

## THYROID FUNCTION IN ME – IS THERE A MAJOR DIAGNOSTIC PROBLEM?

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1. **INTRODUCTION:** It has been suggested that “scandalous medical ignorance leading to an epidemic of undiagnosed thyroid deficiency, underlies the increasing prevalence of ME in modern times”<sup>(1)</sup>. Can such a challenge be ignored? Does it stand up to my own experience of clinical and laboratory medicine in the NHS (including the years of epidemic and pandemic ME between 1965 and 1990)? Of course not! – but first we have to define the thyroid problems under discussion.
2. **DEFINITIONS:** The above quotation refers only to thyroid deficiency and hypothyroidism which, by definition, is the clinical state resulting from underproduction and lack of secretion of the thyroid gland hormones.
3. **PHYSIOLOGY**<sup>(2)</sup>  
Thyroid hormones are unique in that they incorporate an inorganic element (iodine) into the organic structure of both hormones produced in the thyroid gland. These are Tetra-iodo Thyronine (known as Thyroxine or T4 and Tri-iodo-Thyronine (known as T3). The main hormone produced is T4, which acts as a “Pro-Hormone”. T3 is produced in small amounts by the thyroid gland, but is mainly produced in other tissues from chemical conversion of T4. The T4, therefore, acts as a thyroid hormone reservoir from which the body can make T3 as needed. It is this T3 which is responsible for most of the thyroid hormone actually in the body.
4. **THERAPY OF HYPO THYROIDISM**<sup>(2,3,5)</sup>  
Therapeutic replacement of thyroid hormones in deficient individuals by T4 (thyroxine) and not by the more active metabolite (T3) is usually chosen to imitate the physiological situation. The aim is to restore normal levels of thyroxine and (by negative feedback to the pituitary gland) to reduce associated high levels of thyroid stimulating hormone to normal range at the same time.

It can be recognised from the diagram<sup>(Fig 1 Ref: (2))</sup> that the entire process of producing thyroid hormones depends upon a series of interrelated balances and checks. These include inhibiting or releasing hypothalamic and pituitary hormones, while the thyroid gland itself, exerts negative and positive influences over both master (controlling) glands.

The system is also linked (via the pituitary gland and the HPA axis) to the adrenal gland the body’s main defence against stress. Disruption of this axis by overproduction or prescription of thyroid hormones can cause life-threatening adrenal gland failure<sup>(3)</sup>

One has to imagine the hypothalamus, with its input of information derived directly from the central nervous system, as the captain on the bridge of a ship relaying positive and negative messages and receiving positive and negative replies from a crew with many different functions. Lack of co-operation, discipline and control can easily sink even the most solidly built vessel. Unless we have considerable clinical experience and reliable scientific knowledge from laboratory support, we tinker with this finely adjusted system at the peril of our patients.

### 5. **WHAT IS THE FUNCTION OF THE THYROID GLAND?** <sup>(2)</sup>

Thyroid hormones increase the basal metabolic rate of the body and improve oxygen uptake and heat production. Additionally they increase the heart rate, cardiac output, alter body temperature and ventilation rates in support of these activities. Other effects on the brain and skeleton are essential to normal growth and development. A patient who is seriously deficient in thyroid hormones will usually be female, elderly, cold, living in poor conditions and mentally sluggish or comatose – easily distinguishable even from those suffering severe ME. Very mild hypothyroidism can occur at any age and in both genders with non specific symptoms as a normal physiological response to general illness. Both free T4 and T3 are marginally low: treatment for “hypothyroidism” cannot make them feel better because it cannot cure the underlying illness.

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### 6. WHAT ARE THE PRINCIPAL CAUSES OF THYROID UNDERACTIVITY? <sup>(3)</sup>

- (1) Iodine deficiency – this is no longer geographically widespread in developed countries since the introduction of food supplements (eg iodised table salt in the UK).
- (2) Autoimmune disease – this is now the commonest cause in the UK. It occurs almost exclusively in females in middle life and there is usually a family background of the same or various other kinds of autoimmunity.
- (3) Following surgery or similar tissue-destroying treatment for hyper thyroidism.

### 7. WHAT IS THE OUTLOOK FOR PATIENTS WITH THYROID DEFICIENCY? <sup>(3)</sup>

The annual incidence is very low in the UK (0.2% in women) and life expectancy is normal except for acceleration of ischaemic heart disease, which should be subject to regular screening.

### 8. IS THERE A PARTICULAR CONNECTION BETWEEN HYPOTHYROIDISM & ME?

Yes, there are 3 special circumstances in which vigilance is essential:

#### (1) SUB ACUTE THYROIDITIS<sup>(4,5)</sup>

This is a virus induced infection of the thyroid gland caused by enteroviruses, adenoviruses, or mumps virus. It is a common trigger of the onset of ME, but, because it causes pain in the thyroid gland, jaws, ears, head and neck, it is often misdiagnosed as mumps. It is a systemic illness, usually in females aged 20-40 years. Laboratory tests indicate a raised ESR (a blood sedimentation rate associated with infection) and increased production of thyroid hormones for 4-6 weeks. Iodine uptake by the gland is low because of virus damage to the specialist colloid and iodine containing follicles where thyroid hormones are stored. The illness subsides gradually during the next 6 months and may include temporary hypothyroidism accompanied by circulating antibodies. Treatment is with anti-inflammatory drugs. Anti thyroid drugs should not be given during the initial hyper thyroid period. In our clinic at Basildon Hospital (where we screened 420 patients with ME for thyroid problems<sup>(5)</sup>) 15/307 women (5%) suffered from this illness (to which I can find only one reference in modern text books!) <sup>(4)</sup>

(2) SECONDARY THYROID DEFICIENCY<sup>(4)</sup> This is much less common than primary hypothyroidism and sometimes results in shrinkage of the thyroid gland. It is associated with primary defects in hypothalamic and pituitary function (as in ME), It is already known that adrenal function is poor in ME<sup>(3)</sup> and that overload of Thyroid hormones can precipitate adrenal failure.

#### (3) INAPPROPRIATE OR FACTITIOUS (UNINTENTIONAL) OVERDOSAGE OF THYROID HORMONES<sup>(4)</sup>

This may occur when patients, who have suffered a temporary period of hypothyroidism, continue to take thyroid hormone preparations for years without supervision or when thyroid preparations are bought from Health Food shops in order to slim or to achieve athletic prowess. This can alter the normal T4 : T3 ratio and lead to hyperthyroidism as well as suppressing the production and effect of the pituitary stimulating hormone (TSH) on the thyroid. Of only 2 male patients seen at Basildon hospital with thyroid problems, one had been given thyroid supplements without confirmatory laboratory tests, by a kindly London consultant (who thought he was just depressed). Some years later, we had to stop all treatment and start again after laboratory tests – but it took some 6 years to stabilise his initially mild hypothyroidism. Unfortunately it made no difference to his ME, which required early retirement.

### SUMMARY OF LABORATORY DIAGNOSIS OF THYROID DEFICIENCY

PRIMARY HYPOTHYROIDISM:- This involves measurement of the two hormones involved in the “checks and balances” system (fig.1) T4 thyroxine itself and TSH. the pituitary hormone which drives the thyroid gland. Normally the “free T4” (circulating in the blood) is measured because this is the most accurate indicator of the thyroid deficiency. One can expect a high TSH and a low (or lowish-normal) free T4.

SECONDARY HYPOTHYROIDISM:- If the T4 only is low, other tests must be done to make sure the condition is not secondary to other glandular dysfunction (eg: hypothalamus or adrenal as in ME). All ME patients whether diagnosed or suspected must have TSH and free T4 tests as well as a 9am: serum cortisol level performed to avoid adrenal failure!

### DO THYROID SUPPLEMENTS SUPPLIED WITHOUT CONFIRMATORY LABORATORY MONITORING HELP ME PATIENTS?

- (1) Well, not in my clinical and laboratory experience of ME as it makes it more difficult to diagnose any underlying hormone imbalance and to correct it, if necessary, in the right direction<sup>(5)</sup>.
- (2) Where hormone imbalance is so slight as to be virtually incapable of measurement by routine laboratory methods and where (it is claimed by those who advocate hormone supplements without prior laboratory testing) the patient is clinically hypothyroid. I have to ask why all the additional diagnostic tests are not applied? These include haematology (for anaemia) pituitary and hypothalamic hormone levels (to indicate secondary hypothyroidism and the danger of adrenal failure) Immunology (for antibodies) ECG (for associated cardiac defects) and Histology (for lymphoid enlargement or nodular defects of the thyroid gland <sup>(3)</sup> to exclude goitre or cancer.
- (3) Finally, the results of the only randomised double blind placebo controlled trial of thyroxine treatment in patients with symptoms of hypothyroidism (but with thyroid function tests within the reference range), indicate that thyroxine did not improve cognitive function and psychological wellbeing in healthy controls and was no more effective than placebo in patients said to be clinically hypothyroid but with laboratory tests in the normal range.

### CONCLUSION – CAN A LITTLE OF WHAT YOU FANCY DO YOU GOOD?

In the present era of scientific and evidence based medicine one is obliged to count both the monetary and psychological cost of what is prescribed and/or advised for patients.

1. It would appear that the above placebo controlled trial indicates that medication without laboratory monitoring is likely to be expensive in terms of ineffective remedies and possibly of delayed or inappropriate treatment.
2. The costs of psychological disappointment and despair are incalculable.
3. A glance through the Southend Hospital Clinical Chemistry Department library is informative and sometimes terrifying in respect of the safety of alternative remedies advertised equally for slimming, body building and thyroid deficiency. Hazards noted, include interaction with other drugs or laboratory tests and contents include “multi glandular complexes” from raw Bovine meat including liver, lung, spleen, pancreas, kidney and brain. “Armour Thyroid” which is highly recommended by the Practitioners mentioned in reference to these problems<sup>(1)</sup> consists of Bovine thyroid gland which, of course, cannot be sterilised.

**CONCLUSION**

I fully understand the despair of patients and the impelling desire of kindly doctors to prescribe almost anything to relieve their anxiety and pain but, in testing our pet theories against scientific facts and common sense, I am always reminded of an unfortunate Mr Day who tested his firm conviction of right of way against a London bus – he was right, dead right, as he strode along, but he's just as dead as if he were wrong.

As we enter the 21<sup>st</sup> century, there is a greater need than ever for doctors and patients to share knowledge and experience towards a common goal of obtaining fair, speedy and effective means of preventing the current neglect and deterioration of patients with ME.

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