Infective Endocarditis
Diagnostic Testing for Identification of Microbiological Etiology

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Utilization Message

- As you view this presentation, consider the following important points regarding the laboratory testing of endocarditis:
  - Which tests should you use?
  - When should these tests be used?
Introduction

- Infective endocarditis
  - Identification of microbial etiology essential
- Microbiology
  - Staphylococci & streptococci ~80%
  - Enterococci ~10%
  - Gram-negative bacilli (HACEK group, non-HACEK) ~5%
  - Challenging to cultivate organisms → Coxiella burnetii, Bartonella species, Tropheryma whipplei
- Modified Duke criteria
  - ≥2 blood cultures positive, microorganism consistent with infective endocarditis
  - Positive Q fever serology

Importance of Blood Cultures
Blood Cultures
Infective Endocarditis Diagnosis

3 sets of blood cultures - 1 aerobic + 1 anaerobic bottles per set; OR
2 sets of blood cultures - 2 aerobic + 1 anaerobic bottles per set
• Yield directly related to volume blood cultured
• Most/all blood cultures should be positive
• Unnecessary
  • Separation of blood culture draws over time
  • Terminal blind subcultures
  • Prolonged incubation (except *Cutibacterium acnes*)

Culture-Negative Endocarditis

• 2-40% of cases
• Causes
  • Concomitant or antecedent antibacterial therapy
  • Organism does not grow in routine blood cultures
    • *Coxiella burnetii* - 28-37%
    • *Bartonella* species - 12-28%
    • *Tropheryma whippelii* - 6%
    • *Cutibacterium acnes*
    • *Mycoplasma hominis*
    • etc.
Culture-Negative Endocarditis Blood Tests

- Serology
  - *Coxiella burnetii*
    - Anti-phase I IgG *C. burnetii* titers ≥1:800
  - *Bartonella* species
  - *(Brucella* species)*
- Nucleic acid amplification tests
  - *C. burnetii*
  - *Bartonella* species
  - *Tropheryma whipplei*

Excised Cardiac Valvular Tissue Histopathology

- Gross examination: Vegetations soft, friable or firm; size varies
  - Discrete vegetations may be absent
- Representative sections valvular material → histopathology
  - Patterns, degrees of inflammation vary depending on organism
    - High virulence organisms → acute inflammation
    - Less virulent organisms → fibrin deposition, mononuclear cells
  - *Bartonella* species, *Coxiella burnetii, Tropheryma whipplei* endocarditis → chronic inflammation, may be grossly normal
    - *T. whipplei* endocarditis → foamy macrophages
Excised Cardiac Valvular Tissue Histopathology

- Bacteria → basophilic or eosinophilic colonies on H&E stained tissue
- Stains
  - Tissue Gram stain - may fail to highlight some bacteria
  - Grocott-Gomori methenamine silver stain - bacteria
  - Periodic acid-Schiff (PAS) - bacteria
  - Warthin-Starry - non-specific, background
  - Ziehl-Nielson - acid fast bacteria
- Visualization of organisms in tissue ≠ active endocarditis

Excised Cardiac Valvular Tissue Culture

- Low sensitivity
  - Positive cultures – 6-26%
- Low specificity
  - Microorganism different from blood culture or valve
  - PCR ~1/3rd cases
  - Valves from patients without endocarditis falsely-positive (1/4 to 1/3 cases)
**Excised Cardiac Valvular Tissue Culture**

- Avoid valve culture
  - Valve removed for reasons other than endocarditis
  - Blood culture-positive endocarditis
  - Blood culture-negative endocarditis
  - Only perform if sufficient tissue available for all tests of interest
    - Do not prioritize over more sensitive assays (e.g., nucleic acid amplification tests)

**Excised Cardiac Valvular Tissue Nucleic Acid Amplification Tests**

- Broad-range bacterial PCR/sequencing
- Organism-specific PCR assays
  - *Coxiella burnetii* (Q fever) PCR
  - *Bartonella* PCR
  - *Tropheryma whippelii* PCR
  - *Mycoplasma hominis* PCR
HOT TOPIC / Infective Endocarditis: Diagnostic Testing for Identification of Microbiological Etiology