



# Infective Endocarditis

Diagnostic Testing for Identification of Microbiological Etiology

HOT TOPIC / 2018

HOT TOPIC / Infective Endocarditis: Diagnostic Testing for Identification of Microbiological Etiology



*Presenter:*

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## Disclosures

- Board Member: ASM
- Grant Recipient: CD Diagnostics, BioFire, Curetis, Merck, Hutchison Biofilm Medical Solutions, Accelerate Diagnostics, Allergan, The Medicines Company
- Consultant: Curetis, monies paid to Mayo Clinic
- Patent on *Bordetella pertussis/parapertussis* PCR issued, patent on a device/method for sonication with royalties paid to Mayo Clinic, patent on an anti-biofilm substance issued
- DSMB: Actelion, money paid to Mayo Clinic
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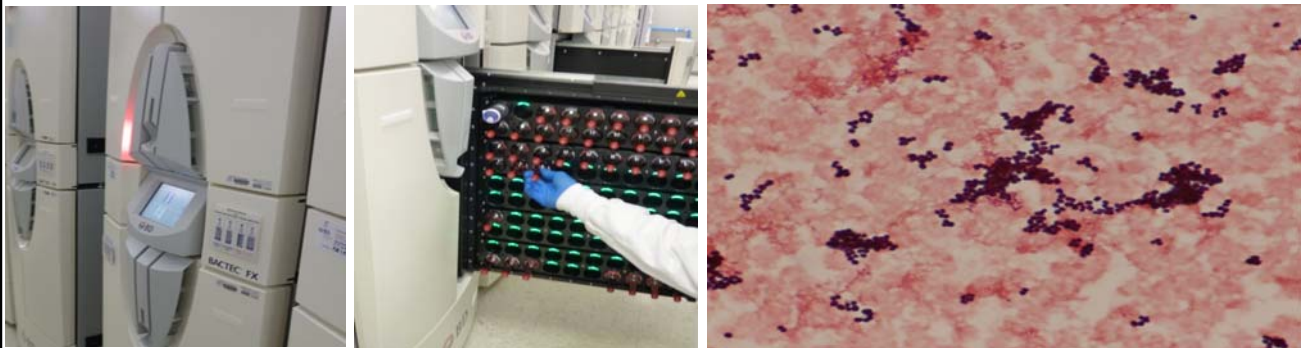
## Utilization Message

- 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 whipplei* - 6%
    - *Cutibacterium acnes*
    - *Mycoplasma hominis*
    - etc.

## Culture-Negative Endocarditis Blood Tests

- Serology
  - *Coxiella burnetii*
    - Anti-phase I IgG *C. burnetii* titers  $\geq 1:800$
  - *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

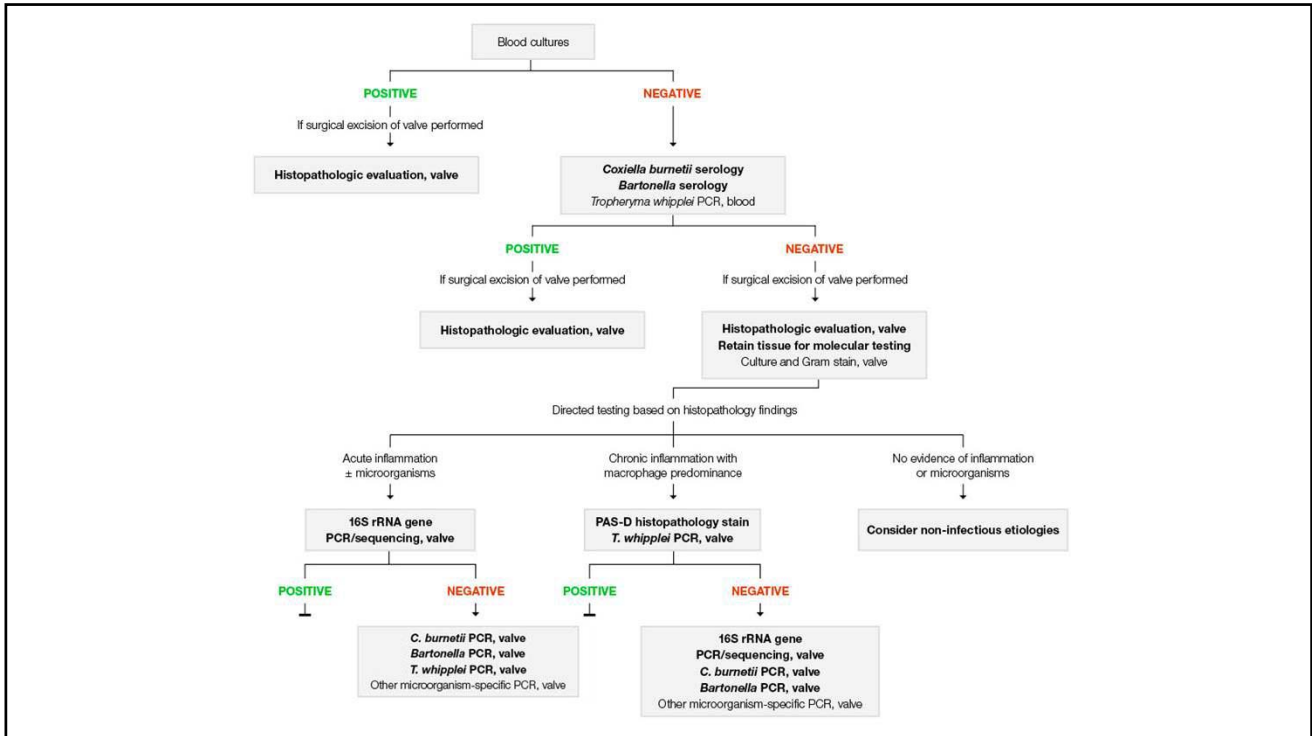
- Low sensitivity
  - Positive cultures – 6-26%
- Low specificity
  - Microorganism different from blood culture or valve  
PCR ~1/3<sup>rd</sup> cases
  - Valves from patients without endocarditis falsely-  
positive (1/4 to 1/3 cases)

## 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 whipplei* PCR
  - *Mycoplasma hominis* PCR



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## Reference

1. Liesman R, Pritt B, Maleszewski J, Patel R: Laboratory Diagnosis of Infective Endocarditis. J Clin Microbiol 2017 Sept 55:2599-2608

## Questions or requests...

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