was looked at but not recommended. Lord Justice Auld also rejected the argument that where a defence lawyer goes on a shopping expedition for a suitable expert all opinions should be disclosed to the court. This was on the basis that our current criminal trials are adversarial and the burden of proof lies with the prosecution.

The question of auditing expert medical evidence is an important one and has not yet been addressed. The courts are not the appropriate place for this. Many experts, including forensic pathologists, work in isolation. Individual cases are not reviewed before a report is prepared, although an annual audit of Home Office pathologists is undertaken in England and Wales. In forensic science laboratories, a second scientist validates each case. A second pathologist checks cancer diagnoses. No such check is routinely performed in autopsy work in England and Wales, despite the fact that the evidence may form the central core of a case that leads to life imprisonment.[6] A second pathologist checking the work of a colleague should be routine in potential criminal cases. Forensic pathology services are currently under review in England and Wales, a region with few established centres. However, in these centres regular audit can take place, and we have instituted such checks on work performed in our centre. Clinical audit is now established. Medicolegal work should be similarly audited and subject to quality assurance.

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Thyroid function tests and hypothyroidism

Measurement of serum TSH alone may not always reflect thyroid status

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It is extraordinary that more than 100 years since the first description of the treatment of hypothyroidism and the current availability of refined diagnostic tests, debate is continuing about its diagnosis and management. Symptoms of thyroid failure are often non-specific, such as weight gain, low mood, and fatigue. Some patients seeking an explanation for feeling "below par" are disappointed when thyroid function tests are normal. Unable to accept that there may be psychosocial reasons for their symptoms, a vociferous minority believe that hypothyroidism may exist with normal serum concentrations of both thyroxine (T_4) and thyroid stimulating hormone (TSH).

Their hypothesis is that a doctor cannot know whether a concentration of free T_4 or TSH within wide reference ranges is normal for that individual. Such an argument, supported by some misguided medical practitioners to justify prescribing various combinations of thyroid hormones, does not appreciate the sensitivity of the pituitary thyrotroph, which modifies the synthesis and secretion of TSH in response to minor changes in thyroid hormone concentrations within their reference ranges. For example, a reduction in free T_4 from 20 pmol/l to 15 pmol/l is likely to cause a rise in serum TSH to above the upper limit of the reference range, and a similar incremental rise in free T_4 to suppress thyrotroph secretion, with a resultant serum TSH concentration of less than 0.05 mU/l.[1] In effect, any significant deviation from the set point for serum thyroid hormone concentrations, which is remarkably constant from day to day in healthy people, will trigger changes in serum TSH.

The finding of raised or undetectable serum TSH with thyroid hormone concentrations within their reference ranges is not usually associated with symptoms, hence the basis for the unsatisfactory terms subclinical hypothyroidism and hyperthyroidism. It is better to consider them as the mildest forms of thyroid failure and thyrotoxicosis, respectively, particularly as a variable proportion of patients with subclinical hypothyroidism benefit from replacement therapy with thyroxine,[2] and endogenous subclinical hyperthyroidism is a recognised risk factor for atrial fibrillation and osteoporosis.[3]

In contrast, patients with non-specific symptoms of hypothyroidism and unequivocally normal T_4 and TSH concentrations do not benefit from treatment with thyroxine.[4] In the paper by Meier et al in this issue we are reminded that in severe primary hypothyroidism with serum TSH greater than 20 mU/l the correlation between TSH concentrations and other end organ responses to a low serum T_4 is poor (p 311).[5] This must not be interpreted as thyrotroph insensitivity but exhaustion after prolonged stimulation[6]; an analogous apparent loss of sensitivity occurs after treatment of hyperthyroidism as the suppressed thyrotroph requires several weeks to recover its responsiveness to falling serum thyroid hormone concentrations.

It is the exquisite sensitivity of the thyrotroph that led to the use of serum TSH measurements as a first line test of thyroid function; a normal TSH indicated euthyroidism whereas only a raised or suppressed concentration prompted the measurement of T_3 or T_4 or both, to assess the degree of hypothyroidism or hyperthyroidism.[7] This approach has been strongly championed by some laboratories to contain costs, but they may provide misleading information. For example, a normal TSH may be recorded in patients with profound hypothyroidism secondary to pituitary or hypothalamic disease,[8] a remediable condition that

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may have serious consequences if not recognised; and rarely hyperthyroidism may be associated with a normal TSH due to pituitary tumour, thyroid hormone resistance, or assay interference.[9]

There is also the difficulty of interpreting a serum concentration of TSH in isolation. A concentration at or near the upper limit of the reference range, particularly if associated with a normal free T_4, may indicate underlying autoimmune thyroid disease. A consensus exists for early treatment of such patients with thyroxine if anti-thyroid peroxidase antibodies are present in the serum, not because any immediate benefit may be expected but because the risk of overt thyroid failure in future years is high,[10] and it makes sense to anticipate morbidity rather than risk loss to follow up.

The other difficulty in interpreting serum TSH concentrations is to decide what value should be aimed for in patients taking thyroxine replacement. It is not sufficient to satisfy the recommendations of the American Thyroid Association[11] by simply restoring both serum T_4 and TSH concentrations to normal, as in our experience most patients feel well only with a dose resulting in a high normal free T_4 and low normal TSH concentration, and those patients with continuing symptoms despite "adequate" doses of thyroxine[12] may be slightly under-replaced. Some patients achieve a sense of wellbeing only if free T_4 is slightly elevated and TSH low or undetectable.[13] The evidence that this exogenous form of subclinical hyperthyroidism is harmful is lacking in comparison to the endogenous variety associated with nodular goitre,[3] and it is not unreasonable to allow these patients to take a higher dose if T_3 is unequivocally normal.

Although the potential improvement in the wellbeing of patients with hypothyroidism while taking a combination of T_3 and T_4 is of great interest,[14] the greatest advantage will be the security of a normal TSH while taking physiological replacement, removing the anxiety about whether a little too much thyroxine alone is harmful. Of course, we are perhaps naive in thinking that patients with autoimmune thyroid disease who continue to complain of non-specific symptoms despite restoration to normal of TSH and T_4 concentrations can be improved by tinkering with the dose and form of thyroid hormone used for treatment. It is just possible that these symptoms arise from the chronic inflammatory basis of the underlying thyroid disease, but that story is largely unwritten.

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The prevention and treatment of jet lag

It's been ignored, but much can be done

The jet lag syndrome emerged with the rise of long haul air travel. The symptoms include disturbed sleep, increased fatigue, loss of concentration, and increased irritability during the new daytime, and yet difficulties in initiating and maintaining sleep at night. Long flights are also often tiring and uncomfortable (travel fatigue), and the dry cabin air contributes to dehydration. These effects can be distinguished from those of jet lag by comparing flights across time zones, for example from Europe to Asia, with flights of similar length along the same meridian, say to southern Africa, which cause travel fatigue but no jet lag. It is worth trying to minimise travel fatigue in its own right, and simple practical advice includes (see box).[1]

Jet lag is due to the desynchronisation between various body rhythms and environmental rhythms. The rhythm most noticeably affected is the cycle of sleep and activity, with the associated changes in physical and mental functioning. All the rhythms are regulated by internal and external factors that interact. For example, the "body clock" controls secretion of melatonin by the pineal gland, an important internal factor, and light turns it off. With a rapid change of time zone, it takes several days for the external factors to shift the phase of the body clock from the time zone

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