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Stopping thyroid medication

AT first sight it may seem that thyroid medication is not a subject of great priority in practice. Thyroxine is cheap, relatively harmless and has few side-effects; its dose and effectiveness are easily monitored clinically and biochemically. However, thyroid medication has often been started in the past for reasons which would nowadays be considered insufficient or inappropriate. Obesity, lymphoedema, depression, infertility, menstrual disorders, constipation and falling hair are among the symptoms for which a 'trial' of thyroid extract may have been undertaken. The placebo response and natural cure have been too readily taken as therapeutic response. A fear that prolonged medication may permanently suppress the thyroid/pituitary axis may act as a deterrent; the difficulty is to know if and when to stop medication. Thyroid therapy may also have been initiated at hospital after definitive treatment for thyrotoxicosis. It is now known that transient hypothyroidism may occur after surgery and radioactive iodine therapy. Sawers and colleagues (1980) recommend that if biochemical hypothyroidism should occur during the first six months after radioactive iodine, replacement therapy should be withheld for a further two months (unless the severity of symptoms demands it) to allow natural recovery of thyroid function to occur. In Hashimoto's thyroiditis, operative intervention is more likely to result in hypothyroidism, so that replacement therapy is often considered mandatory.

Clinically, thyroid disease may be suspected frequently but not so often confirmed biochemically. White and Walmsley (1978) found that the presence of only one or two symptoms rarely (only twice in 442 patients referred for thyroid function studies) indicated thyroid dysfunction. One patient out of 35 with three or four symptoms required treatment, while five or more symptoms indicated dysfunction in 18 out of 23 patients.

Hypothyroidism is a common diagnosis, with prevalence rates of up to 15 or even 20 per thousand adult women. Since treatment is life-long, the resources needed to continue treatment and monitor it assume significant proportions for the general practitioner, the laboratory, occasionally for hospital outpatients, and certainly in financial terms for the National Health Service. The patient must take tablets regularly, obtain prescriptions, attend the doctor, and have blood tests.

Stopping thyroxine in suspected hypothyroid patients is potentially dangerous because of the risk of hypothermia and the insidious onset of myxoedema; hypercholesterolaemia and the attendant cardiovascular threats have to be prevented. In excess, thyroxine can cause tachycardia, angina, nervousness, tremors, diarrhoea, insomnia, sweating, muscle cramps, muscle weakness and wasting, and weight loss, and has the risks of sympathetic overdrive in patients with cardiovascular disease.

The development of a test applicable in general practice, which will enable us to determine whether

continued medication is required, is therefore to be welcomed. Several procedures have been proposed in the past and tested experimentally. Stein and Nicoloff (1971) substituted triiodothyronine (T_3) for previous therapy for four weeks and measured protein-bound iodine and radioactive iodine uptake, and again after a further 10 days off all therapy. Removal of hormonal suppression allowed the thyroid/pituitary axis to recover function in euthyroid patients. Krugman and colleagues (1975) simply withdrew thyroid medication for 35 days, and found that serum thyroxine (T_4) and thyrotropin (TSH) levels reliably differentiated between euthyroid and hypothyroid (low T_4, high TSH) patients.

Now Rizzolo and Fischer (1982), writing from family practice in the USA, have used T_4 and TSH assays to investigate the 24 patients diagnosed as having hypothyroidism in their practice of some 6,000 enrolled patients (a prevalence of 4/1,000). Of these 24, only four had a diagnosis meeting modern criteria, that is a documented low T_4 and elevated TSH level before starting therapy. Only 10 of the remainder could be located and included in the study: four were on thyroxine after subtotal thyroidectomy, two after radioactive iodine therapy, and four had idiopathic hypothyroidism. The method of testing was simple: after basal blood tests, all selected patients were asked to discontinue thyroid hormone therapy for three weeks, when their T_4 and TSH were retested. The six patients with normal results were followed up three months later, and on retesting all were found to be euthyroid. Four with low T_4 and raised TSH were restarted on thyroxine for life. Clinical symptoms and signs did not correlate with biochemical findings.

In their similar study of 46 patients, Krugman and colleagues found that even those who became biochemically hypothyroid were not clinically hypothyroid until the fifth week. Since a low T_4 could occur up to 25 days after stopping therapy, a careful 35 days was advised between tests. At that time the hypothyroid could be reliably differentiated from the euthyroid by high TSH levels. Other workers have indicated that care is necessary with three groups of patients. In clinically euthyroid patients with Hashimoto's disease, raised TSH levels may be found with a normal T_4. This situation may also be found after radioactive iodine therapy for thyrotoxicosis. Presumably the pituitary is driving the thyroid harder to produce normal T_4 output from its remaining functioning tissue in both cases. Both instances would lead to medication being unnecessarily continued, and thus would err on the side of safety. Patients with pituitary disorders may respond variably and need special care.

Both these studies are small in number, and a larger one is obviously needed to substantiate their findings; ideally it should be done in the UK, where clinical practice may differ. Nonetheless, the implications are considerable. We may shortly have another strategy for eliminating unnecessary medication to join the slowly growing library of methods so far developed for digoxin (Manning and Brown, 1977), night sedation (Wells, 1973) and now tranquillizers (pages 745-752 in this issue of the *Journal*). The fine details, especially whether withdrawal should be for 21 or 35 days for maximum reliability, await further elucidation. At the moment, a follow-up examination at three months would be mandatory for those patients taken off treatment; because of the forgetfulness and apathy of hypothyroid patients, it is up to the general practitioner to ensure that this is done.

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Epidemiology and research in a general practice

GEORGE Ian Watson was well known throughout general practice, but particularly in the College as Honorary Director of the Epidemic Observation Unit, as a major figure on the Research Committee, and as a distinguished President from 1970 to 1972. His sudden death in 1979 came before he had finished writing a book that was eagerly awaited by his friends and colleagues, since it described his research in his own