come to assume that many people included in the "normal" sampling are probably those in a hypocaloric state with some symptoms of low thyroid function. When you consider the percentage of people who are trying to lose weight at any point in time, this subset of the population must be skewing the reference range to include those who are actually mildly low thyroid by symptomatic criteria.

In addition to the information provided above, we have seen evidence of other adaptations to altered thyroid hormone levels. Many patients will do fine when maintained on their initial dose of desiccated thyroid. However for others, after several months of treatment, the patient reaches a plateau of weight with the return of low thyroid symptoms. When lab values are obtained, these patients usually have FT₃ and FT₄ which have returned to their previously low pre-thyroid-treatment levels. This demonstrates the body's ability to increase degradation rates of T₃ and T₄ which the body recognizes as being at hyperthyroid levels in the face of a hypocaloric diet. Also, in patients with high rT₃ who have been treated with T₃ only, we generally add some T₄ to the T₃ treatment after rT₃ has decreased to normal levels. Anecdotally, we have noticed that some of our patients with the most challenging weight struggles are those whose rT₃ levels rise dramatically as soon as any T₄ is added to their T₃ dose.

In the larger view, we must accept the fact that scientific knowledge evolves over time and both our understanding of what should be measured and the meaning of the resultant measurements can change. Consider cholesterol. Initially, we assessed total cholesterol with higher levels indicating increased cardiovascular risk. As time went on, we learned of HDLcholesterol and LDL-cholesterol. Limits were set for each, with higher HDL being protective and lower LDL healthier. As the years have gone on, further refinement of the cholesterol parameters have been elucidated as has the importance of inflammatory markers.[16] These refinements are based on clinical outcomes. We should fully expect to see changes in both the parameters assessed and their acceptable values as our understanding increases.

But we will never argue for the dominance of a lab test when signs and symptoms are available. In considering thyroid lab values, we must also be cognizant of known biochemical variants such as receptor and transporter abnormalities which may cause a lab result to be at odds with the signs and symptoms.

It is possible that lifestyle changes in our society have affected thyroid function so that our normal values might be different when compared to people who lived thousands of years ago. Among the environmental changes that may lead to differences in thyroid levels are the amount of food eaten (increases in weight may raise thyroid levels and decreases in weight may lower thyroid levels)[1] and ambient temperature (warmer environments such as heated living and working spaces may lower thyroid levels). It is possible that our "normal" values, especially for those who are trying to lose weight, are in fact lower than what would have been determined from a population of normal people from thousands of years ago. Our "normal" ranges for thyroid tests might tend to be misleading in the same way that testing a population of "normal" people in areas of iodine deficiency hundreds of years ago would have been misleading in guiding people who needed to be treated to improve individual health. Normal values needed to be based on more than two standard deviations outside the range of "normal" people. We need to critically look at the health of those "normals" to see whether a different reference range would better serve the health of our patients. Certainly clinical health must be taken into account as has been done in our evolving understanding of cholesterol and inflammatory markers for cardiovascular disease risk.

While we have arrived at our current approach to thyroid treatment by years of working with patients to find the best approaches, we believe the research community should address these issues with our findings in mind. Controlled experiments studying thyroid treatment during weight loss should be performed monitoring rT_3 and treating with this paradigm (T_3 treatment) versus both untreated control and thyroxine groups.

While 10% weight loss is helpful at decreasing co-morbidities such as hypertension and type 2 DM, attaining normal weight seems out of reach of many obese people. This is partly due to the plateau created by maladaptive hypothyroidism. Ideally, we would like to be able to help many patients reach and maintain normal weight. Given our current environment with freedom from vicissitudes of food availability, this goal is harder than it would otherwise be. In our experience of having a combination of medications to