

source of both T_3 and rT_3) and to replace T_4/T_3 with T_3 only. Over a period of a few months, both the rT_3 and T_4 will fall while the T_3 should remain in the normal range.

Another point is that there are wide reference ranges for thyroid tests. Some patients feel optimally well when their thyroid levels are on the high side and some when the thyroid levels are lower in the normal range. For example, a patient with a history of an anxiety disorder or sensitivity to stimulants such as caffeine may feel better when thyroid levels are on the low sides of their ranges. Some require treatment at the high end of normal to eliminate constipation, cold extremities, and/or other symptoms of low thyroid. We think that optimizing symptoms is a good guide along with complete thyroid testing including FT_4 , FT_3 , and rT_3 , especially during caloric restriction. One can optimize symptoms of constipation or diarrhea, feeling too cold or hot, depression or anxiety, or feeling fatigue (which can result from high or low thyroid), etc., by appropriate dosing of T_3 with or without T_4 .

Patient Number 2. The second patient example is a 46 year old female, 5'2", weight 150 lbs, BMI 28 (range: 18.5-24.9; overweight 25-29.9; obesity >30), with HTN. Her blood pressure was slightly elevated at 148/85 (on lisinopril 5 mg daily). Her medical problems at baseline included history of Hashimoto's thyroiditis, borderline high TSH, elevated lipids, and HTN. Her medications were lisinopril 5 mg daily, estradiol 2 mg daily, and rofecoxib 25 mg daily for osteoarthritis of her large joints. She was started on our comprehensive program. Thyroid treatment was started as well because of initial low thyroid symptoms of fatigue, constipation, and feeling cold along with a TSH of 3.41 uIU/mL (considered elevated by some, but not all groups who set limits for TSH). Desiccated thyroid was prescribed at 60 mg for six days to adjust to the medication, and then advanced to 120 mg daily. Over a period of several years thyroid hormone dose was reduced to 45 mg as dictated by clinical and lab results, and she was feeling relatively well. Her weight remained between 119 lbs and 130 lbs. Her blood pressure and pulse remained in the normal range (100/60-138/78, pulse 64-72) with no antihypertensive medications. Four years into her treatment, desiccated thyroid became unavailable so she was switched to levothyroxine at 75 mcg daily. Within a few weeks she began to feel tired, cold, and depressed and developed constipation and hair loss. Her FT_3 was 2.3

pg/mL (range: 2.2-4.0), FT_4 1.07 ng/dL (range: 0.93-1.70), and TSH was 0.91 uIU/mL. Her levothyroxine was increased to 100 mcg daily and T_3 was added at 5 mcg bid. Two months later, her first test of rT_3 was 379 pg/mL (range: 90-350), FT_4 1.12 ng/dL (range: 0.93-1.70), FT_3 2.4 pg/mL (range: 2.2-4.0). Over the next 4 months her levothyroxine dose was gradually reduced to zero, and she was placed on gradually increasing doses of T_3 only, ending on 25 mcg bid. Her weight was 125 lbs, BP 122/80 on no medications, and pulse was 72. She no longer suffered from hair loss; her bowels were normal, she felt well, and she stated that for the first time in her life she was not cold. Her lipids were also improved compared to baseline. On this regimen her rT_3 was 193 pg/mL (range: 90-350), FT_3 2.5 pg/mL (range: 2.2-4.0), and FT_4 0.67 ng/dL (range: 0.93-1.70).

Comments. This patient failed to achieve her optimum health until her rT_3 was mid-normal on T_3 replacement only. In addition, correcting peripheral vasoconstriction results in improved comfort, better sleep, and improved blood pressure, especially diastolic blood pressure. Patients with untreated hypothyroidism may have elevated blood pressure, especially diastolic hypertension, due to peripheral vasoconstriction. After the T_3 treatment to reduce rT_3 levels, a change from T_3 to desiccated thyroid or other ratio of $T_4:T_3$ dosing would be an option.

Discussion

By the early 1970's, TSH became the gold standard for assessing thyroid function. Part of its prominence as a diagnostic tool appears to have arisen because TSH levels change logarithmically when the levels of circulating thyroid hormones are higher or lower than the set point. However, several issues of basic endocrinology allow one to realize that using TSH alone will have severe limitations. TSH levels will not necessarily distinguish secondary hypothyroidism (of pituitary cause) from normal. A PubMed search of (intracellular) thyroid receptor mutations produced 598 citations and a search for mutations of the proteins which transfer thyroid hormones across cell membranes produced 65 citations. Clearly, this area of research is deemed important and these are only two portions of the pathway involved in generating a metabolic change via thyroid hormones. So assuming normal pituitary function, TSH does not