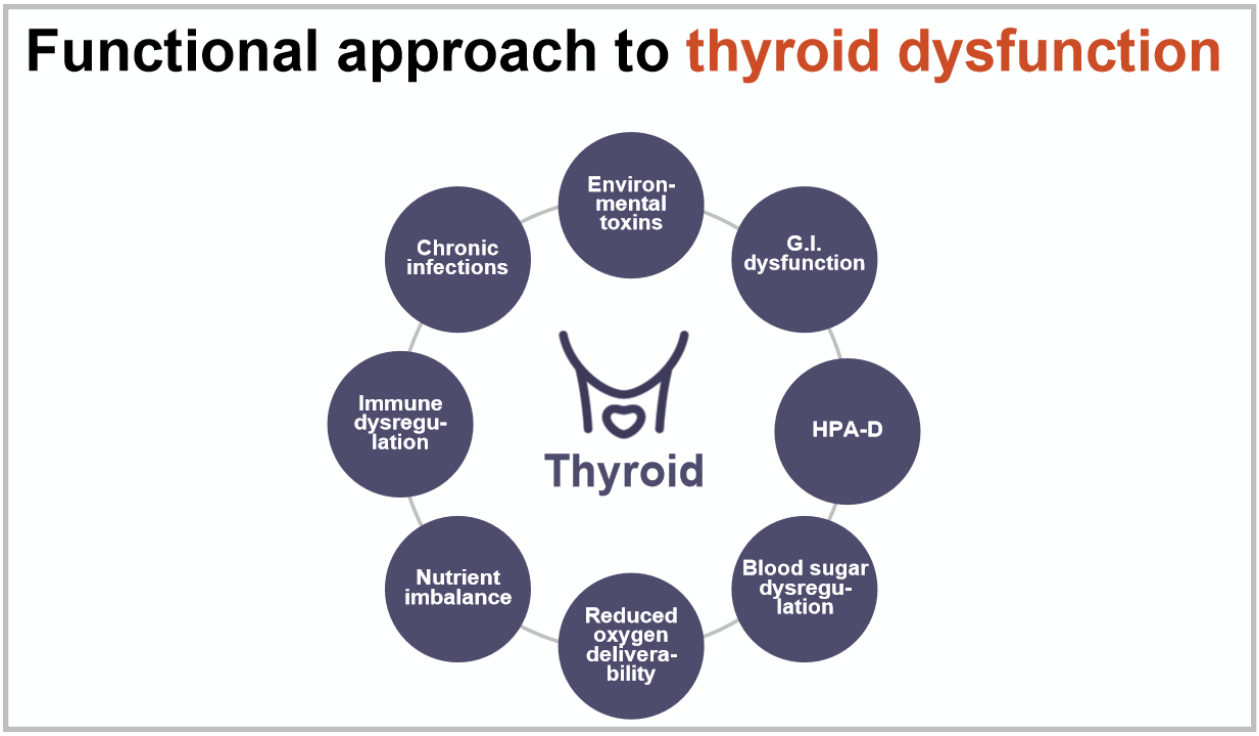


There is a fundamental difference between the conventional and functional approach to hyperthyroidism, just as there is with hypothyroidism. The conventional approach in this case is the suppression model. If TSH is low and thyroid hormones are high, they will suppress production with drugs such as methimazole and PTU, which are toxic to the thyroid gland and thus reduce thyroid hormone production, or they may radioactively ablate the thyroid gland and permanently destroy its ability to produce thyroid hormone, or they may surgically remove the thyroid gland, which, of course, would have the same effect.

In the functional model, as with the other conditions we've already talked about, we, of course, look for the underlying causes of thyroid hyperfunction and autoimmunity and address those. However, in the case of Graves', the risk and complications of hyperthyroidism are greater than with Hashimoto's and hypothyroidism. For example, if T3 is really high, it can lead to a thyroid storm, heart attack, stroke, and even death. In some cases, suppression is necessary to bring T4 and T3 levels under control while you continue to address the underlying mechanisms.

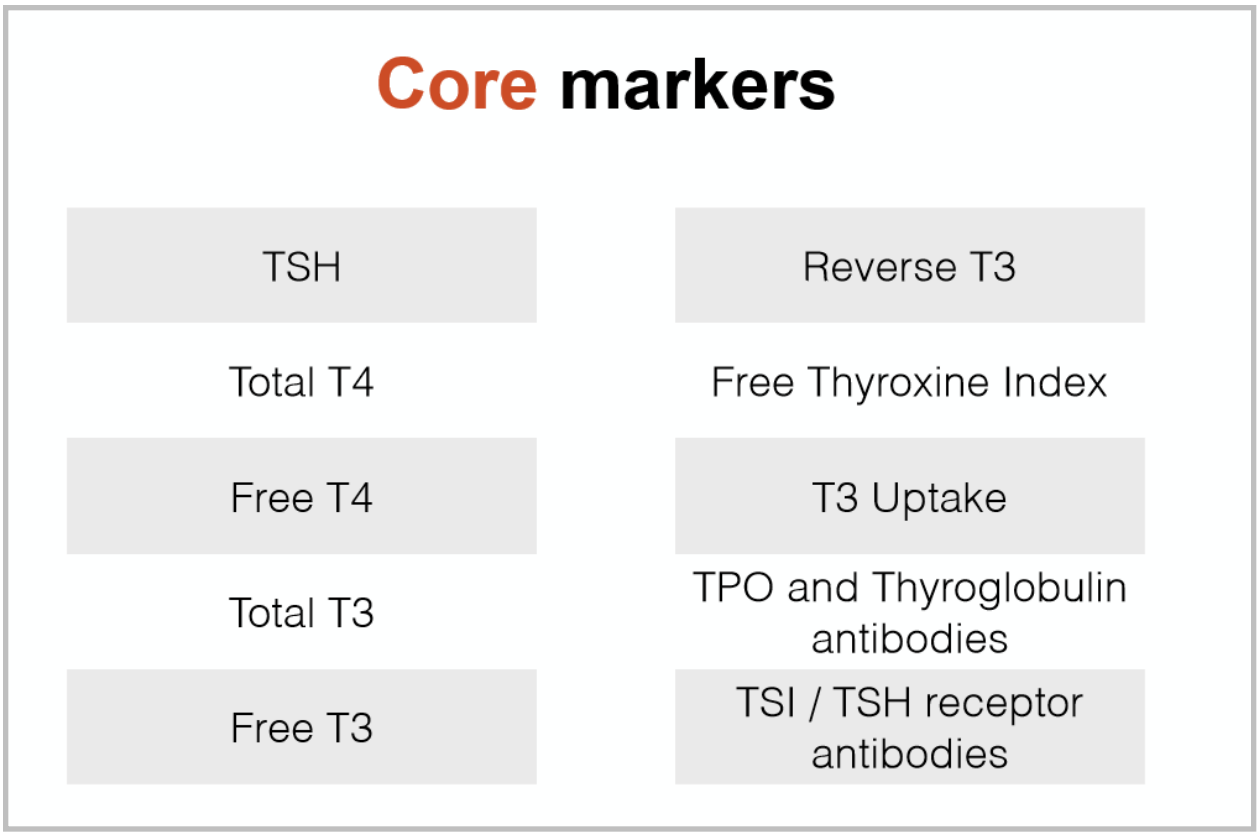
Unfortunately, in the conventional model, little to no attention is paid to these mechanisms. When the patient is diagnosed with Graves', the options offered are PTU or methimazole, radioactive ablation, or surgical removal, depending on the circumstances. There is typically no discussion of the role and triggers of autoimmune disease and the steps that could be taken to address them. The patients I've seen with hyperthyroidism most often have either had their thyroid gland surgically removed or ablated, or they've been on PTU or methimazole for a long time. Fortunately, even when patients have been on thyro-suppressive drugs for decades, it is still possible in some cases for them to stop these drugs and heal more naturally.

That said, you should never take a patient off those drugs without close supervision and monitoring. You don't want to provoke a thyroid storm, so a conservative approach is warranted.



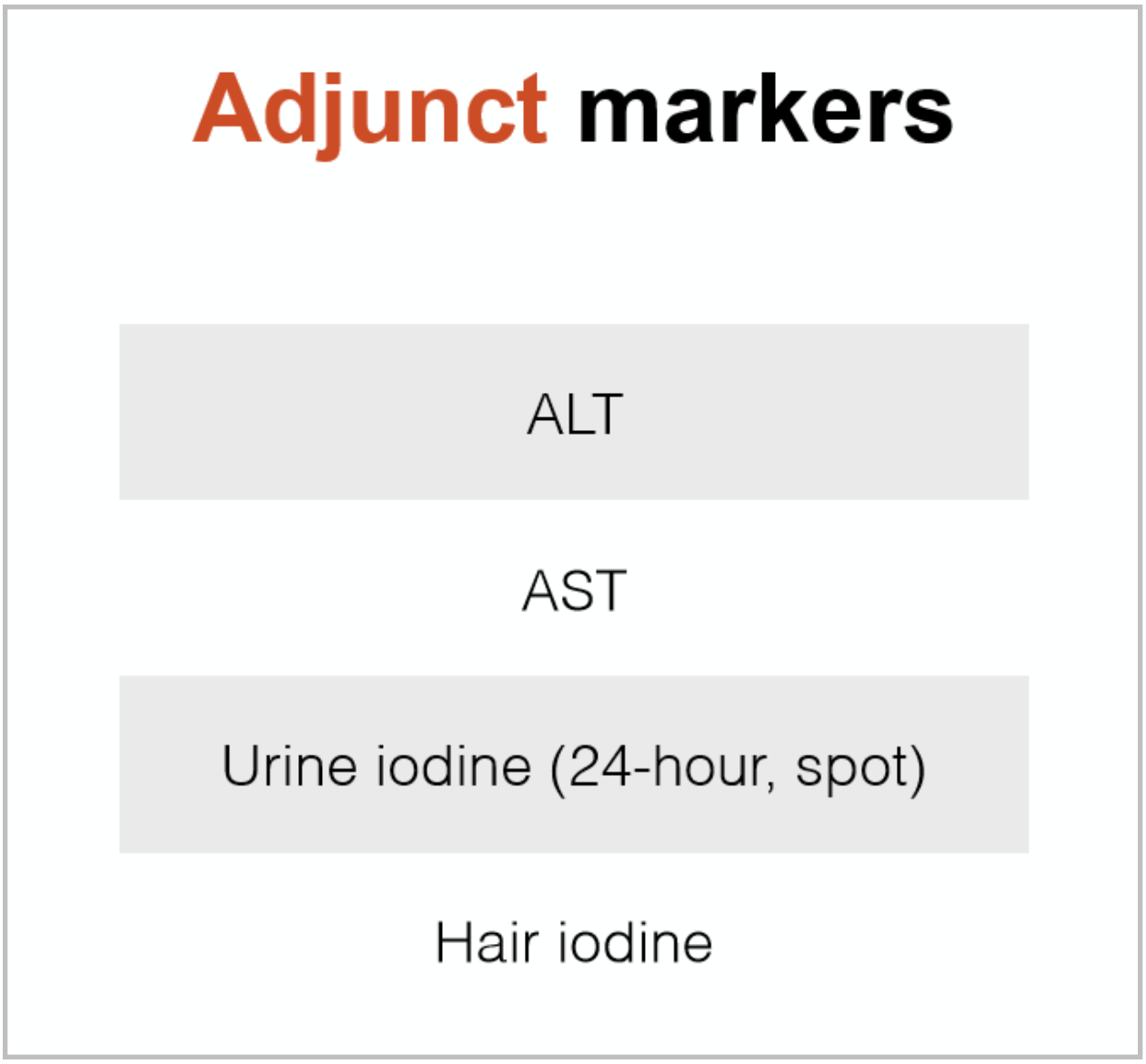
You should recognize this slide from the last presentation on hypothyroidism. It illustrates the numerous interactions between the thyroid gland and the rest of the body. In a complete functional medicine approach to hyperthyroidism, all of these must be considered. Again, the good news is we are covering most of them in this ADAPT Level One course, with the exception of infection and toxins such as molds and metals. If you do a comprehensive case review with all of the suggested labs and address these problems, you're doing 80 to 90 percent of what you need to do to approach the thyroid from a functional perspective. A key point here, as I mentioned in the hypothyroidism presentation, is that thyroid dysfunction is often a symptom or a manifestation of a deeper underlying problem. In the case of Graves' disease, it is an expression of the autoimmunity that is present.

Suppressing thyroid hormone overproduction without addressing the underlying problems is not functional medicine, and it won't get you far. As I said, suppression is sometimes necessary, but it is rarely if ever a good idea to only do that.



Here are the core markers for assessing hyperthyroidism. They are similar to assessing hypothyroidism. The only difference is that it is crucial to add TSI, also known as TSH receptor antibodies. While thyroglobulin, and less commonly TPO antibodies, may also be elevated in Graves', TSI is used to distinguish Graves' from thyroiditis, Hashimoto's, and other causes of hyperthyroidism. In the past, the radioactive iodine uptake test was used to diagnose Graves', but this has been superseded by the availability of TSI. TSI has both the sensitivity and the specificity above 95 percent, so although false negatives or positives are theoretically possible, they are very rare in clinical practice.

Reverse T3, as we discussed, is not a marker of thyroid function per se, but it does provide information about inflammatory signaling. T3 uptake is probably the least important marker on this panel, but it will often be elevated in hyperthyroidism.



Some studies have shown that ALT and AST are elevated in Graves' disease, and you may also want to consider urine and hair iodine in patients who have been supplementing with it to rule out excess iodine as a potential cause.

Functional ranges for core thyroid markers

Marker	Functional range
TSH	0.5–2.0 mU/L
Total T4	6.0–12 ug/dL
Total T3	100–180 ng/dL
Free T4	1.0–1.5 ng/dL
Free T3	2.5–4.0 pg/mL

With hypothyroidism, we discussed how the upper end of the reference range is likely much too high; 4.5 is the upper end of the conventional range, or even 5 with some labs, versus 2 being the upper end of the optimal range. With hyperthyroidism, however, the lower end of the functional and lab ranges are basically the same. However, the upper end of the free T4 and free T3 functional range is a little bit lower, reflecting caution with excess thyroid hormone production. As with all the functional ranges, it doesn't mean if a patient has a single test that is slightly out of the functional range that they have a problem that needs to be treated. It just means that it requires further investigation.

Reference ranges for thyroid antibodies

Marker	Range (IU/mL)
Thyroid peroxidase (TPO) Ab	0–34
Thyroglobulin (TG) Ab	0.0–0.9
TSH receptor Ab (TSI)	0–139

Recall that there is no functional range for TPO and thyroglobulin antibodies, and the same is true for TSI. You would just use the lab ranges, which I've put here on this slide. They do differ slightly in some cases from lab to lab, but they are usually pretty consistent, so you can just use the lab range that shows up on your lab report.