Infective Endocarditis:
Diagnostic Testing for Identification of Microbiological Etiology

Blood cultures\(^1\)

- **POSITIVE**
  - If surgical excision of valve performed
    - **POSITIVE**
      - PATHC / Pathology Consultation\(^4\)
    - **NEGATIVE**
      - If surgical excision of valve performed
        - **POSITIVE**
          - PATHC / Pathology Consultation\(^4\)
        - **NEGATIVE**
          - PATHC / Pathology Consultation\(^4\)

- **NEGATIVE**
  - If surgical excision of valve performed
    - **POSITIVE**
      - PATHC / Pathology Consultation\(^4\)
    - **NEGATIVE**
      - PATHC / Pathology Consultation\(^4\)

Directed testing based on histopathology findings

Acute inflammation ± microorganisms

- **POSITIVE**
  - BRBPS / Broad Range Bacterial PCR and Sequencing
    - **POSITIVE**
      - CBPR / Coxiella burnetii (Q fever), Molecular Detection, PCR
    - **NEGATIVE**
      - BRBPS / Broad Range Bacterial PCR and Sequencing

- **NEGATIVE**
  - BRBPS / Broad Range Bacterial PCR and Sequencing
    - **STOP**

Chronic inflammation with macrophage predominance

- **POSITIVE**
  - PAS-D histopathology stain\(^5\)
    - **POSITIVE**
      - TWRP / Tropheryma whippeli, Molecular Detection, PCR
    - **NEGATIVE**
      - TWRP / Tropheryma whippeli, Molecular Detection, PCR

- **NEGATIVE**
  - TWRP / Tropheryma whippeli, Molecular Detection, PCR
    - **STOP**

No evidence of inflammation or microorganisms

Consider noninfectious etiologies

This algorithm is intended for use in patients with clinical and/or echocardiographic findings suggestive of infective endocarditis, based on the modified Duke criteria.

1 Per American Heart Association, European Society of Cardiology, and British Society for Antimicrobial Chemotherapy guidelines, 2 (or more) blood cultures should be positive for a typical microorganism consistent with infective endocarditis (ie, viridans group streptococci, HACEK group bacteria, Staphylococcus aureus, community-acquired Enterococcus species in the absence of a primary focus) to define a positive result.

2 *C. burnetii* anti-phase I IgG antibody titer ≥1:800 is considered indicative of *C. burnetii* endocarditis.

3 The sensitivity of *T. whippeli* PCR from blood in endocarditis is unknown; a negative result should not be used to rule out *T. whippeli* endocarditis.

4 Histologic examination is used to evaluate for infectious and noninfectious etiologies and correlate with microbiology test results.

5 If surgery is not performed, consider testing for noninfectious etiologies.

6 Ideally, a representative sample of valvular tissue should be collected specifically for molecular testing in the operating room in a sterile fashion.

7 If sufficient valvular tissue is available after sampling for histopathological and molecular (microorganism-specific and broad range) testing, consider culture and Gram stain. Due to the low sensitivity and specificity of culture, molecular testing should be prioritized over culture.

8 PAS-D, periodic acid Schiff with diastase. Macrophages infected with *T. whippeli* will stain PAS positive following diastase digestion. Specialty stains are ordered as appropriate by the reviewing pathologist.