letters to the editor

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Normocalcaemic tetany

Editor – We write to highlight some important flaws in the inferences and conclusions of V Seghal and colleagues in their recent case report (*Clin Med* December 2011 pp 594–5).

The authors' comments regarding several aspects of acid–base and lactate interpretation, and their implication of Hartmann's solution as the causative agent for the alkalosis, appear misguided. They seem to have failed to recognise important physical and pharmacological principles; namely, the implications of volumes of distribution and concentrations. For example, if a total body transfusion using Hartmann's solution took place, the total lactate (and therefore bicarbonate) concentration could not exceed 29 mmol/l (ie that of the administered fluid). How then can they explain their patient's serum bicarbonate of 39.5 mmol/l? The authors have also failed to recognise that the lactate in Hartmann's solution is administered in 'balance' with other strong anions (chloride) and cations (sodium, potassium and calcium). It is inappropriate to focus on the effects on pH of one of the fluid's constituents and not the others; these do not (and cannot) exist in isolation due to the laws of mass action and electroneutrality.[1] These laws dictate that lactate would not be metabolised into bicarbonate if this resulted in profound alkalosis. Such a situation would result in alterations in the dissociation of lactate in the blood and the subsequent uptake by the liver.[2] It would also have effects on the ionisation and distribution of other strong ions. Higher volumes of Hartmann's solution are regularly administered in intensive care/resuscitation environments and in patients with acute renal failure. Indeed lactate- or bicarbonate-buffered dialysate remain the fluids of choice for renal replacement therapy in many intensive care units where it is rare to observe significant alterations in serum lactate or alkalaemic states as a result.

Even if were to ignore the above, the contribution of 116 mmol of lactate (4 litres of Hartmann's solution) to the circulation of any adult patient will be minimal given the normal lactate metabolism of 1 mmol/kg/h. While the kidney plays some role in this metabolism, the liver plays the major role, with the heart making some contribution.

Importantly, the approach used by the authors to interpret the acid–base disturbances (namely, their focus on bicarbonate and hydrogen ions alone) has been shown to 'miss' important components of complex mixed disturbances.[3] Applying either the corrected anion gap (albumin-corrected, albumin-phosphate-corrected, or albumin-phosphate-lactate-corrected) or Stewart model (using the physico-chemical approach) would provide more robust analysis and interpretations.[3,4] For example, hypoalbuminaemia results in alkalosis due to the weak acid effects of albumins; thus the failure to report both the patient's lactate and albumin concentrations make any detailed assessment of their acid-base status impossible.

The authors also demonstrate a common misunderstanding of the complex metabolic processes through which lactate is exposed and its interesting (and contentious) effects on acid–base haemostasis.[2] At physiological pH, the pK of lactate dictates that it exists predominantly in its ionic (acidic) form.[5] Traditional approaches support this through the Henderson–Hasselbalch equation; the Stewart approach supports this through lactate's impact as a strong anion. Either way, the immediate impact of the molecule's presence in blood at physiological pH is acidifying (versus the weak buffering effect in solutions of lower pH). The subsequent effects on pH depend heavily on its metabolism. The authors imply that it is the conversion to bicarbonate that results in an alkalinising effect; in fact there are many possible metabolic fates for lactate (including entry via pyruvate into the tricarboxylic acid cycle, conversion to glucose, transamination, etc) all of which have an alkalinising effect due to the removal of the molecule from the blood in its ionised (strong anion) form (ie removal of an acid rather than generation of an alkali). Again, such an alkalinising effect cannot be considered in isolation of the other ionic and mass action effects.

We believe that the patient they describe demonstrates typical signs and symptoms of alkalosis following severe vomiting (and hyperventilation) and that their report highlights common errors in complex acid-base and lactate interpretation.

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In response

Editor – We were interested to read the comments of Drs Kale and Handy and are pleased that our case report has generated interest and correspondence. We agree that hypoalbuminaemia is a potential cause of a metabolic alkalosis and, in retrospect, we should have included this information in the report. At 40 g/l it was clearly not contributing to our patient's acid–base derangement.

While we acknowledge the interest of the correspondents, we feel they have misconstrued the message of our report. We did not suggest that administration of Hartmann's solution was the sole cause of our patient's severe alkalosis; the patient had symptoms of ionized hypocalcaemia prior to its administration. As both the abstract and the 'key learning points' box clearly state, we were using the case to illustrate various aspects of the diagnosis and treatment of normalcaemic tetany; one of which is that the administration of Hartmann's solution in this situation of volume contraction, alkalosis and paradoxical aciduria due to prevailing secondary hyperaldosteronism, was not appropriate. There seems to be little in the content of their argument that contradicts our conclusions.

In preparing our manuscript, we did not consider that *Clinical Medicine* was the correct forum for an in-depth metabolic discussion, but we would remind the correspondents that the hepatic metabolism of lactate consumes protons and generates bicarbonate. In a starving, volume-contracted patient with reduced renal perfusion, this will be the metabolic fate of the vast majority of infused lactate. As Hartmann himself demonstrated, 1 l of 1/6 molar sodium lactate is potentially equivalent to 290 ml of 5% sodium bicarbonate; non-metabolically orientated readers of the journal may find this easier to comprehend. Kale and Handy's reference to 'total body Hartmann's transfusion' is misleading and detracts from the message that administration of an alkalinizing fluid to an already symptomatically alkalotic patient is potentially hazardous.

Finally, it is well recognised that potassium deficiency and alkalosis cannot be fully corrected unless there is satisfactory replenishment of chloride. The relevant chloride contents of Hartmann's solution and normal saline (111 mEq/l and 154 mEq/l respectively) provide a further reason (not included in our original report) that the latter would have been the most appropriate resuscitation fluid in this clinical scenario.

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Cavitating pulmonary tuberculosis: a global challenge.

Editor – We were concerned that a new treatment for tuberculosis (TB) was being advocated without the benefit of a randomised controlled trial (W Saeed, *Clin Med* February 2012 pp 40–1). The authors argue that cavitary pulmonary TB relapses following therapy in 21–25% of cases and that additional drugs (levofloxacin and amikacin) are required to prevent this. However, in a treatment trial of sputum smear-positive TB (a *sine qua non* for cavitary disease) with relatives supervising therapy in the follow-up phase, a standard six-month regimen with an initial phase of four drugs resulted in negative sputum cultures at 30 months in 94%.[1] Furthermore, while levofloxacin has few adverse effects, irreversible hearing loss is a common finding in those treated with amikacin.[2] Research itself is known to improve patient outcomes. Improved care rather than the addition of two further drugs to the standard treatment regimen for TB may have been responsible for the observed 'complete bacteriological cure at three months and radiological cure at the end of six months' that are reported in an unspecified number of patients from an, as yet unpublished, study.

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Influenza-related pneumonia

Editor – In regard to the CME Respiratory Medicine article by Almond *et al* on influenza-related pneumonia (*Clin Med* February 2012 pp 67–70), I would like to correct a point on when to administer antiviral therapy.

It is stated in the article that based on Department of Health recommendations[1] uncomplicated influenza infection should be treated with prompt commencement of antiviral therapy. However, more recent guidelines from the Health Protection Agency[2] state that generally in an uncomplicated presentation of influenza, treatment, other than symptomatic, is not required.

While it is correct that in the hospital setting all patients with influenza should be given antiviral drugs such as oseltamivir, in the community those patients with an uncomplicated presentation should only receive antiviral treatment if they have underlying health issues such as chronic heart, liver, pulmonary or renal disease.

Oseltamivir does have potential significant side effects such as nausea, vomiting and abdominal pain, and even reports of more serious adverse effects such as