

Myths of Hypothyroidism

The diagnosis and treatment of hypothyroidism seem to be regarded by most health professionals as being relatively simple matters – just run a blood test and if the results lie outside the reference range, administer just enough levothyroxine to bring them back within range.

Those of you who have long felt unwell, suspecting that your thyroid is the cause of your symptoms but repeatedly being told that your blood tests are normal, may by now be thinking rather differently. If this is the case, you will not be surprised to learn that thyroidology is littered with mythology! This article challenges some of that mythology.

The Myth of TSH as the 'Golden Measure' of Thyroid Health

TSH is produced by the pituitary gland (and so is *not* a thyroid hormone). Special cells at the back of the pituitary gland sense the levels of thyroid hormone in the blood. It also receives information from the hypothalamus and other parts of the brain, representing your emotional state, what demands are being made on your body, how warm or cold you are, where in the diurnal cycle you are and so on. The pituitary then works out what the levels of tri-iodothyronine (T3) and thyroxine (T4) in your blood stream should be, compare them to what they actually are and adjusts the production of TSH to make your thyroid gland decrease or increase its production of thyroid hormone accordingly.

That is the old, simplistic explanation of how TSH regulates your thyroid hormone levels, assuming there is only one 'feedback loop' in operation. However, it is now known that it is all much more complicated than that. For example, there are actually multiple feedback loops all working at different molecular levels and timescales, the peripheral conversion of T4 into T3 is also controlled by TSH and is therefore closely integrated with the production of hormones in the thyroid gland, and the hormones secreted by your thyroid gland contain a much higher proportion of T3 than previously thought.

However, if there is something wrong with your pituitary gland, hypothalamus or the information coming into your hypothalamus, the levels of TSH in your blood will be affected.

Dr Anthony Toft has spoken of the "exquisite sensitivity" of the TSH measurement, meaning that a small increase in the free thyroxine (FT4) level is accompanied by a much larger decrease in the TSH level and vice versa. However, recent research¹ has shown that the relationship between the TSH and FT4 levels is not fixed as previously supposed and can at any time change permanently due to such things as illness or stress. It is also affected by body weight and whether or not you are having levothyroxine therapy.

The TSH measurement doesn't actually tell you very much - it won't tell you if:

- you are converting enough T4 into T3
- you are converting too much T4 into reverse T3
- your thyroid is being attacked by antibodies
- you have T3 receptor resistance
- you are suffering from adrenal insufficiency
- you are deficient in those minerals and vitamins essential for good thyroid health

The usual approach to the treatment of hypothyroidism is to limit the levothyroxine dose to that which 'normalises' the TSH level in your blood, returning it to about the middle of the

reference range, assuming that the thyroid hormone levels in the cells will also be normalised. The late Dr John Lowe searched long and hard for scientific evidence that imposing a TSH normalising dose of thyroid hormone really does achieve normal thyroid hormone levels in the cells but being unable to find any, had to conclude that this was a scientifically unproven assumption.

Whilst a full picture of your thyroid health cannot be obtained by checking only your TSH level, very high TSH levels are indicative of hypothyroidism and very low ones of hyperthyroidism but that is about as far as it goes.

The Myth of Blood Tests as the Only Reliable Way of Diagnosing Thyroid Disease

If your TSH test result is 'abnormal' the lab will run an FT4 check as well. Whilst this is an improvement on a TSH only check, it is still fallible and can produce false negatives.

Doctors have been looking for a diagnostic test for thyroid problems ever since the importance of thyroid hormones was recognised late in the eighteenth century. There have been numerous proposals for different tests for thyroid illness prior to the advent of the blood test used today but not one was found to be reliable. Unfortunately, the currently used thyroid function test, based on a blood sample, has its own limitations.

What should really be measured are the thyroid hormone levels in every cell in the body. As it is not practical to do this, they are in effect inferred from those in the blood stream. However, the transfer of thyroid hormones from the blood stream and into the cells is a quite a complicated matter and there are several points in the process where problems may arise.

If, for example, your thyroid has been under-producing for a long time, the receptors on the outside of those cells may for various reasons alter their function with the result that insufficient amounts of hormone manage to get inside where they are needed. The unused hormones will accumulate in the bloodstream where the levels will eventually return to within the reference range but since those in your cells will be low, the blood test results will not line up with the clinical picture. If your clinician dismisses your symptoms as being too general and non-specific to allow a definitive diagnosis to be made from them, your hypothyroidism may well remain undiagnosed. Ideally non-thyroidal blood markers indicating thyroid hormone insufficiency should be identified and these would be more informative.

There are many other problems with thyroid function blood tests, including their interpretation. The use of 'reference ranges' seems to encourage the recognition only of fairly extreme under or over activity of the thyroid gland as if lesser deviations from 'normal' don't make people feel unwell. The reference ranges themselves may be too broad if they were based on a sample of 'healthy individuals' too many of which had mild but unrecognised hypothyroidism or hyperthyroidism. It is not generally appreciated that because the reference ranges are derived statistically, the closer the test result is to one of the limits, the greater the uncertainty as to whether you are ill or not - you don't suddenly fall off a cliff edge the moment the result exceeds the limit, and nor should normality be assumed if your results are within the reference range but close to its limits.

It would be much better if the blood test was generally regarded as a means of confirming a diagnosis already made based on symptoms, medical history, a physical examination and an ultrasound scan of the your thyroid gland and that the benefit of doubt was more readily granted if the blood tests come back 'normal' especially if the patient's symptoms are suggestive of a thyroid problem.

The Myth that it is Possible to Set a Precise Dose of Thyroid Medication

There appears to be a school of thought that the treatment of hypothyroidism can these days be carried out with great precision. This is presumably based on the assumptions that, for instance:

- you can measure the levels of thyroid hormones in the blood very accurately
- the potency of each tablet never varies
- you can find a combination of tablet strengths that make up the precise dose your doctor thinks you need without you having to sub-divide any tablets for yourself
- your thyroid hormone needs never change.

Thyroid Hormone Measurements

No measurement can ever be made which does not have some degree of uncertainty or imprecision. As the concentrations of thyroid hormone in the bloodstream are extremely small, the measurement of them is actually quite difficult. Furthermore, there are several different measurement techniques in use, each having its own reference range. Even two labs in the same city may be using different ones (so it is very important to always ask for a print out of your test results which should give the applicable reference ranges).

TSH blood test measurements made by all the pathology labs throughout the UK are periodically checked using a standard TSH solution supplied by the regulatory authority, as is required by law. Apparently, if all the standard TSH solution results from the all the different pathology labs in the UK were to be compared they would be seen to vary by up to one quarter of the reference range in either direction!

There is no such legal requirement to standardise the FT3 and FT4 blood test measurements, and because of the poorer standards of production by different manufacturers, variation of the measurement can be even greater.

Furthermore, the levels of TSH and FT3 in your bloodstream follow a 24 hour diurnal cycle and, to complicate matters further, the hormones are not secreted continuously, rather as several 'spurts' a day, so ignoring the time of day your blood sample was taken could introduce further errors.

In summary, the TSH blood test is cheaper but relates poorly to the hormone levels in your cells. The FT3 and FT4 blood tests yield better information but are more expensive to do as well as being less accurate.

Potency of Tablets

The potency of the tablets should not vary from batch to batch provided they are produced by a reputable manufacturer who regularly checks the strength of the tablets he makes.

Most medications are available in a range of different strengths and it is possible to combine tablets of different strength to achieve different dosages. It is unlikely, though, that a really precise dose can be obtained without having to divide a tablet, something which is difficult to do with sufficient accuracy.

Thyroid Hormone Needs

Your medication needs will change for various reasons. For instance, if you were hypothyroid for a long time before being diagnosed you might have slowed down a lot since you lacked the energy to do otherwise. When you first start your thyroid hormone replacement therapy you may be fairly inactive. As you recover and become more active, you may require a higher dose to meet your increasing needs. If you then take a holiday somewhere very warm, you may need to reduce your dose because your body will not need to create so much warmth for itself.

Because your true healthy thyroid hormone levels were never measured when you were well there is no well-defined target to aim at to recover those levels by levothyroxine therapy. So, as a compromise, the right dose of thyroid hormone for you is the one at which you feel your health is optimum, and that dose is likely to vary according to how active you are or how warm or cold the weather is. It may not therefore be possible to specify a precise dose of thyroid hormone exactly meeting your needs for evermore and it may change quite significantly as you grow older.

The Myth of Levothyroxine as the Only Thyroid Medication Anybody Might Need

Levothyroxine is regarded as the first line thyroid medication. Most doctors are increasingly unwilling to prescribe anything else. Some people do get better on levothyroxine but others don't and require alternatives such as liothyronine (synthetic T3) or Natural Desiccated Thyroid (NDT).

Whereas levothyroxine is synthetic thyroxine, the first ever medication for hypothyroidism, desiccated porcine thyroid, was a natural substance containing both T4 and T3.

One of several reasons why some people may not respond well to levothyroxine is that lacking an active thyroid they are unable to convert enough T4 into T3. If you give levothyroxine to these people all that happens is that the T4 builds up in the bloodstream to toxic levels whilst their tissues remain woefully short of T3. In such cases, a much better response may well be obtained by taking a medication containing T3, such as liothyronine or NDT, instead of levothyroxine. Taking liothyronine will fundamentally affect the blood test results, causing the T4 and TSH levels to fall dramatically but as the tissues need T3 to work properly, so what? In fact, your thyroid needs enough T3 to work properly so when it gets more T3 there is a possibility that it may eventually start to work better, as indicated by a recovery of the serum T4 levels, even though no T4 is being taken by mouth.

Another possible reason why people may not respond to levothyroxine, or to NDT for that matter, is that they have also developed adrenal insufficiency; the adrenal hormones are needed both to open the T3 receptors in the cells and to facilitate the T4 to T3 conversion. These people may also need to take hydrocortisone, prednisolone, adrenal glandular or 7 Keto DHEA to provide the required adrenal support.

If you are unable to obtain levothyroxine or NDT for any reason you can, of course, take thyroid and adrenal glandulars to support your thyroid and adrenals.

Furthermore, if you have a deficiency in any of the vitamins and minerals necessary for thyroid health, you may need to supplement those as well.

From the above it will be realised there are actually quite a number of ways of treating hypothyroidism and that it is quite wrong to think of levothyroxine as the only medication that might be needed.

The Myth of 'Normality'

We go to our doctor with symptoms and have a blood test but the results come back 'Normal'. What exactly is meant by 'Normal'?

In the case of the blood test, it means that the results are within the reference range - but normal for whom? The reference range is actually determined by measuring the blood serum thyroid hormone levels in members of a group of healthy, symptom free people and looking for the lowest and highest readings that between them contain 95% of the sample group. That means that 5% of those healthy, symptom free people have been arbitrarily declared abnormal and by present beliefs they would be eligible for treatment of their absent symptoms!

One thing that is probably not generally appreciated is that the TSH blood test is unique among blood tests as having a very high inter- and intra-individual variation. In other words, it varies a lot both between individuals at the same time and in the same individual over time. This will not be reflected in the reference range because it is statistically derived from the sample population group and statistical methods are intended to highlight overall trends only, so masking individual variations.

Some researchers are now calling for a much more individualised approach to the interpretation of the blood test results, using new reference criteria based on a combination of TSH, FT3 and FT4 results.

In reality therefore, there is no absolute, definitive 'normal' that can be applied to everybody. Each of us might be 'normal' in some ways and yet be abnormal in lots of other ways because in the final analysis we are all individuals, after all.

So, when the doctor says your blood tests are normal, he means that they fall within the 'normal' or 'reference' range, as it should be called. The problem is that he doesn't know what is 'normal' for you as your truly normal measurements in health are not available.

The Myth that Thyroid Auto-immune Antibodies Never Hurt Anybody

Patients are frequently told that their thyroid antibodies are not harming them. However, the most common cause of hypothyroidism is Hashimoto's disease. In Hashimoto's disease, thyroid autoimmune antibodies attack and destroy the thyroid hormone producing cells in your thyroid gland. Such attacks may initially stimulate the thyroid into over-activity but the autoimmune antibodies gradually turn the thyroid into scar tissue, destroying in the process its ability to produce thyroid hormones.

In reality you should not have any autoimmune antibodies in your body at all. You do of course need normal antibodies to provide you with vital resistance to infectious diseases, etc. If you do have autoimmune antibodies, they will not be doing you any good.

Furthermore, if you have one type of autoimmune antibody active in your body, you may well have others to go with them and they won't be doing you any good either.

In practice, because thyroid antibody levels tend to wax to wane, they may not always show up as being abnormally high in a blood test - the trick is to catch them when they are high!

In the late Dr Bo Wikland's clinic in Sweden, thyroid problems were routinely investigated using the Fine Needle Aspiration (FNA) technique. Dr Wikland's experience, as published in

The Lancet (2001 and 2003), was that FNA is actually very valuable in the demonstration of thyroid autoimmunity; superior, in fact, to antibody testing. Dr Wikland noticed that when the TSH level is suppressed, thyroid antibodies are suppressed also, so here is a further argument against TSH as the 'golden measure' of thyroid health.

The Myth that a Suppressed TSH Leads to Osteoporosis

Bones are living entities, as are muscles and ligaments. If you don't use your muscles they will waste away. On the other hand, you can deliberately build your muscles up through exercise. Bones similarly respond to the demands made of them.

If you are feeling generally listless due to being hypothyroid, you are not going to be terribly active physically and so won't be making very great demands on your bones. This in time leads to a reduction in bone density as would happen to astronauts when they spend many weeks in space stations orbiting the earth in weightless conditions. In fact, astronauts have restrictions placed upon them as to how long they can remain in a weightless condition in space for this very reason. During long missions on the International Space Station they have to exercise regularly.

The idea that suppressed TSH is associated with osteoporosis comes from a number of studies carried out by various researchers. Because these gave conflicting results, a further study, "Long-term Thyroxine Treatment and Bone Mineral Density" was carried out by J.A. Franklin, J. Betteridge, J. Daykin, R. Holder, G.D. Oates, J.V. Parle, J. Lilley, D.A. Heath, M.C. Sheppard and published in the Lancet in 1992. The synopsis reads,

"Studies of the effect of thyroxine replacement therapy on bone mineral density have given conflicting results; the reductions in bone mass reported by some have prompted recommendations that prescribed doses of thyroxine should be reduced. We have examined the effect of long-term thyroxine treatment in a large homogeneous group of patients; all had undergone thyroidectomy for differentiated thyroid cancer but had no history of other thyroid disorders.

The 49 patients were matched with controls for age, sex, menopausal status, body mass index, smoking history, and calcium intake score; in all subjects bone mineral density at several femoral and vertebral sites was measured by dual-energy X-ray absorptiometry. Despite long-term thyroxine therapy (mean duration 7-9 [range 1-19] years) at doses (mean 191 [SD 50] µg/day) that resulted in higher serum thyroxine and lower serum thyrotropin concentrations than in the controls, the patients showed no evidence of lower bone mineral density than the controls at any site. Nor was bone mineral density correlated with dose, duration of therapy, or cumulative intake, or with tests of thyroid function. There was a decrease in bone density with age in both groups. We suggest that thyroxine alone does not have a significant effect on bone mineral density and hence on risk of osteoporotic fractures."

This study was carried out on groups of patients who had undergone thyroidectomies for thyroid cancer and did not have any previous history of thyroid disease. They would therefore have gone straight onto the routinely prescribed dose of levothyroxine after having their thyroidectomies. T3 and T4 are hormones the body should be making for itself so why should taking replacement doses of them by mouth cause osteoporosis? If you are taking too much thyroid hormone, the ensuing symptoms of hyperactivity would surely prompt you to reduce your dose. Conversely, if you aren't taking enough you will feel unwell anyway and so increase your dose until you feel better. When you are taking the right amount to actually feel well again, your TSH will be suppressed because you have taken control of your thyroid hormone input away from your pituitary.

Most patients will not feel well again when a dosage of levothyroxine is imposed on them that merely 'normalises' the blood TSH levels. In fact, many people don't actually feel better until they are on a dose that does suppress their TSH level.

My view is that you are probably more likely to develop weak bones when your blood TSH level is not suppressed and you are still suffering from fatigue and all the other symptoms of hypothyroidism, and consequently are abnormally inactive for a long time.

Summary

We are all individuals with an individual biochemical makeup defining health. Thyroid hormone tests must take this into account and diagnosis simply by categorising patients as 'normal' or 'abnormal' according to whether they are, or are not, in a reference range is unacceptable. Personalised medicine must take over from anonymous assessment.

Glossary of Terms

Thyroxine (T4):	The biologically inactive thyroid hormone molecule having four iodine atoms
Free T4 (FT4)	Free (or unbound) thyroxin as measured via a blood test
Tri-iodothyronine (T3)	The biologically active thyroid hormone molecule having three iodine atoms
Free T3 (FT3)	Free (or unbound) Tri-iodothyronine as measured via a blood test
Levothyroxine	Synthetic Thyroxine (thyroid medication)
Liothyronine	Synthetic Tri-iodothyronine (thyroid medication)
Thyroid Stimulating Hormone (TSH)	The thyroid controlling hormone produced by the pituitary and measured via a blood test
Natural Desiccated Thyroid (NDT)	A thyroid medication containing both T4 and T3 prepared from the desiccated thyroid tissue of pigs

References

1. Hoermann R, Midgley JEM, Larisch R, Dietrich JW. Homeostatic control of the thyroid–pituitary axis: perspectives for diagnosis and treatment. *Front Endocrinol.* 2015 18(6):1-17

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Date created: 12/06/17

Review date: 12/06/19