Lyme Disease

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Overview

- Definition
  - A multisystem disease caused by *Borrelia burgdorferi* sensu *lato*, a group of spirochetes transmitted by Ixodes ticks
  - Characterized by skin, musculoskeletal, neurologic, ocular, and cardiac manifestations
- Symptoms
- Varies widely depending on stages of disease
  - Conjunctivitis: redness
  - Episcleritis: redness, irritation
  - Keratitis: photophobia, blurry vision
  - Intraocular inflammation: photophobia, redness, blurry vision, floaters
  - Optic nerve involvement: visual field and color deficits
  - Orbital inflammation: pain, swelling, diplopia
  - Cranial nerve palsy (CN 4, 5, 6, and 7): diplopia, facial weakness
- Laterality
  - Typically bilateral
- Course
- Applies to both systemic and ocular manifestations
  - Early localized stage: self-limited over 3–4 weeks
  - Early disseminated stage: days to weeks after tick bite
  - Late disseminated stage: months to years after tick bite

    Note: Lyme disease can remain silent for months to years between tick bite and disseminated stages; some patients may never have disseminated disease.

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- Age of onset
  - All age groups affected
- Gender/race
  - Slight male predominance
  - More common during warmer months
  - Reported regularly in North America, Europe, and Asia
    USA: Northeast, Mid-Atlantic, and upper Midwest
    Europe: More common in Eastern Europe (highest prevalence in Austria and Slovenia)
- Systemic association
  - Early localized stage
    Erythema migrans (also called erythema chronicum migrans) (70–80%)
    - Average of 7–10 days after tick bite
    - At least 5 cm diameter, and may expand by 1 cm/day (up to 20–30 cm)

    Fever, malaise, fatigue, myalgia, and arthralgia
  - Early disseminated stage
    Skin
    - Erythema chronicum migrans
    - Borrelial lymphocytoma (rare in the USA, more common in Europe)

    Central and peripheral nervous systems (30–40%)
    - Cranial neuropathy
      - Facial nerve is most commonly involved (1/3 of cases are bilateral, which help differentiate from idiopathic Bell's palsy); usually resolves with or without antibiotics, but chance of Lyme arthritis is much higher in untreated patients
    - Motor and sensory radiculopathy
    - Encephalitis/myelitis

    Cardiac (<5%)
    - AV (atrioventricular) block of different degrees
    - Others: myocarditis, pericarditis
  - Late disseminated stage
    Joints (80%)
    - Chronic or recurrent mono- or oligoarthritis, with each episode lasting days to months
    - Can affect smaller joints, but general predilection for large joints, especially the knee
    - Often asymmetric
    - May be the only Lyme manifestation in children

    Neurologic disease
    - Peripheral nervous system: cranial neuropathies, radiculoneuritis
    - Central nervous system: meningitis, encephalomyelitis, benign intracranial hypertension, encephalopathy

    Acrodermatitis chronica atrophicans
    - Bluish-red lesions found on extremities of older females; eventually wrinkled and atrophic
    - Seen in European cases

Exam: Ocular

As with systemic findings, ocular findings vary with different disease stages, and practically all parts of the eye may be affected:

- Early localized stage
  - Follicular conjunctivitis
  - Episcleritis
- Early disseminated stage
  - Uveitis affecting any segment, but intermediate uveitis with significant vitritis is most common
  - Retinitis and retinal vasculitis
  - Exudative RD (retinal detachment)
  - Optic neuritis/papillitis
  - Neuroretinitis
  - Cranial neuropathy (may affect multiple cranial nerves)
  - Papilledema due to meningitis and increased intracranial pressure
  - Pupillary abnormalities (Horner's syndrome, tonic pupil, mydriasis)
  - Orbital inflammation
- Late disseminated stage
  - Episcleritis
  - Keratitis (bilateral patchy and nebular subepithelial and stromal infiltration)
  - Chronic uveitis

Exam: Systemic

- Skin
  - Erythema chronicum migrans: reddish round rash, which enlarges with central clearing (bull's eye or target lesion), without itching or pain, but may have some warmth. Diameter of at least 5 cm; expands by 1 cm/day up to 20–30 cm
  - Borrelial lymphocytoma (aka lymphadenosis benigna cutis): bluish-red lesions with predilection for earlobes in children and nipples in adults; rare in the USA, more common in Europe
  - Acrodermatitis chronica atrophicans: more often found on extremities of older females, bluish-red lesions that eventually become wrinkled and atrophic; rare in the USA, more common in Europe
- Cardiac: bradycardia
- Joints
  - Asymmetric knee or other joint swelling and erythema
- CNS

  - Facial palsy: 1/3 of Lyme-related facial palsy is bilateral: a crucial distinction from idiopathic Bell's palsy, which tends to be unilateral
  - Multifocal asymmetric weakness
  - Decreased vibratory sensation of the lower distal extremities

Imaging

Due to the varying ocular presentations, there is no specific ocular imaging that would be particularly helpful in differentiating Lyme from other uveitic entities

Laboratory and Radiographic Testing

- ELISA screening for serum Lyme antibodies, with confirmatory Western blot:
  - Both may be negative in the initial 2–4 weeks after infection as it takes time for antibodies to develop

Differential Diagnosis

- Coinfection with *Babesia* and *Anaplasma* should be ruled out in patients with ongoing nonspecific symptoms despite appropriate treatment for Lyme disease, or in the presence of anemia, leukopenia, and or thrombocytopenia
- DDx of erythema migrans:
  - Insect bite hypersensitivity: usually more rapid onset (within hours), shorter duration, and smaller size
  - STARI (Southern tick-associated rash illness following the bite of the Lone Star tick-Amblyomma)
  - Contact dermatitis
  - Bacterial cellulitis
  - Granuloma annulare
  - Hyperkeratotic disorder
- Juvenile idiopathic arthritis.
- Rheumatoid arthritis (symmetric joint involvement; more likely to involve smaller joints than Lyme)
- Systemic lupus erythematosus.

Treatment

- Based on IDSA (Infectious Disease Society of America) guidelines, doxycycline prophylaxis is recommended only if
  - Attached tick is identified as an adult or nymphal *Ixodes scapularis* (deer) tick.

  - Tick is estimated to have been attached for ≥36 hours (based upon how engorged the tick appears or the amount of time since outdoor exposure).
  - Antibiotic can be given within 72 hours of tick removal.
  - Local rate of tick infection with *B. burgdorferi* is ≥20% (known to occur in parts of New England, parts of the mid-Atlantic states, and parts of Minnesota and Wisconsin).
  - Patient can safely take doxycycline (e.g., not pregnant or breastfeeding; not child under 8 years of age).
  - If the person meets ALL of the above criteria, the recommended dose of doxycycline is a single dose of 200 mg for adults and 4 mg/kg, up to a maximum dose of 200 mg, in children ≥8 years.
- Early disease/erythema migrans
  - Doxycycline 100 mg BID for 10–21 days
  - Alternatives: amoxicillin 500 mg TID or cefuroxime 500 mg BID for 14–21 days
- Disseminated disease
  - Doxycycline 100 mg BID for 14–28 days
  - Alternatives: amoxicillin 500 mg TID or cefuroxime 500 mg BID for 14–28 days
- Neurological involvement (including ocular disease involving the posterior segment): may need IV (intravenous) therapy; in Europe, oral antibiotics appear to be as effective as IV therapy for meningitis. In the USA, IV therapy is used more commonly
  - Ceftriaxone 2 g once daily
  - Cefotaxime 2 g Q8H
  - Penicillin G 18–24 MU/day divided Q4H
- Topical corticosteroids for nummular keratitis and anterior uveitis, and oral corticosteroids for posterior segment inflammation, once proper antibiotic has been started

Referral/Comanagement

- Infectious Disease
- Rheumatology
- Dermatology
- Neurology