letters to the editor

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Severe hypercalcaemia can be due to benign disease and give reversible neurological signs

Editor – Crowley *et al* have outlined a sensible approach to a patient with hypercalcaemia (*Clin Med* June 2013 pp 287–90). In addition to the symptoms and signs listed we have also encountered and reported neurological symptoms of imbalance and signs of nystagmus, dysdiachokinesis and ataxia due to biopsy-proven sarcoidosis and a serum-corrected calcium of 4.4 mmol/l (and no evidence of structural lesions on neuro-imaging). All symptoms were resolved with steroid treatment.[1] We also highlight this to illustrate that benign granulomatous disease can sometimes be the cause of very severe hypercalcaemia (above 4 mmol/l), although malignancy is the usual expected cause at this level.

Reference

1 Walters S, Bhatt N, Medford AR. Reversible cerebellar signs due to sarcoid-related severe hypercalcaemia. *QJM* 2013;106:667–9.

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Laboratory samples deemed 'unsuitable for analysis' can be diagnostically useful

Editor – Sen Gupta *et al*'s 'Lesson of the month' (*Clin Med* June 2013 pp 309–11) is a useful reminder of the importance of working together for the benefit of patients, both for those who request and receive the results of laboratory tests and those who analyse and report the results. The increasing tendency for the centralising of laboratories does not facilitate this process. Nonetheless, I would hope that the first occasion on which a sample from a particular patient demonstrated gross hyperlipidaemia or abnormal sample clotting would lead to a telephone call from the laboratory to the requesting practitioner to discuss the findings and the most appropriate action to take.

There are some matters of detail in the examples of analyser artefact that Sen Gupta *et al* present that are worth commenting on.

The 'white cell buffy layer' in the sample tubes shown in Fig 1 is, in fact, a plug of gel. These are serum separator tubes (SSTs).[1] SSTs contain a gel with a mass density between that of serum and blood clot. Once the sample has clotted the tube can be centrifuged with the gel plug rising to form an impermeable barrier between the serum and clot. While this is not suitable for collecting samples for all analyses, SSTs greatly simplify sampling handling in the laboratory and reduce the chance of errors.

Creatinine assays based on the Jaffé reaction are increasingly being replaced by enzymatic assays, which are less subject to interferences which can produce elevations in the creatinine concentration. Alcoholic ketoacidosis (mentioned in Table 1) is not a situation which produces a falsely elevated Jaffé creatinine. The compound that produces this interference in diabetic ketoacidosis is acetoacetate. The ketone body elevated in alcoholic ketoacidosis is beta-hydroxybutyrate, which does not interfere with the Jaffé reaction.[2] Nor does it produce a blue colour with nitroprusside-based test strips for ketones. Laboratory confirmation of alcoholic ketoacidosis requires specific measurement of beta-hydroxybutyrate.

The pseudo hyperlipidaemia associated with a grossly lipaemic plasma sample is found because the proportion of water in the plasma is reduced by the high concentration of lipids. Sodium ions are found in the water fraction of plasma, not in the hydrophobic lipid layer. As Ball points outs in his CME endocrinology review (*Clin Med* June 2013 pp 291–5), the instruments routinely used to measure electrolytes use a dilution step and algorithms assuming 'a normal distribution of the aqueous and non-aqueous phases of venous blood'. An instrument based on direct reading ion selective electrode (ISE) technology, where the sample is not diluted before measurement, is far less susceptible to such errors.[3] The 'Ilyte' referred to by Sen Gupta *et al* in Case 1 is such an instrument.

In summary, clinicians should have a low threshold for talking to their clinical chemists, and clinical chemists should have a lower threshold for talking to the clinicians through whom they serve their patients.

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References

1 Cuhadar S, Atay A, Koseoglu M *et al.* Stability studies of common biochemical analytes in serum separator tubes with or without gel barrier subject to various storage conditions. *Biochem Med (Zagreb)* 2012;22:202–14.
2 Kemperman FA, Weber JA, Gorgels J *et al.* The influence of ketoacids on various routine plasma creatinine assays during a clinical episode of diabetic ketoacidosis. *J Intern Med* 2000;248:511–7.
3 Baron DN, Forrest ARW, Shenkin A. Letter to the editor: Dangerous pseudohyponatraemia. *Lancet* 1980;316:1256.

Is research declining among gastroenterology trainees in the UK

Editor – Clark *et al* comment on the problems of trainees carrying out research (*Clin Med* June 2013 pp 323). As chair of a research ethics committee (REC), I wonder if the authors really needed REC approval for their project.

Using the National Research Ethics Service (NRES) *Defining Research* leaflet,[1] it would appear that their study might well come