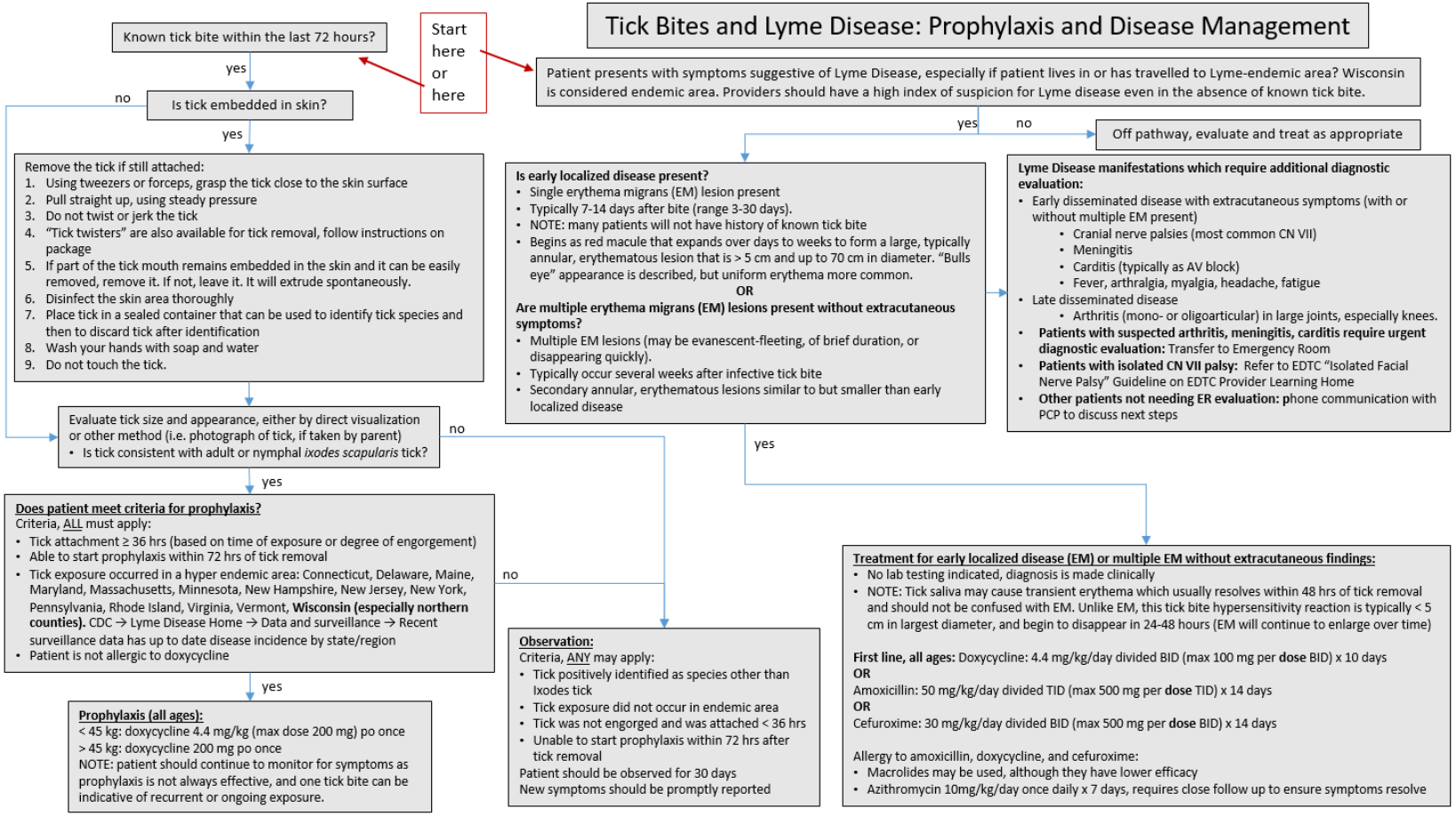
Children's Hospital and Health System
Patient Care Evidence Based Guideline
CW Urgent Care

SUBJECT: Tick Bites and Lyme Disease



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Purpose: To evaluate and initiate treatment of tick bites and suspected Lyme Disease in children.

The most up-to-date recommendations by the CDC can be found at the below link:
https://www.cdc.gov/lyme/index.html

Definition: Lyme disease is the most common reportable tick-borne disease in the United States (U.S.) with 25,000-30,000 cases annually. Most U.S. cases of Lyme disease occur in the upper Midwestern and northeastern U.S.; a smaller number of cases were reported in California, Oregon and Washington. In 2015, 95% of cases were reported from 14 states: Connecticut, Delaware, Maine, Maryland, Massachusetts, Minnesota, New Hampshire, New Jersey, New York, Pennsylvania, Rhode Island, Vermont, Virginia, and Wisconsin. Wisconsin is considered a hyperendemic area, especially in the northern counties.

Children ages 5-10 years old have the highest reported incidence of Lyme disease. People who are at increased risk of developing Lyme disease are those individuals with occupational, recreational or residential exposure to tick-infested fields, yards or woodlands in endemic areas.

Typical symptoms are variable based on the stage of illness.

Early localized disease: presence of single erythema migrans lesion. Typically 7-14 days after tick bite (range 3-30 days)

Early disseminated disease: Occurs weeks to months after a tick bite, due to the spirochete disseminating throughout the body. Can present with multiple erythema migrans (most common), but also cranial nerve palsy, meningitis, or carditis.

Late disease: Occurs weeks to months after infection, most commonly arthritis (mono- or oligoarticular, typically of the knee).

Etiology: Lyme Disease is a bacterial infection that is spread through the bite of infected ticks. In the U.S., it is caused by the spirochete *Borrelia burgdorferi*. It is transmitted to humans through the bite of infected *Ixodes scapularis* (the black-legged tick, commonly called a deer tick) in the eastern and Midwestern portions of the U.S. and *Ixodes pacificus* (the western black-legged tick) on the Pacific coast. It is estimated that 20% to 30% of *Ixodes* ticks are infected with *B. burgdorferi.* Both nymphal and adult *Ixodes* ticks spread Lyme disease.

Studies have shown that transmission of *B. burgdorferi* requires tick attachment for at least 36 hours. Overall risk of infection is 1-3% after an adult tick bite and 8-10% with an infected nymphal tick and engorgement at discovery.

Differential Diagnosis:

Early Localized Disease (Erythema Migrans)	Early Disseminated Disease	Late Disseminated Disease

• Tick bite hypersensitivity reaction
  o Occurs while tick is still attached or within 48 hours after removal
  o May be urticarial
  o Usually begins to disappear within 24-48 hours
• Cellulitis
• Contact dermatitis
• STARI (Southern tick-associated rash illness)
  o Similar rash to erythema migrans
  o May present with flu-like symptoms
  o *Consider when tick bite occurred in a non-Lyme-endemic area*
• Tinea Corporis
• Erythema multiforme
• Nummular eczema
• Granuloma annulare
• Insect bites
	• Bell's palsy
	• Chronic fatigue syndrome
	• Fibromyalgia
	• Systemic Lupus Erythematosus
	• Viral meningitis
	• Bacterial meningitis
	• Myocarditis
		o Bacterial septic arthritis
		o Juvenile idiopathic arthritis
		o Cancer

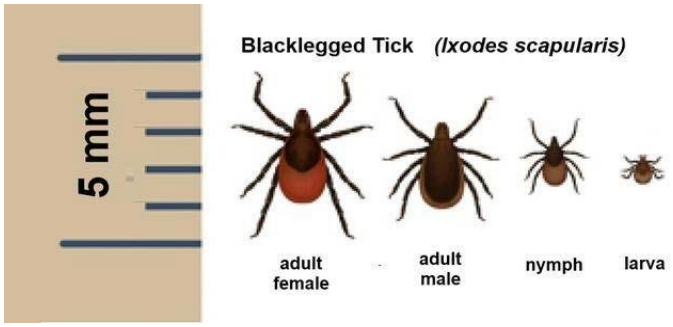
- Co-infection with other tick-borne pathogens,
  - Further evaluation is recommended for:
    - Patients who remain febrile more than 48 hours after starting appropriate antibiotic therapy for Lyme Disease.
    - Unexplained leukopenia, thrombocytopenia and/or anemia.

Guideline

Subjective Data/History

- Possible environmental exposure to tick-infested fields, yards or woodlands in endemic areas.
  - Depending on the stage of the disease, it may have occurred days to weeks or even months prior to the patient seeking medical care.
  - The patient may or may not remember having a tick bite.

- If tick is available, visually identify species and presence or absence of engorgement if possible:



Ixodes scapularis ticks: non-engorged vs. engorged:

Engorged Ixodes scapularis tick

Typical appearance of Erythema Migrans rash (uniform erythema more common, bull's eye pattern less common):

Objective Data: Clinical findings vary based on presence of early localized, early disseminated, or late disease (see next page).

Early Localized Disease *occurs 3 to 30 days (usually 7-14 days) after tick bite*	**Early Disseminated Disease** *occurs weeks to months after tick bite*	**Late Disseminated Disease** *occurs weeks to months after initial infection if not adequately treated*

• Erythema Migrans (EM) rash
  ○ Lesion appears at the site of tick bite 3-30 days (usually 7-14 days) after tick bite
  ○ EM may appear anywhere on body
  ○ Rarely pruritic or painful
  ○ Occurs in 70-80% of patients
  ○ Begins as flat, red macule or papule
  ○ If untreated, expands for days to weeks to form an annular, erythematous lesions that can grow to a foot or more in diameter
  ○ Most often uniformly erythematous or has increased central erythema
  ○ Less commonly, appears in bull's eye pattern
  ○ Warm to touch
  ○ Vesicles or necrotic areas may appear in central part of lesions
• Flu-like symptoms may occur including headache, neck pain, malaise, myalgia, arthralgia
• Lymphadenopathy
	• Multiple EM lesions
	  ○ Usually appear 3-5 weeks after tick bite
	  ○ Appear as multiple annular erythematous lesions similar to but usually smaller than the primary lesions
	• Cranial nerve palsy
	  ○ Bilateral facial palsy is characteristic of Lyme Disease
	  ○ May occur with or without history of EM
	• Ophthalmologic conditions may occur, usually with other neurological symptoms (conjunctivitis, optic neuritis, keratitis, uveitis)
	• Lyme Meningitis
	  ○ Presents similarly to aseptic meningitis
	  ○ Older children: headache, neck stiffness, photophobia, fever may be present
	  ○ Younger children: rash, diarrhea, cough, fever may be present
	  ○ Usually occurs in older children (mean 10.5 years)
	  ○ Longer duration of symptoms at time of diagnosis compared to aseptic meningitis patients
	  ○ Lower temperature than viral meningitis patients
	  ○ Associated with history of EM, cranial nerve palsy, and papillodema
	• Polyradiculitis
	  ○ Initial limb weakness, both proximal and distal
	  ○ Sensory symptoms such as tingling and numbness of hands and feet
	  ○ Motor symptoms (usually predominant side)
	• Flu-like symptoms are common but rarely occur without EM (headache, neck pain, malaise, myalgia, arthralgia)
	• Carditis
	  ○ Common symptoms include lightheadedness, syncope, shortness of breath, heart palpitations, chest pain, fever, body aches
	  ○ Arrhythmia and murmur
	  ○ Partial heart block more common than complete heart block
	  ○ Usually self-limited
		• Arthritis
		  ○ Most common manifestation of late disseminated disease
		  ○ May be monoarticular or oligoarticular
		  ○ May be acute or subacute
		  ○ Affects large joints; knees are involved 90% cases
		  ○ Affected joint is edematous and mildly tender, but severe tenderness is usually absent
		  ○ Child can often walk without difficulty despite limitation in range of motion.
		  ○ Erythema of joint less common
		  ○ Associated fever is uncommon
		  ○ If untreated, arthritis may resolve in several weeks only to recur in different joint
		• Encephalitis and polyneuropathy
		  ○ Different than neurological symptoms of early disseminated disease
		  ○ Extremely rare in children:
		  • Numbness and tingling of extremities
		  • Facial palsy
		  • Memory loss
		  • Dizziness
		  • Inability to concentrate

Diagnosis/Diagnostic Studies

- Early localized disease is diagnosed clinically with the presence of the characteristic finding of an erythema migrans (EM) skin lesion in a patient with the potential for geographic exposure
    - Serology is *not recommended* for patients with early localized disease as it is not sensitive early in the infection.
- Patients with early disseminated disease who present with only multiple erythema migrans (EM) lesions without extracutaneous manifestations should also be diagnosed and treated clinically *without* serology due to risk of false negative results early in illness.
- All other patients with other manifestations of Lyme disease should have their diagnosis confirmed through the combination of typical clinical illness, plausible geographic exposure, and a positive serologic test result.
    - This includes patients with early disseminated disease presenting with extracutaneous manifestations (CN palsy, meningitis, fever, or other systemic symptoms) as well as late disease (arthritis).
    - For patients with 1 or more skin lesion that may be consistent with erythema migrans but are atypical: if provider is unlikely to treat with antimicrobials, initial antibody testing should be performed on an acute-phase sample, followed by a convalescent phase sample at least 2-3 weeks later. If the provider opts to treat with antimicrobials, this testing would be unnecessary.
- Serological testing for Lyme Disease
    - Ideally, serologic testing for Lyme Disease should be obtained either as part of CW ER evaluation (if patient's clinical status warrants transfer for additional reason) or PMD follow up.
        - For patients who present with signs and symptoms that suggest arthritis, carditis, meningitis or other more severe clinical diagnoses, then EDTC transfer is appropriate and serology would likely be performed as part of EDTC evaluation.
        - If a patient has isolated facial nerve palsy, refer to EDTC "Isolated Facial Nerve Palsy" Guideline on EDTC Provider Learning home for diagnosis and management.
        - If empiric therapy for Lyme Disease is not indicated, and the patient does not need evaluation in the ED, serology may still be indicated. Personal (phone) communication with PCP is appropriate to discuss next steps, and ensure that the patient is able to follow up within an appropriate time frame (likely 24-48 hours).
    - Two-step testing with ELISA (for sensitivity) and immunoblot (for specificity) is the recommended testing regime at this time, ordered as "Lyme Antibody with reflex Western Blot." *CW Lab performs the Western Blot reflexively if the ELISA test result is positive.*
        - If the first-tier ELISA result is negative, the patient is considered seronegative and no further testing is indicated.

        - If the ELISA test is equivocal or positive, then second tier testing with Western Blot is indicated.
            - If the ELISA test is equivocal or positive, but Western Blot is negative, then the test result for Lyme disease should be interpreted as negative
            - Western Blot should not be performed without a simultaneous ELISA. Results are uninterpretable when the Western Blot test result is positive without a simultaneous ELISA result.
            - A positive result does not differentiate between a past *B. burgdorferi* infection and a current one as both IgM and IgG antibodies may persist for many years despite treatment and clinical cure of the illness.
- Due to testing challenges, the following tests are NOT recommended:
    - Antibody tests should not be used as screening tests due to high false positive results; poor sensitivity in early Lyme disease
    - Once antibodies to Lyme disease develop, they may persist for years. Once positive, tests for antibodies should not be repeated or used to assess success of treatment.
    - Tick analysis for spirochete infection has poor predictive value
    - *Do not order testing for patients with nonspecific symptoms alone (fatigue, headache or myalgia) due to high prevalence of false positive results.*

Treatment (See algorithm)

- **Tick Removal**
    - Use fine-tipped forceps and grasp the tick as close to the skin's surface as possible
    - Pull upward with steady, even pressure. **Do not twist the tick as this can cause part of the tick to remain embedded in the skin.**
        - If any remaining remnants can be easily removed, remove them.
        - If remnants of the tick mouth remain but cannot be easily removed, do not traumatize the area with attempts to remove them; they will be expelled spontaneously.
    - "Tick Twisters" are available for tick removal, follow instructions on packaging.
    - After removing the tick, clean the tick bite area and your hands with 70% isopropyl alcohol or soap and water.
    - Dispose of a live tick by submerging it in alcohol, placing it in a sealed container or bag, or flushing it down the toilet.
        - Do not crush the tick with your hand.
    - Tick identification: Tick identification can typically be performed using online resources. If additional resources are needed, contact the Wisconsin Medical Entomology Lab Identification Service. See https://wisconsin-ticks.russell.wisc.edu/tick-identification-for-public-health-and-medical-

professionals/ for details. Photos of the tick may be submitted or a tick specimen can be mailed to them.

- **Antibiotic prophylaxis**
  - *Observation for low risk cases* defined as tick attachment brief (< 36 hours) and the tick is flat and non-engorged
    - Parents should monitor the child for skin lesions at the site of the tick bite for 30 days and report any new symptoms to their PMD
  - *Antibiotic prophylaxis* with doxycycline should be started for ALL ages if the following criteria are all met:
    - The patient is not allergic to doxycycline
    - Tick identified as Ixodes spp. vector species
    - Exposure occurred in an hyperendemic area where > 20% of ticks are infected with *B. burgdorferi* (upper Midwest including Wisconsin, northeast, or Pacific coastal areas)
    - Tick attachment ≥ 36 hours or positive tick engorgement
    - Prophylaxis can be started within 72 hours of tick removal
  - **Antibiotic prophylaxis regimen (all ages):**
    - < 45 kg: doxycycline 4.4 mg/kg (max dose 200 mg) once
    - > 45 kg: doxycycline 200 mg po once
    - Patients should be advised to continue to monitor for symptoms as prophylaxis is not always effective, and one tick bite can be indicative of recurrent or ongoing exposure.
- **Antibiotic treatment** is determined by Lyme staging and specific symptoms
  - Patients with early localized disease (single erythema migrans) or multiple erythema migrans without extracutaneous findings are diagnosed clinically and should be treated without need for additional lab testing.
    - **First line, all ages:** Doxycycline: 4.4 mg/kg/day divided BID (max 100 mg per **dose** BID) x 10 days

      OR
    - Amoxicillin: 50 mg/kg/day divided TID (max 500 mg per **dose** TID) x 14 days

      OR
    - Cefuroxime: 30 mg/kg/day divided BID (max 500 mg per **dose** BID) x 14 days

    - If allergic to amoxicillin, doxycycline, and cefuroxime, macrolides may be used, although they have lower efficacy.
      - Azithromycin 10mg/kg/day once daily x 7 days

Education of Patient/Family

- The long-term prognosis for individuals who are treated appropriately with antimicrobials for Lyme disease, regardless of stage of the illness, is excellent.

- The most common persistent symptom after appropriate antimicrobial therapy is myalgia, which may persist for several weeks even in patients with early Lyme disease who are treated successfully.
    - Myalgia may persist for several weeks and usually resolves spontaneously within 6-12 months
    - No benefit to treat with long-term or repetitive antibiotic courses
    - Symptomatic care is recommended

Prevention of Lyme Disease

- Children should be routinely inspected for ticks when returning indoors and ticks should be removed immediately.
- Tick and insect repellents that contain DEET should be applied sparingly only to exposed skin but not to the face, hands or skin that is irritated or abraded.
    - Requires frequent reapplication
    - After returning indoors, skin that was treated with DEET should be washed with soap and water.
    - Serious neurologic complications in children from frequent or excessive application of DEET-containing repellents have been reported, but they are rare, and the risk is low when these products are used according to package labels.

Special Areas of Concern for Lyme Disease

- Congenital Transmission
    - Current studies and understanding do not show increased risk for congenital malformation or serious adverse effects on the fetus if the mother is diagnosed with Lyme disease and is treated appropriately during her pregnancy.
        - Research is controversial when Lyme Disease occurs during pregnancy and is not treated; early research reflects increased risk of placental infection, possible stillbirth or fetal malformation. Recent research does not reflect increased risk; investigation is ongoing.
- Breastfeeding Transmission: has not been documented
- Sexual Activity Transmission: has not been documented
- Chronic Lyme Disease/Post Treatment Lyme Disease Syndrome
        - There is no evidence of chronic Lyme disease as the cause of nonspecific symptoms alone (headache, fatigue, myalgia and arthralgia). The majority of patients labeled as having chronic Lyme Disease demonstrate no evidence of Lyme disease per history or laboratory testing.

This guideline is designed to serve as a reference for clinical practice and does not represent an exclusive course of treatment nor does it serve as a standard of medical care. Providers should apply their professional judgment to the management of individual patient conditions and circumstances. Children's Hospital and Health System (CHHS) does not make any representation with respect to any sort of industry recognized standard of care for the particular subject matter of this clinical guideline. Additionally, CHHS form documents are subject to change, revision, alteration, and/or revocation without notice.

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