Blood cultures

Introduction

Blood cultures assist with the diagnosis and management of bloodstream infections. They identify the causative organism(s) and its antimicrobial sensitivities, and so enable appropriate antibiotic treatment to be given. Taking blood cultures is a practical skill that junior doctors need to be competent at, and one of the procedures that *Tomorrow's Doctors* (General Medical Council, 2009) lists that medical students should be able to perform. Blood cultures can also be taken by other health-care workers, e.g. nurses, phlebotomists, but it is essential that all health-care workers taking cultures have been trained in the collection procedure, and their competence assessed and maintained (Department of Health, 2010).

Reason for taking blood cultures

Blood cultures should be taken when a bacteraemia is suspected clinically. Symptoms and signs which suggest this can include temperature >38°C, focal signs of infection, tachycardia, low or raised blood pressure, increased respiratory rate, chills or rigours, raised or very low white blood cell count, and new or worsening confusion. However, signs of sepsis can be minimal or absent in the very young and elderly, or those on steroids or who are immunosuppressed (Department of Health, 2010).

It has been usual practice that samples are taken at the time of a spike of temperature. In a review in the 1950s, Bennett and Beeson (1954) found that studies suggested that blood should be obtained for culture in the hour preceding the expected chill or spike in temperature. This is based on the principle that the presence of the organism in the intravascular space leads to the production of cytokines, which in turn cause body temperatures to rise (Reidel et al, 2008). Mylotte and Tayara (2000) recommend that because it is not feasible to obtain blood cultures before the onset of symptoms, cultures should be taken as soon as symptoms (e.g. fever, chills) occur. Reidel et al (2008) have also demonstrated that the likelihood of documenting bloodstream infections was not significantly enhanced by collecting samples at the time of temperature spikes.

Dr Susan Dawson *is Consultant Microbiologist in the Department of Microbiology, The Great Western Hospital, Swindon SN3 6BB (susan.dawson@gwh.nhs.uk)*

How to take blood cultures

Blood cultures are usually taken from a peripheral vein. The femoral vein should be avoided as it is difficult to adequately cleanse the skin in this area and contamination may occur. Similarly avoid taking samples from above peripheral line or venflon sites or via peripheral or central lines unless intravenous access is limited. Samples taken via a line may grow organisms colonizing or infecting the line. However, if a central line infection is suspected then paired samples should be taken – one via the central line and the other peripherally – and the peripheral vein sample should be collected first (Department of Health, 2010). If both sets of blood cultures grow the same organism, with growth in the sample from the catheter hub occurring at least 2 hours before that in the peripheral vein sample, then this indicates a catheter-related bloodstream infection (Mermel et al, 2009).

Blood cultures should be taken before antibiotics are administered or, if they have been given, just before the next dose to minimize inhibition of organism growth in the cultures. For patients with a suspected bacteraemia it is generally recommended that at least two sets of blood cultures should be taken at different times and sites (Department of Health, 2007). Microorganisms may be present in the blood intermittently or continuously, depending on the source of infection, and leaving time between sets raises the chance of detecting pathogens that are not present in the blood at all times (Shore and Sandoe, 2008).

For patients with suspected infective endocarditis new guidance from the working party of the British Society of Antimicrobial Chemotherapy now recommends that for those with severe sepsis or septic shock at the time of presentation, two sets of blood cultures should be taken at different times within 1 hour before starting empirical therapy. However, in patients with a chronic or subacute presentation, three sets of blood cultures should be taken with ≥6 hours between them before starting antimicrobial chemotherapy (Gould et al, 2012).

Taking more than one set ensures that sufficient blood is sampled to improve the yield of organisms and to assist with interpreting the clinical significance of positive blood cultures. If only one set is positive this may reflect contamination, particularly if the organism cultured is a skin flora-type organism such as coagulase staphylococci or diphtheroids, but if two sets are positive contamination is less likely.

When taking blood cultures it is important to use an aseptic non-touch technique to prevent contamination. Cultures can be taken using a needle and syringe, a winged blood collection set and adapter cap, or via a central line. Taking cultures with a winged blood collection set is the preferred method (Department of Health, 2010) as it leads to less contamination and some have a needle safety device which helps prevent a needlestick injury. Details are given in *Table 1*. For blood cultures taken via a central line, Dwivedi et al (2009) demonstrated that discarding the initial 10 ml after an initial saline flush does not decrease the contamination rate. If the sample is taken using a needle and syringe technique it was previously recommended to change needles before bottle inoculation as this led to a lower contamination rate (Spitalnic et al, 1995), but this is no longer advocated (Department of Health, 2010) because of the increased risk of accidental needlestick injury (Mylotte and Tayara, 2000; Thompson and Madeo, 2009).

The most common source of contaminated percutaneous blood cultures is often thought to be the skin of the patient at the site where the cultures are obtained (Hall and Lyman, 2006). There are several antiseptics that are commonly used – alcohol, chlorhexidine and iodine products

Table 1. How to take blood cultures

Method
1. Collect all equipment needed for the procedure
2. Wash hands with soap and water. Remove caps from blood culture bottles and clean septum using 2% chlorhexidine in 70% isopropyl alcohol swab. Allow the tops to dry to fully disinfect
3. Confirm the patient's identity. Apply a disposable tourniquet. Palpate to identify vein then cleanse the area using a 2% chlorhexidine in 70% isopropyl alcohol impregnated swab. Allow to fully evaporate
4. Wash hands again or apply alcohol hand rub and put on clean examination gloves
5. Attach a winged blood collection set to blood collection adapter cap. Do not repalpate the cleaned site before inserting the needle and taking a sample
6. Place adapter cap over bottle and pierce septum. Inoculate the bottles upright and fill up to graduation mark (usually 10 ml)
7. Release tourniquet then remove needle. Cover site with sterile dressing
8. Discard winged blood collection set into a sharps container. Remove gloves and wash hands
9. Record patient details and date and time of procedure on blood culture bottles and form
10. Document in the patient's notes that blood cultures have been taken

For more details please refer to Department of Health guidance (2010)

(Caldeira et al, 2011). Current UK guidance recommend 2% chlorhexidine in 70% isopropyl alcohol to clean the skin before venepuncture for blood cultures (Department of Health, 2010).

A review of skin antisepsis by Caldeira et al (2011) concluded that alcoholic chlorhexidine solutions showed statistically significant reduction in blood culture false positives compared with aqueous povidone-iodine and non-significant with alcoholic iodine, and that overall alcoholic products appeared to be superior to non-alcoholic solutions as skin antisepsis before venous puncture in prevention of blood culture contamination.

To be effective as an antiseptic the agent needs time to dry which has practical implications. In their review Caldeira et al (2011) found studies that showed that alcoholic chlorhexidine needs 15–30 seconds to dry, iodine tincture 30 seconds and povidone iodine needs about 2 minutes. As well as cleaning the skin, bottle tops also need to be cleaned as Schifman et al (1998) found that this was significantly associated with a lower contamination rate.

Blood culture bottles should be filled according to the manufacturer's instructions – this is usually 10 ml per bottle. One bottle is incubated aerobically and the other anaerobically. If bottles are under-filled yield of organisms may be less. The order in which the bottles should be filled differs with the method of taking the sample. If using a winged blood collection set (with adapter cap) the aerobic bottle should be inoculated first, whereas when using a needle and syringe the anaerobic bottle should be inoculated first to prevent accidental inoculation of air into the system (Thompson and Madeo, 2009). If taking blood for other tests then blood culture bottles should be filled first before filling any other tubes, e.g. those containing EDTA, as these may not be sterile and can lead to contamination (Jumaa and Chattopadhyay, 1994). Once taken the blood cultures should be transported to the laboratory promptly or put in an incubator at 37°C to allow the organisms to continue growing.

Blood culture systems

The bottles contain a liquid culture medium which is a mixture of nutrients that support growth of a wide range of bacteria and some fungi. Some bottles may contain resin which can neutralize a wide range of antibiotics in the patient's blood and this allows growth of organisms. Most laboratories now have automated blood culture systems, and the machine regularly scans the bottles (usually every 10 minutes) to detect microbial growth. Bottles are incubated in the machine for 5–7 days. If slow-growing organisms are suspected or the patient has infective endocarditis then the laboratory needs to be informed so that the bottles are incubated for longer. These will be incubated for 14 days to allow growth of organisms such as the HACEK (*Haemophilus* spp., *Aggregatibacter actinomycetemcomitans*, *Cardiobacterium hominis*, *Eikenella* spp. and *Kingella* spp.) group in patients with infective endocarditis.

However, the working party of the British Society of Antimicrobial Chemotherapy has now suggested that, for patients with suspected infective endocarditis, routine incubation of blood cultures for >7 days is now not necessary (Gould et al, 2012).

Interpretation of positive and negative cultures

If the machine indicates that the bottles are growing organisms, then an aliquot is removed from the bottle for Gram staining and subcultured on to medium to grow the organism. The result of the Gram stain is relayed by the microbiologists or infectious diseases physician to the clinical team. Details of the patient's symptoms, inflammatory marker results and antibiotic therapy are needed to evaluate if it is significant (i.e. indicates a bacteraemia) and assess whether the patient is likely to be on appropriate therapy or if the result indicates likely contamination. Organism identification will be available with sensitivities after a minimum of a further 24 hours. This will then allow further rationalization of antibiotic therapy.

If a patient is clinically septic but blood cultures yield no growth then discussion with a microbiologist or infectious diseases physician can be valuable to discuss further testing strategy and antibiotic therapy. Although blood cultures are still the main method by which causative organisms of bacteraemia are detected they do have several limitations which affect the sensitivity of the test. Culture results can depend on total volume of blood cultured, timing of sampling, if patient has received antibiotics, and type of underlying infection, i.e. producing continuous or intermittent bacteraemia (Mylotte and Tayara, 2000; Shore and Sandoe, 2008). Blood cultures can also be negative if the organism is non-culturable in the broth medium, and other tests may be needed, e.g. serum antibody tests for leptospirosis, Q fever. The clinical

microbiologist or infectious diseases physician can assist with evaluating which would be the most appropriate tests based on the patient's symptoms.

Another major limitation of blood cultures is the time before a culture result is available and this limits its influence on early antibiotic management. However, methods are being developed based on new molecular technology to increase the sensitivity and speed up the process. Two basic approaches have been taken in assay design, using either specific primers that detect a particular organism or universal primers that bind to conserved sequences in bacterial but not human DNA (Dark et al, 2009). Commercial systems have now been developed and trials have started evaluating use in clinical practice.

Contamination of samples

Another limitation of blood cultures is that they may grow contaminants. These may delay initiation of the correct treatment or lead to inappropriate antimicrobial prescriptions (Shore and Sandoe, 2008). Alahmadi et al (2011) showed that they can increase patients' hospital length of stay, costs of laboratory tests and use of antibiotics.

Contamination can occur from a number of sources – the patient's skin, the hands of the person taking the blood sample, equipment used to take the sample and transfer it to the culture bottle, the tops of culture bottles, or the general environment. Reports from NHS trusts and equipment suppliers suggest that the contamination rate could be as high as 10% (Department of Health, 2007). Current Department of Health guidance (2010) suggests that contaminant rates should be less than 3%.

To lower contamination rates Thompson and Madeo (2009) suggest a variety of strategies are needed such as sufficiently educating clinicians on the correct techniques, provision of appropriate resources and equipment, and monitoring of contamination rates. Other have found the introduction of a dedicated phlebotomy team, using pre-packed blood culture kits, and feedback on contamination rates with further training for health-care workers with contaminants have helped with lowering rates (Weinstein, 2003; Larkin et al, 2010; Thomas et al, 2011). BJHM

Conflict of interest: none.

Alahmadi YM, Aldeyab MA, McElnay JC et al (2011) Clinical and economic impact of contaminated blood cultures within the hospital setting. *J Hosp Infect* **77:** 233–6

Bennett IL, Beeson PB (1954) Bacteremia: a consideration of some experimental and clinical aspects. *Yale J Biol Med* **26:** 241–62

Caldeira D, David C, Sampaio C (2011) Skin antiseptics in venous puncture-site disinfection for prevention of blood culture contamination: systematic review with meta-analysis. *J Hosp Infect* **77:** 223–32

Dark PM, Dean P, Warhurst G (2009) Bench-to-bedside review: The promise of rapid infection diagnosis during sepsis using polymerase chain reaction-based pathogen detection. *Crit Care* **13:** 217

Department of Health (2007) *Taking Blood Cultures A summary of best practice.* Department of Health, London

Department of Health (2010) *Taking Blood Cultures A summary of best practice.* http://hcai.dh.gov.uk/files/2011/03/Document_Blood_culture_FINAL_100826.pdf (accessed 12 March 2012)

Dwivedi S, Bhalla R, Hoover DR, Weinstein MP (2009) Discarding the initial aliquot of blood does not reduce contamination rates in intravenous-catheter-drawn blood cultures. *J Clin Microbiol* **47**(9): 2950–1

General Medical Council (2009) *Tomorrow's Doctors Outcomes and standards for undergraduate medical education.* General Medical Council, London

Gould FK, Denning DW, Elliott TSJ et al (2012) Guidelines for the diagnosis and antibiotic treatment of endocarditis in adults: a report of the Working Party of the British Society for Antimicrobial Chemotherapy. *J Antimicrobl Chemother* **67**(2): 269–89

Hall KK, Lyman JA (2006) Updated review of blood culture contamination. *Clin Microbiol Rev* **19**(4): 788–802

Jumaa PA, Chattopadhyay B (1994) Pseudobacteraemia. *J Hosp Infect* **27:** 167–77

Larkin S, Baker N, Anderson R, Ward S, Forde S (2010) An interactive approach to reducing blood culture contamination. *J Hosp Infect* **76:** 273–5

Mermel LA, Allon M, Bonza E et al (2009) Clinical Practice Guidelines for the diagnosis and management of intravascular catheter-related infection: 2009 Update by the Infectious Diseases Society of America. *Clin Infect Dis* **49:** 1–45

Mylotte JM, Tayara A (2000) Blood Cultures: Clinical aspects and controversies. *Eur J Clin Microbiol Infect Dis* **19:** 157–63

Reidel S, Bourbeau P, Swartz B et al (2008) Timing of specimen collection for blood cultures from febrile patients with bacteraemia. *J Clin Microbiol* **46**(4): 1381–5

Schifman RB, Strand CL, Meier FA, Howanitz PJ (1998) Blood culture contamination: A College of American Pathologists Q-Probes study involving 640 institutions and 497134 specimens from adult patients. *Arch Pathol Lab Med* **122:** 216–21

Shore A, Sandoe J (2008) Blood cultures. *Student BMJ* **16:** 324–5

Spitalnic SJ, Woolard RH, Mermel LA (1995) The significance of changing needles when inoculating blood cultures: a meta-analysis. *Clin Infect Dis* **21:** 1103–6

Thomas S, Cheesbrough J, Plumb S et al (2011) Impact of a blood culture collection kit on the quality of blood culture sampling: fear and the law of unintended consequences. *J Hosp Infect* **78:** 256–9

Thompson F, Madeo M (2009) Blood cultures: towards zero false positives. *J Infect Prevent* **10**(1): s24–26

Weinstein MP (2003) Blood Culture Contamination: Persisting Problems and Partial Progress. *J Clin Microbiol* **41**(6): 2275–8

KEY POINTS

- Blood cultures are important tools for the diagnosis and management of bloodstream infections.
- It is essential that all health-care workers taking cultures have been trained and their competence assessed.
- When taking blood cultures an aseptic non-touch technique should be used to minimize contamination.
- At least two sets of blood cultures should be taken from different sites and at different times to maximize yield of organisms and to assist with interpretation of possible contamination.
- Limitations of blood cultures include length of time needed to grow organisms, lack of sensitivity if insufficient blood volume or organisms sampled, prior antibiotics or organism non-culturable in medium and possible contamination.

TOP TIPS

- Collect everything that you need together before starting to take blood cultures, including access to a sharps box to discard sharps.
- Preferably use a system with a needle safety device to decrease risk of a sharps injury.
- Always ensure enough time is allowed for the skin antiseptic to dry before taking cultures.
- Do not repalpate the vein after cleaning the site as this will increase the contamination rate.
- Ensure that blood culture bottles are labelled correctly with the patient details as unlabelled samples may not be processed by the laboratory.