

Neurosciences

Ticks

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Definition of Ticks

- Ticks are blood-feeding parasites. Once aboard, ticks crawl until they find a suitable spot to feed, then burrow their mouthparts into the skin for a blood meal.
- Ticks feed anywhere from several minutes to weeks depending on their life stage, type of host, and species of tick.
- It is during feeding that infected ticks can transmit disease to their hosts.

- Ticks are members of the **class Arachnida**. There are three families of ticks, two of which are known to transmit disease to humans.
- The **family Ixodidae** (hard ticks) includes 13 genera, of which Amblyomma, Dermacentor and Ixodes transmit disease to humans in the United States. The **family Argasidae** (soft ticks) contains five genera; only Ornithodoros is known to transmit disease to humans in the United States.

Life cycle

- Ticks have four life stages; **egg**, 6-legged **larva**, 8-legged **nymp**h and 8-legged **adult**.
- Most **hard ticks** undergo a 2-year life cycle in which they begin as 6-legged larvae. The larvae hatch from eggs in summer and begin seeking hosts in August; these ticks have only 6 legs and are the size of the period.
- If the larvae do not find a host for a blood meal, they die. Larvae that successfully feed then fall off the host and live in the soil and decaying vegetation over the winter.

- The next spring, most often in May and June, the larvae molt into 8-legged nymphs. These nymphs are quite small and seek their blood meal from a small vertebrate.
- Humans may be infected as accidental hosts at this point in the cycle.
- Then, the nymph either dies (if it fails to find a blood meal) or lives in the soil to molt into an adult in the fall season.
- The 8-legged adult tick is somewhat larger and seeks a larger host for its required blood meal. Hard ticks feed once during each stage.

- The adult ticks mate on the preferred host over the winter months. The adult female lays several thousand eggs and then dies. Eggs that survive the winter hatch into larvae the next season, and the 2-year cycle begins anew.
- **Soft ticks** have no hard shell (scutum). In the U.S. only ticks of the genus *Ornithodoros* transmit human disease, namely, **relapsing fever**. The biology of soft ticks differs from that of hard ticks in that meals last for only short periods (<1 h), and disease can be transmitted in less than 1 minute.

Amblyomma americanum, adult female, and a nymphal form of the same species



A soft-bodied tick of the genus *Ornithodoros*



Pathogenesis and clinical disease

- The mechanism of transmission of disease through tick bites is not well understood.
- During a blood meal, pathogens harbored in the gut of ticks may migrate to their salivary glands and then are transmitted to the host. When a tick attaches to a human, prostaglandins in the tick saliva are passed into the skin. These may decrease the production of IL-1 and TNF-alpha by macrophages and the secretion of IL-2 and interferon gamma by T-lymphocytes.

- These actions have an inhibitory action on the host's local immune response.
- Apyrase, an enzyme in tick saliva, may maintain blood flow into the bite by stimulating local vasodilation and preventing platelet aggregation. There are also inhibitors of the coagulation cascade in tick saliva that enhance blood flow to the lesion.
- These factors combine to enhance the blood meal of the tick and facilitate transmission of infectious agents to the host

Major tick-borne diseases include:

- **Bacteria**
- **Lyme Disease:**
 - Organism: *Borreila burgdorferi* (bacterium)
 - Vector: deer tick (*Ixodes scapularis* (=I. dammini), *I. pacificus*, *I. ricinus* (Europe), *I. persulcatus* (Asia))
 - Endemic to: North America and Eurasia
- **Rocky Mountain Spotted Fever** Organism: *Rickettsia rickettsii*
 - Vector: Wood tick (*Dermacentor variabilis*), *D. andersoni*
 - Region (US): East, South West
 - Vector: *Amblyomma cajennense*
 - Region (Brazil): Sao Paulo, Rio de Janeiro, Minas Gerais

- **Erlichiosis anaplasmosis** (human granulocytic E.) Organism: *Ehrlichia chaffeensis*, *E. equi* and *Ehrlichia sennetsu*
 - Vector: lone star tick (*Amblyomma americanum*), *I. scapularis*
 - Region (US): *South-Atlantic South-Central*
- **Relapsing fever**
 - Organism: *Bprrrelia species*
 - Vector: *Ornithodoros species*
 - Region (US): West
- **Tularaemia**
 - Organism: *Francisella tularensis*, *A. americanum*
 - Organism: *D. andersoni*, *D. variabilis*
 - Region (US): Southeast, South-Central, West, Widespread

- **Virus**

- **Tick-borne meningoencephalitis**

- Organism: **TBEV** aka FSME virus, a **flavivirus**
- Vector: deer tick (*Ixodes scapularis*), *I. ricinus* (Europe), *I. persulcatus* (Russia + Asia)
- Endemic to: Europe and Northern Asia **Colorado tick fever**

- **Colorado tick fever**

- Organism: *Coltivirus*
- Vector: *D. andersoni*
- Region (US): West

- **Crimean-Congo hemorrhagic fever**

- Organism: *Rhipicephalus bursa*
- Organism: *Hyalomma marginatum marginatum*
- Region (Turkey)

- **Protozoa Babesiosis**
- Babesiosis
 - Organism: *Babesia microti*, *B. equi*
 - Vector: *I. scapularis*, *I. pacificus*
 - Region (US): Northeast West Coast
- Cytauxzoonosis
 - Organism: *C. felis*
 - Vector: *D. variabilis* (American Dog Tick)
 - Region (US): South, Southeast
- **Toxin**
- Tick paralysis
 - Cause: Toxin
 - Vector: *D. andersoni*, *D. variabilis West*
 - Region (US): East

Lyme Disease

- Acute Lyme disease is characterized by fever, a migratory “bull’s eye” skin rash, muscle and joint pains, often with evidence of meningeal irritation.
- In a chronic form evolving over several years meningo-encephalitis, myocarditis, and a disabling recurrent arthritis may develop.
- *B. burgdorferi* is transmitted to humans by *Ixodes scapularis* (black-legged tick).

EPIDEMIOLOGY

- *B. burgdorferi* exists in a complex cycle involving ticks, mice, and deer. Lyme disease occurs when the ticks feed on humans who enter their wooded habitat.
- The disease is endemic in many parts of the world. The primary reservoir of *B. burgdorferi* is rodents, particularly white-footed mice.
- Infection is transmitted by *Ixodes ticks*, Ticks feed on mice and then deer. Adult & nymph stages can infect humans.
- Deer are essential to the mating and survival of the tick (no deer, no disease).

Clinical manifestations

- Lyme borreliosis is a highly variable disease involving multiple body systems.
- The skin lesion spreading from the site of the tick bite is its most characteristic finding. Relapsing arthritis is the most persistent finding. Lyme disease is rarely fatal, but if untreated, is often a source of chronic illness.
- Erythema migrans and febrile aches mark acute disease.
- Meningitis, cranial nerve palsies, peripheral neuropathy and cardiac findings appear later.

DIAGNOSIS

- The diagnosis of early Lyme disease is based on exposure and typical clinical findings. Culture and PCR are not yet practical.
- Diagnosis in later stages of disease usually rests on the demonstration of circulating antibodies to *B. burgdorferi*. Serologic tests are not diagnostic as they still lack the sensitivity and specificity.
- The current recommendation is to first perform a sensitive screening test (EIA or fluorescent antibody) followed by a more specific Western blot.

TREATMENT

- **Doxycycline** and **amoxicillin** are the first-line antimicrobics for the treatment of early Lyme disease and arthritis.
- **Cefuroxime** is an alternative for oral therapy.
- Intravenous therapy with **ceftriaxone** or **penicillin G** is recommended for patients with neurologic involvement or cardiovascular findings such as atrioventricular heart block.
- The response to treatment is typically slow requiring the continuation of antimicrobics for 30 to 60 days.

PREVENTION

- Avoiding places where ticks often live.
- The most useful preventive measures in endemic areas are the use of clothes that reduce the likelihood of the infected nymph reaching the legs or arms, careful search for nymphs after potential exposure and removal of the tick by its head with tweezers.
- Some insect repellents may provide added protection.
- Vaccine is directed against the feeding tick.

Rocky Mountain Spotted Fever

- It is an acute febrile illness that occurs in association with residential and recreational exposure to wooded areas where infected ticks exist. It is caused by the bacterium known as *Rickettsia rickettsii*. The disease has a significant mortality (25%) if untreated.
- It was originally called “black measles” because of the look of its rash in the late stages of the illness, when the skin turns black.

Epidemiology

- Ticks are naturally infected. Wood tick (*Dermacentor andersoni*), dog tick (*Dermacentor variabilis*) and Lone Star tick (*Amblyomma americanum*) are dis. vectors.
- *R. rickettsii* does not kill its arthropod host, so the parasite is passed through unending generations of ticks by transovarial spread.
- Adult females require a blood meal to lay eggs and thus may transmit the disease.
- More than two thirds of cases are in children less than 15 years of age.

Manifestations

- Incubation period 2–6 days after tick bite.
- Fever, headache, rash, toxicity, mental confusion, and myalgia are the major clinical features. The rash usually develops on the second or third day of illness as small erythematous macules that rapidly become petechial. The lesions appear initially on the wrists and ankles and then spread up the extremities to the trunk in a few hours.
- A diagnostic feature is frequent appearance of the rash on the palms and soles.

Diagnosis

- Rising antibody titers confirm the diagnosis.
- Prompt initiation of therapy is based on clinical and epidemiologic considerations.

Treatment

- Appropriate antibiotic therapy is highly effective if given during the first week of illness. **Doxycycline** is the treatment of choice.
- Death results in patients in whom diagnosis and therapy are delayed into the second week of illness.

Prevention

- The major means of preventing RMSF is avoidance or reduction of tick contact. Frequent deticking in tick-infested areas is important, because ticks generally must feed for 6 hours or longer before they can transmit the disease.
- Killed vaccines prepared from infected ticks, or rickettsias grown in embryonated eggs and cell cultures have been developed. None is licensed for clinical use at present.

EHRlichIA

- The *Ehrlichia* genus includes several species of white blood cell-associated bacteria (small, gram-negative, pleomorphic, obligate intra-cellular organisms) that cause human disease. *Ehrlichia sennetsu*, the first species to be identified as a cause of human disease is restricted to Japan and Malaysia.
- In the U.S., the principal causes are:
- Human monocytic ehrlichiosis (HME) due to *Ehrlichia chaffeensis*; and
- Human granulocytic ehrlichiosis (HGE) due to *Anaplasma phagocytophilum*.

- They are transmitted by deer or dog ticks.
- On occasion, the diagnosis of ehrlichiosis may be suggested by observation of characteristic ehrlichial intracytoplasmic inclusions (morulae) in granulocytes (HGE) or mononuclear cells (HME).
- Confirmation is usually made serologically by a fourfold or greater rise in antibody & PCR.
- **Doxycycline** is the drug of choice for ehrlichiosis. The risk of infection can be reduced by avoiding wooded areas and tick bites.

Babesiosis

- Babesiosis is a tickborne, malaria-like parasitic disease that can be found worldwide.
- In most people, babesiosis is a mild disease. It can, however, be very serious or even fatal. Those who suffer the most serious cases include the elderly, people who don't have a spleen, transplant patients, and those with other diseases associated with immunosuppression, such as HIV infection.

Epidemiology

- It is a vector-borne illness usually transmitted to humans by the bite of an infected deer tick, *Ixodes scapularis*. This is the same tick that transmits Lyme disease.
- Usually is caused by a parasite called *Babesia microti* that attacks RBCs in much the same way as that causes malaria.
- Disease in Europe is usually due to infection with *Babesia divergens*.

Manifestations

- Most people with babesiosis do not have symptoms. If you do have symptoms, they will usually appear 1 to 4 weeks after you have been infected with the parasite. Symptoms include chills, fever, headache, muscle aches, sweating, fatigue, nausea, vomiting and weakness.

Treatment

- Most cases of babesiosis resolve without any specific treatment. **Quinine** and **Clindamycin**, or **Atrovaquone** and **Azithromycin** have been used.

TULAREMIA

- Tularemia is a disease of wild mammals caused by *F. tularensis*, a small, facultative, coccobacillary, Gram-negative rod.
- Humans become infected by direct contact with infected animals or through the bite of a vector (tick or deer fly).

Epidemiology

- Infecting dose is low (100 organisms), Acquired by tick bites or directly from wild mammal. Distribution throughout Northern hemisphere.

Manifestations

- Incubation period of 2 to 5 days.
- Ulceroglandular, oculoglandular, typhoidal, and pneumonic forms exist.
- Without treatment, mortality ranges from 5 to 30%, Ulceroglandular has lowest mortality.

Diagnosis

- Culture on special media. Serodiagnosis is the most common, Single high antibody titers.

Treatment and Prevention

- **Streptomycin** is the drug of choice, Tetracyc. & chloram. Use rubber gloves & eye protection.