Tick- Born Diseases
الامراض المنتقلة بالقراد

Borrelia burgdorferi (Lyme disease)

- Lyme disease is named after the town of Lyme, where clusters of cases in children were identified.
- Lyme disease is caused by the spirochete *B. burgdorferi* and is transmitted to humans by the bite of a small *Ixodes tick*.
- Ticks are hematophagous *ectoparasites* that become infected with *B. burgdorferi* by feeding on one of the majors reservoirs for the Spirochete, e.g. certain strains of *mice, deer, birds, and lizards*.السحلً
- The disease has early manifestations with a characteristic skin lesion, **erythema migrans**, along with **flu-like symptoms**, and late manifestations often with **arthralgia** and **arthritis**.

![Image](https://example.com/image.jpg)

**Typical Organisms**

- *B. burgdorferi* is a spiral organism, highly motile.
- Transmission of *B. burgdorferi* to humans is by injection of the organism in tick saliva or by regurgitation of the tick's midgut contents.
- The organism **adheres to proteoglycans** on host cells; After injection by the tick, the organism migrates out from the site, producing the characteristic skin lesion.
- Dissemination occurs by lymphatics or blood to other skin and musculoskeletal sites and to many other organs.
- *B. burgdorferi* can spread throughout the body during the course of the disease, and has been found in the skin, heart, joints, PNS, and CNS. Many of the signs and symptoms of Lyme disease are a consequence of the **immune response to the spirochete**. Lyme disease occurs in different stages with early and late manifestations.

**A. Early localized infection**

- Early localized infection can occur when the infection has not yet spread throughout the body. Only the site where the infection has first come into contact with the skin is affected. The classic sign of early local infection with Lyme disease is a **circular, outwardly expanding rash, erythema Migrans**, which occurs at the site of the tick bite 3 to 32 days after the tick
bite. The rash is red, and may be warm, but is generally painless with the appearance of a **bull's eye**.

**B. Early disseminated infection**

- Within days to weeks, the Borrelia bacteria may begin to spread through the bloodstream. Various acute neurological problems, termed neuroborreliosis, appear in 10–15% of untreated people. These include facial palsy, as well as meningitis, which involves severe headaches, neck stiffness, and sensitivity to light. Inflammation of the spinal cord nerve roots can cause shooting pains that may interfere with sleep, as well as abnormal skin sensations. Mild encephalitis may lead to memory loss, sleep disturbances, or mood changes.

**C. Late disseminated infection**

- After several months, untreated or inadequately treated patients may go on to develop severe and chronic symptoms that affect many parts of the body, including the brain, nerves, eyes, joints, and heart. Many disabling symptoms can occur, including permanent impairment of motor or sensory function of the lower extremities.

- Unfortunately, many Borrelia strains have evolved ways to resist the complement system. **B. burgdorferi can bind factor H** (H regulates complement activation by possessing both cofactor activity for the Factor I mediated C3b cleavage, and decay accelerating activity against the alternative pathway C3-convertase, C3bBb) produced by the complement system, and thereby avoid complement-mediated opzonisation, formation of membrane attack complexes and phagocytosis, thus escaping unharmed from this first line of defense.

- The cells of the innate immune system, e.g. monocytes, macrophages, dendritic cells (DCs) and granulocytes, first encounter *B. burgdorferi* locally at the site of the tick bite where the spirochete usually remains localized for some time. The cells of the innate immune system sense the presence of pathogens by recognizing certain pathogen-associated molecular patterns (PAMPs) through Toll-like receptors (TLRs).
- TLRs recognize different microbial ligands such as lipoproteins, lipopolysaccharides (LPS), lipotechoic acid (LTA) and cell-wall peptidoglycan

**Diagnosis**

Lyme disease is diagnosed **clinically based on symptoms**, as well as serological blood tests. The EM rash is not always a bull's eye, i.e., it can be solid red.

Polymerase chain reaction (PCR) tests for Lyme disease have also been developed to detect the genetic material (DNA) of the spirochete.

Lumbar puncture is more definitive of diagnosis of antigen capture in the CSF. OspA antigens, shedded by live Borrelia bacteria, are detected by Western blot, and ELISA. Anti-OspA immunoglobulin G (IgG) antibody concentrations correlate directly with the severity and duration of Lyme arthritis.

**Tick-borne encephalitis virus (TBEV)**

Tick-borne encephalitis virus (TBEV), belonging to the tick-borne Flavivirus group, genus Flavivirus, family Flaviridae
TBEV is the causative agent of tick-borne encephalitis in humans, usually after the bite of an infected tick. Two types of host are required for TBEV circulation in nature. The first is the tick as the reservoir and carrier of TBEV and the second the vertebrate animal whose blood is the nutrient source for ticks and also the way in which the virus is transmitted from infected to non-infected ticks by their feeding on the same animal. The virus circulates between vector ticks and some of their hosts, mostly deer and rodents with humans being as accidental hosts.

**There are three TBEV subtypes:**

1. **Far-Eastern (FE-TBEV)**, mainly in the Russian Far East, formerly known as Russian Spring Summer encephalitis virus, RSSEV, transmitted by *Ixodes persulcatus*.

2. **Siberian (S-TBEV)**, which are transmitted by *Ixodes persulcatus*, is commonest in Siberia, the European part of Russia, the Baltic countries and Finland.

3. **European (Eu-TBEV)**, which is transmitted by *Ixodes ricinus*.

Each TBEV subtype has specific nucleotide substitutions in the protein E gene (Envelop protein E) and their classification is based on this characteristic.
➢ After an infected tick bite, TBEV replication occurs locally.
➢ **Dendritic skin cells (Langerhans cells)** are assumed to be the first cells for viral replication and to transport the virus to local lymph nodes.
➢ From this initial site the TBEV then disseminate to extraneural tissues, especially **spleen, liver** and **bone marrow**, where further multiplication maintains viremia for several days.
➢ During the viremic phase the virus probably **reaches the brain**. The exact mechanism by which TBEV breach the blood-brain barrier is not known.

**Four possible routes have been postulated:**

(1) **peripheral nerves**
(2) **highly susceptible olfactory neurons**
(3) **transcytosis through vascular endothelial cells of brain capillaries**
(4) **diffusion of the virus between capillary endothelial cells.** The primary targets of TBEV infection in CNS are neurons.

Schematic drawing of the steps during TBE virus infection. (1) TBE virus transmission from an infected tick, (2) TBE virus replication in regional lymph node, (3) primary viremia, (4) replication of the virus in other organs and tissues, (5) secondary viremia, (6) TBE virus crossing of the blood-brain barrier, and (7) virus infection of the brain
Cerebral and spinal meninges usually show diffuse infiltration with lymphocytes and sometimes neutrophils.

Pathological lesions consist of

- lymphocytic perivascular infiltrations
- accumulation of glial cells
- nerve cells necrosis
- neuronophagia

Blume العصبىنات are localized in the grey matter and are most often present in the medulla oblongata, pons, cerebellum, brainstem, basal ganglia, thalamus, and spinal cord.

Manifestations of TBEV infection

- The large majority of infections with TBEV are asymptomatic.
- The incubation period of TBE ranges from 2 to 28 d and is usually 7-14 d.
- Disease with the European TBEV has a typical biphasic course.

The initial phase correlate with viremia and usually presents with non-specific symptoms such as moderate fever, headache, body pain (myalgia and arthralgia), fatigue, general malaise, anorexia, nausea, and others. This phase lasts for 2 to 7 d and is followed by an asymptomatic interval that usually lasts for about 1 wk.

The second phase appears in approximately 50% of adult patients it presents as meningitis, in about 40% as meningoencephalitis, and in around 10% as meningoencephalomyelitis.

- Meningitis and encephalitis are the most frequent clinical forms of TBE. Meningitis typically manifests with high fever, headache, nausea and vomiting; many patients have photophobia, and some vertigo. Meningeal signs are present in most of patients. Other manifestations comprise personality changes, behavioral disorders, concentration and cognitive function disturbances, and tremor of extremities

- Cranial neuritis most commonly affects ocular, facial, pharyngeal and vestibular nerves
Occasionally, patients with TBE have pronounced variability in heart rate or other signs of autonomic nervous system dysfunction

**DIAGNOSIS**

A case of TBE is diagnosed by the presence of:

1. symptoms/signs indicating meningitis or meningoencephalitis
2. an elevated cerebrospinal fluid cell count (> 5 × 10⁶ cells/L)
3. Serologic evidence of TBEV infection (the presence of specific IgM and IgG antibodies).

Routine laboratory confirmation of the TBEV infection is based mainly on the demonstration of **specific antibodies in serum and CSF**. In the majority of patients specific serum IgM and IgG antibodies are present at the beginning of the meningoencephalitic phase of the disease.

World Health Organization (WHO) recommends vaccination to people of all age groups, including children, in highly endemic areas.