Laboratory techniques

Blood cultures: where do we stand?

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Septicaemia in hospital patients is common. Its prevalence has increased over the past decade from 10 to around 15 cases/1000 admissions, with a corresponding increase in morbidity and mortality. In this hospital the number of clinically important isolates from blood cultures has doubled in the past four years, with an increasing proportion of Gram positive organisms, especially coagulase negative staphylococci.

In cases of suspected septicaemia the culture of blood for bacteria or fungi is mandatory. Early treatment with appropriate antimicrobial agents is essential to reduce mortality.^{1,2} Kreger *et al* found that the wrong choice of antibiotics led to an increase in the number of patients who developed "shock" or who died,¹ irrespective of their underlying clinical condition.¹ Weinstein *et al* found that patients who received the wrong antimicrobial treatment had a mortality three times that of patients receiving appropriate treatment based on *in vitro* susceptibility results.² The antibiotics selected for use should therefore have a high probability of being clinically effective when used on a "best guess" basis. Speed and accuracy in providing the relevant information to clinicians is imperative to allow them to select the most appropriate directed spectrum antibiotics. In a case of septicaemia, for example, can the use of blood cultures help clinicians to do this? It does not seem so at the moment. While a blood culture isolate can provide a result that is clinically definitive and aetiologically specific, this does not necessarily change the management of an acutely ill patient. Often, once a blood culture has been taken, the septicaemic patient is placed promptly and, appropriately, on a "blind" antibiotic regimen. More important, the clinician needs to know what the likely infecting organism is and which antibiotic(s) should be given. The distinction between Gram positive and Gram negative septicaemia is probably not possible, but evidence suggests that the aetiological organism in septicaemia has an independent role in predicting morbidity and mortality.³ Microbiologists should supply this information which will vary between different groups of patients such as the immunocompromised or

immunocompetent. Each laboratory must provide rapid accurate epidemiological data for local clinicians, and the widespread use of microcomputers and suitable software packages makes this feasible.⁴ So if microbiologists are to provide such a service they must use the most appropriate media which will allow the recovery of *all* organisms present in the blood stream, not necessarily in the shortest time. Even in non-urgent cases such as subacute bacterial endocarditis, the mortality of patients with blood culture negative disease exceeds that of patients from whom an organism has been isolated and identified.

A major problem for medical microbiologists is finding the most appropriate blood culture system for their hospital. Many reviews on this subject have been published.⁵⁻⁷ The question was posed in the Royal College of Pathologists' Final Examination in October 1987. It would be illuminating to see the diversity of answers that I am sure were received. Part of the problem is that the type and number of different media used for the isolation of organisms from blood have long been controversial subjects. In 1983 I looked at blood culture techniques in over 100 hospitals throughout Great Britain. Some 10 different liquid media were used, with brain heart infusion broth being the most common. The media were used in different combinations, the number of bottles varied from one to three; volume of media and blood sampled varied, materials were "home-made" or commercial, and the time of subculture was spread over 21 days. Automated techniques, primarily radiometric,⁸ were only used by a few laboratories. Today, five years later, the picture is still muddled. The number of radiometric devices had increased to 143 systems in use in the United Kingdom in 1987.⁹ Other commercial systems have also been introduced into an already crowded market place: biphasic slide cultures,¹⁰ lysis centrifugation,¹¹ gas-capture,¹² and an automated impedance device.¹³

But which system should clinical medical microbiologists choose? Each has advantages and disadvantages whether it be the latest "state of the art" or a technique such as the pour plate, a method first described in 1917 by Muir and Ritchie.¹⁴ Adequate control of new lots of media is necessary, although

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difficult to perform properly. Many have been shown to differ in their ability to support the growth of test micro-organisms.¹⁵ Traditional methods lack the standardisations required of an important diagnostic technique. The introduction of radiometric systems has facilitated considerable progress in standardisation, but interlaboratory variation still exists.

Whatever system is used, the ability to detect septicaemia depends on the primary factor that at least one viable organism must be present in the blood sampled, but in many the number of patients with less than 1 cfu/ml of blood can be as high as 62% of those infected with an *Escherichia coli* septicaemia.¹¹ Investigators have confirmed a direct correlation between the volume of blood culture and the ability to recover micro-organisms. This is a feature of both traditional¹⁶ and modern automated detection techniques.¹⁷ An increase in the amount of blood sampled from 10 to 30 ml produces a considerable increase in the number of septicaemias detected. Collection of 20–30 ml of blood for each culture is optimal for adults, but more blood culture bottles have to be used which is more expensive. Septicaemic neonates and children usually have higher numbers of circulating bacteria, requiring less blood to be sampled.^{18, 19}

In this issue of the Journal are reports which have examined some of the new blood culture systems in children and adults; gas capture which detects gaseous pressure by means of simple monometry; infrared analysis of microbial generated carbon dioxide; and the measurement of conductivity changes in the culture media as a result of substrate metabolism. Each system examined still has problems such as contamination and the production of false negative or false positive results. A major problem is cost, both capital and maintenance: the capital cost of the new Bactec infrared analyser, which has been shown to be comparable with the earlier radiometric machine,⁹ is about £45 000—five times the salary of a laboratory worker—to which the cost of bottles must be added. The gas-capture system, on the other hand, requires no capital expenditure, but has added revenue consequences, especially if more than one bottle is used. Every new system has been found to be more expensive and less efficient when compared with a traditional system of three blood culture bottles plus pour plate, when at least 30 ml of blood are sampled.

Clinical microbiology remains largely a confirmatory rather than a diagnostic speciality.²⁰ All automated methods, whether using radiometric, infrared, or impedance techniques, still depend to a considerable degree on a conventional culture phase entailing at least overnight incubation for identification and antibiotic susceptibility.⁵ This all takes time, and therefore any claim that automated innovations are speedier does not stand up to critical evaluation. I

am not a Luddite. I would like to see progress as much as the next medical microbiologist, but while we continue to rely on traditional culture methods, with or without automation we will never be able to climb out of our Petri dishes into a "Brave New World". Louis Pasteur or Robert Koch would soon find themselves at home in all our laboratories. The Gram stain, over 100 years old, still remains the standard against which rapid diagnostic tests must be measured. Too often they fail. Hopefully, the introduction of molecular biology with DNA probes²¹ and monoclonal antibodies²² will allow us to provide a truly diagnostic service for our clinical colleagues. In the meantime we remain tied to our Bunsen burner and trapped in our Petri dish.

The papers in this issue of the Journal still leave us with the feeling that the definitive system for blood culture has yet to be invented. Of the many articles written on blood cultures, what stands out is the fact that the more blood you sample the more isolates you get—whatever system is used.

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