Infectious Disease Society of America (IDSA) Clinical Practice Guidelines

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About the IDSA

- The IDSA is a member organization of over 12,000 physicians, scientists, and public health experts who specialize in infectious diseases
- Mission: to improve the health of individuals, communities, and society by promoting excellence in patient care, education, research, public health, and prevention relating to infectious diseases
- Clinical Practice Guidelines: developed by a panel of experts who perform a systematic review of the available evidence, assess the quality/certainty of the evidence, and develop evidence-based recommendations to inform clinical decision making

Requirements for Guideline Development

- IDSA requires that guideline developers adhere to all of the following (minimum requirements):
  1. The IDSA Handbook for Clinical Practice Guidelines Development
  2. The Institute of Medicine's (IOM) Standards for Developing Trustworthy Clinical Practice Guidelines
  3. The GRADE Working Group approach: Grading of Recommendations Assessment, Development and Evaluation (GRADE) – assesses the quality (or certainty) of evidence & strength of recommendations

https://www.idsociety.org/practice-guideline/clinical-practice-guidelines-development-training-and-resources/

1. Rating the quality of the evidence

1. Establish initial level of confidence

Study design	*Initial confidence in an estimate of effect*
Randomized trials ➔	High confidence
Observational studies ➔	Low confidence

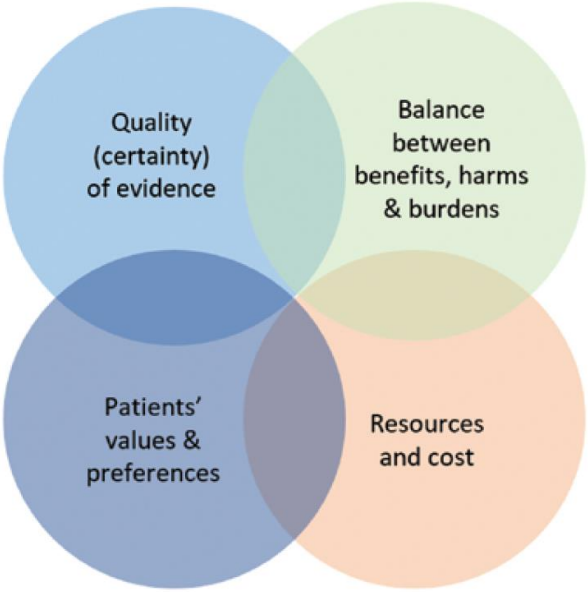
2. Consider lowering or raising level of confidence

Reasons for considering lowering or raising confidence	
↓ Lower if	↑ Higher if
Risk of Bias	Large effect
Inconsistency	Dose response
Indirectness	All plausible confounding & bias • would reduce a demonstrated effect or • would suggest a spurious effect if no effect was observed
Imprecision	
Publication bias	

3. Final level of confidence rating

Confidence in an estimate of effect across those considerations
High ⊕⊕⊕⊕
Moderate ⊕⊕⊕◯
Low ⊕⊕◯◯
Very low ⊕◯◯◯

2. Determinants of the Strength of Recommendation



3. Implication of the Strength of Recommendation

Strong

- ❖ Population: Most people in this situation would want the recommended course of action and only a small proportion would not
- ❖ Health care workers: Most people should receive the recommended course of action
- ❖ Policy makers: The recommendation can be adapted as a policy in most situations

Weak

- ❖ Population: The majority of people in this situation would want the recommended course of action, but many would not
- ❖ Health care workers: Be prepared to help people to make a decision that is consistent with their own values/decision aids and shared decision making
- ❖ Policy makers: There is a need for substantial debate and involvement of stakeholders

Organizations That Follow GRADE

https://www.gradeworkinggroup.org/

NH DIVISION OF Public Health Services
Department of Health and Human Services

Clinical Practice Guidelines Developed by IDSA

- Lyme Disease
- Babesiosis
- Community-Acquired Pneumonia
- Hospital-acquired and Ventilator-associated Pneumonia
- Urinary Tract Infections (uncomplicated cystitis and pyelonephritis)
- Asymptomatic Bacteriuria
- Periprosthetic Joint Infections
- Vertebral Osteomyelitis
- Skin and Soft Tissue Infections
- Treatment of Drug-Susceptible TB
- Treatment of Drug-Resistant TB
- Nontuberculous Mycobacterial (NTM) Diseases
- COVID-19
- Influenza
- Clostridium difficile
- Neurocysticercosis
- Leishmaniasis
- Coccidioidomycosis
- Aspergillosis
- Candidiasis
- Infectious Diarrhea
- Hepatitis C Virus (HCV) Guidance
- Endocarditis
- Prevention and Treatment of Opportunistic Infections Among Adults, Adolescents, and Children
- Antimicrobial Prophylaxis in Adults with Cancer-related Immunosuppression
- Vancomycin

https://www.idsociety.org/practice-guideline/practice-guidelines/#/date_na_dt/DESC/0/+/?Status=Current

Clinical Practice Guidelines for the Prevention, Diagnosis and Treatment of Lyme Disease (*Updated 11/30/2020*)

- Guidelines authored by the IDSA, American Academy of Neurology (AAN), and the American College of Rheumatology (ACR)
- Followed the systematic processes used in the development of IDSA, AAN, and ACR clinical practice guidelines
- Guideline Panel composed of 36 people from multiple other disciplines

https://www.idsociety.org/practice-guideline/lyme-disease/

Guideline Panel Composition

- Infectious Disease Society of America (IDSA)
- American Academy of Neurology (AAN)
- American College of Rheumatology (ACR)
- American Academy of Family Physicians (AAFP)
- American Academy of Pediatrics (AAP)
- American College of Physicians (ACP)
- Child Neurology Society (CNS)
- Pediatric Infectious Diseases Society (PIDS)
- Entomological Society of America (ESA)
- Association of Medical Microbiology and Infectious Disease (AMMI) Canada
- European Society of Clinical Microbiology and Infectious Diseases (ESCMID)
- Members representing disciplines of cardiology, microbiology, pathology, and methodologist with expertise in GRADE
- 3 patient representatives
- 1 healthcare consumer representative

General Principles: Diagnostic Testing

- Antibody tests are first-line for the laboratory diagnosis of Lyme disease
- Antibody tests are “highly sensitive” in patients with extracutaneous manifestations that develop weeks to months after initial infection
- Untreated patients that are negative for *B. burgdorferi* IgG antibodies with months to years of symptoms “essentially rules out the diagnosis of Lyme disease”

General Principles: Diagnostic Testing

- Antibody tests should be performed using clinically validated assays in either:
  - a standard 2-tiered testing protocol, in which an enzyme immunoassay (EIA) or indirect fluorescent antibody test (IFA) is followed by IgM and IgG immunoblots, or
  - a modified 2-tiered testing protocol in which 2 different EIAs are performed sequentially or concurrently without the use of immunoblots
- Antibody tests are intended for use in a 2-tiered testing protocol, rather than as stand-alone tests because this improves specificity (i.e., prevents false-positive results)

Limitations of Antibody Tests

- It can take a few weeks after exposure to any pathogen for a person to develop antibodies
- Therefore, antibody tests can/will be falsely negative in the first days to weeks after an initial exposure
  - When someone develops erythema migrans, for example, most people will test negative
- Alternatively, antibodies (both IgM and IgG) can persist for decades after an infection – so antibody tests don't tell you when an infection necessarily occurred
- There is no "test of cure"

Limitations of Antibody Tests

- People can be infected multiple times – so for someone with known past history of Lyme disease, diagnosis may have to rely on clinical features and exclusion of alternative diagnoses
- False-positive test results can occur (there can be cross-reactive antibodies to other microbes or due to autoimmune disease)
  - Clinicians should be selective when ordering tests in patients with a low probability of Lyme disease
  - Prevalence and “pre-test probability” of disease influences the positive-predictive value of a test

Specific IDSA Diagnostic Testing Recommendations

Testing of Asymptomatic Patients Following Tick Bites

1. "We recommend <u>against</u> testing asymptomatic patients for exposure to *B. burgdorferi* following an *Ixodes* spp. Tick bite."
   (strong recommendation, moderate-quality evidence)

Rationale

- Immediately following a tick-bite, an asymptomatic patient would have a negative antibody test, unless the patient had a prior infection.
- Although follow-up testing 4-6 weeks after the tick bite could detect asymptomatic seroconversion (antibody positivity), IDSA recommends against testing because there is insufficient evidence that patients with asymptomatic antibody positivity (seropositivity) should receive antibiotic therapy.

Testing for Erythema Migrans (Early Disease)

1. "In patients with potential tick exposure in a Lyme disease endemic area who have 1 or more skin lesions compatible with erythema migrans, we recommend clinical diagnosis rather than laboratory testing"
   (strong recommendation, moderate-quality evidence)
2. "In patients with 1 or more skin lesions suggestive of, but atypical for erythema migrans, we suggest antibody testing performed on an acute-phase serum sample (followed by a convalescent-phase serum sample if the initial result is negative)"
   (weak recommendation, low-quality evidence)

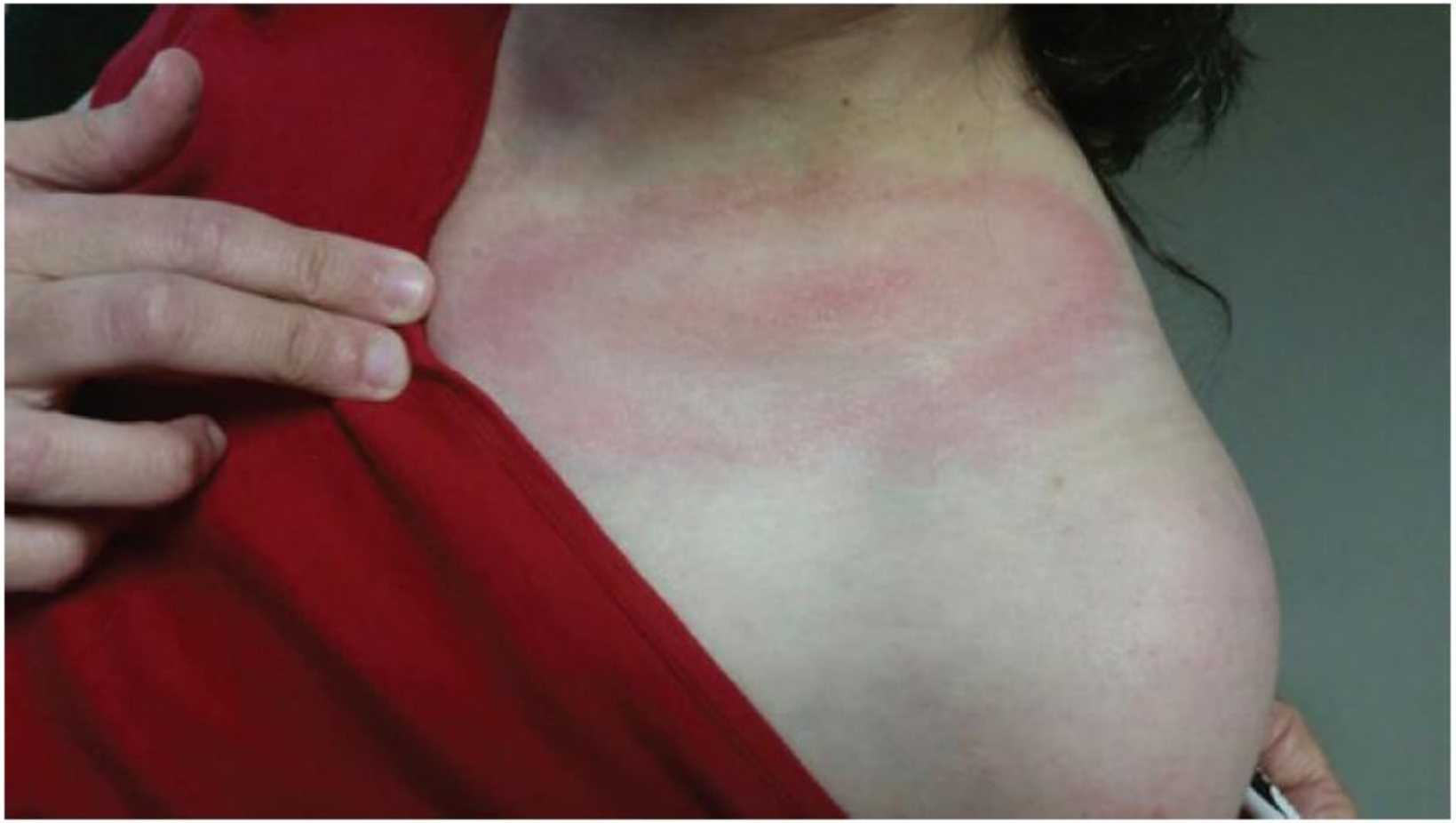


Figure 7. Early Lyme rash.

Rationale

- “acute” and “convalescent” antibody tests should be collected at least 2-3 weeks apart (to give antibodies a chance to develop)
- If antibody testing is done within the 1-2 weeks after noticing the erythema migrans rash, as few as 20-40% of people will test positive

Testing for Lyme Neuroborreliosis (neurologic Lyme disease)

1. "When assessing patients for possible Lyme neuroborreliosis involving either the PNS or CNS, we recommend serum antibody testing…"
   (strong recommendation, moderate-quality of evidence)
2. "If CSF testing is performed in patients with suspected Lyme neuroborreliosis involving the CNS, we… recommend obtaining simultaneous samples of CSF and serum for determination of the CSF:serum antibody index, carried out by a laboratory using validated methodology…"
   (strong recommendation, moderate-quality)

Rationale

- Neurological symptoms typically develop several weeks after initial infection, which should be sufficient time for the development of a detectable serum antibody response
- Therefore, most patients with early Lyme neuroborreliosis are seropositive by conventional 2-tiered testing at the time of initial clinical presentation
- If initially antibody testing is negative, they should be positive on repeat testing several weeks later

Testing for Lyme Arthritis (symptoms of an infected swollen joint)

1. "When assessing possible Lyme arthritis, we recommend serum antibody testing over PCR or culture of blood or synovial fluid/tissue"
   (strong recommendation, moderate-quality evidence)
2. "If seropositive patients for whom the diagnosis of Lyme arthritis is being considered but treatment decisions require more definitive information, we recommend PCR applied to synovial fluid or tissue rather than *Borrelia* culture of those samples"
   (strong recommendation, moderate-quality evidence)

Rationale

- “Lyme disease serology, particularly IgG seroreactivity, is invariably positive in people presenting with Lyme arthritis…”
- “Numerous studies and meta-analyses have demonstrated that the sensitivity of serum antibody testing in the diagnosis of Lyme arthritis, using conventional 2-tiered testing with Western immunoblotting, is very high – in the range of 95-100%”
- There is moderate to high diagnostic accuracy with use of *B. burgdorferi* PCR on synovial fluid or tissue (reported sensitivity ranges from 71% to 100%)

Summary

- Antibody testing remains the primary diagnostic test to diagnose all stages of Lyme disease except for very early symptoms of lyme disease (i.e., erythema migrans) when diagnosis is clinical
- 4+ weeks after initial infection, antibody tests should be positive and a negative test in most cases "essentially rules out the diagnosis of Lyme disease"
- Re-infection can be difficult to diagnose because antibody tests can be positive for years/decades
- A 2-tier test approach is important to maximize test sensitivity and specific and reduce false-positives