Positive blood culture Gram stain interpretation guide

University Hospitals of Leicester NHS
NHS Trust

Trust Ref number: B48/2024

1. Introduction

This guideline aims to give clinicians information to help them assess their patients who have been found to have positive blood cultures. Until now, Gram stains for positive blood cultures have been verbally reported (as well as electronically) to clinicians by the microbiology medical staff along with some advice regarding sources of infection and antibiotic choice. The laboratory is transitioning into 24 hour reporting of blood cultures. In future, Gram stain results of newly positive blood cultures will be rung out to the relevant clinical area by the Biomedical Scientist staff and reported electronically. This guideline is a substitute for the initial microbiology consultation. The laboratory biomedical scientist will point the receiving clinician in the direction of this guideline.

Medical microbiologists will continue to have close liaison with the clinicians regarding positive blood cultures, but by the time these discussions take place there will be more information available and clearer advice can be issued.

Background information on blood cultures

1. Importance of blood cultures

Blood cultures should be collected in patients with suspected serious infections, prior to the administration of antimicrobials. Ideally, two separate sets of blood cultures should be collected, as increasing the volume of blood collected increases the diagnostic yield. It is also important that each blood culture bottle is filled to the marked fill line (10 ml of blood per bottle for adults, please refer to paediatric blood culture e-learning on HELM for paediatric samples). Identifying causative pathogens of infection is important in order to use appropriate antimicrobials on the individual patient level, and to monitor resistance patterns and influence our guideline antibiotic choices on a wider scale.

2. Blood culture process

Once collected (as per local policy), blood culture bottles should be sent urgently to the laboratory. This is to ensure the samples are incubated at the correct temperature as soon as possible, and to reduce the risk of viable organisms dying in transit. Once received, samples are loaded onto an automated analyser. The analyser detects production of CO_2 in the blood culture bottles, and once a threshold is reached, the analyser "flags" this sample as positive. The sample is then unloaded for further work. This part of the process can take up to 5 days, and if the bottle hasn't "flagged" positive at this point, then it is deemed negative.

3. Gram stain

A drop of the positive blood culture sample is smeared across a glass slide and fixed with heat. A Gram stain is then performed, offering a rapid (within 15 minutes) preliminary shortlist of potential pathogens. Drops of the blood culture sample are also cultured onto different agars to be able to identify the organism(s) to species level using various laboratory tests, and obtain antimicrobial susceptibilities (this can take anywhere from an additional 18 hours to several days).

It is important to note that the Gram stain is not perfect, and often conventional Gram positive organisms (e.g. *Streptococcus pneumoniae*) can look Gram negative. Therefore, Gram stain results need to be interpreted with the clinical picture.

2. Scope

This guidance applies to all staff responsible for the medical care of patients who have positive blood cultures.

3. Recommendations, Standards and Procedural Statements

3.1 General advice when receiving a positive blood culture report:

1. Review the patient and gather information.
    a. Is there a clear source of infection?
    b. Does the blood culture Gram stain correlate with the clinical picture (refer to below sections)?
    c. Are they on antimicrobials? If so which ones?
    d. Is the antimicrobial they are on likely to be effective (refer to below sections)?
    e. Are they clinically stable or not? Is there a clinical deterioration?
    f. Is there any history of resistant organisms (MRSA, VRE, MDR, XDR, CRO)?
2. Patient stable, afebrile or improving?
    a. Continue current treatment based on the appropriate trust guideline.
    b. If non-urgent microbiology advice is required as a result of this result, then please get in contact via electronic advice request (ICE).
3. If the patient is unstable or clinically deteriorating, consider discussion with on call microbiologist via switchboard.
    a. Please note, this is a non-resident on call service and the on-call consultant / registrar is expected to work the following day. Between the hours of 00:00 and 07:00, the on call microbiologist should be contacted in emergency situations only and by a doctor of ST3 grade equivalent or above.
4. See the sections below for further advice on specific Gram stain results. Note, restricted antibiotics will need a verification code before prescribing if they are not being used for their guideline indication, even out of hours. Please liaise with microbiology if this is required (electronic advice request 09:00-16:00 on normal working days, on call via switchboard outside of these times).
5. Document the review on Nervecentre.

3.2 Blood culture Gram stain report "organisms not seen". This would not usually be rung out.

What could this mean?

- False positive due to:
    - Very high white cell count (white cells may also produce CO_2)
    - Excess blood volume in bottle
- Organism has died prior to the sample being stained
- Slow growing / indolent organism needs further incubation

The laboratory will perform further work on the sample to try to isolate potential pathogens. If further information becomes available, this will be communicated to the clinical team.

3.3 Blood culture report "Gram positive cocci in clusters"

Common pathogens and infective sources

- *Staphylococcus aureus* (most virulent and most important)
    - Skin and soft tissue
    - Bone and joint including discitis
    - Endocarditis
    - Prosthetic material
- *Coagulase negative staphylococci*
    - Most common contaminant of blood cultures (usually from patient's own skin)
    - Infections of prosthetic material, particularly:
        - Vascular lines – PICC, midlines, Hickman line, dialysis catheters etc.
        - Prosthetic heart valves, pacemaker leads
        - Endovascular prosthetic material

Antibiotics

- Most empiric antibiotic choices will treat a *S. aureus* infection, e.g.
    - Flucloxacillin, co-amoxiclav, piperacillin-tazobactam, meropenem, vancomycin, teicoplanin, linezolid, cefazolin, cefuroxime, cefotaxime, ceftriaxone
- MRSA infections will not be treated by the beta lactam antibiotics mentioned above, active options include:
    - Vancomycin, teicoplanin, linezolid
- Drugs with minimal or no activity against *S. aureus* include:
    - Benzylpenicillin, amoxicillin, gentamicin, ciprofloxacin

Further action (in addition to advice in section 3.1)

- If working diagnosis is an infection of prosthetic material or endocarditis, ensure multiple blood culture sets have been obtained.
- If working diagnosis is a vascular line infection ensure paired line and peripheral cultures have been sent.
- Consider early involvement of microbiology if known MRSA colonisation (see "IP Alerts" section on Nervecentre).

3.4 Blood culture report "Gram positive cocci in pairs or chains"

Common pathogens and infective sources

- Streptococci
    - Beta-haemolytic (groups A, B, C, G, usually mid to long chains)
        - Skin, soft tissue, necrotising fasciitis, bone, joint, neonatal sepsis
    - *S. pneumoniae* (usually pairs)
        - Pneumonia, meningitis
    - Other streptococci
        - Lung, liver, brain abscesses
        - Endocarditis
- Enterococci (usually pairs or short chains)
    - Intra-abdominal infection, particularly biliary
    - Urinary
    - Endocarditis

Antibiotics

- Most of our empiric antibiotic choices as per guidelines will treat most streptococcal infections
    - Benzylpenicilin, amoxicillin, flucloxacillin, co-amoxiclav, piperacillin-tazobactam, meropenem, cefotaxime, ceftriaxone, vancomycin, teicoplanin, linezolid)
- Most Enterococci will be killed by amoxicillin, piperacillin-tazobactam, meropenem, vancomycin and teicoplanin.
- If known VRE (Vancomycin Resistant Enterococci, see "IP Alert" section on Nervecentre), consider early microbiology involvement.
- *S. pneumoniae* is most commonly penicillin sensitive, however beware of patients with recent travel abroad as there is increasing penicillin resistance in certain regions.

Further action (in addition to advice in section 3.1)

- If working diagnosis is endocarditis, ensure multiple blood culture sets have been obtained.
- Consider early involvement of microbiology if there is a VRE alert, travel history in a patient with suspected *S. pneumoniae* bacteraemia, or possibility of necrotising fasciitis.

3.5 Blood culture report "Gram positive bacilli"

Common pathogens and infective sources

- *Corynebacterium, Cutibacterium (Propionibacterium), Bacillus* species
    - Usually contaminants, however may cause infection of prosthetic material (e.g. long intravenous lines, pacemakers, prosthetic heart valves.
- *Listeria* species
    - Neonatal sepsis
    - Sepsis and meningo-encephalitis in immunosuppressed and elderly
- *Clostridium* species
    - Anaerobic bacteria, usually originate from GI tract
    - Gas gangrene
    - Note - empiric therapy for abdominal infections will usually cover these organisms.

Antibiotics

- No treatment is required for probable contaminants.
- Gram positive bacilli are a diverse range of organisms, and different species require different treatment.
- Empiric guidelines for meningitis include antibiotics active against *Listeria* (amoxicillin, meropenem, co-trimoxazole) in those at risk. Ceftriaxone and cefotaxime are not active against *Listeria.*
- Empirical treatment for line related infections (vancomycin, teicoplanin and linezolid) are usually active against *Corynebacterium / Cutibacterium / Bacillus* species.

Further action (in addition to advice in section 3.1)

- If working diagnosis is a vascular line infection ensure paired line and peripheral cultures have been sent.
- Consider early discussion with microbiology if there is a concern of necrotising soft tissue infection, gas gangrene, or *Listeria* infection.

3.6 Blood culture report "Gram negative cocci or coccobacilli"

Common pathogens and infective sources

- *Neisseria meningitidis* (usually diplococci)
    - Septicaemia, meningitis
- "HACEK" group
    - Infective endocarditis, joint infections.
- *Haemophilus influenzae*
    - Pneumonia, epiglottitis, meningitis. Vaccine history important.
- *Acinetobacter* species
    - Prosthetic material, hospital acquired infections, occasional contaminant in blood cultures.
- *Brucella*
    - Rare but important, causative agent of brucellosis, travel history essential.

Antibiotics

- *Neisseria meningitidis* will be treated by guideline antibiotics for meningitis (ceftriaxone, cefotaxime, meropenem).
- Antibiotics have variable activity against other organisms.
- *Acinetobacter* species can be particularly drug resistant (look for "IP Alerts" – MDR, XDR, or CRO).

Further action (in addition to advice in section 3.1)

- Consider early discussion with microbiology to ensure an appropriate antibiotic and dose is used.
- If working diagnosis is endocarditis, ensure multiple blood culture sets have been obtained.
- Consider early microbiology involvement if IP alert with MDR/XDR/CRO, or history of foreign travel.

3.7 Blood culture report "Gram negative bacilli"

Common pathogens and infective sources

- Enterobacterales (e.g. *E. coli, Enterobacter* species, *Klebsiella* species, *Proteus* species)
    - Urinary tract, biliary, other intra-abdominal infections.
- *Pseudomonas aeruginosa*
    - Catheter associated UTI, ventilator associated pneumonia, complicated hospital acquired infections
- *Salmonella typhi / paratyphi*
    - Typhoid fever / enteric fever
    - Travel history important
    - Patient needs isolation with contact precautions if this is suspected.
- Anaerobes e.g. *Bacteroides* species
    - Biliary and other intra-abdominal infections
- *Fusobacterium* species
    - Lemierre's disease – septic thrombophlebitis. Consider in patient with severe sore throat and sepsis.

Antibiotics

- Enterobacterales should be covered by empiric antimicrobial choices in the relevant guidelines (co-amoxiclav, ciprofloxacin, piperacillin-tazobactam, meropenem, cefotaxime, ceftriaxone, gentamicin), but resistance is becoming more common – check for MDR/XDR/CRO alerts on Nervecente.

- Anti-pseudomonal antibiotics include ciprofloxacin, piperacillin-tazobactam, meropenem, ceftazidime, amikacin, tobramycin.
- Typhoid/enteric fever has a standalone guideline.
- Antibiotics with anaerobic activity include co-amoxiclav, piperacillin-tazobactam and meropenem.
- *Fusobacterium* species should be empirically treated with antibiotics used for tonsillitis/quinsy (metronidazole and benzylpenicillin).

Further action (in addition to advice in section 3.1)

- Review previous microbiology results to look for previous resistant organisms.
- MDR/XDR/CRO IP alert may indicate the need for early microbiology involvement.

3.8 Blood culture report "yeasts"

Common pathogens and infective sources

- *Candida* species
    - Usually originate from GI tract (e.g. perforation, post-operative collection, anastomotic leak), but once in blood stream can disseminate (endocarditis, endophthalmitis)
    - Frequently infect lines and other prosthetic material e.g. PICC lines, central lines, catheter associated UTI.

Further action (in addition to advice in section 3.1)

- Review patient for potential sources of infection referring to the above.
- New yeast in blood culture or patient unstable (high EWS, critically unwell) or deteriorating on current treatment?
    - Review patient and discuss with microbiology.
- Already known candidaemia on treatment and stable?
    - Continue current therapy, review with microbiology during normal working hours.

4. Education and Training

N/A.

5. Monitoring and Audit Criteria

All guidelines should include key performance indicators or audit criteria for auditing compliance,

if this template is being used for associated documents (such as procedures or processes) that support a Policy then this section is not required as all audit and monitoring arrangements will be documented in section 8 of the Policy.

Key Performance Indicator	Method of Assessment	Frequency	Lead
Documentation of review on nervecentre (recommendation point 5 in 3.1)	Audit	Annual	George Hills

6. Supporting Documents and Key References

UKSMI B 37 – Investigation of blood cultures (for organisms other than Mycobacterium species). Available at:

https://www.rcpath.org/profession/publications/standards-for-microbiology-investigations/bacteriology.html

7. Key Words

"blood culture", "Gram stain"

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This table is used to track the development and approval and dissemination of the document and any changes made on revised / reviewed versions

DEVELOPMENT AND APPROVAL RECORD FOR THIS DOCUMENT		
Author / Lead Officer:	George Hills	**Job Title:** Consultant in microbiology and infectious diseases
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Approved by:	**Policy and Guideline Committee**	**Date Approved: 19 April 2024**

REVIEW RECORD			
Date	**Issue Number**	**Reviewed By**	**Description Of Changes (If Any)**

DISTRIBUTION RECORD:			
Date	**Name**	**Dept**	**Received**