



This document provides guidance for best practices for blood cultures in diagnoses of bloodstream infection due to bacterial, mycobacterial and fungal infection.

[Section 1:](#) Blood Culture for Bacteremia and Candidemia

[Section 2:](#) Blood Culture for Disseminated Mycobacterial Infection

[Section 3:](#) Blood Culture for Disseminated Mold Infection

### Section 1. Blood Culture for Bacteremia and Candidemia

Blood cultures are the critical specimens for diagnosing bloodstream infection. Ninety percent of blood cultures are negative. In Interior Health, 1-3% of positive blood cultures are contamination. Unrestricted repeating of blood cultures increases the risk of contamination, leading to false-positive results, additional cultures and imaging, and unnecessary antibiotic use. This document provides guidance on the indications for INITIAL and FOLLOW-UP blood cultures, and when the FOLLOW-UP blood culture is not required.

**NOTE:** Discuss with a Medical Microbiologist or Infectious Diseases if any questions about a specific scenario.

#### Indications for INITIAL Blood cultures in adult patients:

- **Blood cultures are INDICATED in the following scenarios:**
  - Sepsis/septic shock
  - Systemic signs of infection AND asplenia
  - Fever with signs of infection in severely immunosuppressed patients (e.g., neutropenia, hematopoietic stem cell or solid organ transplant)
  - Syndromes with high risk of bacteremia (>50%):
    - Endovascular infection
      - Infective endocarditis
      - Septic thrombophlebitis
      - Infected cardiac/vascular devices
    - Central nervous system (CNS) infections
      - Meningitis
      - Epidural abscess
    - Musculoskeletal infections
      - Native joint septic arthritis
      - Vertebral discitis/osteomyelitis
    - Catheter-related bloodstream infection
  - Syndromes with intermediate risk of bacteremia (>10%, <50%):
    - Cholangitis
    - Pyelonephritis
    - Severe pneumonia
    - Severe cellulitis/skin soft tissue infection (SSTI) (e.g., necrotizing soft tissue infection)
    - Non-severe cellulitis/SSTI with significant comorbidities (e.g., severely immunocompromised, end-stage renal or liver disease)

- **Blood cultures are NOT indicated in the following scenarios:**
  - Syndromes with low risk of bacteremia (<10%)
    - Non-severe cellulitis/SSTI
    - Lower urinary tract infection (e.g. cystitis, prostatitis)
    - Non-severe community-acquired pneumonia (CAP)
    - Non-severe diabetes related foot infection
    - Colitis (including *C. difficile*)
    - Aspiration pneumonitis
    - Uncomplicated cholecystitis, diverticulitis, or pancreatitis
  - Fever or leukocytosis explained by a non-infectious cause (e.g., drug withdrawal, trauma, pulmonary embolism, etc.)
  - Isolated fever or leukocytosis without symptoms and signs of systemic infection
  - Post-operative fever within 48 hours
  - Persistent fever or leukocytosis in patient with negative blood culture in past 48-72 hours with out new localizing signs of infection
    - Other cultures or imaging to look for a source control issue would be more appropriate than blood cultures
    - Consider Infectious Diseases consultation
  - Surveillance blood cultures in patients without suspicion of bacteremia (e.g., from central line prior to TPN initiation, prior to central line replacement)

**Indications for FOLLOW-UP Blood Culture to Document Clearance of Bloodstream Infections:**

**NOTE:** Follow-up blood culture should be collected at least 48 hours from the initial positive blood culture, AND after effective antibiotics have been started, AND after source control has been achieved.

- Bacteremia caused by the following organisms:
  - Carbapenemase producing *Enterobacterales*
  - *Enterococcus spp.*
  - *Pseudomonas aeruginosa*
  - *Salmonella spp.*
  - *Staphylococcus aureus*: repeat blood culture every 72 hours until blood cultures are negative on two separate days
  - *Staphylococcus lugdunensis*
  - Yeast
- Suspected/proven intravascular infection, regardless of which microorganism was detected on initial blood culture
  - Endocarditis
  - Previous history of endocarditis
  - Cardiac comorbidities
    - Heart transplant-associated valvulopathy
    - Unrepaired congenital heart disease, repaired congenital heart disease with residual shunt or valvular regurgitation, or repaired congenital heart disease within the first six months post-repair)
  - Intra-cardiac medical device(ICD)/pacemaker
  - Vascular graft
  - Septic thrombophlebitis/septic emboli

- Other clinical indications, regardless of which microorganism was detected on initial blood culture
  - Epidural abscess
  - Persistent symptoms and lack of clinical improvement
  - Febrile neutropenia patient
  - Catheter-related bloodstream infection when attempting catheter retention

**The Following Conditions DO NOT Require FOLLOW-UP Blood Culture:**

- Single positive blood culture (i.e. 1 bottle positive or 2/4 from the same venipuncture) with skin flora, AND no clinically suspicious/ proven intravascular infection or other clinical indications for follow-up blood culture
  - *Actinomyces spp.*
  - *Bacillus spp.*
  - Coagulase-negative staphylococci
  - *Corynebacterium spp.*
  - *Cutibacterium acnes*
  - *Kocuria spp.*
  - *Micrococcus spp.*
  - Viridans group streptococci
- Uncomplicated gram-negative bacteremia
  - Clinically improving after 48 hours effective antibiotic treatment and source controlled

For ordering information and collection instructions, refer to the Interior Health Microbiology Laboratory Test Directory (“Blood Culture”): [microbiology-guide-to-specimen-ordering-collection-and-transport-information.pdf](#)

## Section 2. Blood Culture for Disseminated Mycobacterial Infection

### The Facts:

- Routine Blood culture bottles are NOT useful for detecting mycobacterial bloodstream infection (disseminated infection). Myco/F lytic blood culture bottles are designed for mycobacterial bloodstream infection (disseminated infection) including disseminated tuberculosis (TB) and non-TB mycobacterial (NTM) infection such as BCG infection from urinary tract cancer treatment, disseminated diseases due to Mycobacterium avium complex (MAC) and slow grower infections.
- The major predisposing conditions for disseminated tuberculosis include Immunodeficiency/suppression, hematologic disorders, severe diabetes and alcoholism.
- Mycobacterial blood culture doesn't add to the diagnostic yield of conventional tests used routinely for tuberculosis and NTM infection, namely sputum microscopy and culture, or biopsy specimens. Furthermore, tissue biopsy has better yield for diagnosing mycobacterial infection compared to mycobacterial blood culture. When no localized infection site is identified and the clinical presentation suspected disseminated mycobacterial infection, blood culture is helpful.

### Indications for Mycobacterial Blood Culture:

- Suspected disseminated mycobacterial infection in patients with clinical risk factor (*e.g.* immunosuppression\* or certain chronic illnesses) and relevant exposure history (for TB)
- History of bladder cancer with prior BCG irrigation therapy with subsequent clinical presentation compatible with suspected disseminated BCG infection

### Mycobacterial Blood Culture Is NOT Indicated for the Following:

- Localized Mycobacterial Infection: targeted specimens (*e.g.* sputum or biopsy) preferred and provide much higher diagnostic yield.

For ordering information and collection instructions, refer to the Interior Health Microbiology Laboratory Test Directory ("TB/Mycobacteria"): [microbiology-guide-to-specimen-ordering-collection-and-transport-information.pdf](#)

## Section 3. Blood Culture for Disseminated Mold Infection

### The Facts:

- Routine blood culture bottles are excellent for yeast detection but not good for detecting mold. Myco/F lytic blood culture bottles are designed for detecting fungemia caused by disseminated mold infection.
- Since mold blood culture yield is extremely low and turn around time is long, most positive mold blood cultures result in no immediate clinical impact due to other microbiological tests available sooner, such as targeted culture specimens from biopsy or respiratory sources, serology, antigen tests, and PCR. Furthermore, most of the positive mold blood culture isolates are deemed to be false positive results, if clinical suspicion is low.

### Indications for Fungal Blood Culture:

- Clinical suspicion of disseminated mold infection in Immunocompromised\* patients when other faster targeted tests (e.g. bronchoscopy or biopsy cultures, serology, antigen tests) are not possible
- Clinical suspicion of disseminated dimorphic mold infection (e.g.: *Histoplasma*, *Blastomyces*) in patients with relevant travel history, if other faster directed tests (e.g. respiratory or biopsy cultures, serology, antigen tests) are not possible

### Mold Blood Culture Is NOT Indicated for the Following:

- Detection of yeast (e.g. *Candida* or *Cryptococcus* species) since these can be detected in routine blood cultures
- Diagnosis of disseminated mold infection in patients for whom other more rapid targeted tests are available (e.g. bronchoscopy or biopsy culture, serology, antigen tests)

For ordering information and collection instructions, refer to the Interior Health Microbiology Laboratory Test Directory ("Fungal Culture, Deep"): [microbiology-guide-to-specimen-ordering-collection-and-transport-information.pdf](#)

### **\*Immunocompromised/immunosuppressive Conditions**

[healthbc.sharepoint.com/sites/IPCPortalIH/SharedDocuments/Forms/All.aspx?id=%2Fsites%2FIPCPortalIH%2FShared Documents%2FDefinition %26 Management of Immunocompromised Patients%2Epdf&parent=%2Fsites%2FIPCPortalIH%2FShared Documents](http://healthbc.sharepoint.com/sites/IPCPortalIH/SharedDocuments/Forms/All.aspx?id=%2Fsites%2FIPCPortalIH%2FShared Documents%2FDefinition %26 Management of Immunocompromised Patients%2Epdf&parent=%2Fsites%2FIPCPortalIH%2FShared Documents):

- Hematopoietic stem cell transplant patients in the first 24 months after transplant
- Patients with neutrophil count  $< 0.5 \times 10^9 / L$  for duration  $\geq 48$  hours
- Patients receiving corticosteroid therapy equivalent to prednisone  $\geq 20\text{mg/day}$  for duration of  $\geq$  two weeks
- HIV positive patients with  $CD4 < 200 \times 10^6 / L$
- Patients with inflammatory bowel disease, rheumatologic conditions, multiple sclerosis, or solid organ recipients receiving immunosuppressive therapy, such as, infliximab, etanercept, and methotrexate
- Oncology patients receiving chemotherapy
- Patients with extensive loss of skin/mucous membrane barrier defenses e.g., graft versus host disease, Steven-Johnson syndrome, scalded skin syndrome, major burns
- Patients with congenital or acquired hypogammaglobinemia or agammaglobulinemia, severe combined immunodeficiency or other congenital immune deficiency syndrome

## References:

- Canzoneri CN, Akhavan BJ., Tosur Z., Alcedo Andrade PE., Aisenberg GM. CID 2017: 65 (1):1776-9
- CLSI M47: Principles and procedures for blood cultures. 2<sup>nd</sup> edition, 2022
- Doern GV, Carroll KC, Diekema DJ, et al. Practical Guidance for Clinical Microbiology Laboratories: A Comprehensive Update on the Problem of Blood Culture Contamination and a Discussion of Methods for Addressing the Problem. *Clin Microbiol Rev.* 2020 Jan; 33 <https://doi.org/10.1128/cmr.00009-19>
- Doern GV. Detection of bacteremia: Blood cultures and other diagnostic tests. UpToDate 2023 [Detection of bacteremia: Blood cultures and other diagnostic tests - UpToDate](#)
- Fabre V, Carroll KC, Cosgrove SE. Blood Culture Utilization in the Hospital Setting: a Call for Diagnostic Stewardship. *J Clin Microbiol.* Mar 16 2022;60(3):e0100521. doi:10.1128/jcm.01005-21
- Fabre V, Sharara SL, Salinas AB, Carroll KC, Desai S, Cosgrove SE. Does This Patient Need Blood Cultures? A Scoping Review of Indications for Blood Cultures in Adult Nonneutropenic Inpatients. *Clin Infect Dis.* Aug 22 2020;71(5):1339-1347. doi:10.1093/cid/ciaa039
- Mushtaq A., Bredell BX, and Soubani AO. Repeating blood cultures after initial bacteremia: When and how often? *Cleveland Clinic Journal of Medicine* 2019 Feb; 86 (2): 89-92
- Nebraska Medicine: Blood culture guidance in Non-severely immunocompromised adult inpatients
- Oldberg K., and Rasmussen M. Enterococcus faecalis in blood cultures-a prospective study on the role of persistent bacteremia. *Diagnostic Microbiology and Infectious Disease* 2021: 101 (1) 15433 <https://doi.org/10.1016/j.diagmicrobio.2021.115433>
- Siegrist EA, Wungwattana M, Azis L, Stogsdill P, Craig WY, Rokas KE. Limited Clinical Utility of Follow-up Blood Cultures in Patients With Streptococcal Bacteremia: An Opportunity for Blood Culture Stewardship. *Open Forum Infect Dis.* Dec 2020;7(12):ofaa541. doi:10.1093/ofid/ofaa541
- Tungsiripat M: Follow-up blood cultures are often needed after bacteremia. *Cleveland Clinic Journal of Medicine* 2019 Feb; 86 (2): 93-94
- Thaden JT., Cantrell S., Dagher, M, Tao Y., Ruffin F., Maskarinec SA., Goins S., Sinclair M., Parsons JB., Eichenberger E., Fowler VG.. Association of follow-up blood cultures with mortality in patients with Gram-negative bloodstream infections: A systematic review and meta-analysis. *JAMA Network Open* 2022, 5(9): e2232576
- Pappas Pg., Kauffman CA., Andes DR., Clancy CJ., Marr KA., Ostrosky-Zeichner L., Reboli AC., Schuster Mg., Vazquez JA., Walsh TJ., Zaoutis TE, and Sobel JD. Clinical Practice Guideline for the management of candidiasis: 2016 Update by the Infectious Diseases Society of America. *CID* 2016, 62(4): 1-50.
- Crump JA and Reller LB. Two Decades of Disseminated Tuberculosis at a University Medical Center
- Herrera LN et al. Clinical Utility of Routine Use of Fungal Blood Cultures. *American J Med* 2023 <https://doi.org/10.1016/j.amjmed.2023.01.037>
- Chavez MA et al. Clinical impact of positive fungal blood cultures for diagnosis and treatment of fungal infections. *OFID* 2022;9 (Suppl 2) S224.
- Valencia-Shelton F. et al. Clinical laboratory considerations after discontinuation of the Isolator tube lysis-centrifugation system for fungal and mycobacterial blood culture. *American Society For Microbiology* 2024 ([Clinical Laboratory Considerations After Discontinuation of the Wampole Isolator Lysis-Centrifugation System for Fungal and Mycobacterial Blood Cultures | ASM.org](#))

- Von Gottberg A et al. Utility of blood cultures and incidence of mycobacteremia in patients with suspected tuberculosis in a South African infectious disease referral hospital. Intern J Tuberculosis and Lung Dis 2001, 5:80-86.