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CORRESPONDENCE

Urgent cerebrospinal fluid analysis: is it necessary?

Sir,

Rapid diagnosis and treatment is imperative to improve morbidity and mortality in bacterial meningitis. In general, history and physical examination alone lack sufficient sensitivity and specificity to confirm or exclude the diagnosis. Hence, patients are often hospitalised and treated empirically until additional laboratory results are available. Cerebrospinal fluid (CSF) biochemistry and microscopy improve the diagnostic yield to a certain extent. Predictive models which incorporate a combination of history, examination findings and laboratory results are available to improve the diagnostic accuracy of bacterial meningitis.[1–3] Although these predictive models have good positive and negative predictive values, no test reliably excludes bacterial meningitis. Thus, physicians rely on additional tests such as culture and molecular testing, which increasingly can be performed in a real time manner, before making a definitive diagnosis. Pending these definitive results, most clinicians would continue empiric therapy regardless of initial CSF biochemistry and microscopy results.

Data regarding the role or need for urgent CSF cell count and its influence on patient management in the current molecular era are lacking. Urgent processing of samples continues to be expected from diagnostic laboratories despite considerable inter and intrapersonal variability in CSF cell count results, changing cell count dynamics in early compared to later samples (especially in viral meningitis) and the influence of host immune responses on counts such that normal cell counts fail to rule out meningitis.[4] Current automated systems are unable to perform counts accurately,[5] necessitating ongoing manual processing. In laboratories that do not operate 24 hours / 7 days, this leads to scientific staff call-backs after-hours resulting in disruption to the routine work flows and additional laboratory costs.

Following ethics approval, we conducted a retrospective study at the Royal Prince Alfred Hospital (RPAH), Sydney, to determine whether these CSF call-backs after-hours influenced clinical management.

All CSF call-backs (i.e., between 10pm and 6am) for an 8 month period between January and August 2013 were identified through the laboratory information system, as were CSF parameters [gram stain, white cell counts, subsequent culture and polymerase chain reaction (PCR) results]. After excluding traumatic taps, a leukocyte count of $\leq 5 \times 10^6$/L was regarded as normal, except in patients under the age of one month in whom $\leq 20 \times 10^6$/L was considered normal. Demographic data, location [e.g. Emergency Department (ED) versus ward] of the patient at time of lumbar puncture (LP), indication for LP and final discharge diagnosis were retrieved from the medical records. Similarly, management decisions were retrieved and defined as (1) definite when direct documentation linked CSF cell count to alteration in prescribed antimicrobials, patient discharge or forming an alternative diagnosis; and (2) probable when the aforementioned actions occurred in the absence of a direct documented link.

In total, 71 CSF call-backs occurred during the 8 month study period, equating to at least two call-backs weekly. Of these, 68 (96%) LPs were performed in ED. Three (4%) were performed on the ward following two direct ward admissions and one request from neurosurgical intensive care. Patients' ages ranged from 0 to 79 years with a male predominance (62%). Seventeen paediatric (24%) after-hours LPs were performed, of which the majority ($n = 15$) were under the age of one.

Overall, normal CSF parameters were observed in 61 (86%) patients. Two of these patients (2/61; 3%) had a confirmed microbiological diagnosis based on a positive PCR result for enterovirus. In the remaining LPs (10/71; 14%), the CSF leukocyte counts ranged from 12 to 5508×10^6/L. Three of these patients (3/10; 30%) had an established microbiological diagnosis; positive enterovirus and herpes simplex virus PCR one each, and a positive *Streptococcus pneumoniae* culture ($n = 1$).

A provisional diagnosis of a central nervous system (CNS) infection requiring a LP was made in only 72% of cases with overall management altered based on the CSF cell count in 36 (51%) patients (Table 1). In most cases, CSF cell count assisted in ruling out a CNS infection ($n = 34$) with 13 of the 34 patients subsequently discharged directly from ED. Alternatively, an abnormal cell count was used to rule in CNS infection in two patients.

In contrast, 35 (49%) patients did not have an alteration to management based on CSF leukocyte count. A total of 26 patients were continued on empiric treatment until further results became available (i.e., negative CSF culture and PCR). This included 14 paediatric patients who had LPs performed as part of 'septic work-up'. In addition, in patients with a provisional diagnosis of subarachnoid haemorrhage (SAH; $n = 10$), further testing was based on the presence of CSF xanthochromia rather than red cell count in 80% of cases. One patient from the neurosurgical intensive care unit had no indication for cell count as the LP was performed to improve CNS pressure only.

Call-backs of microbiology laboratory scientists were helpful in the majority (51%) of patients. In patients with a high index of suspicion for a CNS infection (based on the documented LP indication), a normal CSF cell count facilitated an alternate diagnosis, despite two microbiologically confirmed infections having normal CSF parameters. Similarly, in patients with a low pre-test probability for meningitis, although the need for LP could be questioned, a normal CSF cell count facilitated early patient discharge and prevented unnecessary antibiotic usage.

On the other hand, 37% of patients were admitted for empiric treatment regardless of the initial LP indication or microbiological parameters. No clinical or microbiological features were identified which would allow us to distinguish these patients from those whose therapy was altered.

In contrast, when the provisional diagnosis was SAH, xanthochromia alone determined patient management as microbiological testing including red cell clearance is unable to reliably distinguish between SAH and traumatic tap.[6,7] Thus if the laboratory could ensure accurate ordering, call-backs could be averted for this indication. Similarly, LPs as part of 'routine septic work-up' in paediatrics could be processed during normal hours as all patients received antibiotics for 24 to 48 hours irrespective of initial CSF cell count. However, given the sensitive nature of medical management of children, a

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Table 1 Number of patients in whom the management decision was altered based on initial cerebrospinal fluid cell count

	Normal CSF microbiological parameters	CSF pleocytosis (WCC 12–5508 × 10^6/L)	Total
Management decision altered by initial CSF parameters			
Yes	33	3	36[*] (51%)
No	28	7	35[†] (49%)
Total	61[‡]	10[§]	71

[*] Appropriate treatment commenced based on CSF results ($n = 2$), cell count used to rule out CNS infection ($n = 21$) and discharged from emergency department based on CSF results ($n = 13$).
[†] Treatment continued until PCR/culture results were available ($n = 26$), only xanthochromia was necessary ($n = 8$), and no real indication for CSF ($n = 1$).
[‡] Confirmed microbiological diagnosis ($n = 2$; both positive for enterovirus PCR).
[§] Confirmed microbiological diagnosis ($n = 3$; one case each positive for enterovirus PCR, herpes simplex virus PCR and *S. pneumoniae* culture).
CNS, central nervous system; CSF, cerebrospinal fluid; PCR, polymerase chain reaction; WCC, white cell count.

delay in processing the CSF until working hours is unlikely to be widely acceptable, especially as some concern exists about degradation of CSF leukocyte counts with delayed processing.[8]

Given the heterogeneity of indications for LP and clinical management decisions, we were unable to construct a call-back algorithm for triaging CSF requests. However, scope for improvement is possible with education of need for LP and appropriate testing requests likely to result in a reduced number of call-backs.

There are several limitations of our study which include the retrospective nature of data collection, being a single centre study, and having a small sample size, with an even smaller proportion (15%) of patients having a CNS infection. Whether these results hold true for other infections such as tuberculous, fungal or bacterial meningitis is unknown. There is also a valid concern that CSF cell parameters degrade over time.[8,9] However, methods including the addition of serum containing medium can be used to preserve the cells from degradation,[10–12] thus allowing a delay in CSF processing and eliminating the need for call-backs. It is likely in the future that the nature of testing will evolve such that definitive testing is performed in a real-time fashion and management decisions are based on microbiological results as opposed to an interpreted surrogate, namely CSF cell count. This will, as with CSF cell count, require optimisation of ordering and diagnostic work flows.

Despite common belief, this study highlights that in a large number of patients (49%), urgent CSF results did not influence initial clinical decision making. However, in this study, we were unable to determine the factors that differentiated when CSF cell count altered patient management. As a result, we continue to offer this service after-hours at RPAH. Further multicentre prospective studies (including paediatric-only centres) are necessary in order to determine the true utility of initial CSF microbiological parameters in this molecular era.

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Multidrug resistant, *bla*$_{VEB}$ positive *Pseudomonas aeruginosa* causing high mortality among haematology patients

Sir,
We recently described an outbreak of multidrug resistant *Pseudomonas aeruginosa* (MDR-PAE) involving three patients in a haematology unit in 2009 that was associated with contaminated sink drains.[1] In retrospect, *P. aeruginosa* with the same antimicrobial susceptibility profile (resistant to