Journal of Hospital Infection 102 (2019) 351–357

Available online at www.sciencedirect.com

Journal of Hospital Infection

journal homepage: www.elsevier.com/locate/jhin

Letters to the Editor

Oxygenating the argument for consistent performance of anaerobic blood cultures and blood volumes collected

Sir,

We read with interest two articles in the February issue describing high levels of failure of empirical antibiotic therapy due to multidrug-resistant Gram-negative bacilli [1,2]. There was an association with higher mortality rates although underlying comorbidities also needed to be considered. Whilst rapidly screening patients for carbapenemase-producing organisms may help to reduce/correct empirical antibiotic failure in the sepsis, there is a danger of overprescription of the few remaining active agents in the absence of identifying the definitive pathogen(s).

Significant positive blood culture results are increasingly important in this era of antibiotic resistance. The concept of diagnostic stewardship is straightforward: utilizing timely laboratory test results to best manage antimicrobial prescribing for optimal patient benefit. The blood culture pathway is central to this objective. Greatest benefit from diagnostic stewardship will be achieved when microbiological confirmation of blood stream infection (BSI) is maximized, leading to appropriate targeted antimicrobial therapy.

The pre-analytical phase is critical to many pathways but so often attracts little attention. Patient selection, correct sample collection and prompt placement on the blood culture analyser are important variables.

Considerable energies have been expended in debate regarding the necessity (or otherwise) of an anaerobic bottle based mainly on the relatively uncommon incidence of anaerobe pathogens, their association with mostly identifiable clinical scenarios, and availability of antimicrobial agents with predictable efficacy [3]. In parallel, despite existing guidance on blood culture collection in consensus documents (i.e. SMI B37 recommends two blood culture sets/adult in order to culture at least 30 mL of blood), such advice is frequently not adhered to. In the UK, therefore, routine practice can vary from collection of a single aerobic bottle in adults, a single set (aerobic plus anaerobic bottle), to multiple sets.

Our disquiet regarding potential delay in pathogen identification led us to perform a retrospective analysis using data from two hospitals utilizing the same media – an aerobic bottle containing antibiotic inactivating resins and a lytic anaerobic bottle (improves detection by lysing white/red cells and releasing intracellular pathogens). Analysis included records relating to 500 (hospital A) and 555 (hospital B) consecutive positive blood cultures identified by interrogating the Laboratory Information Management System (LIMS).

Excluding likely contaminants, 474 significant positive blood cultures (paired aerobic/anaerobic cultures) were eligible for analysis. Two-hundred and fifty-eight sets proved positive in both bottles, thereby allowing comparison of time to positivity. The results were significant. In 42 instances there was no difference noted, while in 55 cases the aerobic culture proved faster (*Streptococcus pneumoniae* 27 instances – combination of an oxygen detoxifying enzyme permitting unrestricted fermentation and less buffering in aerobic bottle means this bottle either signals first or at same time as anaerobic – the latter never signalled first). However, in 161 cases, anaerobic cultures were positive first. More specifically, although the time differential was modest, 60 min in 40% of cases, in 19% of cultures this extended to $\geq$6 h with 10% being $\geq$12 h. Most UK laboratories do not provide a 24/7 routine blood culture service, instead implementing a cut-off at varying times of the day for examination of the final positive blood culture. In that context, small delays can make a difference, whereby a delay of just 1 h can impede availability of results for 24 h.

We further assessed the impact of volume of blood collected on tests, broadening our comparison of records to those from four hospitals. In 1975, J.A. Washington showed that the "the higher the volume of blood cultured, the higher the yield" [4]. With the introduction of continuous monitoring blood culture equipment and improved media, it might be anticipated that the requirement for culturing large volumes of blood would be lessened. However, this is not the case. Studies show that sampling blood volumes of 20, 40, and 60 mL was associated with sensitivities of 65.0–75.7%, 80.4–89.2%, and 95.7–97.7%, respectively [5–8]. In our study, average blood volumes cultured varied from 6.9 to 10.83 mL/ blood culture set (ideally 16–20 mL/set), making it possible that as much as 50% of bacteraemias are missed.

The UK has implemented successful national programmes targeting improvements in both management of sepsis and antimicrobial stewardship recognizing, in a sense, the start and finish points of a continuum. Bridging these points is the blood culture pathway. We believe that focus needs to remain on ensuring that both recommended levels of blood volumes are collected and, crucially, that anaerobic cultures are performed consistently. Appropriate speed to positive blood culture

remains the imperative if effective diagnostic stewardship, reduction in length of stay and potentially improved patient outcomes are to be achieved.

Conflict of interest statement
None declared.

Funding sources
None.

References

[1] Alvares PA, Arnoni MV, da Silva CB, Safadi MAP, Mimica MJ. Carbapenem-resistant Gram negative bloodstream, infections in critically ill children: outcome and risk factors in a tertiary teaching hospital in South America. J Hosp Infect 2019;101:188—9.
[2] Sabino S, Monroy H, Jara C, Lopez O, Ramos F, Falci DR, et al. Impact of extended-spectrum β-lactamases and carbapenem-resistant Gram-negative on sepsis mortality at the emergency department department: a cohort study. J Hosp Infect 2019;101:190—5.
[3] Sharp S. Routine anaerobic blood cultures: still appropriate today? Clin Microbiol 1991;13:179—81.
[4] Washington J. Blood cultures: principles and techniques. Mayo-Clin.Proc. 1975;52:91—8.
[5] Cockerill F, Wilson J, Vetter E, Goodman K, Torgerson C, Harmsen W, et al. Optimal testing parameters for blood cultures. Clin Infect Dis 2004;38:1724—30.
[6] Bouza E, Sousa D, Rodrıguez-Creixems M, Lechuz J, Munoz P. Is the volume of blood cultured still a significant factor in the diagnosis of bloodstream infections? J Clin Microbiol 2007;45:2765—9.
[7] Lee A, Mirrett S, Reller L, Weinstein M. Detection of bloodstream infections in adults: how many blood cultures are needed? J Clin Microbiol 2007;45:3546—8.
[8] Patel R, Vetter E, Scott W, Schleck C, Fadel HJ, Cockerill 3rd FR. Optimised pathogen detection with 30- compared to 20-milliliter blood culture draws. J Clin Microbiol 2011;49(12):4047—51.

M. Weinbren[a,*]
V. Weston[b]
S. Woods[c]
M. Collins[d]
A. Coultas[a]
N.H. O'Connell[c]
C.P. Dunne[e]

[a]*Department of Microbiology, King's Mill Hospital NHS Foundation Trust, Sutton-in-Ashfield, UK*

[b]*Department of Microbiology, Nottingham University Hospitals NHS Trust, Nottingham, UK*

[c]*Department of Microbiology, University Hospital Limerick, Dooradoyle, Co. Limerick, Ireland*

[d]*Department of Microbiology, Chesterfield Royal Hospital, Calow, Chesterfield, UK*

[e]*Graduate Entry Medical School, University of Limerick, Limerick, Ireland*

* Corresponding author. Address: Department of Microbiology, King's Mill Hospital NHS Foundation Trust, Mansfield Road, Sutton-in-Ashfield, NG17 4JL, UK.
E-mail address: mweinbren1@googlemail.com (M. Weinbren).

Available online 8 April 2019

https://doi.org/10.1016/j.jhin.2019.04.002

Effectiveness of early use of fidaxomicin in preventing recurrence of *Clostridium difficile* infection

Sir,

We read with interest the manuscript by Biggs and colleagues [1].

We agree with the authors that fidaxomicin is optimally used for treatment of initial *Clostridium difficile* Infection (CDI), which is consistent with our previously reported findings [2]. Since fidaxomicin has a narrow spectrum of activity and allows reconstitution of indigenous gut flora, it is logical that the most beneficial effect is obtained before further collateral damage to the microbiome has struck.

This is supported by the findings of a randomized study comparing faecal microbiota transplantation (FMT) to fidaxomicin in 64 patients with multiply recurrent CDI [3]. This study recruited patients with average of four previous episodes of CDI, so it is perhaps unsurprising that FMT was significantly better than fidaxomicin in achieving clinical cure.

However, we disagree with the authors' proposal of reserving fidaxomicin for non-severe cases. Since 2012 at Guy's and St Thomas' NHS Foundation Trust we have administered fidaxomicin to all adult patients with CDI as a first-line therapy, including those with severe disease. To date we have treated over 600 patients, with excellent clinical outcomes as evidenced by a reduction in recurrence rates from 16% to 5% during this period. Extended-pulsed dosing of fidaxomicin has been shown to be superior to vancomycin for sustained clinical cure in addition to significantly reducing rates of recurrence. This novel dosing regimen reduces recurrence rates to 7% without incurring additional cost compared with standard dosing [4].

We have also observed a significant reduction in environmental contamination in rooms of patents with CDI who have been treated with fidaxomicin, compared to those treated with vancomycin and/or metronidazole (37% vs 58%, $P=0.02$) [5]. This is presumably due to sporicidal activity of fidaxomicin and possibly also related to reduced time to resolution of diarrhoea. This finding could have significant infection-prevention benefits, reducing in-hospital transmission and new infections.

This is likely to be a contributory factor in our organization having the lowest CDI rate in the Shelford group (of 10 leading academic English healthcare organizations), a position that has been held for the last four financial years. Our organization had a rate of 16.5 infections/100,000 occupied bed days (OBD) in 2017/18, half that of the next-best-performing Shelford group organization (the National rate during this time-period was 38.3 infections/100,000 OBD) [6].

Biggs and colleagues incorrectly state that there are 'limited data on fidaxomicin and its effect/usefulness in the treatment of rCDI and severe CDI'. In fact, the two large