Chapter 11

Is your thyroid to blame?

When it comes to seizing control over coronary plaque, conventional notions of thyroid health may need to be thrown out the window.

Marginal thyroid dysfunction is common and can be an important contributor to distortions of LDL cholesterol, Lp(a), and body weight. Correction of even subtle degrees of thyroid dysfunction is important to gain full control over coronary plaque growth. It also can make you feel happier, more energetic, and thinner.

The thyroid gland modulates metabolism, fine-tuning the function of virtually every tissue, from lowly cells at the base of the fingers making fingernails, to the neurons in your brain guiding memory and thought, to the cells lining your arteries.

Hypothyroidism, or deficiency of active thyroid hormones, can wreak devastating effects on health. It’s been known for decades that, when severe, signs of hypothyroidism are obvious and advanced degrees of atherosclerosis and heart failure develop. However, more recently, it has come to be recognized that even mild degrees of hypothyroidism can also contribute to heart disease. Mild hypothyroidism is also proving to be far more common than previously suspected. Because it is less dramatic, it can go undetected longer, doing damage slowly over many years, including allowing growth of coronary plaque. Subtle degrees of hypothyroidism can also be trickier to diagnose. Add to this the debate among the medical community over the boundary between “normal” and abnormally “low” thyroid function, not to mention the widespread tendency to treat only laboratory values while ignoring the patient.
It is *Track Your Plaque*’s mission to help identify every possible advantage for stopping or reversing plaque growth. To that end, normal—no, *perfect*—thyroid function may be key.

**Thyroid disease: Emerging from the dark ages**

For many years, the condition of hypothyroidism (*hypo-*, underactive) proved a mystery, doctors standing by helplessly while the patient became bloated and swollen, lost hair, weakened, often with a fatal end. While the grotesque degenerative changes that struck sufferers fascinated physicians through the ages, insight into its causes didn’t emerge until the late 19th century.

An 1878 description of a woman in life, followed by the autopsy descriptions after her death, paint a picture of the profound nature of the disease:

“. . . *there was a marked slowness of perception, and a marked slowness of response of muscles to voluntary or reflex nerve-impulse. She stated that she could not act or think quickly, that her thoughts would only come slowly; there where any operation, such as dressing, took her half an hour formerly, it now took her two hours . . . She felt always tired, so that her life was utterly wretched.*”

After her death, the woman’s autopsy showed that “*the arteries were everywhere thickened, the larger ones atheromatous . . . Overgrowths appear to have led to the obliteration of arteries . . .*”

The woman was only 54 years old.

The author, Dr. William Ord, was so struck with the edema that was evident in every organ that he dubbed the condition “myxedema.” Despite the detailed observations of the woman in both life and death, Dr. Ord ascribed her condition to “. . . the evil result of a restricted indoor life, [without] the benefits of out-door exercise, of bracing air, of the exposure in journeyings by sea.” In other words, she didn’t get enough fresh air.
Subsequent research pinpointed the cause of the mysterious myxedema as deficient thyroid function. Physiologist Moritz Schiff later demonstrated that thyroid extract taken from the thyroid glands of animals and administered orally to humans could successfully correct myxedema.

While we might chuckle today at the misguided notions of the 19th century, controversy over diagnosis and management of thyroid disorders persists even today. The unfortunate woman in Dr. Ord’s description would be readily diagnosed today, but a hotly contested question remains in discerning the boundary between normal and low.

For us, the debate is not just academic: New data suggest that not only are such factors as physical stamina impacted, but there are implications for lipids, lipoproteins, and coronary plaque.

The thyroid gland: A primer
The thyroid is a three inch-wide, butterfly-shaped gland located in the front of the neck. Though bridging across the trachea (airway) and located just beneath the surface of the skin, you should not be able to feel a normal thyroid. Enlarged thyroids can be felt, however.

The thyroid gland produces hormones that regulate body metabolism:

**T4 (thyroxine)**
T4 accounts for roughly 80% of the hormones produced by the thyroid gland. T4 is a “prohormone,” or precursor hormone, converted to the physically active hormone, T3, via the action of deiodinase enzymes in body tissues that remove one iodine atom. T4, with an elimination half-life of about 7 days (i.e., 7 days to drop to half its level), acts as a “reservoir” for supplying the much shorter-lived T3 to the body.

**T3 (triiodothyronine)**
T3 is the “real” thyroid hormone that controls metabolic rate at the cellular level by mediating the rate of oxygen consumption of virtually every tissue in the body. The thyroid produces only small amounts of T3 directly (roughly 15-20% of bodily requirements), relying mostly on
conversion of T4 to T3 in various organs, mostly the liver and kidney. T3 is a particularly powerful hormone, such that the body requires only picogram (trillionths of a gram) quantities per deciliter of blood to function properly.

The conversion of T4 to T3 can go awry: the deiodination process also creates what is known as “reverse” T3 (rT3), structurally similar to T3 except for the location at which T4 loses an iodine atom. rT3 is indistinguishable from T3 on most diagnostic tests. rT3 also binds to the same tissue receptor sites as T3 but is inactive and therefore blocks the action of “real” T3. It is thought that the body regulates T3 and rT3 production as a means of increasing and decreasing metabolism in response to conditions such as sickness, stress, and scarcity of food. (A controversial condition known as Wilson’s Syndrome, in which a disproportionate amount of rT3 is produced due to overproduction of cortisol by the adrenal glands during excessive stress, is currently being debated as the cause of certain forms of hypothyroidism.)

**T2** (diiodothyronine), **T1** (monoiiodothyronine)
The thyroid produces only trace amounts of T2 and T1 with additional production occurring from the further activity of deiodinase enzymes on T3. Little is known about the effects or purpose of T2 and T1. Recent research suggests they may be necessary for conditions in which rapid energy utilization is required, such as cold exposure or overfeeding and may also be involved in reducing weight via regulating effects on fat storage.

The thyroid gland is under the control of the pituitary gland (deep within the brain). The pituitary produces *thyroid-stimulating hormone*, TSH, to stimulate thyroid production of thyroid hormones, T4 and T3. If tissue levels of T4 and T3 are low, the pituitary responds by increasing TSH. The TSH level is therefore the mostly commonly used clinical blood test used to diagnose hypothyroidism.

After release into the blood, T3 and T4 are transported through the body by attaching to the blood protein, thyroxine-binding globulin (TBG). T3 and T4 are only active when disassociated from TBG and in their “free” form. Reflecting their impressive potency, less than 1%
of all T3 and T4 are present in their free state, but it is the “free” form, the biologically active form, that we are most interested in.

**Thyroid disease basics**
 Disorders of the thyroid can be broken down into two general categories: *hypothyroidism* (underactive thyroid) and *hyperthyroidism* (overactive thyroid). By a wide margin, hypothyroidism is the more insidious that often evades diagnosis, unrecognized for years while contributing to growth of coronary plaque. Hyperthyroidism, while important, is far less common and carries less implication for our plaque-control efforts and will therefore not be the focus of our discussion.

Hypothyroidism is a condition in which the thyroid produces inadequate amounts of thyroid hormones, T4 and T3.

Overt hypothyroidism nowadays tends to be recognized before it reaches the extreme stage of Dr. Ord’s day, manifesting itself by high TSH levels (>10mIU/L) and usually accompanied by one or more symptoms including:

- Substantial drop in energy; fatigue; need for more sleep
- Feeling cold when other people feel warm; reduced or absent sweating
- Dry, itchy skin
- Dry, coarse, brittle hair; hair loss or thinning
- Loss of appetite with weight gain (5-20 pounds) and difficulty losing weight
- Short-term memory impairment, slowed thinking
- Feelings of pins and needles in the hands and feet (paresthesias)
- New constipation
- Puffiness around eyes, hands, ankles, and feet due to fluid retention
- Carpal tunnel syndrome
- Heavier and/or more frequent menstrual periods, worse cramps, worse premenstrual symptoms
- Depression, sadness or indifference
- Goiter (swelling in the front of the neck, caused by enlargement of the thyroid)
- Abnormally slow heart rate
- Higher diastolic blood pressure (bottom value)
- Iron deficiency anemia, low ferritin (an iron storage protein)

Diagnosing hypothyroidism can be difficult if based purely on symptoms, as symptoms are not specific to hypothyroidism. Symptoms may also be vague. Levels of thyroid hormones, free T3 and T4, along with TSH, are therefore used to confirm the diagnosis.

Diagnosis can be especially troublesome in lesser degrees of underactive thyroid function. The frequency of hypothyroidism increases with age and, though estimates vary due to differing cut-points for TSH, most estimates cite a range of 2-4% early in life to as high as 15-20% later in life, with greater prevalence in females (Andersen 2002).

TSH remains the primary method of confirming that symptoms may be attributable to hypothyroidism. Unfortunately, there is extensive disagreement about what constitutes a “normal” TSH level.

The standard (though disputed) TSH ranges (in mIU/L) from the American Thyroid Association are listed below.

<table>
<thead>
<tr>
<th>Level</th>
<th>Condition</th>
</tr>
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<tbody>
<tr>
<td>0.0 – 0.4</td>
<td>Hyperthyroidism</td>
</tr>
<tr>
<td>0.4 – 2.5</td>
<td>Normal Range</td>
</tr>
<tr>
<td>2.5 – 4.0</td>
<td>At Risk: (repeat TSH test at least once a year)</td>
</tr>
<tr>
<td>4.0 – 10.0</td>
<td>Sub-clinical (mild) hypothyroidism</td>
</tr>
<tr>
<td>Above 10.0</td>
<td>Hypothyroidism</td>
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</tbody>
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Other commonly used laboratory tests to gauge thyroid function include:

**Free T4 (fT4) and free T3 (fT3)** are the preferred tests that measure T4 and T3 unbound to protein and therefore active, excluding the 99% of hormone bound to proteins. Reference ranges for free T4 and T3 are supplied by the test lab. As with TSH, what is “normal” for the
standard population may not be normal for every individual and there can be considerable differences in the T4 or T3 levels ideal for each person.

There are a number of other thyroid tests, such as T4 uptake and T3 uptake, that have been replaced by direct measurement of free T4 and free T3 and should therefore not be used.

Thyroid inflammation can be responsible for both hypo- and hyperthyroidism and can be identified by antibodies against thyroid components:

**Thyroid Peroxidase Antibody (TPO Ab)**
Thyroid peroxidase (TPO) is a thyroid enzyme responsible for manufacturing thyroid hormones. A common autoimmune condition results in the body attacking the TPO enzyme. Approximately 90% of sufferers of the inflammatory thyroid disorder, Hashimoto’s thyroiditis, will test positive for elevated TPO antibodies (Carlé 2006).

**Thyroglobulin Antibody (TG Ab)**
Another common autoimmune condition results in the body attacking thyroglobulin. Approximately 60% of Hashimoto’s thyroiditis sufferers will test positive for elevated thyroglobulin antibodies. Testing positive for both TPO and TG antibodies increases the likelihood of Hashimoto’s thyroiditis to 95% (Carlé 2006).

**Sidebar**

**Iodine: Essential trace mineral for thyroid health**
Iodine is essential for health.

Just as deficiency in vitamin C will lead to teeth falling out, open sores over the body, and eventually death, so will iodine deficiency lead to debilitating disease. Simply meeting the Recommended Daily Allowance (RDA) of 150 mcg per day will keep goiter (enlarged thyroid from lack of iodine) from developing and maintain thyroid hormone production at a “normal” level for the majority of people. Because Americans increasingly avoid use of iodized salt, more people are developing iodine deficiency.
A century ago, Americans were plagued with goiters, with as many as a third of the inhabitants of some parts of the country (e.g., the Great Lakes region, AKA the “goiter belt,” and much of the Midwest) affected. The connection between goiter and deficiency of iodine wasn’t made until a family doctor in Cleveland, Ohio, conducted an experiment on schoolgirls in 1916. Dr. David Marine administered what we now recognize as a very large dose of iodine: 170-340 mg (170,000 – 340,000 micrograms, mcg) sodium iodide per day to 900 girls. Virtually none of the girls receiving iodine supplementation developed goiters, compared to 22% of the control group not receiving iodine (Zimmerman 2008).

This led to the introduction of iodized salt in 1924 with FDA advice to use more salt. Fast forward to the 21st century and many health-conscious people proudly declare their assiduous avoidance of salt, especially iodized table salt. Others have turned to alternative preparations of sodium chloride, such as sea salt (very little iodine content), Kosher salt (no iodine), and potassium chloride-based salt substitutes (no iodine). As a result, iodine deficiency and goiters are making a comeback.

If iodine is unavailable to the thyroid gland, production of thyroid hormones, T3 and T4 (the “3” and “4” referring to the number of iodine atoms per molecule of T3 and T4), begins to suffer, production drops, hypothyroidism ensues. Iodine deficiency over time leads to a thyroid gland that enlarges, or “hypertrophies,” an attempt to overcompensate by growing larger and better able to extract the little iodine available from the body. It is not necessary to have a goiter for thyroid dysfunction to develop.

Athletes and persons engaged in heavy physical effort lose considerably more iodine than other people in their perspiration, increasing need for iodine (Smyth 2005; Mao 2001). Vegetarians also have substantially greater likelihood of iodine deficiency than carnivorous people (Remer 1999).

What is not clear is just how much iodine we all need for optimal health. Does alleviating goiter also mean that thyroid function is optimized? Goiter may simply represent the grossly visible
manifestation of hypothyroidism. Is there an intake of iodine that can further improve thyroid function, even after goiter is reversed or suppressed?

To further complicate the situation, what is the quantity of iodine required in the presence of now ubiquitous environmental blockers of thyroid function, such as bromine (pesticides like polychlorinated biphenyls (PCBs), flame retardants like polybrominated diphenyl ethers, brominated pool water); bisphenol A (from polycarbonate plastics, plastics with recycling code 7, microwaveable plastic, and the resin lining of canned foods); perchlorates (fertilizers, explosives in fireworks)? All of these substances have been shown to block thyroid action; having sufficient iodine helps prevent these chemicals from entering thyroid tissue (Blount 2006; Schmutzler 2007). How should this factor into our decisions on dose of iodine?

Simply adhering to the RDA of 150 mcg per day for adults or thereabouts is likely just enough for most people. Note that many multivitamins or multi-minerals contain the RDA for iodine. Obtaining iodine through the use of iodized salt is both unreliable and unhealthy, since salt increases blood pressure in the susceptible, causes fluid retention, and can accelerate osteoporosis. Iodine in salt is also inconsistent, poorly absorbed, and volatile (evaporating from the container within weeks of opening).

If there is any indication of hypothyroidism, then strong consideration should be given to an increase in iodine intake to the 500-1000 mcg (microgram, not milligram) per day range, preferably from an iodine supplement such as kelp tablets, a form that approximates the natural, ocean-derived source. Iodine is also available from health food stores as potassium iodide drops, capsules, and tablets. Also, note that there may be a mild increase in TSH for several months after iodine is initiated, only to drift back down over time (Clarke 2003).

Thyroid testing can suggest iodine deficiency by the pattern of a low free T4, e.g., at or below the “reference range,” along with a slightly-higher—than-optimal TSH of 2.5 mIU/L or greater. This is usually corrected after 3-6 months of iodine replacement if iodine deficiency is the cause, especially if any thyroid enlargement is present.
Keep in mind that, if hypothyroidism or goiter is present, iodine intake may need to be individualized by your healthcare provider. Rarely, someone with hypothyroidism or goiter will develop abnormal thyroid responses to iodine. This occurs because of iodine deficiency present before correction distorts thyroid function; adding iodine can actually worsen the situation temporarily. Iodine replacement may therefore be best undertaken alongside monitoring of thyroid function by you and your health care provider. Alternatively, some people have success by increasing the dose of iodine gradually, e.g., starting at the RDA of 150 mcg per day, building up by 50-100 mcg increments gradually over 6 months until the desired dose, e.g., 500 mcg per day, is achieved.

Unfortunately, dose-escalating studies for iodine that track thyroid function have not been thoroughly explored. If the RDA for iodine of 150 mcg yields some improvement of thyroid measures, would 300 mcg, 600, 900, even 10,000 mcg further improve thyroid function or other aspects of health? Sadly, sufficient study has not yet been done to answer these questions.

Should we take a lesson from the Japanese, who, through their dietary reliance on seaweed (e.g., kelp, kombu, nori, etc.) and abundant seafood, have iodine intakes 30- to 100-fold higher (5,280-13,800 mcg per day) without excessive thyroid disease and reduced incidence of fibrocystic breast disease and breast cancer (Patrick 2008)? This is also unclear, though it suggests that much higher intakes of iodine are, for the majority, safe. It may even be preferable.

References:


Hypothyroidism: Lipids, lipoproteins, and other factors
Hypothyroidism of all degrees has been linked to distortions in lipid and lipoprotein patterns. Recognizing this connection can provide a unique and effective means of gaining better control over these measures.

LDL Cholesterol
Hypothyroidism increases LDL cholesterol and all related measures. The higher the TSH, the higher the LDL cholesterol, as well as apoprotein B and LDL particle number (NMR).

Although the blunted metabolic state of an underactive thyroid results in reduced LDL cholesterol production, cellular uptake of LDL is also reduced to a greater degree, resulting in net accumulation of LDL. Correction of hypothyroidism therefore reduces LDL. This relationship has been confirmed in a number of studies in thousands of subjects.
The magnitude of reduction of LDL cholesterol, apoprotein B, and LDL particle number is inversely proportional to TSH, with a larger reduction in those with the highest TSH levels (more severe hypothyroidism). In persons with mild hypothyroidism, LDL and apoprotein B reductions of 20 mg/dl are typical (Monzani 2004).

The HUNT Study likely closes the door for good on this argument. This large Norwegian study examined the thyroid hormone levels of 35,000 people. Thyroid hormone levels were then correlated with various parameters. As in previous studies, a clear relationship between higher TSH levels (i.e., hypothyroidism) and higher LDL levels was observed. However, the HUNT Study was unique not only for the extraordinary size of the group studied, but because the investigators extended the analysis to TSH levels ordinarily considered to be within the normal range: TSH levels as low as 1.0 mIU marked the start of a gradual increase in LDL (Asvold 2007).

What about small vs. large LDL? Here the data are not so clear, with conflicting observations. However, the best information emerges from the one study that used NMR lipoprotein analysis, which suggested that the large, less atherogenic (plaque-causing) fraction doubled with lower thyroid function (higher TSH). This suggests that, while LDL cholesterol increases with diminishing thyroid and rising TSH, it is the less harmful large fraction (Pearce 2008). However, in the Track Your Plaque experience, the effect is more likely to be variable, often depending on weight effects, diet, and other factors.

Higher TSH levels are also associated with greater levels of oxidized LDL. Oxidized LDL is more likely to contribute to coronary plaque by triggering LDL particle ingestion by macrophage inflammatory cells. Correction of hypothyroidism reversed the excessively oxidized state (Duntas 2002).

**HDL Cholesterol**

In the HUNT Study, as TSH increased above 1.0 mIU/L, LDL increased, but HDL decreased. However, the effect is quite small, amounting to a difference of no more than 2 mg/dl. This is similar to the findings of other studies.
Triglycerides
As you might expect, along with increases in LDL, hypothyroidism is accompanied by increased triglycerides; the higher the TSH, the higher the triglycerides. The degree of increase parallels the increase in LDL, though is slightly less (usually 10-20 mg/dl in mild hypothyroidism) (Asvold 2007). Correction of hypothyroidism reduces triglycerides.

Homocysteine
While increasing levels of homocysteine are unquestionably associated with increasing levels of cardiovascular risk, several randomized clinical trials have failed to show reduction of risk with reduction of homocysteine using a combination of B vitamins (folic acid, B6, B12). Nonetheless, the observation that hypothyroidism is associated with higher homocysteine levels and that correction of hypothyroidism leads to reduction of homocysteine (-44%) raises some interesting questions about the thyroid’s role underlying homocysteine as a predictor of cardiovascular events (Hussein 1999).

Could homocysteine serve, at least to some degree, as a surrogate measure of low thyroid function? While some authorities are ready to dismiss homocysteine as a dead end, significant questions remain that may, in time, yield important insights into just what role homocysteine should play in our coronary plaque control efforts.

Until then, a high homocysteine (>10 µmol/L) should at least cause you to consider an underactive thyroid gland as a contributor.

Lipoprotein(a)
Though the effect is variable (as with all other aspects of Lp(a)), many people with Lp(a) show substantial reductions in Lp(a) with thyroid correction. Thyroid correction is one of the most important strategies we have for reduction of Lp(a).
Clinical studies suffer from variation in the method of Lp(a) measurement and the substantial genetic variation in Lp(a) size (Kung 1995; Becerra 1999; Tzotzas 2000; Yildirimkaya 1996). Another factor is time: Lp(a), for unclear reasons, requires at least 3-4 months to respond to any intervention; reassessment before this time period yields misleading results (Kung 1995).

Correction of T3, in particular, may be especially important in people with Lp(a). A small Dutch study in patients after thyroid removal demonstrated 50 mg/dl reduction of Lp(a) with T3 supplementation (Dullart RP et al 1995). Whether adding T3 to T4 treatment adds to Lp(a)-reducing effect has not been systematically examined, but has proven helpful in many cases in the Track Your Plaque experience. This means using both T4 and T3 thyroid preparations or using combination preparations, such as Armour® thyroid, to correct even subtle degrees of thyroid dysfunction to gain control over Lp(a).

**Endothelial dysfunction**
Thyroid hormones, especially T3, enhance the action of nitric oxide in the arterial wall, which causes a reduction in arterial tone and blood pressure. This effect is similar to that of l-arginine. People with mild hypothyroidism have been observed to have impaired artery dilating responses, corresponding to a rise in diastolic blood pressure, an effect which reverses when hypothyroidism is treated (Taddei 2003).

**Heart rate and parasympathetic tone**
Beat-to-beat variation in the interval from one heartbeat to the next is a desirable feature, a condition of heightened parasympathetic tone (opposite of sympathetic “fight-or-flight”). Increased variability is seen in healthy people, high levels of fitness, and people who meditate. People with hypothyroidism display diminished beat-to-beat variability, reflecting impaired parasympathetic tone, a potential marker for poor health and adverse outcomes (Kahaly 2000).

**Sidebar**
Do-it-yourself-at-home thyroid test: Basal body temperature
The regulation of body temperature—thermoregulation—is a reflection of the body’s capacity to adapt to the external environment and maintain body temperature within a narrow range. Deviations from the narrow range of body temperature can suggest disruption of internal control. If it weren’t for our ability to regulate body temperature, we’d have to lie in the sun like snakes and crocodiles to control body temperature.

Should thermoregulation go haywire due to external influences that overwhelm it, trouble results. Anyone who has experienced a fever of 104º F or hypothermia from cold exposure knows that just a few degrees in either direction is distinctly unpleasant, even life-threatening.

What is normal body temperature? Recent analyses, as well as a comprehensive review of temperature data from studies from 1935 to the present, suggest that normal oral temperature ranges from 96.3º F/35.7º C to 99.9º/37.7º C (Sund-Levander 2002; McGann 1993). This differs from the 98.6º F/37.0º C often quoted as normal, a relic of 19th century observations on human temperatures.

Body temperature also undergoes a predictable circadian rhythm, with highest temperature of the daily 24-hour cycle at around 8 p.m., lowest at around 4 a.m. It is the temperature low that is most reflective of thyroid status.

There is no question that the thyroid gland and thyroid hormones, T3 and T4, play a crucial role in temperature regulation. A principal sign of advanced hypothyroidism (high TSH, low thyroid hormone levels) is low body temperature, while hyperthyroidism (low TSH, high thyroid hormone levels) is associated with increased body temperatures.

When can low temperature be attributed to hypothyroidism and not other causes? There are frustratingly few data that explore this relationship. While there is no dispute that low temperatures can accompany hypothyroidism, it is not clear how reliable an indicator it is, since the relationship has not been studied in a formal manner. In anecdotal experience in many clinical practices, however, low body temperature is commonly used to identify hypothyroidism.
We have used first-upon-arising oral temperatures in the *Track Your Plaque* program and they can indeed be useful. At a practical level, any first a.m. temperature (immediately upon arising) consistently less than 97.3º F or 36.0º C is *suggestive* of hypothyroidism; the *lower* the temperature, the *more likely* it represents hypothyroidism. A temperature of 94.7º F, for instance, is more strongly suggestive of hypothyroidism than a temperature of 97.1º F.

Followers of the experience of Dr. Broda Barnes adhere to his original belief that axillary (armpit) temperatures are the preferred method to assess body temperature. However, of the various ways to measure body temperature, axillary is the *least* reliable and the one most prone to inaccuracy. More so than other methods, axillary temperatures are subject to external ambient temperature, amount of clothing worn, sweating, whether right or left arm is used (since there is variation of up to 2.0º F degrees from right to left), the amount of cutaneous (skin) dilation or constriction of blood vessels. Axillary temperatures track internal (rectal) temperature poorly, with wide variation in the day-to-day and minute-to-minute fluctuations of temperature, and especially marked divergence from rectal temperature in morning (temperature nadir) and evening (temperature peak) hours, with as much as 1.8-2.7º F/1.0-1.5º C variation within several minutes (Cattaneo CG et al 2000; Kelly G 2006). Axillary temperatures are therefore too variable and unreliable for use in assessing thermoregulation and thyroid status and should *not* be used to assess thyroid status.

Despite its uncertainties, temperature is still a useful tool to identify hypothyroidism, particularly when laboratory values like TSH, free T3, and free T4 are borderline or equivocal, or when symptoms are unusual or atypical. Low temperature may *suggest* low thyroid status even when all other measures, including TSH, are normal, but this is on more shaky ground scientifically. Temperature can also be useful to follow *trends* over time to gauge the adequacy of thyroid replacement.

There are several lessons to keep in mind if we are to use temperature to assess our body’s capacity for thermoregulation and thyroid status:
Normal immediately-upon-arising oral temperature is 97.3\(^\circ\) F or 36.0\(^\circ\) C.

Oral temperatures are best used as a gauge of thyroid status alongside symptom assessment and thyroid laboratory evaluation that includes TSH, free T3, and free T4.

Oral temperatures only should be used (unless internal temperatures are available). Oral temperatures track most truly to internal temperatures. Axillary temperatures do not track with internal temperatures and are subject to unacceptable variation and should not be used.

Oral temperatures should be assessed immediately upon awakening without drinking water or other liquids or eating any food; alcoholic beverages should be avoided the evening prior. Temperature should not be assessed during calorie restriction, fasting, or a period of substantial sleep deprivation.

The temperature nadir (bottom) usually occurs between 3 am and 6 am. If oral temperature is taken upon awakening at, say, 8 a.m., it will be higher than the true nadir. Waking temperatures later than 6 a.m. can be adjusted to the “6 a.m. equivalent” by subtracting 0.18\(^\circ\) F/0.1\(^\circ\) C for every hour after 6 a.m.

Menstruating females should take oral temperatures during the first 7 days after beginning menstrual bleeding during the follicular phase, the phase that does not show the exaggerated increase in temperature triggered by ovulation or progesterone.

Temperature represents a simple means to gauge metabolic rate and thereby thyroid status. It is another measure like blood pressure or blood sugar, a simple assessment you can perform on your own and track over time.

References:

Hypothyroidism and coronary plaque
Not only have overt and mild hypothyroidism been associated with worsening of factors in the coronary risk profile, but they are also associated with increased risk for heart attack. Risk develops with TSH values even commonly regarded as “normal.”

The Rotterdam Heart Study showed that, among 1149 women participants, those with TSH >4.0 mIU/L showed a 70% greater likelihood of aortic atherosclerosis and more than double the likelihood of heart attack (Hak 2000). (Widely quoted “normal” or “reference ranges” for TSH are usually less than 4.5 or 5.5 mIU/L.)

Individual studies showed widely varying magnitude of increased risk with hypothyroidism (as high as 80% in a 2005 study Walsh 2005). An analysis of 10 combined studies (a “meta-analysis”) examining a total of 14,500 participants showed that mild hypothyroidism was associated with 20% increase in risk for heart attack (Ochs 2008). A small study using coronary angiography showed that 5 of 7 people with “adequate” thyroid replacement (150 mcg levothyroxine) showed no progression of coronary disease, compared to a group “inadequately” treated (<100 mcg levothyroxine) all of whom showed progression (Perk 1997).

The HUNT Study extended these observations by analyzing risk for fatal cardiovascular events over eight years along the entire spectrum of TSH levels, even down into the “normal” reference range <3.5 mIU/L. By breaking their groups down by TSH levels, the group with TSH 1.5-2.4 mIU/L showed a 41% increase in events; the group with TSH 2.5-3.5 mIU/L showed a 69% increase in events, when groups
were compared to the group with TSH 0.50-1.4 mIU/L. The relationship was stronger in women than in men (Asvold 2008).

Unfortunately, clinical studies demonstrating the effects of thyroid correction on cardiovascular risk are limited.

In a large anecdotal experience in 1,110 patients treated with thyroid hormones (mostly Armour® thyroid) over an average of 5.6 years, four heart attacks were observed, compared to the “expected” number of 72 heart attacks in a demographically similar group of people not taking thyroid (i.e., not a true control group) (Barnes 1973).

A study dating back to 1971 suggested reduced risk with thyroid replacement. 347 patients with coronary or peripheral arterial disease, nearly all of whom started without hypothyroidism, were given a combination thyroid preparation equivalent to Armour® thyroid, starting at ½ grain (30 mg) and increasing as tolerated to 2-3 grains (120-180 mg) and observed over 5 years. Total cholesterol was reduced by 22% and mortality reduced by 44% when compared to the expected death rate (judged by actuarial tables, not a true control group) (Wren 1971).

A small study of 45 people with mild hypothyroidism (median TSH 6.31 mIU/L) compared to 32 controls (median TSH 1.19 mIU/L) demonstrated that those with hypothyroidism began with higher LDL cholesterol levels (+25 mg/dl), equivalent HDL levels, higher triglycerides (+14 mg/dl), higher Lp(a) (3 mg/dl), and greater carotid intimal-medial thickness (CIMT; +19%), a measure of atherosclerosis in the carotid artery. After 6 months of treatment with T4 to achieve TSH of 1.32 mIU/L, the participants with starting hypothyroidism showed 11% regression of CIMT. In addition, LDL was reduced by 20 mg/dl; Apo B by 9 mg/dl; triglycerides by 6 mg/dl; Lp(a) by 2.3 mg/dl (Monzani F et al 2004).

At the very least, maintaining ideal thyroid hormone status shifts lipids and lipoproteins in the right direction. In many people, the reduction in LDL cholesterol/apoprotein B/LDL particle number is sufficient to achieve Track Your Plaque targets without statin drugs. Because thyroid replacement also typically causes weight loss or makes weight loss occur more readily, weight-sensitive measures, such as
small LDL and HDL, can improve substantially, as well. While the data are incomplete in telling us whether maintaining ideal thyroid status will facilitate atherosclerotic plaque regression, preliminary experiences suggest, including our large anecdotal experience, that it does indeed play an important role for many people.

**The Track Your Plaque approach to hypothyroidism**

In many people, subtle degrees of hypothyroidism with TSH values within the “normal” range can act as a coronary risk factor and drive plaque growth. Correction of hypothyroidism is also accompanied by many positive side-benefits: people feel more energetic; they are happier; weight loss is accelerated; LDL cholesterol, triglycerides, and Lp(a) values are reduced; and more people enjoy better control over coronary plaque.

The first step in achieving correction of thyroid function is to ensure adequate iodine intake. This is especially important for people who avoid use of iodized salt, exercise or work in hot environments, in people with the low free T4/high TSH pattern, and people with any degree of thyroid enlargement.

The conventional approach to thyroid management, as practiced by most primary care physicians and endocrinologists, is not ideal for coronary health. Given experiences like the HUNT Study, we aim to keep TSH 1.5 mIU/L or less, along with free T3 and free T4 levels in the upper half of the reference range; this has maximized lipid and lipoprotein benefits, generally maximizes a sense of well-being, and has proven practical and effective from a plaque-control viewpoint.

It is also necessary to look beyond thyroid testing measures to gauge the adequacy of thyroid function. TSH serves as an unreliable index of thyroid function in some people and can be falsely low or “normal” even when hypothyroidism is truly present. Recent data appear to support this argument, with one recent study, for instance, showing that, as we age, the increase in TSH with low thyroid function is 75% less compared to younger people (Carlé 2007). Attention to symptoms is therefore essential for detecting persons suffering from hypothyroidism underestimated by standard laboratory testing.
Synthetic T4 (e.g., Synthroid®) is not sufficient to resolve symptoms of hypothyroidism in a substantial proportion of persons with hypothyroidism, since not everyone converts T4 to active T3 with equal efficiency. Indeed, low-T3 has been documented to be a predictor of death in patients with congestive heart failure (Iervasi 2003). T3 supplementation has positive effects on psychological symptoms of hypothyroidism with several studies showing that well-being, mood, and cognitive functions are improved; weight loss may also be greater with added T3 (Saravanan 2002; Bunevicius 1999; Appelhof 2005). T3 supplementation tailored to symptom relief can also address the issue of reverse T3 by providing an external source of effective T3 (Gaby 2004).

Claims that synthetic T4 drugs are superior to natural thyroid drugs in consistency, potency, and stability are false, largely driven by drug industry marketing efforts. The hormones found in porcine (pig) thyroid are chemically identical to that found in humans. Worries over consumption of the animal proteins in desiccated pig thyroid are also unfounded, as they are regularly consumed whenever eating ham, pork chops, or bacon. While this may pose a problem on religious grounds for some people, it offers no impediments on medical grounds. Claims of impurity are also misrepresentation propagated by pharmaceutical marketing. In fact, both Synthroid® (synthetic T4) and Armour® Thyroid (porcine thyroid) have both had similar struggles with potency and stability in past. Unfortunately, many doctors and patients have only heard about problems with Armour® Thyroid. The Department of Health and Human Services has twice issued cease and desist orders to the manufacturer of Synthroid® for misleading advertising. Prior to the development of synthetic T4 in the 1950’s, natural thyroid hormone products were the only treatment for hypothyroidism since their introduction in the late 1800’s. In that time, they have developed an extensive track record for safety and efficacy, and products such as Armour® Thyroid are now produced under the same USP standards as synthetic T4.

In the *Track Your Plaque* experience, we favor symptom management over TSH, assessment of T3 as well as T4, and the use of natural thyroid preparations like Armour® Thyroid over levothyroxine or Synthroid®. For anyone who wishes to add T3 but
wants to avoid the animal-sourced product, a synthetic T3, liothyronine or Cytomel®, is also available (by prescription).

Mild hypothyroidism and the Track Your Plaque program: practical tips

- All levels of hypothyroidism, regardless of how mild, appear to increase heart disease risk. Risk for cardiovascular events may extend to TSH levels as low as 1.4 mIU/L.
- Synthetic T4 (i.e., levothyroxine, Synthroid®) only to treat hypothyroidism may not represent optimal treatment in everyone. Natural hormone therapy (e.g., Armour® Thyroid) that provides T3 replacement may be more efficacious for many, perhaps most, people with hypothyroidism. Lower levels of T3 and/or less than optimal symptom relief on T4 alone may suggest potential for benefit by adding T3 (liiothyronine) or converting to a preparation like Armour® Thyroid.
- Correction of mild hypothyroidism can reduce LDL, triglycerides, Lp(a), and homocysteine, and may help normalize endothelial function. Our experience suggests that it also facilitates atherosclerotic plaque regression.