Interfering antibodies – artefactual elevation in TSH.
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Case History:
We describe a 83 year old lady who presented in 1999 with fatigue. She had the typical biochemistry of primary hypothyroidism, with a raised TSH and low fT4. She was treated with 125mcg thyroxine, and improved clinically. Of note from her extensive medical history, she had rheumatoid factor positive rheumatoid arthritis, and was AMA antibody positive.

In 2006, her TSH was noted be dramatically raised with her fT4 was at the upper limit of the reference range. These abnormalities persisted despite endocrinologist advice to reduce her levothyroxine dose, and therefore in 2007 she was referred to Barnet Hospital for further review. Reducing her dose of thyroxine to 50mcg produced little biochemical change, whilst the patient did experience symptoms of hypothyroidism. Furthermore, although subsequent raising of her levothyroxine dose to 75mcg reduced the TSH level, it remained three times above the upper limit of normal, and was accompanied by the symptoms of hyperthyroidism.

Investigations and method:
Three potential causes for the abnormally high TSH were postulated and investigated. She was felt to have a low clinical probability for a TSH-secreting pituitary tumour, and this was supported by a negative MRI pituitary, negative test for pituitary hormone α-subunit, and a degree of TSH suppression with increasing thyroxine doses. TSH-resistance was excluded via a negative family history and normal TFTs in her daughter. Samples were therefore sent to the Clinical Biochemistry Laboratory in Addenbrooke’s Hospital, Cambridge for analysis. Use of Centaur assay showed a raised TSH, whilst DELFIA assays, plus PEG precipitation, reduced the TSH level, suggesting antibody interference leading to the high TSH levels. There was no evidence of antibody interference on the fT4 assay using the DELFIA platform, and it was felt that the high fT4 was a response to maintain clinical euthyroidism. Gel filtration chromatography showed a high molecular weight TSH also suggestive of antibody interference. Her rheumatoid factor was postulated as the interfering antibody, but her GFC pattern was atypical for this. Before further serological testing could be undertaken to investigate the interfering antibody, the patient died of heart failure due to an unrelated cardiomyopathy in 2009.

Conclusions and points for discussion:
Antibody interference is well documented in hormone assays. In thyroid function testing, three main groups of antibodies cause interference: rheumatoid factor, thyroid auto-antibodies, and heterophile antibodies. Whilst the incidence of these antibodies causing abnormal thyroid function results is rare, the effects can be significant, with patients being erroneously diagnosed and treated. Therefore, if the clinical presentation is at odds with the laboratory results, or thyroid function tests are discordant, it is worth considering assay interference as a potential cause.