Dr Bill Reeder

Integrative and Biomedical Medicine

5 May 2014

The Thyroid Dilemma
And *Functional* Hypothyroidism

Treating thyroid patients with desiccated thyroid, also known as Armor, Natural Thyroid, Whole Thyroid, Desiccated Thyroid and other T4, T3 synthetic combinations.

Over 30 years I have seen many patients with hypothyroid disease, usually auto-immune (AID) but not always, who are already on L-thyroxine but who are anything but well. Whilst their TSH shows the patient as 'euthyroid' – what does that mean, when the patient indicates how unwell they still feel?

When the AACE (The American Association of Clinical Endocrinologists) established new TSH Guidelines (0.3 - 3.0 vs. 0.5 - 5.0) the number of people estimated to be affected by abnormal thyroid function doubled.

According to the AACE, the number of people affected by Thyroid Disease now surpasses the number of people diagnosed with Diabetes or Heart Disease.

• *27 Million: The number of Americans estimated to suffer from Thyroid Disease*
• *13 Million: The number of Americans estimated to suffer from Thyroid Disease...but remain undiagnosed.*
• *14 Million: Estimated number of Americans affected by Hashimoto's Thyroiditis (Autoimmune Thyroiditis / Hypothyroidism).*
• *8 out of 10: Patients with Thyroid Disease are women*
• *5x - 8x: Women are 5 to 8 times more likely to suffer from Hypothyroidism than men.*
• *25%: Approximate number of women that will develop permanent hypothyroidism.*

As doctors we are required to follow 'best practice' guidelines. But what exactly are these? They may apply to the majority but not every single case. Human individuality, genetics, epigenetics and other factors come into play so complicating interpretation and treatment strategies.
So when the patient who is on L-thyroxine, with in-range TSH, says 'why do I still not feel well' and after we exclude other differential diagnoses – what then? SSRI?
Or do we ask:

- Is the Thyroxine actually the right dose for them, *despite* the TSH saying it is?
- Is the TSH the only determinant for our judgement – is every patient exactly the same in response?
- Should we be more guided by our patients reporting – in other words what do we value most - the clinical presentation of the patient or that lab reference range result?
- Is the synthetic T4 – largely a pro-hormone, actually working?
- Is it converting to T3? Is there selenium or zinc deficiency?
- Maybe our focus on TSH could be flawed – at least for some of our patients. Is low TSH really bad when the patient feels normal?

- There is a lot of literature condemning the blind adherence to TSH – and even relevance of T4 and T3 'normal ranges' for that matter.

Here is one typical review -

Table 1. Percentage of 860 hypothyroid patients with various symptoms despite treatment

Symptom	Percentage still suffering from
• Fatigue	92%
• Inability to lose weight despite diet/exercise	65%
• Feel sluggish & lethargic	62%
• Trouble concentrating	60%
• No sex drive	58%
• Pains, aches, stiffness	51%
• Depression	45%
• Hair loss	43%
• Eyes dry & light sensitive	38%
• Strange feeling in neck or throat	38%

A cases study, which shows the situation on careful history taking. So we *could* assign these to depression, stress and so on. But most of these symptoms can resolve with a different approach.

And we should ask – what are normal values anyway?

They are a bell curve range of values in a supposedly healthy cohort of people. Some may be well or ill outside of the lower or higher centiles…..they are population observations only. In fact they are NOT *normal* ranges but Laboratory *Reference* Ranges.
Someone in the low range of 'normal' may well be far better and normal clinically being in the top range of 'normal' or even above.
Biochemical individuality is key – especially in atypical responses. Humans aren't clones but highly complex.
Happily many hypothyroid patients do just very well on just L Thyroxin replacement using TSH. This not the group of concern, its that big group above.

So why aren't they responding?

Assuming we rule out other differential diagnoses and are left with symptoms typical of persisting hypothyroidism – with 'normal' TSH.

First look at the biochemistry:

In response to circulating T4, T3, T2 and maybe T1 and any other 'T's' – the hypothalamus will instruct the pituitary to secrete TSH, or not.
T4 is produced and circulates where in the liver and periphery (some in the thyroid) it converts to the active hormone T3 – requiring enzyme de-iodination steps and co-factors Selenium and Zinc. (Potential for Se deficiency here in NZ and zinc is important for many other enzymes)
So with our lab testing guidelines, ALL we are evaluating is the circulating TSH – and if we can or will, test T4 and its success in converting to T3.
That's as far as our 'guidelines' allow us to be concerned as doctors.

But that is only the start of the biochemistry and physiology – what happens next is crucial:

- Iodine has to be oxidised and by organification converted to thyroxin. TSH required.
- T3 has to be actively transported across cell membranes (transporter proteins) .
- It has to locate intracellular receptors in mitochondria and genes – their numbers and availability are influences by many factors.
- Is there disruption of transport and Na/symporter mechanisms.
- Are there disruptive molecules already occupying receptors?
- What about molecular mimicry? Xeno-chemicals from environmental pollution, personal care products etc?
- There is vast evidence of hormonal mimicry and other disruptor activity – well documented. Women appear to most at risk with thyroid disruption.
- And there are less common genetic disorders.
- Auto-antibodies play a role in dysfunction as well.
- Goitrogens can block iodine. Peanuts, soy, brassica vegetables, halides incl bromine and fluoride.
- Mercury displaces iodine.
- Polyunsaturated fats (long chain seed oils) can be anti-thyroid and promote weight gain, which doesn't happen with stable sat fats like medium chain coconut oil! It now appears we have been incorrect in over-promoting PUFA oils at the expense of saturated fats.

So what?

Internationally, the problem is well recognised, but still not so much by mainstream where TSH is THE reference point.
Depending on the presentation and possible things like selenium, conversion etc – a consistently good solution has been the prescribing of the combined gland extract which contains T4, T3, T2, T1 etc.
It used to be THE treatment for hypoT, but got superseded by synthetic T4 which was more consistent in quality.
But as high quality 'extract' became available so did results become consistent and more effective in certain cohorts. Indeed, peer reviewed articles have demonstrated superior results from combined T4 T3 therapy than T4 alone (NEJM 1999 -340)

So for the 'still symptomatically hypothyroid' patient who is on appropriate T4 dosing – and after considering T3 issues etc, the term *T3 resistance* is useful to describe what may be taking place. Akin to metabolic syndrome, which was once highly controversial but now very mainstream.

The patient is then offered a trial on WTE (whole thyroid extract) in incremental dosing until they achieve clinically acceptable outcome. This requires proper supervision.

The TSH always suppresses. T3 usually increases to high normal range and sometimes above.

T4 will sometimes increase but more likely reduce as feedback suppresses endogenous T4. That's not such an issue as T3 is the active hormone.

> Most patients have good to excellent response and THEY report results and THEY know which treatment gets their life back to some normality again.

I should add that the patients all have thyroid questionnaires databases, clinical exam, temperature charting to strengthen the diagnosis.

The final confirmatory test is the Trial Of Treatment.

What about the suppressed TSH.

All my research as well as that of the WTE experts and that's well cited – shows that suppressed TSH below the 'normal' range is NOT an issue unless high risk cardiac patient when closer monitoring and small dosing required. But these patients are also required to have optimal thyroid function too. Not just near enough.
The risks of cardiac events and osteoporosis is extremely rare. Of course we are assuming the patient is not already exhibiting significant IHD or OP. TSH suppression remains controversial. Data is mixed. However the risks are small but consider the very significant poor health already suffered by these patients.
Yes, these risks do occur in the disease thyrotoxicosis – which is different from exogenous thyroid replacement in the subset who appear to have T3 resistance.

Of course, as WTE is increased to get tissue responsiveness, we do indeed monitor for hyper-stimulation. Its very rare even on some necessarily high T4 T3 doses. Tissue response is not uniform. In other words, before we get to a dose to eliminate cellular fatigue, cardiac sensitivity with increased basal pulse rate may preclude any further increase in dose. Uncommon but its an example.

T3 Treatment

Rare cases still may not respond and are quite difficult. There may be many reasons but once filtered, there are cases, which will respond very well to T3 only. This requires divided dosing as one a several options. It's a more complex subject and beyond this discussion.
Suppressing endogenous T4 to very low levels and using only T3 seems to be a solution here. It *may* be linked to reverse T3 (rT3) occupying receptor sites.

I hope this will in some way provide a brief explanation of a very intriguing, very common situation in this epidemic of clinical and subclinical hypothyroidism particularly in women, poorly responsive to guideline based treatment.

References

- T3 has been used in combination with T4 in certain situations. 49% of T4 patients preferred combo treatment in one study. (Eur J Endo 2009.).
- DTE therapy *did not result in a significant improvement in quality of life; however, DTE caused modest weight loss and nearly half (48.6%) of the study patients expressed preference for DTE over L-T_4. DTE therapy may be relevant for some hypothyroid patients. J Clin Endo Metab 2013. *(My note: in saying that – the study actually reported 48% preferred DTE, they were 'significantly better', and lost weight. Typical of controversial medical topics, the conclusion still can revert to the preferred result of the researchers!)

With kind regards,

Dr Bill Reeder
Integrative Medicine
Hamilton
New Zealand