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AS WE SEE IT

Defying the Reference Ranges

When physicians review a patient's blood test results, their only concern is when a particular result is outside the normal laboratory "reference range." The problem is that standard reference ranges usually represent "average" populations, rather than what the optimal range should be to maintain good health.

The lethal consequences of faulty reference ranges have been discussed for many years in Life Extension magazine. As more studies show that a person's health can be severely impaired when physicians rely on standard reference ranges, it becomes imperative for Life Extension members to educate themselves about "optimal" ranges to avoid becoming a victim of medical ignorance.

It now appears that most standard reference ranges are too broad to adequately detect health problems or prescribe appropriate therapies on an individual basis.



William Faloon



An example of flawed reference ranges can be seen in blood tests used to assess thyroid status. A long-standing controversy has been how to best diagnose thyroid deficiency. Conventional doctors rely on thyroid blood tests, whereas alternative physicians also look for other signs and symptoms of thyroid deficiency. A recent article in *The Lancet* reveals surprising new findings about reference ranges that may shake up current theories about assessing individual thyroid status.

Before discussing *The Lancet* article, the reader should be acquainted with the serious consequences of a thyroid hormone deficiency. Aging people encounter a variety of ailments that doctors often attribute to problems other than thyroid deficit. Some of the most noticeable symptoms caused by low thyroid are poor concentration, memory disturbances, cold hands and feet, accumulation of excess body fat, difficulty in losing weight, menstrual problems, dry skin, thin hair and low energy. Some specific disorders related to thyroid deficiency include depression, elevated cholesterol, migraine headaches, hypertension and infertility.[1-9]

Broda O. Barnes, M.D., Ph.D. was a physician-scientist who dedicated more than 50 years of his life to researching, teaching and treating thyroid and related endocrine dysfunctions. In his book entitled, *Hypothyroidism: The Unsuspected Illness*, Dr. Barnes described over 47 symptoms that may be related to poor thyroid function. During his many years of research and practice, Dr. Barnes condemned conventional doctors who ignored obvious clinical manifestations of thyroid deficiency. According to Dr. Barnes:

"The development and use of thyroid function blood tests left many patients with clinical symptoms of hypothyroidism undiagnosed and untreated."

In lieu of blood tests, Dr. Barnes advocated that patients measure their temperature upon awakening. If the temperature is consistently below normal ranges, this is indicative of a thyroid deficiency. The box below provides specific instructions on how best to measure your body temperature in order to assess your thyroid hormone status.

Dr. Broda Barnes believed that 40% of the adult population suffers from thyroid deficiency. Based on the percentage of adults now taking prescription drugs to treat depression, elevated cholesterol, high blood pressure and other conditions, Dr. Barnes' observations about the epidemic of thyroid deficiency may now be validated.

What's wrong with thyroid blood tests?

The Lancet is one of the most prestigious scientific journals in the world. It often reports new medical findings that defy conventional wisdom. According to an article published in the August 3, 2002 issue of *The Lancet*, the problem with thyroid blood tests may be

faulty “Reference Ranges” that fail to reflect what the optimal level of thyroid hormone should be in a particular individual.[10]

As stated earlier in this article, standard laboratory reference ranges represent “average” populations, rather than what the optimal range should be. Back in the 1960s, for instance, the upper reference range for cholesterol extended to 300 (mg/dL). This number was based on a statistical calculation indicating that it was “normal” to have total cholesterol levels as high as 300. At that time, it was also “normal” for men to suffer fatal heart attacks at relatively young ages. As greater knowledge accumulated about the risk of heart attack and high cholesterol, the upper limit reference range gradually dropped to the point where it is now 200 (mg/dL).[11]

The same situation occurred with homocysteine reference ranges. Up until recently, it was considered normal to have a homocysteine blood reading as high as 15 (mm/L).[12] Most reference ranges now provide a chart showing that homocysteine levels above 7 increase risk of heart attack and stroke.[13]

It’s not just blood laboratory reference ranges that fail to provide physicians and patients with optimal numbers. For example, when your blood pressure is checked, a diastolic number up to 90 (mm Hg) is considered normal. Yet a diastolic blood pressure reading over 85 is associated with an increased stroke risk. A high percentage of people over age 60 have diastolic readings over 85 and this is the age group most vulnerable to stroke.[14] So when your doctor checks your blood pressure and says it’s normal, your response should be that “normal” is not good enough, since it is also normal for people over age 60 to suffer a stroke. Instead, you should ask your doctor what is the “optimal” range. In the case of diastolic blood pressure, taking steps to keep it at 85 or below could greatly reduce long-term vascular damage. It is important to note that mid-life hypertension predisposes people to stroke later in life, so keeping blood pressure readings in optimal ranges is important at any age.

Scientists are now examining thyroid hormone reference ranges and their findings indicate that it may be time to change the way laboratories report TSH results.

The Thyroid Stimulating Hormone (TSH) Test

The standard blood test used to determine thyroid gland hormone output is the thyroid stimulating hormone test (TSH). When there is a deficiency in thyroid hormone, the pituitary gland releases more TSH to signal the thyroid gland to produce more hormones.

When the TSH test is in “normal range,” doctors usually assume that the thyroid is secreting enough thyroid hormone. The question raised by The Lancet authors, however, is whether today’s reference range for TSH reflects optimal thyroid hormone status.

The TSH reference range used by many laboratories is between 0.2 to 5.5 (mU/L). A greater TSH number is indicative of a thyroid hormone deficiency. That is because the pituitary is over-producing TSH based on lack of thyroid hormones in the blood. Any reading over 5.5 alerts a doctor to a thyroid gland problem and that thyroid hormone therapy may be warranted.

The trouble is that the TSH reference range is so broad that most doctors will interpret a TSH reading as low as 0.2 to be as normal as a 5.5 reading. The difference between 0.2 and 5.5, however, is an astounding 27-fold. It would seem almost absurd to think that a person could be in an optimal state of thyroid health anywhere along this 27-fold parameter, i.e. TSH readings between 0.2 and 5.5.

A review of published findings about TSH levels reveals that readings over 2.0 may be indicative of adverse health problems relating to insufficient thyroid hormone output. One study showed that individuals with TSH values over 2.0 have an increased risk of developing overt hypothyroid disease over the next 20 years.¹⁵ Other studies show that TSH values over 1.9 indicate abnormal pathologies of the thyroid, specifically autoimmune attacks on the thyroid gland itself that can result in significant impairment.[15]

Thyroid Self Testing

Upon awakening before you get out of bed, put a thermometer under your arm with no clothing between the bulb and your armpit. Leave it there for 10 minutes (use snooze alarm if you wake up to an alarm clock). Just drowse for that time lying still. If the armpit method is too inconvenient, you can put the thermometer in your mouth for three minutes (or until the electronic thermometer registers a temperature).

After the appropriate number of minutes take the thermometer out and read it, writing down the result right away. This is known as your Early AM Basal Temperature, and the “normal” should be between 97.8 and 98.2. The reading taken by armpit is somewhat lower and somewhat more accurate than by mouth. If you have a low-grade infection your temperature may read higher than your “normal.” If it is within the range mentioned above, you should repeat the procedure every other day for two weeks. If you are a menstruating female, do it on the 2nd and 3rd day of your period.

If your average temperature over a two-week period is lower than 97.8 to 98.2, you are probably hypothyroid. If it is higher, then you are probably hyperthyroid (or you have an infection somewhere).



More ominous is a study showing that TSH values over 4.0 increase the prevalence of heart disease, after correction of other known risk factors.[16] Another study showed that administration of thyroid hormone lowered cholesterol in patients with TSH ranges of 2.0 to 4.0, but had no effect in lowering cholesterol in patients whose TSH range was between 0.2 and 1.9.[17] This study indicates that in people with elevated cholesterol, TSH values over 1.9 could indicate that a thyroid deficiency is the culprit causing excess production of cholesterol, whereas TSH levels below 2.0 would indicate no deficiency in thyroid hormone status.

Doctors routinely prescribe cholesterol-lowering drugs to patients without properly evaluating their thyroid status. Based on the evidence presented to date, it might make sense for doctors to first attempt to correct a thyroid deficiency (based on a TSH value over 1.9) instead of first resorting to cholesterol-lowering drugs.

In a study to evaluate psychological well being, impairment was found in patients with thyroid abnormalities who were none-the-less within “normal” TSH reference ranges.[18]

Defying the reference ranges

The authors of The Lancet study stated that, “the emerging epidemiological data begin to suggest that TSH concentrations above 2.0 (mU/L) may be associated with adverse effects.”

The authors prepared a chart based on previously published studies that provide guidance when interpreting the results from TSH blood tests. Here are three highlights from their chart that may be useful in determining what your TSH values really mean:

TSH greater than 2.0	Increased 20-year risk of hypothyroidism and increased risk of thyroid autoimmunity[15]
TSH greater than 4.0	Greater risk of heart disease[16]
TSH between 2.0 and 4.0	Cholesterol levels decline in response to thyroxine (T4) therapy[17]

Despite presenting these intriguing findings, The Lancet authors stated that more studies are needed to define optimal TSH level as between 0.2 and 2.0 instead of between 0.2 and 5.5. As a health conscious person, however, this type of precise information provides an opportunity to correct a medical condition that has been unresponsive to mainstream therapies, or possibly prevent disorders from developing in the first place.

This means if you suffer from depression, heart disease, high cholesterol, chronic fatigue, poor mental performance or any of the many other symptoms associated with thyroid deficiency, you may want to ask your doctor to “defy the reference ranges” and try thyroid replacement therapies.

Measuring thyroid hormone levels

TSH is just one blood test that doctors use to assess thyroid status. Other blood tests measure the actual amount of thyroid hormone found in the blood.

The primary hormone secreted by the thyroid gland is called thyroxine (T4). The T4 is then converted in the peripheral tissues into metabolically active triiodothyronine (T3).

Doctors often test for TSH and T4 together, but this may not accurately reflect thyroid deficiency in tissues throughout the body. One study found that psychological well being could be improved if T3 (like the drug Cytomel) is added to T4 (like the drug Synthroid) therapy, while maintaining thyroid function broadly within the standard reference ranges.[19,20] What this means is that even when TSH and T4 blood tests are within normal ranges, a person can still be deficient in peripheral T3 and benefit from Cytomel therapy.

Since T3 is the metabolically active form of thyroid hormone, some doctors use it exclusively in lieu of T4 drugs like Synthroid. The FDA’s recent notice to ban synthetic T4 drugs like Synthroid because of inconsistent potencies helps to validate the following statement made by Dr. Broda Barnes more than 50 years ago:

“Patients taking thyroid replacement therapy have much better improvement of symptoms with natural desiccated thyroid hormone rather than synthetic thyroid hormones.”

While the FDA has found many problems with T4 drugs, the T3 drug Cytomel has produced consistent clinical results and is not a

subject of the FDA's proposed ban. Dr. Barnes fought the drug companies over synthetic T4 drugs for years and recommended desiccated thyroid (Armour) as the therapy of choice for most patients.

An article in the New England Journal of Medicine described a study in which patients with hypothyroidism showed greater improvements in mood and brain function if they received treatment with Armour thyroid rather than Synthroid (thyroxine). The authors also detected biochemical evidence that thyroid hormone action was greater after treatment with Armour thyroid.[21]

It would appear that Dr. Broda Barnes has been vindicated.

All hormone reference ranges may be antiquated

It's not just thyroid hormone deficiency that goes unrecognized by so many physicians. Conventional medicine has neglected virtually all the hormone imbalances that develop as a part of growing older. The result is that aging people suffer a variety of discomforts and lethal diseases that are correctable and preventable if simple hormone adjustments are made.

Standard versus Optimal

A person's risk of contracting lethal disease, suffering debilitating disorders and prematurely aging can be partially predicted based on the findings of blood tests that assess hormone levels. What follows are the Standard Reference Ranges compared to the Optimal Ranges for a 60-year old male:

Hormone	Standard Reference Range	Optimal Range
DHEA	42-290	280-500 ug/dL
Insulin (fasting)	6-27	Under 5 uU/mL
Free Testosterone	6.6-18.1	15-22 pg/mL
Estradiol	0-54	10-30 pg/mL
TSH	0.2-5.5	Under 2.1 mU/L

Aging men, for instance, often suffer from excess production of insulin and estrogen, with simultaneous deficiencies of free testosterone and DHEA. If a physician were to test blood levels of all four of these hormones, the standard "reference ranges" are so wide that most men would fall into the so-called "normal" category.

Standard reference ranges indicate that dangerously high insulin and estrogen levels are "normal" in elderly men. So are heart attacks, stroke, cancer, benign prostate enlargement, weight gain, Type II diabetes, kidney impairment and a host of other diseases that are associated with excess insulin and estrogen.

For instance, the standard reference ranges for free testosterone and DHEA show that very low levels are perfectly "normal" for aging men. It's no coincidence that these same aging men (with low testosterone/DHEA) suffer high rates of depression, memory loss, atherosclerosis, senility, impotency, high cholesterol, abdominal obesity, fatigue and a host of other diseases related to low blood levels of testosterone and DHEA.[22-34]

When it comes to assessing hormone status, standard reference ranges have failed aging humans in a terrible way. The reason is that reference ranges are adjusted to reflect a person's age. Since it is normal for an aging person to have imbalances of critical hormones, standard laboratory reference ranges are not flagging dangerously high levels of estrogen and insulin or deficient levels of testosterone, thyroid and DHEA. The box "Standard versus Optimal" on this page shows standard hormone blood reference ranges for men and compares them to what the "optimal" ranges should be.

Most doctors still believe that imbalances of life-sustaining hormones are "normal" for aging people. These physicians think that nothing should be done to restore hormone profiles to youthful ranges (and almost never test hormone levels anyway).

The problem is that aging people no longer accept that they should contract the diseases that happen to fit into their age category. In other words, more 65-year olds are demanding



Aging people who adjust their hormone profiles to fit a

the health and vitality enjoyed by a younger person. This is not possible if 65-year olds allow their hormone levels to stagnate in today's archaic reference ranges. If you are 80 years old and are told that your hormone profile is normal for your age, tell your doctor that you would prefer the hormone profile of a 25-year old since you perceive a 25-year old as having more vitality and a reduced risk of contracting lethal diseases than an 80-year old.

Optimizing your hormone levels

The Life Extension Foundation has published extensive protocols relating to optimal male and female hormone modulation. If you log on to www.lef.org , you can access the following updated hormone-related protocols:

- Male Hormone Modulation
- Female Hormone Modulation
- Thyroid
- DHEA Replacement Therapy

If you are a Foundation member and don't have access to a computer, call 1-800-544-4440 and we will print out and mail these protocols to you at no charge.

Aging people who adjust their hormone profiles to fit a more youthful profile can turn back some of the effects that time has inflicted on their bodies. In order to accomplish this, however, you must defy the standard laboratory reference ranges and seek the blood values of a much younger person.

If your doctor won't prescribe these critical blood hormone tests, or if the retail cost is prohibitive, call 1-800-208-3444 to find out how you can obtain these tests by mail order at prices below those charged by commercial laboratories.

For longer life,



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