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Laboratory Methods for the Detection of Lyme Disease and Other Tick-Transmitted Diseases

Background

Despite many advances, the algorithm for the laboratory diagnosis of Lyme Disease (LD) and other tick-transmitted diseases remains complex. Laboratory diagnostics must still be considered an adjunct to the clinical diagnosis of LD. The characteristic erythema migrans (EM) rash is quite specific when an experienced clinician examines the patient.

Lyme Disease

Serologic Studies

Serologic methods (i.e. the detection of antibodies directed against *Borrelia burgdorferi*, the causative agent of LD) remain the primary method of LD diagnosis. Current CDC recommendations are based upon a now standard two-tier approach:

1. Screen with Enzyme Immunoassay (EIA):
    a. A negative result rules out LD. If clinically indicated, consider retesting by EIA in two weeks, especially if the tick exposure was recent.
2. If screen results are positive or equivocal, confirm with Western Blot (WB):
    a. IgG and IgM WB if duration of symptoms is $\leq$ 4 weeks.
    b. IgG WB alone if duration of symptoms is > 4 weeks.

WB is considered the definitive serologic test due to its superior specificity over the EIA. However, it should NOT be used as a screening tool since it is a) no more sensitive than EIA; b) has a longer turn-around time compared to EIA; and c) more expensive than EIA.

The CDC two-tier algorithm has been found to have the following performance:

LD Type	Sensitivity (%)
Acute	40
Post EM convalescence	68
Neuroborreliosis	87
Lyme arthritis	99

Because of the lower sensitivity of the algorithm in early disease, negative or equivocal results during this period should be repeated in 2 weeks if LD is clinically suspected. Since anti-*Borrelia* antibodies have been found to rise, fall, or remain unchanged in LD, serologic testing is only useful to initially demonstrate seroconversion. It should not be used as a test of cure, to monitor progress of the disease, or to rule out reinfection. Serological testing in cases presenting with classical primary EM is unwarranted, since the sensitivity of serological tests is at its lowest in early Lyme disease, and their use may therefore result in confounding false negative results.

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Borrelia Culture of Skin

Skin culture using special techniques is most appropriate for:

1. Patients having skin lesions suspicious for, but not pathognomonic of EM.

2. When the primary lesion occurs outside the usual tick season (i.e. December – April).

3. After tick exposure in a geographical area where an enzootic cycle of *B. burgdorferi* has not been established with certainty.

Skin culture is usually not cost-effective in disseminated EM since the lesions are typically diagnostic. Culture of sources other than skin (e.g. synovial fluid, CSF and blood) is not routinely recommended due to the extremely low yield. Contact the laboratory if special circumstances exist which warrant culture.

***B. burgdorferi* PCR**

1. PCR testing can be helpful in establishing a diagnosis of Lyme arthritis (synovial fluid) or neuroborreliosis (CSF), and to help in the assessment of response to therapy. The clinical utility of PCR is better established for synovial fluid than for CSF (i.e. a negative PCR on CSF does not exclude neuroborreliosis).

2. If LD is specifically suspected, *B. burgdorferi* PCR should be ordered instead of a direct specimen 16S rRNA sequencing study, since the former is more sensitive for *B. burgdorferi* than is the latter.

CSF Lyme Index

This test determines the CSF:Serum ratio of anti-*B. burgdorferi* antibodies. A ratio of > 1 is considered suggestive of neuroborreliosis. This test is not available in an FDA-approved format, and has in general been replaced by the *B. burgdorferi* PCR. Contact the microbiology lab for more information.

Blood Smear

In contrast to other agents of tick-borne illness, *B. burgdorferi* does not cause a significant bacteremia. Blood smears are consequently not recommended.

Other Tick-Borne Diseases

In cases where the patient has symptoms consistent with LD, (especially if tick exposure has been documented) but LD serology is negative, other tick-borne diseases should be considered in this order: Human Granulocytic Anaplasmosis (*Anaplasma phagocytophilum*), Babesiosis (*Babesia microti*). Laboratory diagnostics indicated for these two diseases are:

1. Antibody studies
2. Blood smear
3. PCR, blood

Contact Information

Marshfield Labs Customer Service 800-222-5835.

Questions or Comments

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- Thomas Novicki, Ph.D., Clinical Microbiologist
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Selected Readings

CDC. Notice to readers: caution regarding testing for Lyme disease. MMWR 2005. 54:125

CDC. Recommendations for test performance and interpretation from the Second National Conference on Serologic Diagnosis of Lyme disease. MMWR 1995. 44:590

Ledue, TB, MF Collins, and WY Craig. New laboratory guidelines for serologic diagnosis of Lyme disease: evaluation of the two-test protocol. J Clin Microbiol 1996. 34:2343

Reed, KD. Laboratory testing for Lyme disease: possibilities and practicalities. J Clin Microbiol 2002. 40:319

Aguero-Rosenfeld, ME, G Wang, I Schwartz, and GP Wormser. Diagnosis of Lyme borreliosis. Clin Microbiol Rev 2005. 18:484

Tugwell, P, DT Dennis, A Weinstein *et al*. Laboratory evaluation in the diagnosis of Lyme disease. Ann Intern Med 1997. 127:1109

GP Wormser, RB Nadelman, RJ DAttwyler *et al*. Practice guidelines for the treatment of Lyme disease. Clin Infect Dis 2000. 31(suppl 1): S1.