


**TABLE 93-4** NONSPECIFIC LABORATORY TESTS FOR INFECTIVE ENDOCARDITIS

LABORATORY FINDINGS	PERCENTAGE
Anemia	70-90
Leukocytosis	20-30
Elevated ESR	90-100
C-reactive protein (CRP)	100
Histiocytes in blood smear	25
Positive rheumatoid factor (RF)	50
Circulating immune complexes	65-100
Microscopic hematuria	30-50

Data from Bruschi JL: Clinical manifestations of endocarditis. In Bruschi JL, editor: Infective endocarditis, New York, 2007, Informa Healthcare, pp 143-166.  
ESR, Erythrocyte sedimentation rate.

vegetations. A difficult infectious CNE diagnosis is Q fever. Q fever SBE may be suggested by a history of animal contact. Clinical findings of Q fever are often present, but the diagnosis can be missed because Q fever vegetations are not easily visualized.

### Laboratory Findings

With IE, many nonspecific laboratory abnormalities may occur (Table 93-4); when placed in the appropriate context, these can be a significant aid to diagnosis.

Echocardiography is an important element in diagnosis and management; it should be performed for all patients with suspected IE. In those with a low likelihood of having IE or small body habitus, a transthoracic echocardiogram (TTE) may be sufficient. Although TTE is often sufficient to screen for NVE, the “gold standard” remains transesophageal echocardiogram (TEE), which is more sensitive at detecting smaller vegetations, paravalvular abscess, and PVE. If the TTE or TEE demonstrates a vegetation but blood cultures remain negative, the diagnosis of infectious CNE should be considered. A tiered diagnostic approach to such cases is presented in Table 93-5.

Diagnosis of *Legionella*-related IE is based on an antecedent pneumonia and elevated titers of urinary antigen. *Brucella*-related IE is confirmed by titers or by polymerase chain reaction or both. A clue to Q fever CNE is enhanced valve uptake on positron-emission tomography (PET) or computed tomography (CT), and such a result should prompt testing for Q fever. With the advent of sophisticated microbiologic testing, HACEK organisms (*Haemophilus* spp, *Aggregatibacter actinomycetemcomitans* [formerly called *Actinobacillus actinomycetemcomitans*], *Cardiobacterium hominis*, *Eikenella corrodens*, and *Kingella kingae*) grow relatively rapidly and no longer manifest as CNE.

Radiologic testing in IE is primarily focused on identifying complications of IE. Although echocardiography is still the preferred method for detecting vegetations, improvements in multislice CT scans have allowed chest CT to detect vegetations and valvular abnormalities in addition to the septic emboli seen in right-sided IE. Magnetic resonance imaging (MRI) of the spine is useful in patients with IE who report back pain; it is the preferred method to detect the presence of vertebral osteomyelitis caused by IE. Mental status changes should prompt CT or MRI imaging of the head to assess for septic emboli to the brain. Although it is less invasive than TEE, cardiac MRI often lacks the special resolution to detect smaller vegetations; however, it may

**TABLE 93-5** DIAGNOSTIC APPROACH TO CULTURE-NEGATIVE ENDOCARDITIS

#### VALVULAR BIOPSY UNAVAILABLE

1. Q fever and *Bartonella* serology: If negative, then use lysis-centrifugation system for blood cultures and inform microbiology laboratory of concern for fastidious organisms to allow use of special media and culture techniques: thioglycolate-, pyridoxal hydrochloride-, or L-cystine-enriched media for *Abiotrophia*; buffered charcoal yeast extract (BCYE) agar for *Legionella*; prolonged incubation for HACEK organisms\*
2. Rheumatoid factor (RF), antinuclear antibodies (ANA)
3. PCR for *Bartonella* spp and *Tropheryma whippelii*
4. Nested PCR for fungi, tissue for *Cryptococcus neoformans* capsular antigen and urine for *Histoplasma capsulatum* antigen: If negative, then obtain serum serology studies for *Mycoplasma pneumoniae*, *Legionella pneumophila*, *Brucella melitensis*, and *Bartonella* spp by Western blot

#### VALVULAR BIOPSY AVAILABLE

1. Broad-range PCR for bacteria (16S rRNA) and fungi (18S rRNA)
2. Histologic examination with direct staining for *Chlamydia* spp, *Coxiella burnetii*, *Legionella* spp, fungi, and *T. whippelii*
3. Primer extension enrichment reaction (PEER) or autoimmunohistochemistry (AIHC)

Modified from Fournier PE, Thuny F, Richet H, et al: Comprehensive diagnostic strategy for blood culture-negative endocarditis: a prospective study of 819 new cases, Clin Infect Dis 51:131-140, 2010; and Mylonakis E, Calderwood SB: Infective endocarditis in adults, N Engl J Med 345:1320, 2001.

PCR, Polymerase chain reaction; rRNA, ribosomal RNA.

\*HACEK organisms: *Haemophilus* spp, *Aggregatibacter actinomycetemcomitans*, *Cardiobacterium hominis*, *Eikenella corrodens*, and *Kingella kingae*.

be helpful in identifying aortic root pseudoaneurysms, sinus of Valsalva aneurysms, and embolic vascular lesions.

### Differential Diagnosis and Mimics

The diagnosis of SBE is based on an otherwise unexplained high-grade or continuous bacteremia caused by a known endocarditis pathogen plus a cardiac vegetation. Depending on the duration before presentation (usually 1 to 3 months), IE may be accompanied by peripheral manifestations such as Osler's nodes, Janeway's lesions, splinter hemorrhages, or conjunctival hemorrhages. Splenomegaly or embolic phenomena may also accompany SBE. However, peripheral manifestations that are seen in SBE may also be present in other disorders. Before ascribing peripheral manifestations to SBE, physicians need to rule out other systemic disorders and confirm the diagnosis of SBE.

Clinically, the disorders most likely to mimic SBE are Libman-Sacks endocarditis (associated with systemic lupus erythematosus [SLE]), marantic endocarditis (caused by a malignancy, usually lymphoma, lung cancer, or pancreatic cancer), and atrial myxoma. Myocarditis of any etiology may mimic SBE with fever, murmur, and peripheral embolic phenomena. Cardiomegaly, which is usually present with myocarditis, is typically absent with SBE. Leukopenia and thrombocytopenia may be clues to viral myocarditis, and either finding argues against a diagnosis of SBE. Cardiac echocardiography shows myocarditis but no vegetations, and bacteremia is not present.

SLE, particularly between flares, may mimic SBE with low-grade fevers, murmur, peripheral manifestations, and splenomegaly. Laboratory findings in SLE include the anemia of chronic disease and a mildly to moderately elevated erythrocyte sedimentation rate (ESR). Even if Libman-Sacks vegetations are present, SBE is rare in SLE. A lupus flare may resemble ABE with high fevers (>102° F), tender fingertips (mimicking Osler's