

Asymptomatic
bacteremia and
CDC's Antimicrobial
Resistance Laboratory
Network in Nevada

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Objectives

- At the completion of the presentation, attendees will be able to:
 - Compare and contrast bacteremia, sepsis and asymptomatic bacteremia
 - Describe asymptomatic bacteremia
 - Identify other diagnostic tests that might help distinguish between bacteremia, sepsis and asymptomatic bacteremia
 - Identify reasons why asymptomatic bacteremia may not warrant treatment
 - Describe occult bacteremia in children and contrast this with asymptomatic bacteremia

What is bacteremia?

2017 ICD-10-CM Diagnosis Code R78.81 Bacteremia

Clinical Information

The presence of viable bacteria circulating in the blood. Fever, chills, tachycardia, and tachypnea are common acute manifestations of bacteremia. The majority of cases are seen in already hospitalized patients, most of whom have underlying diseases or procedures which render their bloodstreams susceptible to invasion.

Symptoms and Signs

Some patients are asymptomatic or have only mild fever.

Development of symptoms such as tachypnea, shaking chills, persistent fever, altered sensorium, hypotension, and GI symptoms (abdominal pain, nausea, vomiting, diarrhea) suggests sepsis or septic shock. Septic shock develops in 25 to 40% of patients with significant bacteremia. Sustained bacteremia may cause metastatic focal infection or sepsis.

Other definitions

Bacteremia

Bacteremia is the presence of bacteria in the blood as evidenced by a positive blood culture. It is often transient and of no consequence; however, sustained bacteremia may lead to widespread infection and sepsis.

Systemic Inflammatory Response Syndrome (SIRS)

Establishes a clinical response to a nonspecific condition of either infectious or noninfectious origin. SIRS criteria include:

- Fever of more than 38°C (100.4°F) or less than 36°C (96.8°F)
- Heart rate of more than 90 beats per minute
- Respiratory rate of more than 20 breaths per minute or arterial carbon dioxide tension (PaCO₂) of less than 32mm Hg
- Abnormal white blood cell count (>12,000/μL or < 4,000/μL or >10 percent immature [band] forms)
- There are two codes for SIRS of a non-infectious origin in ICD-10-CM, with assignment depending on the presence or absence of associated organ dysfunction: R65.10, systemic inflammatory response syndrome (SIRS) of non-infectious origin without acute organ dysfunction and R65.11, systemic inflammatory response syndrome (SIRS) of non-infectious origin with acute organ dysfunction.

More definitions...

Sepsis

Sepsis can be defined as the presence of both an infection and a systemic inflammatory response. The clinical features include two or more of the SIRS criteria occurring as a result of a suspected or documented infection, taking into consideration the entire clinical picture of the patient.

Septicemia

Older term, In ICD-10, May be used as a synonym for sepsis, unspecified organism.

Severe Sepsis

When a patient has sepsis with evidence of organ dysfunction, this is known as severe sepsis

Classification of bacteremias

Transient bacteremia → tooth brushing, biopsy



Intermittent bacteremia → abscess



Persistent/sustained bacteremia → intravascular



From: The Clinical Importance of Microbiological Findings in the Diagnosis and Management of Bloodstream Infections

Clin Infect Dis. 2009;48(Supplement_4):S238-S245. doi:10.1086/598188

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True vs. asymptomatic bacteremia?

- Bacteremia is the presence of bacteria in the bloodstream.
- May occur spontaneously, during certain tissue infections, with use of indwelling GU or IV catheters, or after dental, GI, GU, wound-care, or other procedures.
- Some patients are asymptomatic or have only mild fever.
- Differentiate true from asymptomatic bacteremia by looking for development of other symptoms:
 - Usually suggests more serious infection, such as sepsis or septic shock
 - Look for tachypnea, shaking chills, persistent fever, altered sensorium, hypotension, and GI symptoms (abdominal pain, nausea, vomiting, diarrhea) suggests sepsis or septic shock. Septic shock develops in 25 to 40% of patients with significant bacteremia.
 - Sustained bacteremia may cause metastatic infections, including endocarditis, especially in patients with valvular heart abnormalities.
- Diagnosis is by blood culture and exclusion of focal infection.

Common causes of asymptomatic bacteremia

- Bacteremia may occur during
 - Certain ordinary activities e.g. vigorous tooth brushing
 - Dental or medical procedures
 - Typically after manipulation of nonsterile body sites
 - Dental procedures: tooth cleaning, tooth extraction, peridontal work
 - Gastrointestinal biopsy
 - Rectal or prostate biopsy
 - Percutaneous catheterization of the vascular system, bladder, or common bile duct
 - Surgical debridement or drainage
 - Certain bacterial infections
 - May see transient bacteremia in intestinal *Campylobacter* infection
 - Injection of recreational drugs

Diagnosis of bacteremia

- Clinical:
 - Look for focal infection(s)
 - Medical history to see if explanation for bacteremia
- Laboratory
 - Cultures: blood and any other suspected sites
 - Single isolates of known pathogenic bacteria generally considered to be true positive results
 - Same pathogen from blood and suspected site highly significant
 - How long did it take for the culture to turn positive
 - Cultures that grow multiple isolates or nonpathogenic bacteria are considered contaminated
 - Consider viral diagnostic studies to rule out typical/seasonal viruses (e.g. Influenza)
 - Look for other inflammatory markers
 - CBC
 - WBC
 - Absolute Neutrophil Count
 - Consider procalcitonin or C-Reactive Protein

Common organisms found in asymptomatic bacteremia

Procedure	Source	Examples
Dental procedure	Oral microflora	Streptococci Enterococci Oral anaerobes
Gastrointestinal/Rectal/ Prostate Biopsy	GI flora (including Gram Negative Rods and Anaerobes	Escherichia coli Klebsiella and Enterobacter spp. Bacteroides spp. Prevotella spp.
Percutaneous catheterization of the vascular system, bladder, or common bile duct	Skin flora or genitourinary flora	Staphylococcus aureus Coagulase-negative Staph. Streptococcus spp. Enterococcus spp. Escherichia coli Klebsiella and Enterobacter spp.
Surgical debridement or drainage	Skin flora or microbial flora from infected area	Above organisms plus Pseudomonas aeruginosa Acinetobacter baumannii

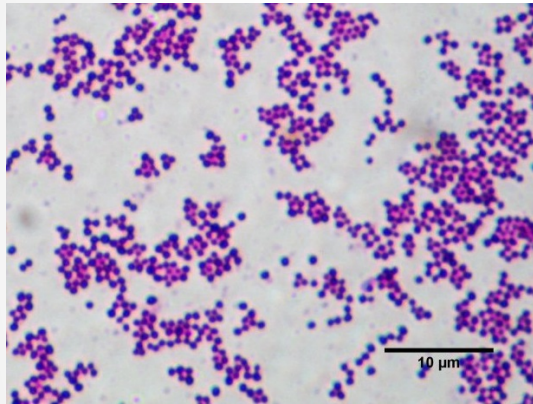
Considerations for treatment of asymptomatic bacteremia

- If it is truly asymptomatic/transient bacteremia:
Typically would not treat
- Important exceptions:
 - Is it a classic pathogen (not readily explained) or one that is known to be associated with occult bacteremia
 - *Neisseria meningitidis*
 - *Staphylococcus aureus*
 - *Streptococcus pneumoniae*
 - *Clostridium septicum*
 - Patient characteristics:
 - Patient is immunocompromised
 - Patient has prosthetic
 - Valve
 - Joint

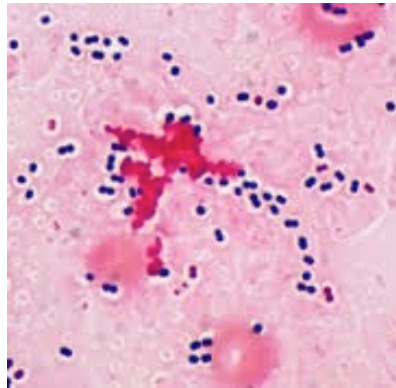
Pay special attention to these organisms

Classic pathogens

Staphylococcus aureus

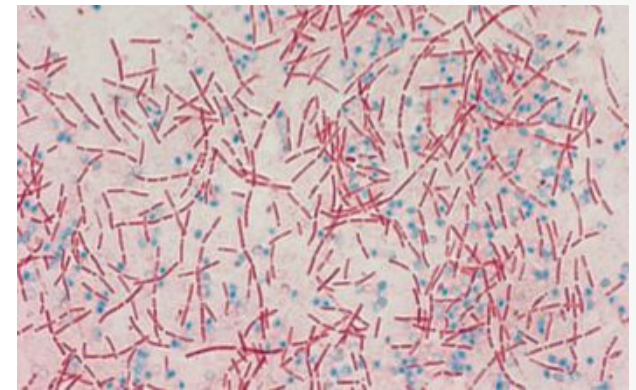


Streptococcus pneumoniae



Unusual pathogens

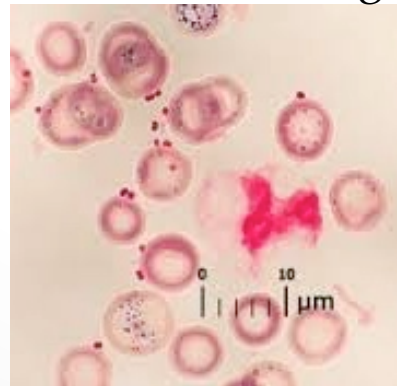
Clostridium septicum



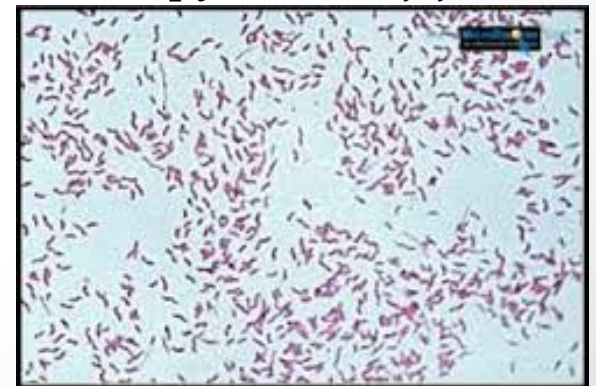
Haemophilus influenzae



Neisseria meningitidis



Campylobacter jejuni



If you do consider antimicrobial therapy, consider

- Antimicrobial stewardship:
 - Optimization of antimicrobial therapy
 - Review of microbiology results / revision / de-escalation of empiric prescribing
- Goal: Ensure the 5 D's of optimal antimicrobial therapy:
 - Diagnosis: Does the condition require antibiotic therapy?
 - Drug: Is the bacteria susceptible?
 - Dose: What is the recommended dose?
 - Duration: What is the recommended duration?
 - De-escalation Can the antibiotic be switched from IV to oral?
- Misuse and Consequences
 - Antibiotic resistance, multidrug-resistant organisms
 - Adverse drug effects or drug interactions
 - Secondary infections (*Clostridium difficile*)
 - Increased cost of care

A word of caution about infants and children

- Children greater than 3 years of age almost always look ill and have an identifiable (ie, non-occult) focus of infection
- However, does not necessarily apply to children, especially those less than 3 years of age
 - Before conjugate vaccines, about 3 to 5% of children aged 3 to 36 mo with a febrile illness (temperature $\geq 39^{\circ}$ C) and no localizing abnormalities (ie, fever without a source) had occult bacteremia
 - 80% *Streptococcus pneumoniae*
 - 10% *Haemophilus influenzae* type b
 - 5% *Neisseria meningitidis*
 - Now rare except in rare except in underimmunized or nonimmunized children, and in children with immunodeficiency
- Febrile infants < 3 mo of age have greater risk of serious bacterial infection. Typically:
 - group B β -hemolytic *Streptococcus*, *S. pneumoniae*, and *H. influenzae* type b.

Summary

- Look for symptoms beyond bacteremia
 - Differentiates between asymptomatic bacteremia and sepsis
 - Look for foci of infection
 - Employ other diagnostic tests including imaging
 - Talk to the microbiology laboratory
- If simple transient, asymptomatic bacteremia, treatment may not be necessary, but remember the exceptions
- If treatment is deemed advisable, then follow guidelines of antimicrobial stewardship

Questions



The CDC Healthcare-Associated Infections and Antimicrobial Resistance Program

- Prevent infections (e.g., CDI, CRE, MRSA)
- Enhance HAI/AR detection and response infrastructure, establish AR expertise in HAI/AR programs
- Promote appropriate antibiotic use
- Increase state laboratory capacity for CRE testing
- Establish regional laboratories as a national resource for AR testing and characterization

CDC AR Program

Increase state laboratory capacity for CRE testing

- Targeted organisms include:
 - CRE: *Escherichia coli*, *Enterobacter* spp, and *Klebsiella* spp.
 - CRP: non-mucoid *Pseudomonas aeruginosa*
 - CRA: *Acinetobacter baumannii*
- Generally includes ability to test for:
 - Antimicrobial resistance
 - Either Kirby-Bauer, E-Test, Automated system, or broth microdilution
 - For surveillance, doesn't necessarily include all antibiotics of interest
 - Phenotypically test for presence of a carbapenemase
 - Either mCIM or CARBA-NP
 - Genetically test for the specific carbapenemase
 - May prescreen with phenotypic test, if positive then test genetically
 - Has advantage that might find novel or unusual resistance
 - Either Cepheid Carba-R or CDC (or other in-house developed test)
 - Phenotypically screen for colistin resistance
 - If positive then test for mobile colistin resistance (mcr) gene

Phenotypically screen for carbapenemases

mCIM

- Modified carbapenem inactivation method
- Uses commercially available materials
- Use with Enterobacteriaceae and *Pseudomonas aeruginosa*
- Incubate organism with meropenem disk, then plate disk on lawn of *E. coli*
- If carbapenemase present, no/reduced antibiotic remaining in disk
- Overnight test

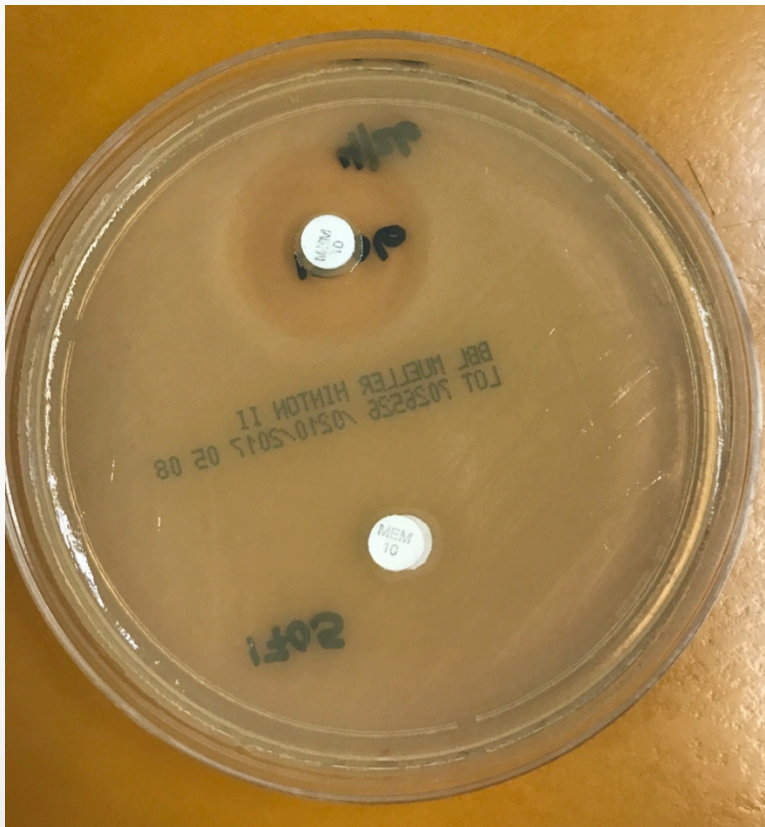
Carba-NP

- Colorimetric micro tube assay
- Not commercially available in US
- Use with Enterobacteriaceae, *Pseudomonas aeruginosa*, *Acinetobacter* spp.
- Detects hydrolysis of imipenem by color change compared to control
- Read at time intervals up to 2 hours

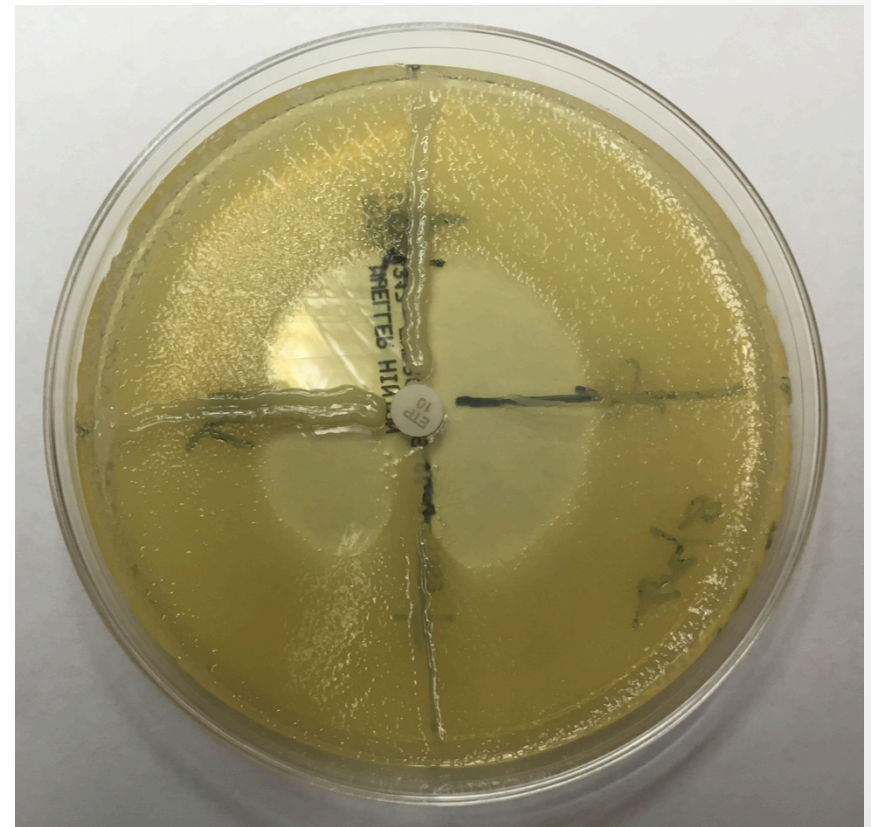
Phenotypic detection of carbapenem

~~Modified Hodge Test~~
(MHT)

mCIM



Pos = 6 - 15 mm; Neg \geq 19 mm



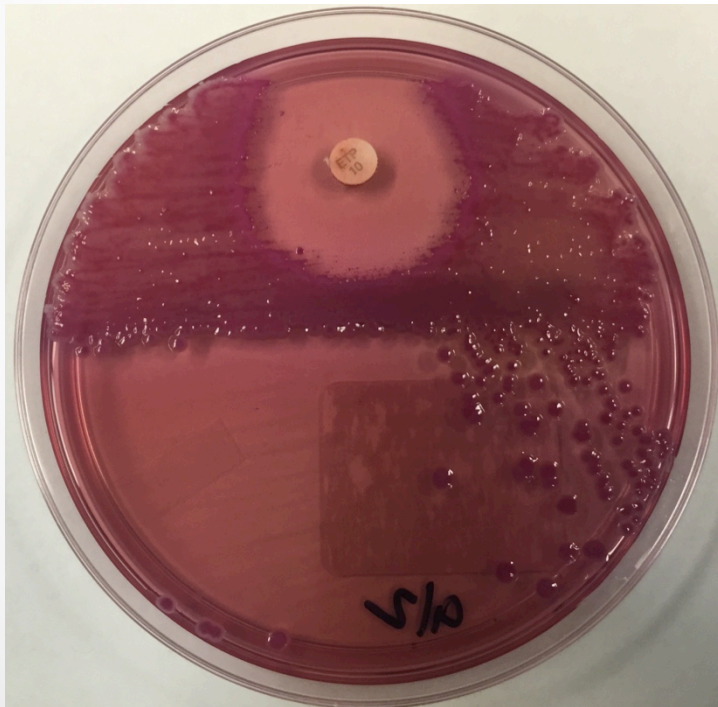
Pos: Cloverleaf; Neg: No cloverleaf

More about phenotypic detection

- CLSI subcommittee has recommended that MHT be removed in January 2018
- mCIM and Carba-NP will be the recommended phenotypic detection methods
- Although Carba-NP currently listed for Acinetobacter in CLSI, subcommittee has recommended removal in January 2018, so must test Acinetobacter genetically
- If you want to consider adding mCIM:
 - Consider validation:
 - Request isolates from CDC AR Bank
 - Use isolates that you submitted for testing elsewhere (but be careful to compare mCIM against mCIM rather than against previous MHT)

Establish regional laboratories as a national resource for AR testing and characterization

- Contact surveillance or point prevalence study
 - Cepheid approved by FDA
 - Direct plating

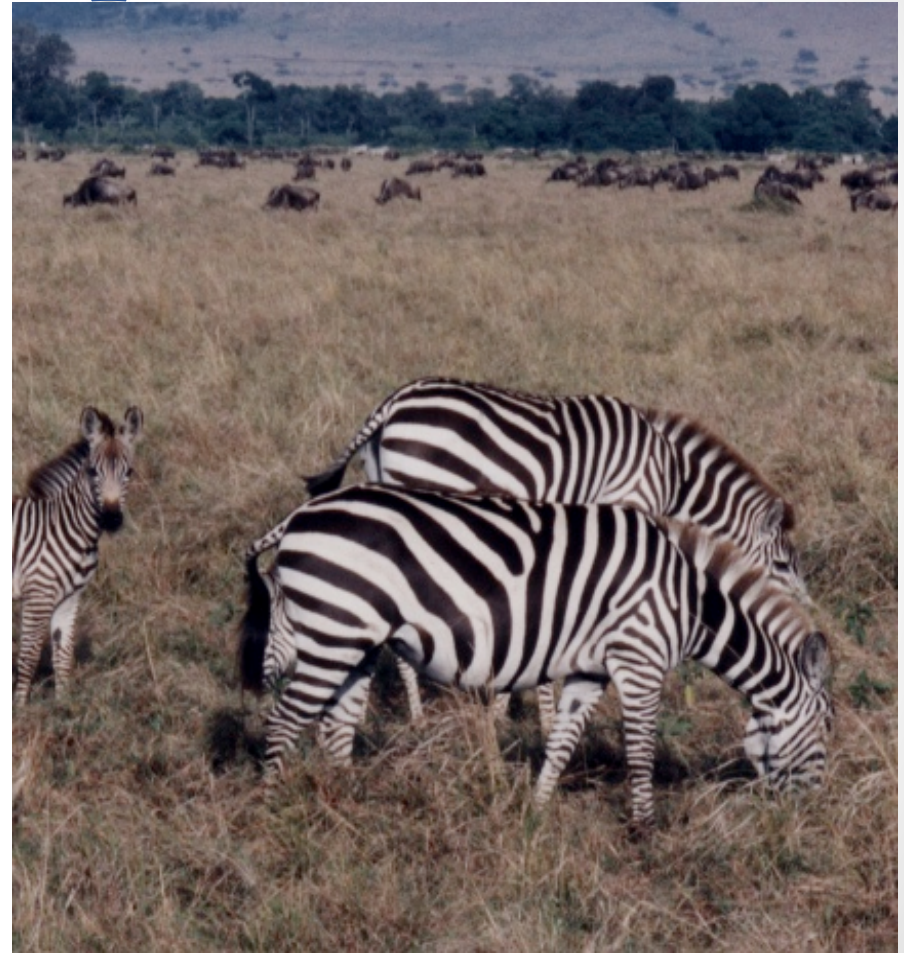


- Regional Lab
 - Broth Microdilution
 - Able to detect carbapenemases that Cepheid does not
 - Mcr testing
 - Help with contact surveillance
 - May help with outbreak investigation
- CDC resources
 - Provide testing for additional antimicrobials
 - Help with outbreak investigation if approved
 - Will provide epi help and advise re facility investigation/monitoring/surveillance

Key partners for detecting an unusual problem



Astute microbiologist/laboratorian



Astute facility personnel

Questions



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