letters to the editor

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Vetting requests for molecular diagnostics for CNS infections based on cerebrospinal fluid measurements undermines the quality of patient care

Editor – We read with interest the study by Mamoojee and Chadwick on the appropriateness of polymerase chain reaction (PCR) requests on cerebrospinal fluid (CSF) in suspected central nervous system (CNS) infections (*Clin Med* December 2011 pp 554–57). We are, however, concerned about their recommendation that CSF parameters may be used to screen requests for PCR assays in adults and that this will have 'little detriment to patient care and considerable cost savings'.

The authors used CSF abnormality as a major criterion for judging the appropriateness of viral and bacterial PCR requests. When this was combined with clinical criteria in a subset of their cohort, they showed that CNS infections were unlikely in 45 out of 98 acute medicine patients. This observation raises the possibility of misclassification bias which may have reduced the diagnostic yield.

Furthermore, corresponding data on paediatric and neurology patients were not presented (n=249).

In keeping with previously published data,[1,2] the authors found that 50% of children with enteroviral CNS infection detected by PCR had normal CSF. Current evidence suggests that acute infectious and non-infectious CNS disorders cannot be distinguished accurately using clinical case definitions or CSF parameters either solely or in combination.[3] Even in the devastating yet potentially treatable herpes simplex encephalitis (HSE), there was no CSF pleocytosis in 11% of cases in a recent UK study,[3] a finding consistent with other studies showing normal CSF cell count in 10–20% of early HSE.[4]

Furthermore, rigorous first-line testing using molecular and serological methods has been shown to reduce the proportion of cases of acute encephalitis with unknown aetiology from the previously reported rate of 60% to 45%, with multidisciplinary case reviews contributing an additional 8% reducion.[5,6]

We believe that the sole use of CSF parameters as a trigger for PCR requests potentially compromises patient safety and represents false economy. Requests for viral, bacterial, or fungal PCRs on CSF should be informed by clinical, neuro-radiological, and neuro-physiological findings together and not just by cellular or biochemical CSF abnormality. With rapid turnaround of results to clinicians (usually 48 hours), adopting CSF PCR testing can help establish early definitive diagnosis of viral CNS infections, reduce the length of hospital stay and its associated cost, and rationalise the use of antimicrobial therapy.[7–9] The current cost of a PCR assay can never be compared to the high costs arising from litigation and life-long care for sufferers of missed diagnoses of CNS infections such as HSE.

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In response

We are grateful for Drs Babiker and Mutton pointing out the pitfall of using CSF parameters solely to determine whether CSF PCRs are requested in patients with suspected CNS infections. They rightly point to studies illustrating the limitations of using such parameters, with or without clinical information, in diagnosing CNS infections. We agree that there is no basis for suggesting the *sole* use of CSF parameters in deciding whether CSF PCRs are indicated, and our article emphasised that further studies were required to assess the sensitivity of using CSF parameters in conjunction with clinical information in identifying patients without CNS infections, in order to validate whether this approach might avoid

unnecessary CSF assays. We also believe that until results of such studies are available it would be prudent for clinicians to continue to request viral PCR assays on adults as well as children with suspected CNS infections. Nonetheless a proportion of adults present predominantly with headaches (without other features of encephalitis or CNS infections) and it may be appropriate in some cases not to order CSF PCRs if CSF parameters are normal and symptoms improve or resolve rapidly. One of the benefits of a retrospective study such as ours, albeit a relatively small study, was being able to determine eventual outcomes and also assess readmissions of patients. Although readmissions were not discussed in our manuscript, it was evident that there were no patients readmitted with features of CNS infections or suffering significant morbidity due to missed CNS infections following negative PCR results, and this gives some credence to a potential strategy of deferring or avoiding PCR tests in a subset of patients with normal CSF.

We would take issue with the assertion that because 'in herpes simplex encephalitis there was no CSF pleocytosis in 11% of cases in a recent UK study',[1] this always mandates testing CSF samples for HSV PCR where there are normal CSF parameters. The study they cite had a case definition of altered consciousness, irritability or behavioural change, and these features probably occur in a minority of adults admitted acutely who undergo lumbar punctures.

Reference

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Lessons of the month

Editor – Rapid availability of blood and serum results helps clinicians to make immediate bedside decisions, but their interpretation continues to pose challenges in clinical practice as witnessed in the two interesting cases of high educational value in the 'Lesson of the month' published in the December issue (*Clin Med* December 2011). For nephrologists, absolute numbers of blood and fluid parameters along with their trends are paramount. We would like to share additional learning points out of these two cases.

In the first case, severe hypomagnesaemia (<0.1 mmol/l) caused seizures. If this result is viewed as a reflection of the fact that there is only 1% of the total body magnesium in the extracellular space, this would have provided a fuller picture of absolute magnesium deficiency, as the renal and gut mechanisms would have failed to correct extracellular magnesium in the long term. This information could have translated into maximal initial correction of serum magnesium using 2 mmol/kg IV dose, a repeat serum magnesium check in a week or two by the GP and then timely oral magnesium supplementation if required. A normal PTH may still be abnormal as PTH resistance is common in magnesium deficiency. A normal 24 hour urinary magnesium in someone during severe magnesium deficiency may not add further valuable information.

Similarly, if the second case of normal corrected calcium and tetany was viewed in terms of the compartments of total serum calcium, this, applied to someone acutely vomiting and losing acid, would help identify the pathology early and allow appropriate management using the right fluid initiated without adding further insult to the injury.

These broad principles are not limited to these cases, but can be applied to most biochemical test results if interpreted as reflections of the concentration in the accessible 10% extracellular fraction of the total body water. Recognition of this volume model of body composition is increasingly applied in correction of electrolytes, minerals and fluid homeostasis due to major chronic conditions like heart failure, chronic kidney disease and chronic liver disease.

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Let's hear it for the medical registrar

Editor – In the December 2011 issue of *Clinical Medicine*, you mentioned in your own editorial, 'Lets hear it for the medical registrar' (*Clin Med* December 2011 pp515–516), the issue of involvement in the acute take and the role of the generalist in hospital general internal medicine. In the same issue, Goddard and colleagues reported a national survey of medical registrars' experience and attitudes to their future careers – in particular, the reluctance of nearly half of them to continue active involvement in the acute take on becoming consultants.[1] Here too, the issue of generalism versus specialism was raised. I believe that this needs further reflection and exploration before we rush headlong to the creation of 'hospitalists' (in other words, re-creation of general physicians), for a number of reasons.

1. We already have what is probably the most extensive training in general internal medicine of any health system: two years at CMT level, rotating through several specialties, followed by five or six years higher specialty training, with GiM dual accreditation throughout for many CCST holders. Are we proposing even longer or more rigorous training in General Internal Medicine? Will 'hospitalists' be any better trained in GiM than current dually accredited consultants?
2. With the expansion of acute medicine as a specialty, as well as a growing focus on medical admission units with very intensive 'front door' involvement of consultants, is there a large cohort of patients remaining in hospital beyond 48 hours who don't fit fairly comfortably into one 'organ specialty' or other, as defined by their principal presenting