LYME DISEASE

- Lyme disease is a bacterial disease, transmitted through the bite of *Ixodes spp*. or blacklegged ticks.
- Lyme disease is caused by the bacterium *Borrelia burgdorferi* and rarely, *Borrelia mayonii*.
- Typical symptoms include fever, headache, fatigue, and a characteristic skin rash called erythema migrans. If left untreated, infection can spread to joints, the heart, and the nervous system.
- *B. burgdorferi* bacteria only enter the bloodstream transiently, and direct detection methods such as culture or PCR are typically insensitive for most specimen sources (e.g., blood, spinal fluid, etc.). Due to this limitation, diagnostic testing for Lyme disease relies on indirect detection of infection by measuring a patient's antibody response to the spirochete.
- During the evaluation of the variety of testing platforms, it was determined that no single serologic test for Lyme disease was sufficiently sensitive and specific on its own. A standard two-tiered testing (**STTT**) method for serologic diagnosis of Lyme disease was agreed upon to maximize clinical utility.
- All US Food and Drug Administration (FDA) cleared tests were based on the STTT method until 2019, when the FDA cleared assays for use in a modified two-tiered testing (**MTTT**) method, as an alternative serologic approach for detection of Lyme disease.

https://www.cdc.gov/lyme/index.html

https://www.aphl.org/aboutAPHL/publications/Documents/ID-2021-Lyme-Disease-Serologic-Testing-Reporting.pdf

LYME DIAGNOSIS -KEY POINTS TO REMEMBER

- Most Lyme disease tests are designed to detect antibodies made by the body in response to infection.
- Antibodies can take several weeks to develop, so patients may test negative if infected only recently.
- Antibodies normally persist in the blood for **months or even years** after the infection is gone; therefore, the test cannot be used to determine cure.
- Infection with other diseases, including some tickborne diseases, or some viral, bacterial, or autoimmune diseases, can result in **false positive** test results.
- Some tests give results for two types of antibody, IgM and IgG. **Positive IgM results should be disregarded if the patient has been ill for more than 30 days**.

https://www.cdc.gov/lyme/diagnosistesting/index.html

LYME DISEASE CLINICAL PRESENTATION

For the full definition please refer to the ADHS Case Definition Manual

A systemic, tick-borne disease characterized by one of the following early or late-stage manifestations, as reported by a healthcare provider, and in the absence of another known etiology:

- Erythema migrans (EM) rash: For purposes of surveillance, EM is defined as a skin lesion (observed by a healthcare provider) that typically begins as a red macule or papule and expands over a period of days to weeks to form a large round lesion, often with partial central clearing. A single primary lesion must reach greater than or equal to 5 cm in size across its largest diameter.

  Note: Secondary lesions also may occur. Annular erythematous lesions occurring within several hours of a tick bite represent hypersensitivity reactions and do not qualify as EM. For most patients, the expanding EM lesion is accompanied by other acute symptoms, particularly fatigue, fever, headache, mildly stiff neck, arthralgia, or myalgia. These symptoms are typically intermittent. Local reactions to insect bites and stings are often misidentified as EM. As a result, it is important to get additional information about the lesion, including (1) general description (shape and color), (2) was it itchy, painful, or warm to-the-touch, (3) when did the lesion first appear, (4) how many days did it persist, and (5) how much it expanded.

- Musculoskeletal system: Recurrent, brief attacks (weeks or months) of objective joint swelling in one or a few joints, sometimes followed by chronic arthritis in one or a few joints.

  Note: Objective joint swelling may sometimes be followed by chronic arthritis in one or a few joints.

- Nervous system: Any of the following signs that cannot be explained by any other etiology, alone or in combination: lymphocytic meningitis; cranial neuritis, particularly facial palsy (may be bilateral); radiculoneuropathy; or, rarely, encephalomyelitis.

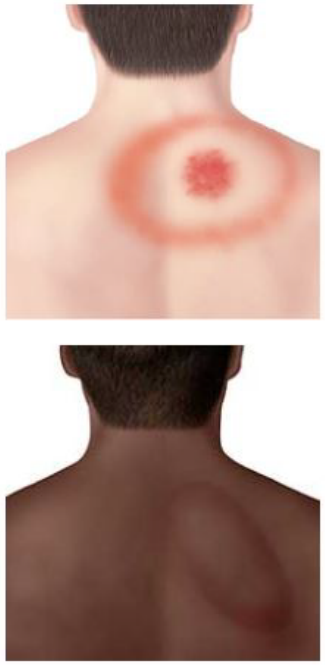
  Note: Headaches, fatigue, paresthesia, or mild stiff necks alone are not criteria for neurologic involvement.

- Cardiovascular system: Acute onset of high-grade (2nd degree or 3rd degree) atrioventricular conduction defects that resolve in days to weeks

  Note: Atrioventricular conduction defects may sometimes be associated with myocarditis.

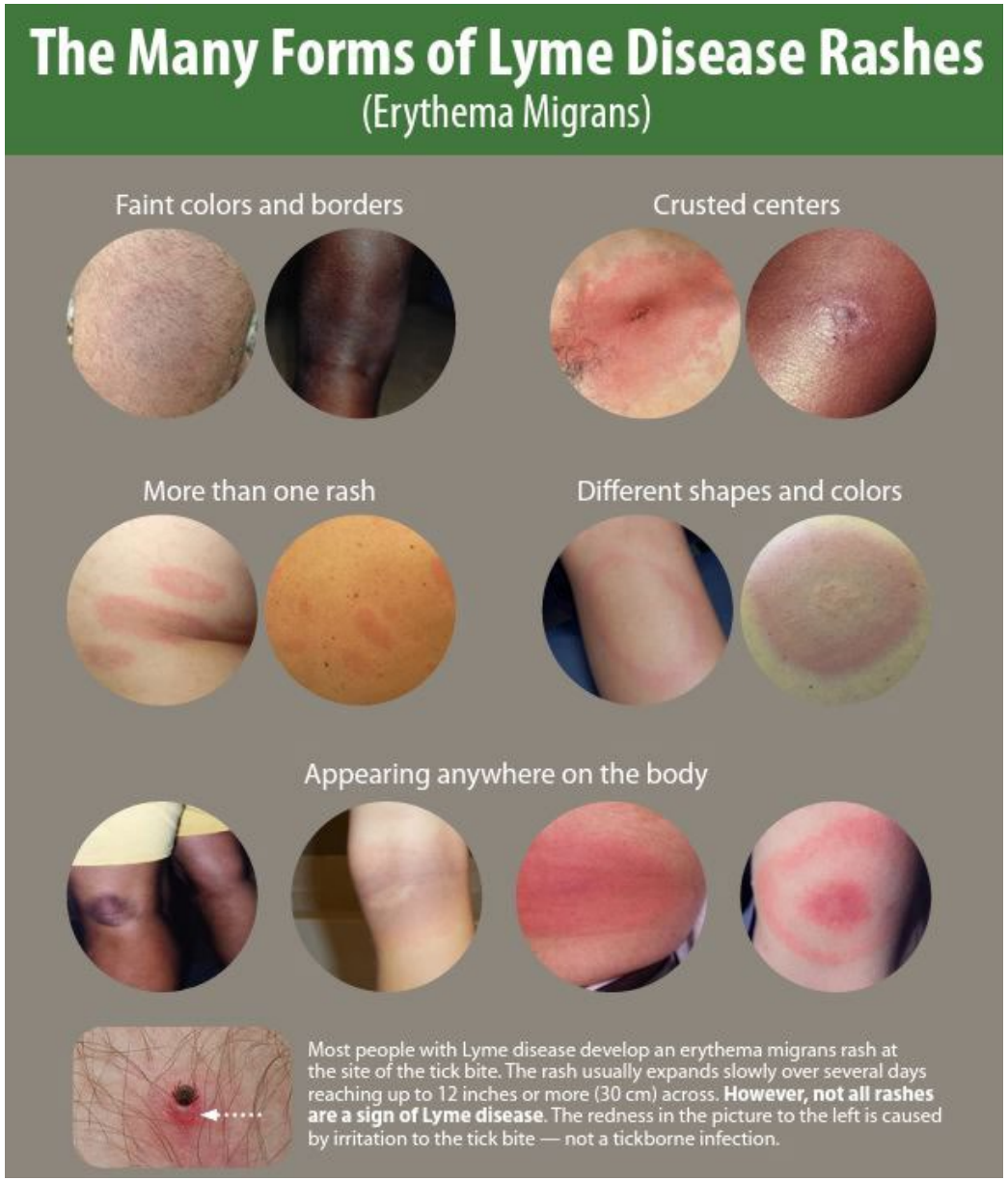
LYME DISEASE CLINICAL PRESENTATION

Early Signs and Symptoms (3 to 30 Days After Tick Bite)



The appearance of the erythema migrans rash can vary widely.

- Fever, chills, headache, fatigue, muscle and joint aches, and swollen lymph nodes may occur in the absence of rash
- Erythema migrans (EM) rash (see photos):
  - Occurs in approximately 70 to 80 percent of infected persons
  - Begins at the site of a tick bite after a delay of 3 to 30 days (average is about 7 days)
  - Expands gradually over several days reaching up to 12 inches or more (30 cm) across
  - May feel warm to the touch but is rarely itchy or painful
  - Sometimes clears as it enlarges, resulting in a target or "bull's-eye" appearance
  - May appear on any area of the body
  - Does not always appear as a "classic" erythema migrans rash



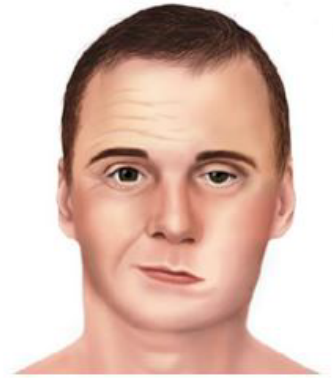
See photos of rashes here: https://www.cdc.gov/lyme/signs_symptoms/rashes.html
https://www.cdc.gov/lyme/signs_symptoms/index.html

https://www.cdc.gov/lyme/resources/NCEZID_rash_poster3r1-508.pdf

LYME DISEASE CLINICAL PRESENTATION

Later Signs and Symptoms (days to months after tick bite)

Swollen Knee



Facial Palsy

- Severe headaches and neck stiffness
- Additional EM rashes on other areas of the body
- Facial palsy (loss of muscle tone or droop on one or both sides of the face)
- Arthritis with severe joint pain and swelling, particularly the knees and other large joints.
- Intermittent pain in tendons, muscles, joints, and bones
- Heart palpitations or an irregular heart beat (Lyme carditis)
- Episodes of dizziness or shortness of breath
- Inflammation of the brain and spinal cord
- Nerve pain
- Shooting pains, numbness, or tingling in the hands or feet

https://www.cdc.gov/lyme/signs_symptoms/index.html

LYME DISEASE - CONFIRMATORY LAB EVIDENCE FOR LOW-INCIDENCE JURISDICTIONS (ARIZONA) (adopted in 2022)

- A positive **culture** for *Borrelia burgdorferi* or *B. mayonii*, OR
- Detection of *B. burgdorferi* or *B. mayonii* in a clinical specimen by a *B. burgdorferi* group-specific **NAAT** assay, OR
- Detection of *B. burgdorferi* group-specific antigens by **immunohistochemical assay** on biopsy or autopsy tissues, OR
- Positive **serologic tests in a two-tier or equivalent format**, including:

    - **Standard two-tier test (STTT):**
        - a positive or equivocal first-tier screening assay, often an enzyme immunoassay [EIA] or immunofluorescence assay [IFA] for IgM, IgG, or a combination of immunoglobulins, followed by
        - a concordant positive IgM or IgG **immunoblot** interpreted according to established criteria, OR

    - **Modified two-tier test (MTTT):**
        - Positive or equivocal **first-tier screen**, followed by
        - a different, sequential positive or equivocal **EIA** in lieu of an immunoblot as a second tier test

LYME STANDARD TWO-TIERED TESTING (STTT)

The **STTT** consists in:

1. An immunoassay detecting IgM or IgG antibodies to *B. burgdorferi*: either an **enzyme immune assay (immunoassay) or, newer generation assays (lateral flow, fluorescence and chemiluminescence, e.g CIA =**chemilluminescence immunoassay**) – Tier 1**

    - If the immunoassay(s) are negative, no further testing is necessary.

2. If the total IgM/IgG immunoassay, or either one or both of the first tier IgM and IgG immunoassays are positive or equivocal, **reflex testing by immunoblot** is required **– Tier 2**

    - For samples collected from patients with symptoms lasting 30 days or less, both IgM and IgG specific anti-B. burgdorferi immunoblots should be performed and interpreted to guide clinical decisions.
    - For samples collected **>30 days post symptom onset**, only the anti-B. burgdorferi **IgG** immunoblot should be performed or interpreted.

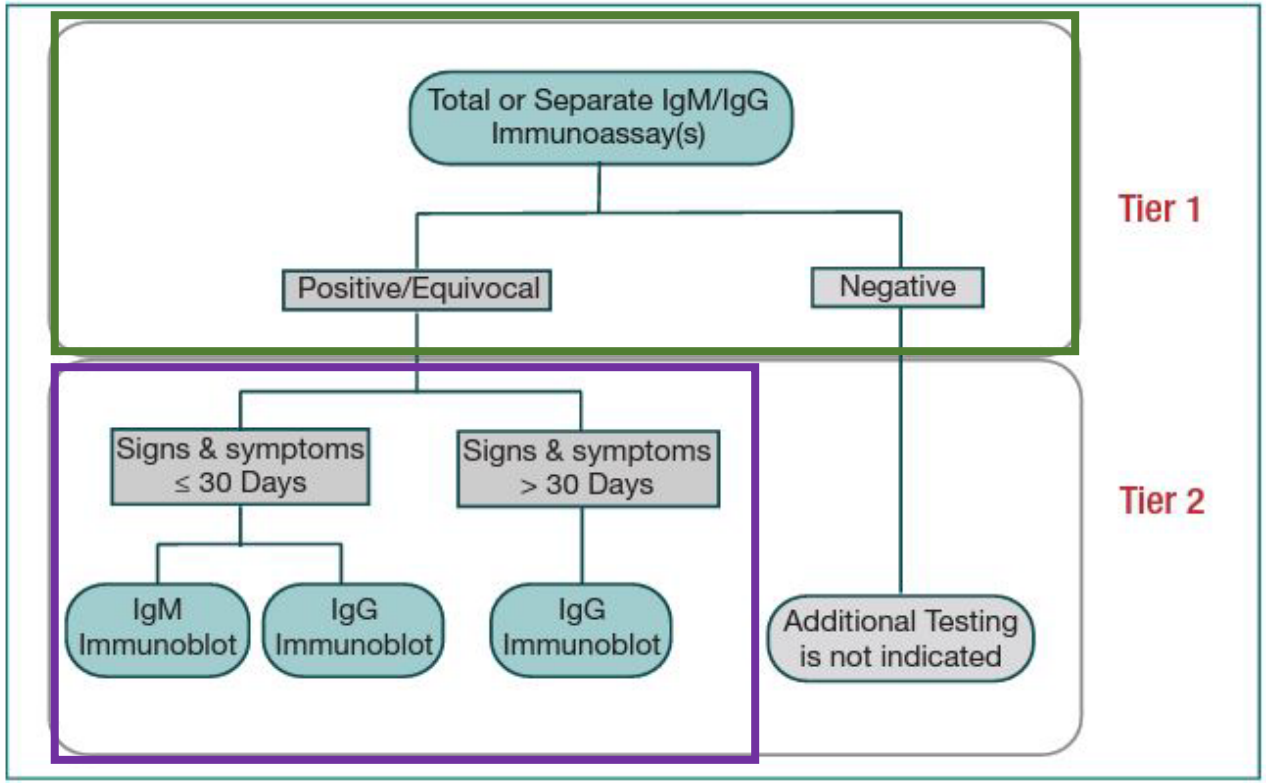


Figure 1: Standard Two-Tiered Testing (STTT)

APHL GUIDANCE: https://www.aphl.org/aboutAPHL/publications/Documents/ID-2021-Lyme-Disease-Serologic-Testing-Reporting.pdf

Test Sequence			Interpretation for Laboratories	Interpretation for Providers	Comments / Further Actions (may be included on the laboratory report)
Tier 1 *Total Ig Immunoassay*	Tier 2a *IgM Immunoblot* [a,b]	Tier 2b *IgG Immunoblot* [c]			
Negative	Testing Not Indicated[d]	Testing Not Indicated[d]	Negative for antibodies to *B. burgdorferi* (Lyme disease).	No laboratory evidence of infection with *B. burgdorferi* (Lyme disease).	Negative results may occur in patients recently infected (≤14 days) with *B. burgdorferi*. If recent infection is suspected, repeat testing on a new sample collected in 7-14 days is recommended.
Positive/ Equivocal	**WBIgM-** Negative	**WBIgG-** Negative	Antibodies to *B. burgdorferi* (Lyme disease) not confirmed.	No laboratory evidence of infection with *B. burgdorferi* (Lyme disease).	Negative results may occur in patients recently infected (≤14 days) with *B. burgdorferi*. If recent infection is suspected, repeat testing on a new sample collected in 7–14 days is recommended.
		IgG Detected Against: (list)[e]			
Positive/ Equivocal	**WBIgM+** Positive	**WBIgG-** Negative	IgM-class antibodies to *B. burgdorferi* (Lyme disease) detected.	Results are consistent with acute or recent infection with *B. burgdorferi* (Lyme disease).	IgM immunoblot results should only be considered as indicative of recent infection in patients presenting within 30 days of symptom onset. Consideration of IgM immunoblot results in patients with symptoms lasting >30 days is discouraged due to the risk of false positive IgM immunoblot results or prolonged IgM seropositivity following disease resolution. Testing of a new specimen collected in 7–14 days to demonstrate IgG seroconversion may be considered to confirm infection.
	IgM Detected Against: (list)	IgM Detected Against: (list)[e]			
Positive/ Equivocal	**WBIgM-** Negative	**WBIgG+** Positive	IgG-class antibodies to *B. burgdorferi* (Lyme disease) detected.	Results are consistent with *B. burgdorferi* (Lyme disease) infection in the recent or remote past. IgG-class antibodies may remain detectable for months to years following resolution of infection.	Results **should not** be used to monitor or establish adequate response to therapy. Response to therapy is confirmed through resolution of clinical symptoms; additional laboratory testing **should not** be performed.
		IgG Detected Against: (list)			
Positive/ Equivocal	**WBIgM+** Positive	**WBIgG+** Positive	IgM- and IgG-class antibodies to *B. burgdorferi* (Lyme disease) detected.	Results are consistent with *B. burgdorferi* infection (Lyme disease) in the recent or remote past. Antibodies may remain detectable for months to years following resolution of infection.	Results **should not** be used to monitor or establish adequate response to therapy. Response to therapy is confirmed through resolution of clinical symptoms; additional laboratory testing **should not** be performed.
	IgG Detected Against: (list)	IgG Detected Against: (list)			

Tier1= Total IgG+IgM

WB Positive

WB Negative

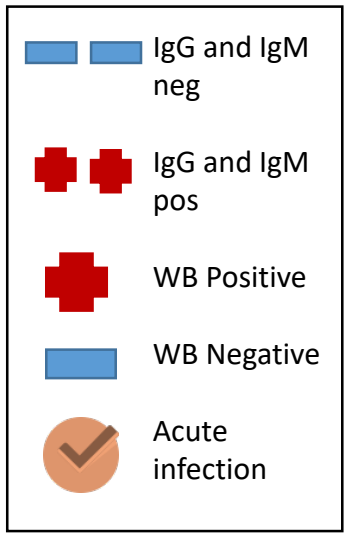
Acute infection

APHL GUIDANCE: https://www.aphl.org/aboutAPHL/publications/Documents/ID-2021-Lyme-Disease-Serologic-Testing-Reporting.pdf

Test Sequence					
Tier 1	Tier 2a	Tier 2b	Interpretation for Laboratories	Interpretation for Providers	Comments / Further Actions (may be included on the laboratory report)
Total Ig Immunoassay	*IgM Immunoblot* [a,b]	*IgG Immunoblot* [c]			
Tier 1 IgM and IgG Immunoassay results in concordance					
Negative	Testing Not Indicated[d]	Testing Not Indicated[d]	Negative for antibodies to *B. burgdorferi* (Lyme disease).	No laboratory evidence of infection with *B. burgdorferi* (Lyme disease).	Negative results may occur in patients recently infected (≤14 days) with *B. burgdorferi*. If recent infection is suspected, repeat testing on a new sample collected in 7–14 days is recommended.
Positive/ Equivocal by both IgM and IgG assays	Negative	Negative	Antibodies to *B. burgdorferi* (Lyme disease) not confirmed.	No laboratory evidence of infection with *B. burgdorferi* (Lyme disease).	Negative results may occur in patients recently infected (≤14 days) with *B. burgdorferi*. If recent infection is suspected, repeat testing on a new sample collected in 7–14 days is recommended.
		IgG Detected Against: (list)[e]			
Positive/ Equivocal by both IgM and IgG assays	Positive	Negative	IgM-class antibodies to *B. burgdorferi* (Lyme disease) detected.	Results are consistent with acute or recent infection with *B. burgdorferi* (Lyme disease).	IgM immunoblot results should only be considered as indicative of recent infection in patients presenting within 30 days of symptom onset. Consideration of IgM immunoblot results in patients with symptoms lasting >30 days is discouraged due to the risk of false positive IgM immunoblot results or prolonged IgM seropositivity following disease resolution. Testing of a new specimen collected in 7–14 days to demonstrate IgG seroconversion may be considered to confirm infection.
	IGM Detected Against: (list)	IgG Detected Against: (list)[e]			
Positive/ Equivocal by both IgM and IgG assays	Negative	Positive	IgG-class antibodies to *B. burgdorferi* (Lyme disease) detected.	Results are consistent with *B. burgdorferi* (Lyme disease) infection in the recent or remote past. IgG-class antibodies may remain detectable for months to years following resolution of infection.	Results **should not** be used to monitor or establish adequate response to therapy. Response to therapy is confirmed through resolution of clinical symptoms; additional laboratory testing **should not** be performed.
		IgG Detected Against: (list)			
Positive/ Equivocal by both IgM and IgG assays	Positive	Positive	IgM- and IgG-class antibodies to *B. burgdorferi* (Lyme disease) detected.	Results are consistent with B. burgdorferi infection (Lyme disease) in the recent or remote past. Antibodies may remain detectable for months to years following resolution of infection.	Results **should not** be used to monitor or establish adequate response to therapy. Response to therapy is confirmed through resolution of clinical symptoms; additional laboratory testing **should not** be performed.
	IgM Detected Against: (list)	IgG Detected Against: (list)			
Tier 1 Discordant IgM and IgG Immunoassay results					
IgM Positive/ Equivocal IgG Negative	Negative	Not Indicated *or* Negative	Negative for antibodies to *B. burgdorferi* (Lyme disease).	No laboratory evidence of infection with *B. burgdorferi* (Lyme disease).	Negative results may occur in patients recently infected (≤14 days) with *B. burgdorferi*. If recent infection is suspected, repeat testing on a new sample collected in 7–14 days is recommended.

Tier1= Separate IgG and IgM

Part 1



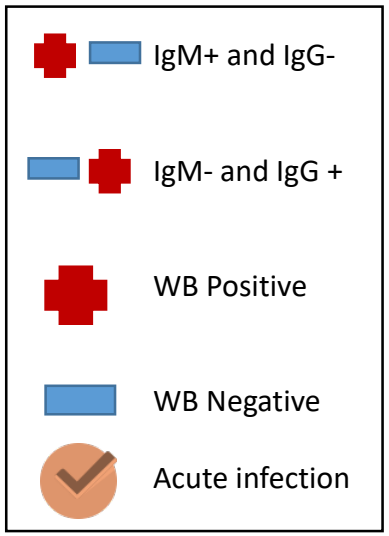
APHL GUIDANCE: https://www.aphl.org/aboutAPHL/publications/Documents/ID-2021-Lyme-Disease-Serologic-Testing-Reporting.pdf

Test Sequence					
Tier 1	Tier 2a	Tier 2b	Interpretation for Laboratories	Interpretation for Providers	Comments / Further Actions (may be included on the laboratory report)
Total Ig Immunoassay	*IgM Immunoblot* [a,b]	*IgG Immunoblot* [c]			
IgM Positive/ Equivocal IgG Negative	Positive	Not Indicated *or* If performed, results should not be considered for clinical care.	IgM-class antibodies to *B. burgdorferi* (Lyme disease) detected.	Results are consistent with acute or recent infection with *B. burgdorferi* (Lyme disease).	IgM immunoblot results should only be considered as indicative of recent infection in patients presenting within 30 days of symptom onset. Consideration of IgM immunoblot results in patients with symptoms lasting >30 days is discouraged due to the risk of false positive IgM immunoblot results or prolonged IgM seropositivity following disease resolution. Testing of a new specimen collected in 7–14 days to demonstrate IgG seroconversion may be considered to confirm infection.
	IgM Detected Against: (list)				
IgM Negative/ Not performed IgG Positive/ Equivocal	Not Indicated *or* Negative	Negative	Negative for antibodies to *B. burgdorferi* (Lyme disease).	No laboratory evidence of infection with *B. burgdorferi* (Lyme disease).	Negative results may occur in patients recently infected (≤14 days) with *B. burgdorferi*. If recent infection is suspected, repeat testing on a new sample collected in 7-14 days is recommended.
		IgG Detected Against: (list)[e]			
IgM Negative/ Not performed IgG Positive/ Equivocal	Not Indicated or If performed, results should not be considered for clinical care.	Positive	IgG-class antibodies to *B. burgdorferi* (Lyme disease) detected.	Results are consistent with *B. burgdorferi* (Lyme disease) infection in the recent or remote past. IgG-class antibodies may remain detectable for months to years following resolution of infection.	Results **should not** be used to monitor or establish adequate response to therapy. Response to therapy is confirmed through resolution of clinical symptoms; additional laboratory testing **should not** be performed.
		IgG Detected Against: (list)			
Tier 1 & 2 Discordant IgM and IgG Results					
IgM Positive/ Equivocal IgG Negative	Negative	Positive IgG Detected Against: (list)	Inconclusive	Repeat testing using the standard two-tiered or modified testing algorithm for Lyme disease is recommended.[f]	Consider further testing or alternate diagnosis.
IgM Negative/ Not performed IgG Positive/ Equivocal	Positive	Negative	Inconclusive	Repeat testing using the standard or modified two-tiered testing algorithm for Lyme disease is recommended.[f]	Consider further testing or alternate diagnosis.

a Immunoblots for IgM antibodies to *B. burgdorferi* are interpreted as "negative" if <2 *B. burgdorferi*-specific proteins are detected. Conversely, if ≥2 out of a possible 3 *B. burgdorferi*-specific proteins are detected, the immunoblot is interpreted as "positive" for IgM-class antibodies to *B. burgdorferi*. The *B. burgdorferi*-specific proteins that may be detected include: p23, p39, p41.
b Testing for IgM antibodies to *B. burgdorferi* is not indicated in patients presenting >30 days post-symptom onset.
c Immunoblots for IgG antibodies to *B. burgdorferi* are interpreted as "negative" if <5 *B. burgdorferi*-specific proteins are detected. Conversely, if ≥ 5 out of a possible 10 *B. burgdorferi*-specific proteins are detected, the immunoblot is interpreted as "positive" for IgG-class antibodies to *B. burgdorferi*. The *B. burgdorferi*-specific proteins that may be detected include: p18, p23, p28, p30, p39, p41, p45, p58, p66, p93.
d In accordance with the current standard two-tiered testing algorithm, testing by the IgM and IgG blots is not indicated due to negative initial screening immunoassay.
e Reporting of individual IgG bands is recommended even when the overall test result is negative, because some physicians may use this information to guide decisions about treatment or repeat testing after more time.
f https://www.cdc.gov/lyme/diagnosistesting/index.html

Tier1= Separate IgG and IgM

Part 2



APHL GUIDANCE: https://www.aphl.org/aboutAPHL/publications/Documents/ID-2021-Lyme-Disease-Serologic-Testing-Reporting.pdf

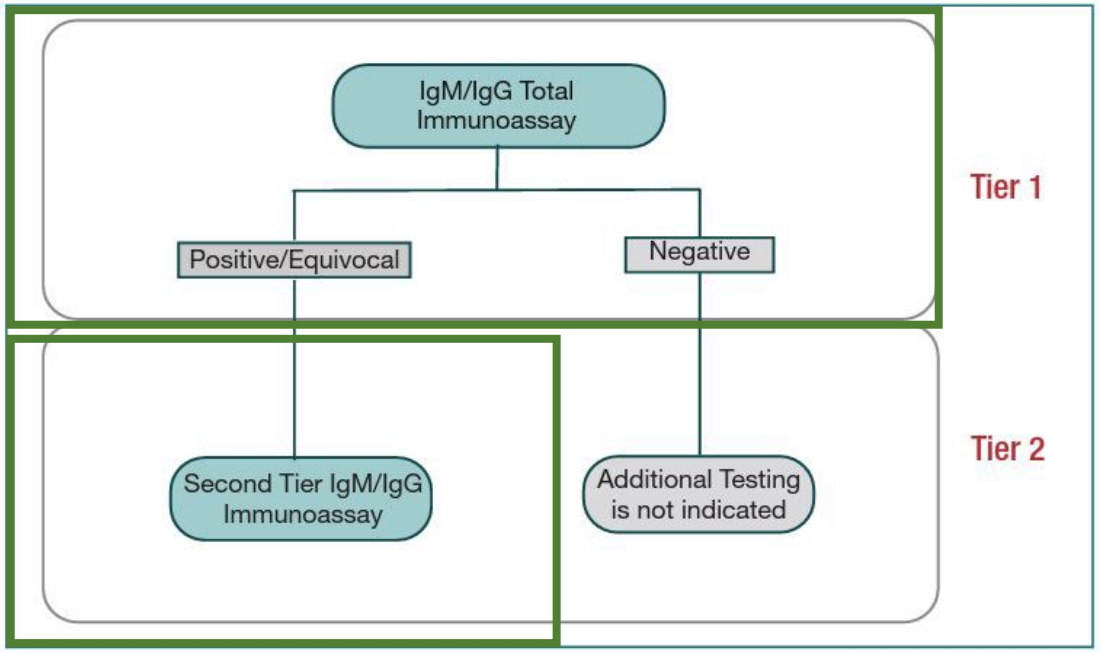
LYME MODIFIED TWO-TIERED TESTING (MTTT)

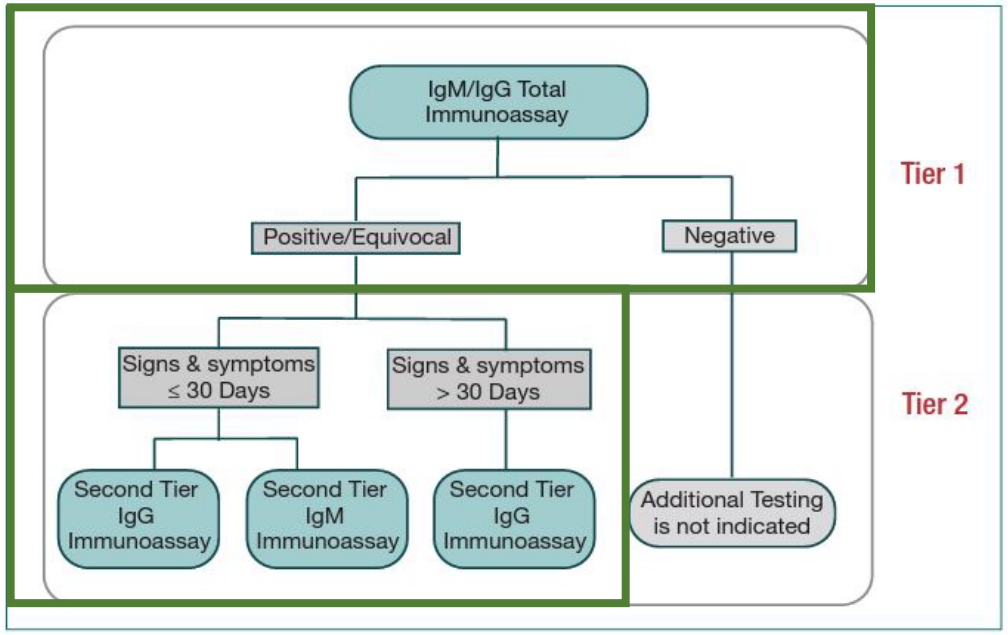
The **MTTT** method utilizes two immunoassays, based on multiple B. burgdorferi antigens, that have been cleared by FDA for this use:

1. The MTTT begins with an **immunoassay** detecting antibodies to *B. burgdorferi* **- Tier 1**

   - Samples negative by this first tier test do not require further testing.
   - If the total IgM/IgG immunoassay is positive or equivocal, **reflex testing by a second immunoassay is required**.

2. The **second immunoassay** may be either **total IgM/IgG** **(FIG 1 below)** or **separated IgM and IgG** **(FIG 2 below)** **- Tier 2**





APHL GUIDANCE: https://www.aphl.org/aboutAPHL/publications/Documents/ID-2021-Lyme-Disease-Serologic-Testing-Reporting.pdf

MEDSIS EXAMPLE
LABCORP MODIFIED TWO-TIERED TESTING (MTTT)

LABCORP LYME MTTT https://www.labcorp.com/assets-media/2849

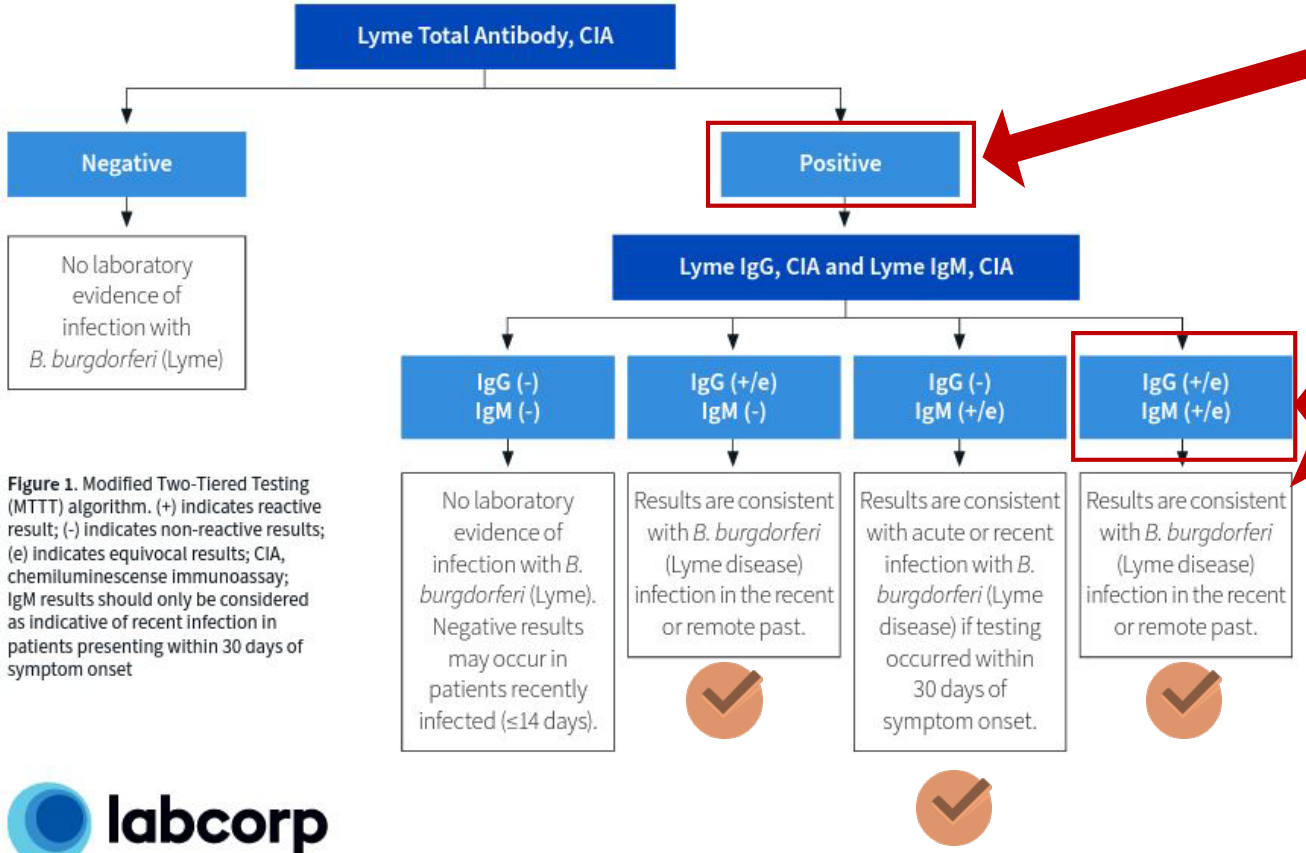


Figure 1. Modified Two-Tiered Testing (MTTT) algorithm. (+) indicates reactive result; (-) indicates non-reactive results; (e) indicates equivocal results; CIA, chemiluminescense immunoassay; IgM results should only be considered as indicative of recent infection in patients presenting within 30 days of symptom onset

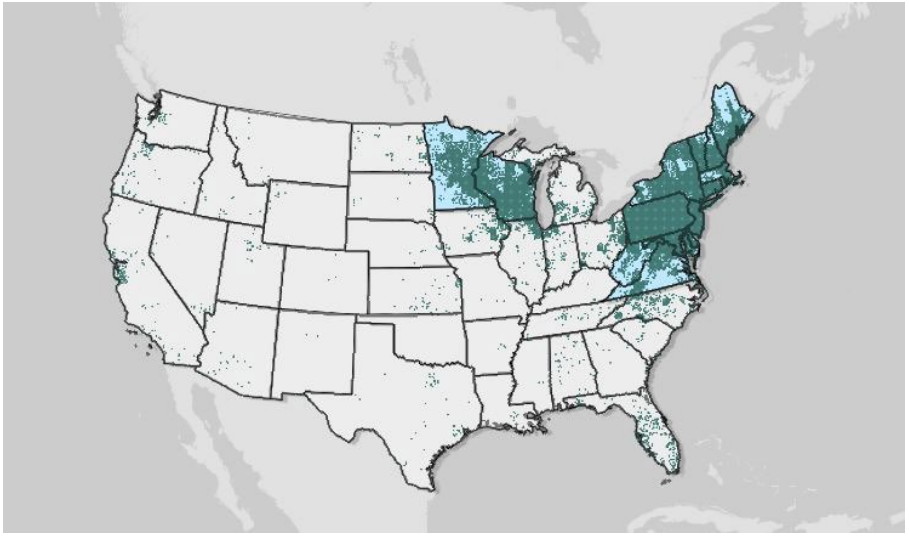
labcorp

MEDSIS LAB SCREENSHOT

Test Performed	Test Results
83081-0 Borrelia burgdorferi Ab.IgG+IgM (Lyme Total Antibody CIA)	10828004 Positive SCT P= Positive
16480-6 Borrelia burgdorferi Ab.IgG (Lyme IgG CIA)	10828004 Positive SCT P= Positive
40612-4 Borrelia burgdorferi Ab.IgM (Lyme IgM CIA)	10828004 Positive SCT P= Positive
101358-0 Borrelia burgdorferi Ab (Lyme Interpretation)	120714000 Borrelia burgdorferi antibody SCT LYMMG Lyme IgM/IgG Abs Detected

LYME DISEASE – LOW AND HIGH INCIDENCE JURISDICTIONS

- **High-incidence jurisdictions:** those with an average Lyme disease incidence of at **least 10 confirmed cases / 100,000** for the **previous three reporting years**. At the time of this statement (spring 2021), those jurisdictions are: Connecticut, Delaware, Maine, Maryland, Massachusetts, Minnesota, New Hampshire, New Jersey, New York, Pennsylvania, Rhode Island, Vermont, Virginia, West Virginia, Wisconsin, and the District of Columbia (http://www.cdc.gov/lyme/stats/tables.html) .
- **Low incidence jurisdictions**: those that have **not** had an average Lyme disease incidence of ≥10 confirmed cases/100,000 population for a period of three consecutive years. Once ≥10 confirmed cases/100,000 population have been observed in a low-incidence jurisdiction for a period of three consecutive years, they become a high-incidence jurisdiction for the purposes of surveillance and should permanently switch reporting criteria.
- For determining incidence for case classification and reporting purposes, calculations should be made at the state or territory level. Case classification for reporting should not be differentially applied at the subdivision level.



https://www.cdc.gov/lyme/datasurveillance/lyme-disease-maps.html

Case Definitions for Public Health Surveillance

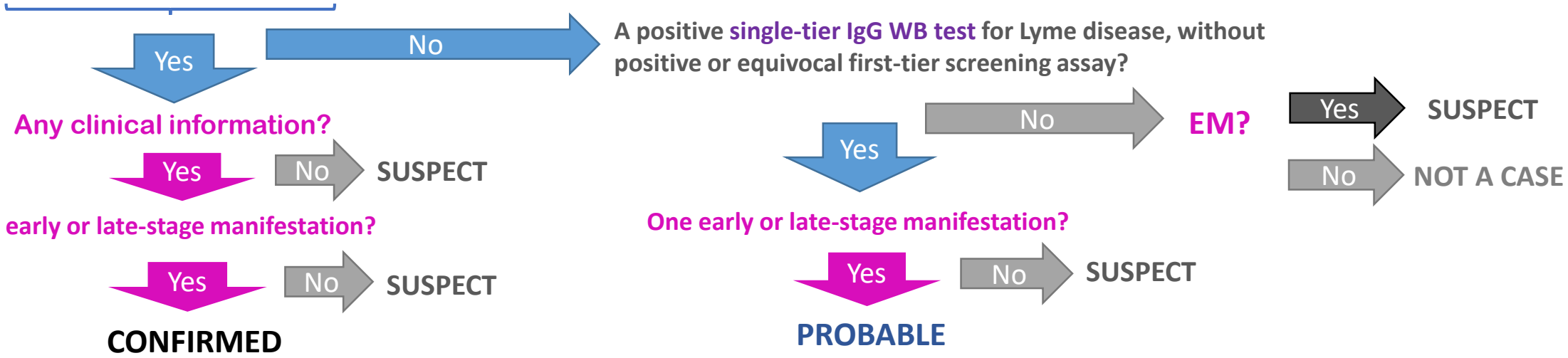
LYME DISEASE CASE CLASSIFICATION ALGORITHM FOR LOW-INCIDENCE JURISDICTIONS (ARIZONA) (adopted in 2022)

For the full definition please refer to the ADHS Case Definition Manual

For more details on Lyme Testing see the APHL Guidance.

Confirmatory lab evidence of infection?

- Positive **culture** for *Borrelia burgdorferi or B. mayonii* , OR
- Detection of *B. burgdorferi* or *B. mayonii* in a clinical specimen by a *B. burgdorferi* group-specific **NAAT** assay, OR
- Detection of *B. burgdorferi* group-specific antigens by immunohistochemical assay **(IHC) on biopsy or autopsy tissues**, OR
- Positive serologic tests in a two-tier or equivalent format, including Standard two-tier test **STTT** or Modified two-tier test **MTTT**



STTT: a positive or equivocal first-tier screening assay, often an enzyme immunoassay [**EIA**] or immunofluorescence assay [**IFA**] for IgM, IgG, or a combination of immunoglobulins, followed by a concordant positive **IgM or IgG WB** interpreted according to established criteria.

MTTT: Positive or equivocal first-tier screen, followed by a different, sequential positive or equivocal EIA in lieu of a WB as a second tier test. The MTTT algorithm should be performed using assays specifically cleared by the US Food and Drug Administration (FDA) for this purpose. (Mead et al, 2019) .

EIA= enzyme immunoassay; **IFA**= immunofluorescent assay; **WB**= western immunoblot.

IgM WB is considered positive when **at least 2** of the following bands are present: 24kDa (OspC)*, 39 kDa (BmpA), and 41 kDa (Fla). **Disregard IgM WB results for specimens collected >30 d after onset.**

IgG WB is considered positive when **at least 5** of the following bands are present: 18 kDa, 24 kDa (OspC)*, 28 kDa, 30 kDa, 39 kDa (BmpA), 41 kDa (Fla), 45 kDa, 58 kDa (not GroEL), 66 kDa, and 93 kDa.

*Depending upon the assay, OspC could be indicated by a band of 21, 22, 23, 24, or 25 kDa.

One early or late-stage manifestation: EM =Erythema migrans, a skin lesion that typically begins as a red macule or papule and expands over a period of days to weeks to form a large round lesion, often with partial central clearing. A single primary lesion must reach greater than or equal to 5 cm in size across its largest diameter; Recurrent, brief attacks (weeks or months) of objective joint swelling in one or a few joints, sometimes followed by chronic arthritis in one or a few joints; lymphocytic meningitis; cranial neuritis, particularly facial palsy (may be bilateral); radiculoneuropathy; or, rarely, encephalomyelitis; Acute onset of high-grade (2nd degree or 3rd degree) atrioventricular conduction defects that resolve in days to weeks.

Last updated: 3.17.2022