Why would we consider moving a patient from monotherapy with LT4, which we've used for many, many decades. Certainly, it's been pretty much the way of things since the 1980s. Why would we consider that? Well, we know that there's about 10% to 16% of patients who can get normalized lab levels if we looked at the biomarkers of adequate circulation of the thyroid hormone in those labs that we currently have. You've done it. You've got them right on target, but the patients aren't feeling better. We know there's about 10% to 16% of patients who will continue to be symptomatic even though you've normalized the thyroid labs. There's many causes for this. There's many concomitant conditions. Other autoimmune disorders as medications. There's many things that can actually affect sufficient circulation or penetrance of T3. There's even genetic polymorphisms that will cause that.

I want to pause here and just mention one thing. TSH is a very sensitive indirect indicator inverse relationship to circulating T4. Very sensitive. Significantly sensitive too. TSH will go up and down based on the certain level of T4, but it's not that sensitive we're finding out to T3 levels, particularly in the low levels. In high levels, yes. You'll see TSH will drop at high levels of T3. But in low levels like we see in hypothyroidism, not only can we truly assay the well in the lab with T4, and 3T, and reverse T3, they're just not as accurate. We're not able to get there. But TSH does not move in the direction, so you might have a T4 that is elevated, going up nicely and TSH is coming down nicely.

With not much of a movement in T3, you can't really adequately look at that T3 level. It's not really telling you not only the true amount of circulating T3, but also, there's an issue with cell penetrance of T3 or T3 receptor down regulation. Many things can affect. Cytokines, adapines, there's a lot of things that can affect that. So we're not there yet to have the great labs I guess is the bottom line. So what we have to do is just look at those labs, and we have to listen to patients, because they have symptoms. They have depression. They have constipation or cardiac-- the feeling of actually malaise for some of them that is not predominantly and was not primarily a neurologic or mood disorder, so we need to pay attention to that.

When that happens, though, we have to use that as a way to tell us this might be a time we should be looking at adding T3 in combination to the LT4. And those patients, they will present themselves. They're still complaining. Do not discount what they're complaining about. You do it to their peril and your own. Again I mention it's very important, because we're missing the boat on this. We do not have very good biomarkers to look for tissue penetrance of T3. So the next thing, if you've decided if the patient's still having symptoms according to guidelines-- you've got the TSH, 3T4, and the like are at the target, what is set, and they're still having symptoms, certainly after six months if they let you go that long, when they're having continued symptoms, it's time to be looking at adding T3 in combination.