# 12th ESCMID Summer School, 2013, Vravrona

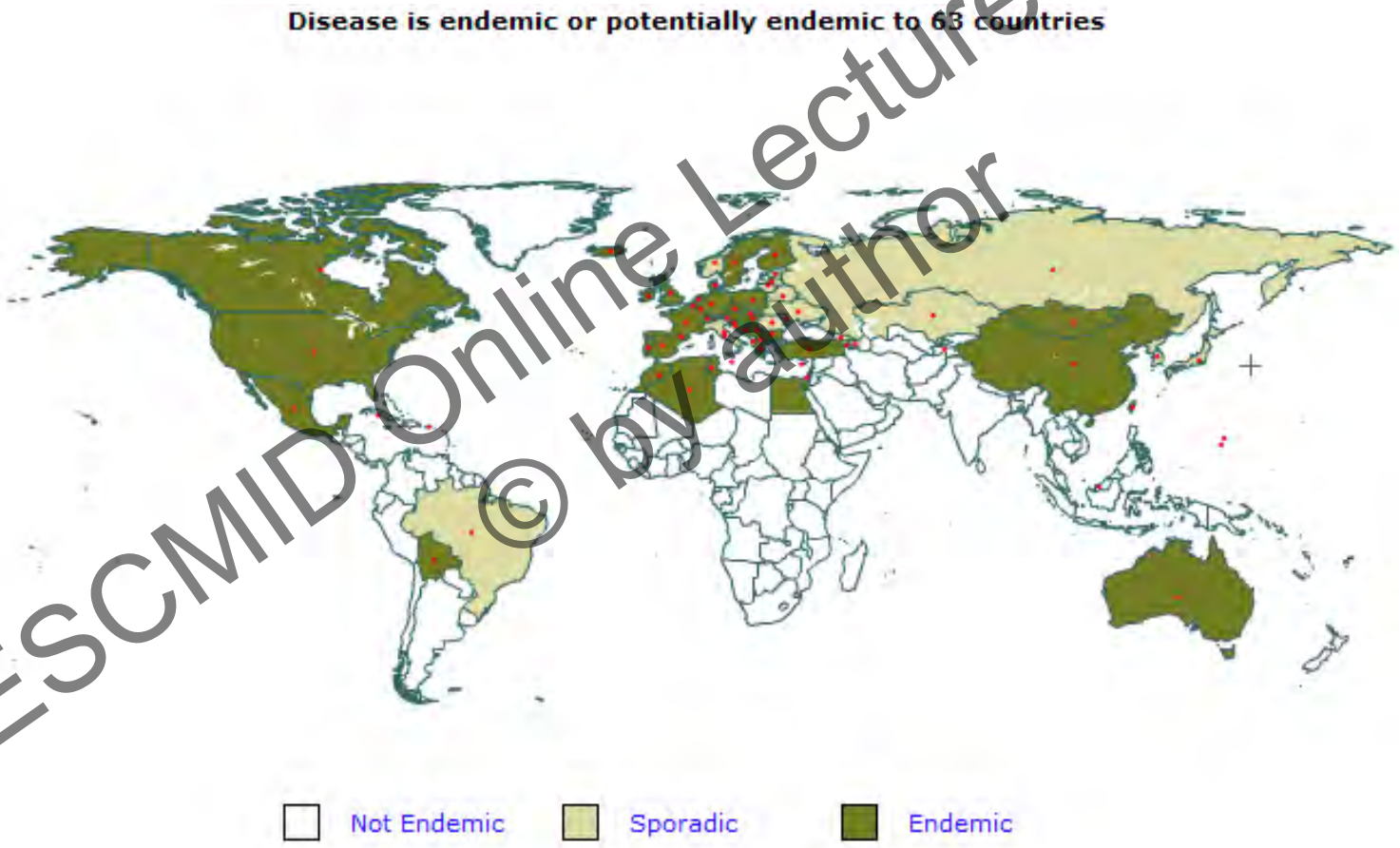

## Lyme Borreliosis in Europe

Nikolaos V. Sipsas, M.D.
National and Kapodistrian University of Athens

# Lyme borreliosis

- A tick-transmitted bacterial infection caused by some members of the spirochete group
  - *Borrelia burgdorferi sensu lato.*
- It is the most prevalent tick-transmitted infection in temperate areas of:
  - Europe,
  - North America
  - Asia

# Epidemiology



# The organism

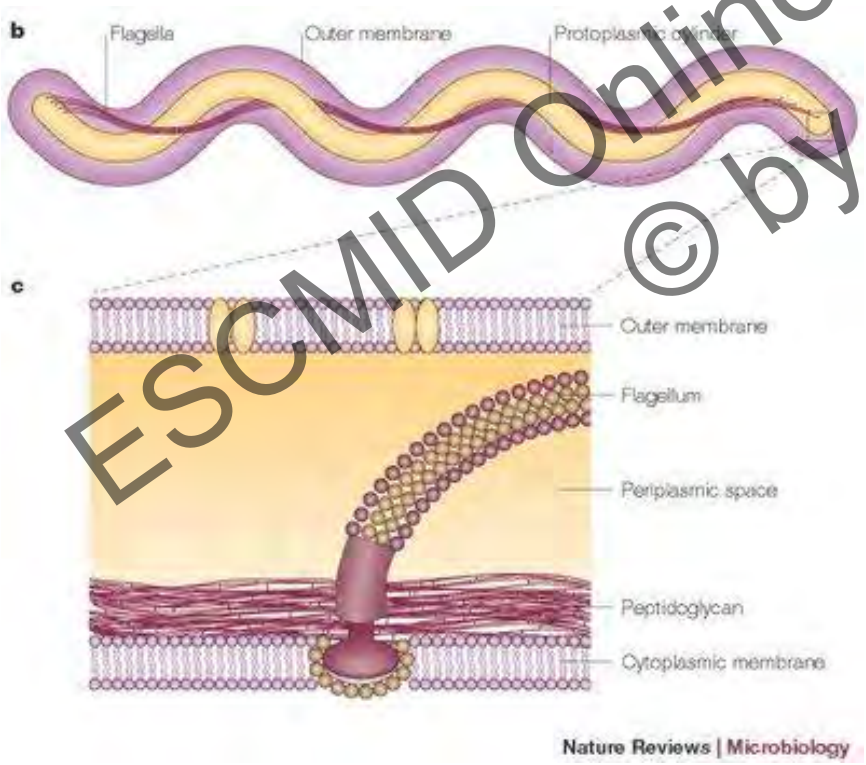
- The B. burgdorferi complex comprises at least 15 genospecies worldwide
- Only five are significantly pathogenic to humans.

# Lyme Borreliosis in Europe

- Borrelia afzelii (skin manifestations)
- B. garinii (neurological manifestations)
  - the major pathogenic genospecies found in Europe
- B. burgdorferi sensu stricto is present in some parts of Europe
  - neurological and arthritic complications
- B. bavariensis, neurological complications
- B. spielmanii.
- B. valaisiana and B. lusitaniae rarely cause disease in humans.

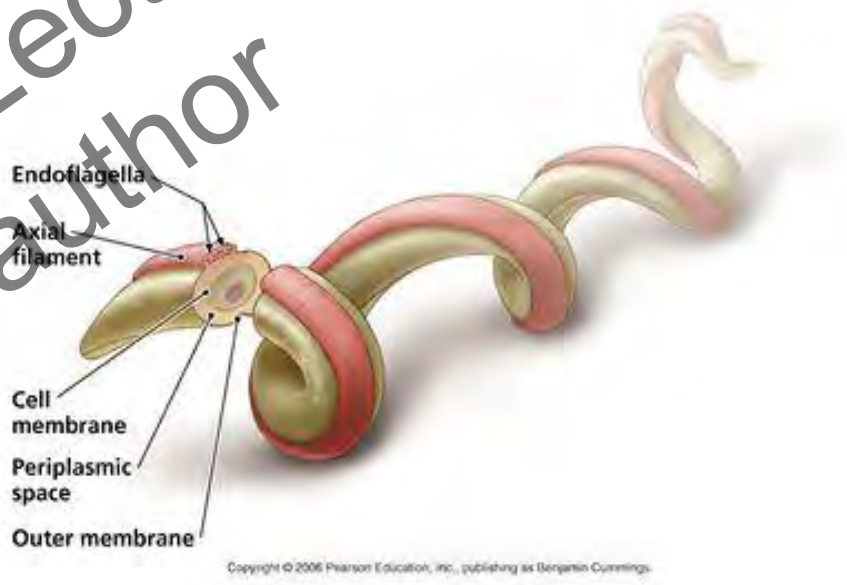
# Lyme Borreliosis in Europe

- *Borrelia burgdorferi*
- Spirochete
- Obligate Intracellular pathogen




# ORGANISM:

*Borrelia burgdorferi*



# Transmission

- Transmitted by ticks
  - Ixodes ricinus species complex

# Ticks

# Global distribution of the vectors (Ixodes ricinus species complex) of Lyme borrelia

# Developmental stages of Ixodes ricinus



Larva, Nymph, Adult female, Adult male

European Concerted Action on Lyme Borreliosis.

# Infectious cycle of the European Borrelia genospecies

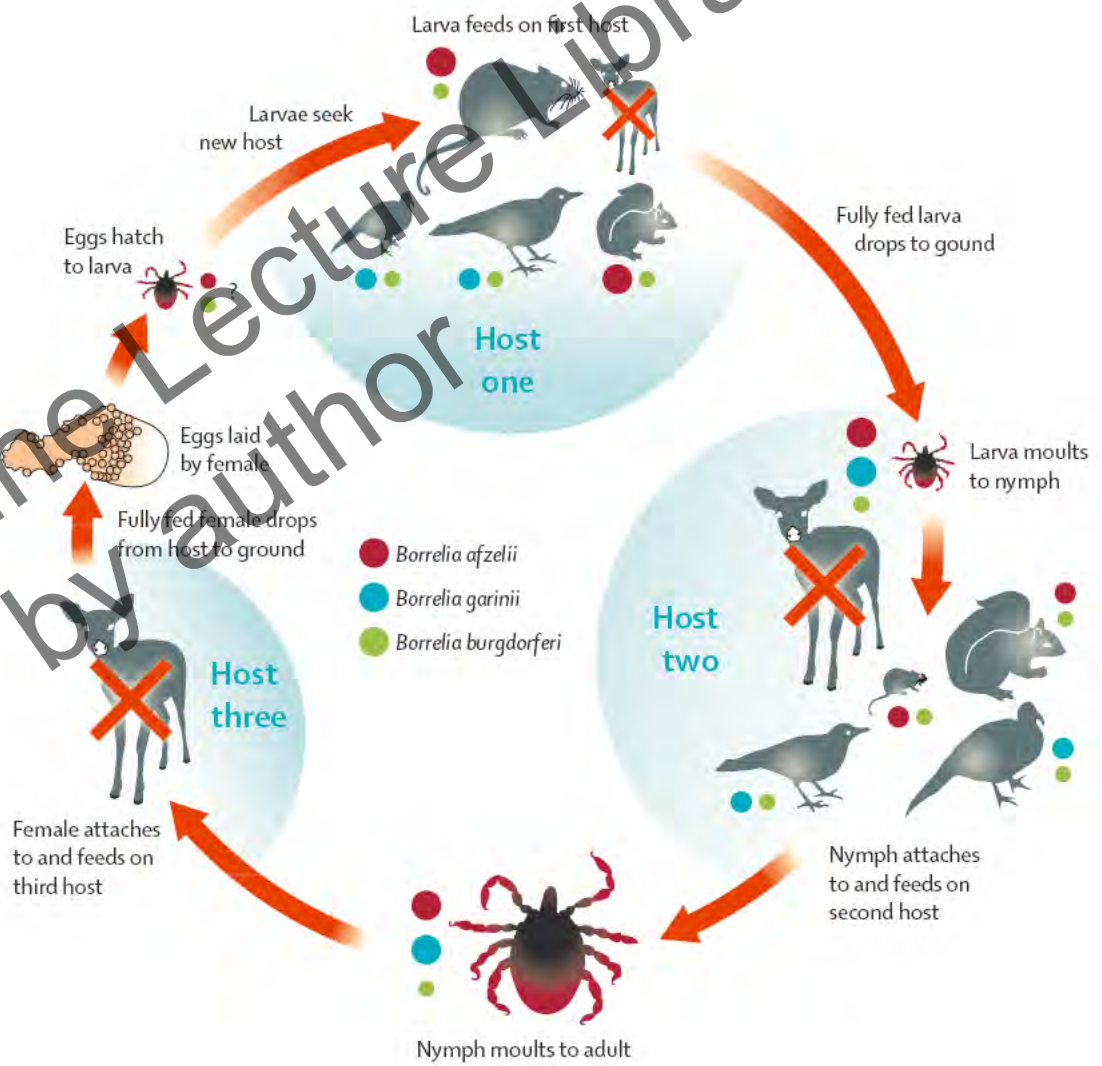
- B. burgdorferi

  circulates between

  - hard ticks
  - vertebrate hosts
    - small mammals
    - ground-feeding birds

# Infectious cycle of the European Borrelia genospecies

Adult ticks usually feed on larger animals such as deer, which are not reservoirs for borrelia, but help to maintain the ticks' reproductive stage



# Lyme Borreliosis in Europe

- The overall mean prevalence of *B. burgdorferi* genospecies in ticks in Europe : 12%
- The regions with highest tick infection rates (nymphs > 10%; adult ticks > 20%) are located in central Europe
  - Austria,
  - Czech Republic,
  - Southern Germany,
  - Switzerland,
  - Slovakia
  - Slovenia.

# Where are the ticks?

- The most suitable microhabitats for ticks have > 85% relative humidity.
  - woodland,
  - heathland,
  - open grassy meadows
  - suburban and urban environments,
    - urban parklands.

# Transmission mode of *B. burgdorferi*

- Bite from an infected tick,
  - a nymph
  - an adult tick.

- Larval tick bites do not pose a significant risk, as it is rare for larvae to carry infection

# Transmission mode of B. burgdorferi

- *B. burgdorferi* normally lives within gut epithelium of tick
- Organism must migrate to salivary glands to be secreted into host

# Transmission mode of *B. burgdorferi*

- As blood flows into gut, the temperature change appears to cause shift of *B. burgdorferi* from gut epithelium to the hemolymph, and then to salivary glands.
- While feeding the tick secretes anti-inflammatory agents, anti-coagulants, and analgesic agents to permit undetected persistence of tick.

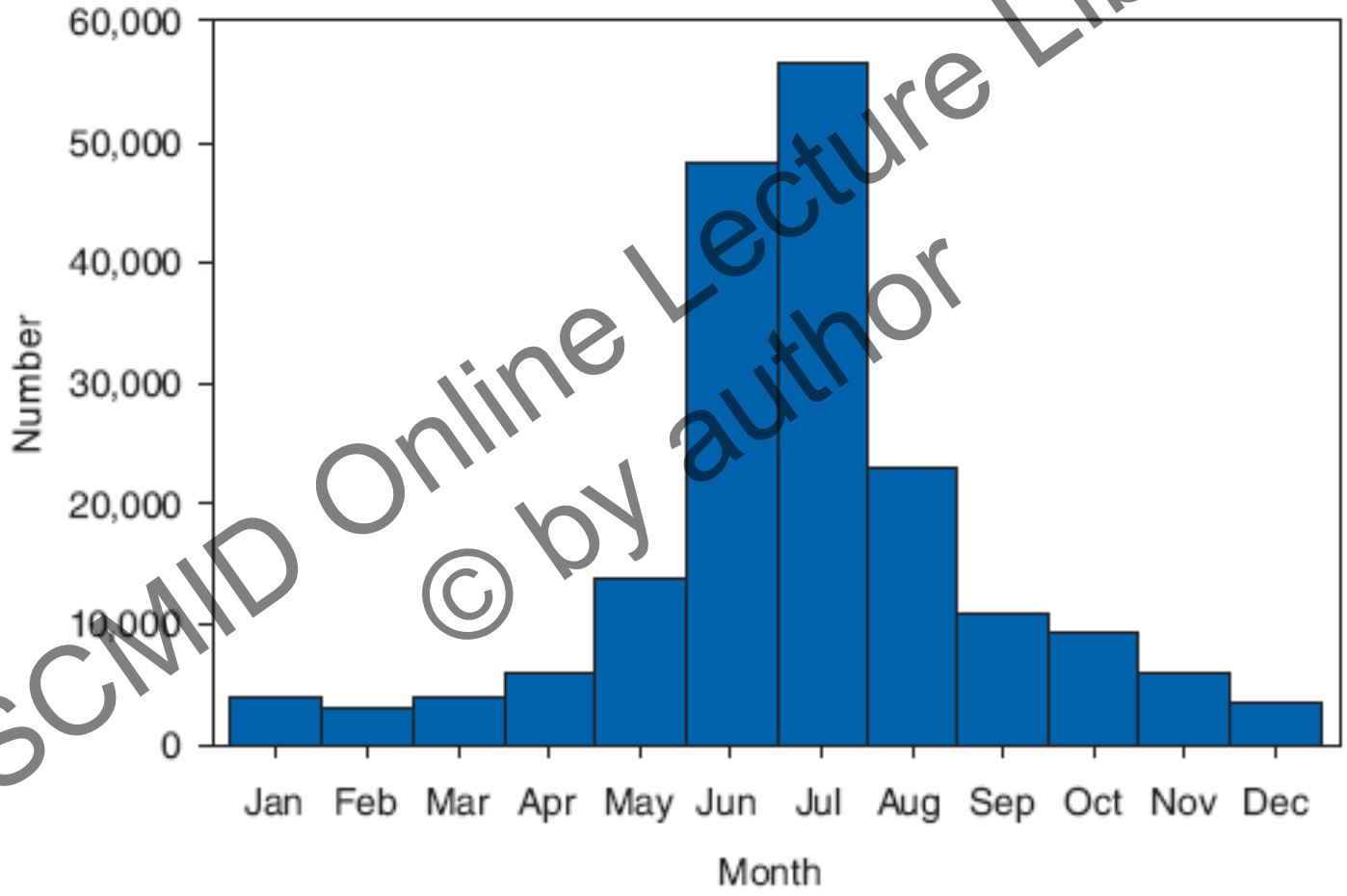
# Transmission mode of *B. burgdorferi*

- Nymphs are most likely to transmit because of inconspicuously small size to permit feeding for as much as several days.

# Transmission mode of B. burgdorferi

- Infected ticks are unlikely to transmit the organisms in the early hours of a feed, but the risk rises steadily with increasing duration of the blood meal
- It needs 24h to transmit
- Early removal of attached ticks within the first hours is very useful in reducing transmission risk.

**FIGURE 5. Number* of reported Lyme disease cases, by month of illness onset — United States, 1992–2006**




* N = 188,340.

*Borrelia burgdorferi* infection can be asymptomatic.

# CLINICAL FEATURES

# Early manifestation – localized disease (first several days)

- Erythema migrans
  - outwardly expanding rash
  - 80-90% of cases.
  - not significantly raised or painful.
  - Usually present; look everywhere
- 'flu-like' illness but without significant respiratory symptoms.
  - Best treatable stage!

James Gathany / CDC

# Early manifestations – localized disease (first several days)

- Borrelial lymphocytoma
  - is an uncommon early skin manifestation
  - affecting
    - earlobe
    - nipple
    - scrotum.
  - It may persist for some months
  - can be mistaken for cutaneous lymphoma because of its associated intense lymphocytic infiltrate

# Borrelial lymphocytoma

- reddish-blue nodule

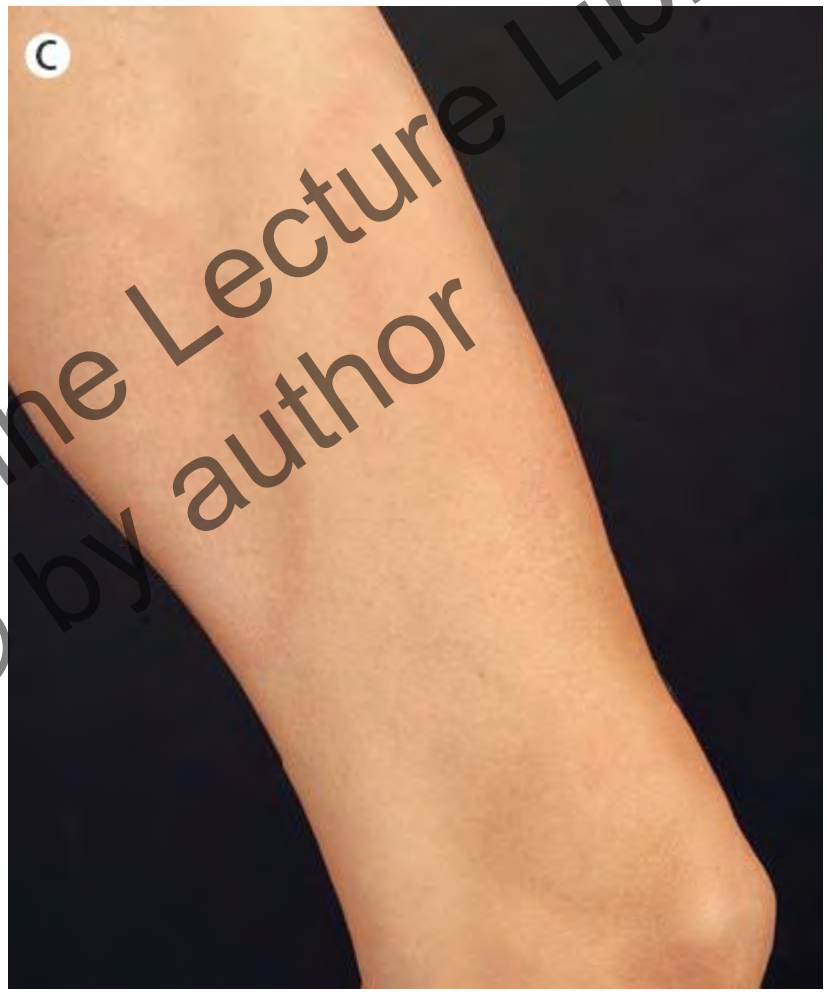
  on the ear lobe.

# 2nd stage (early disseminated) days to weeks

- hematogenous dissemination
- may have multiple bull's eye lesions distributed to other sites of the body
- Also pain in muscles, joints, and tendons, heart palpitations, severe headaches
- Early meningoradiculitis or CN palsy (esp VII)
- Early AV conduction defects (first degree)

# 2nd stage (early disseminated)

days to weeks



# 2nd stage (early disseminated)
# days to weeks

# 3rd Stage: Persistent infections (months later)

- Late Lyme borreliosis can affect
  - the skin,
  - nervous system
  - musculoskeletal system

# Late presentations - Skin

- acrodermatitis chronica atrophicans,
  - a persistent skin infection usually affecting the extremities, causing:
    - inflammation of the skin
    - thinning of the affected skin
    - neuropathy.

## Acrodermatitis chronic atrophicans

(A) ulnar and hand lesions,

(B) bluish-red lesion on the back of a patient's hand and waxy appearance of the skin of fingers,

(C) lesions on a patient's left foot and lower leg.

# Late presentations – CNS - Joints

- Late neuroborreliosis
  - usually presents as an encephalomyelitis and can resemble multiple sclerosis.
  - cranial nerve palsies (VII),
  - Meningoradiculitis
  - Irreversible neural injury may develop unless treated.
- Lyme arthritis
  - usually affects a large joint, most commonly the knee.
  - painful arthralgias

# Late presentations

- Uveitis
- Heart blocks (first degree most common); myoepicarditis
- All are caused by active infection which will respond to antibiotic therapy

# Post-Lyme borreliosis syndrome

- some patients (median of 11·5% 15·4%) report long-term (≥6 months) persistence of
  - fatigue,
  - weakness
  - musculoskeletal pain,
  - difficulties with concentration
  - Cognitive impairment
- Similarity to other chronic spirochetal infections, such as syphilis

# Diagnosis

- No laboratory tests are required in the diagnosis of erythema migrans, which depend on a clinical evaluation and an assessment of tick exposure risk.
- Laboratory tests are necessary to confirm a diagnosis of later stage infection.
- Antibodies to *B. burgdorferi* are usually detectable within 4-8 weeks of infection.

# Diagnosis

- Neuroborreliosis
  - antibody testing and borrelial DNA detection studies on CSF
- Erythema migrans and acrodermatitis chronica atrophicans
  - Borrelia DNA detection on skin biopsies
- Lyme arthritis
  - antibody testing and Borrelia DNA detection on synovial fluid

# Prevention

- Best method: avoid exposure to vector ticks
- If exposure to I. ricinus ticks is unavoidable,
  - Use both protective clothing and tick repellents
    - long trousers and long-sleeved shirts
    - DEET repellents on skin and clothes
  - Check entire body for ticks daily
  - Promptly remove attached ticks before transmission

# Removal of attached ticks

- with tweezers or fine-pointed forceps,
  - grasping the tick as closely as possible to the skin,
  - pulling gently upwards and
  - trying not to break off the mouth parts.
- The risk of borrelial infection is not increased if tick mouth parts are left behind.
- A skin disinfectant should be applied afterwards to prevent pyogenic infection.

# Areas to check for ticks

- skin-folds as ticks seek out more humid areas for attachment
  - groins,
  - armpits,
  - under breasts,
  - waist band area,
  - backs of knees
- young children
  - The head (including scalp) and neck area

# Prevention

- For prevention of Lyme disease after a recognized tick bite, routine use of antimicrobial prophylaxis or serologic testing is not recommended.
- Adverse reactions of doxycycline outweigh benefits.

# Medical Prevention with Caveats

- A single dose of doxycycline may be offered to adult patients (200 mg dose) and to children >8 years of age (4 mg/kg up to a maximum dose of 200 mg)
- Criteria:
  - 1. Attached tick can be reliably identified as an adult or nymphal (I. ricinus) tick.
  - 2. Estimated attachment >36 h (degree of engorgement or certainty about time of exposure).
  - 3. Prophylaxis can be started within 72 h of the time that the tick was removed.
  - 4. Ecologic data indicate that local rate of infection of ticks >20%.
  - 5. Doxycycline treatment is not contraindicated.

# Treatment of Early Localized or Early Disseminated Lyme Borreliosis

- Doxycycline
- Amoxicillin
- Cefuroxime axetil
- Duration: 14-21 days
- Verify absence of specific neurologic manifestations (e.g., VII palsy) or advanced atrioventricular heart block (A-I)

# Treatment of Lyme Meningitis or Radiculopathy in Adults

- Ceftriaxone (2 g once per day IV)
- Cefotaxime (2 g IV every 8 h)
- Penicillin G (18–24 million U per day)
- For patients who are intolerant of β-lactam antibiotics, doxycycline (200–400 mg per day in 2 divided doses orally
- Duration of treatment
  - Range: 10–28 days

# Treatment of Lyme Carditis

- Patients with AV heart block and/or myoepicarditis may be treated with either oral or parenteral antibiotic therapy for 14 days (range, 14–21 days).
- Hospitalization and continuous monitoring for symptomatic patients with:
  - syncope, dyspnea, or chest pain
  - second- or third-degree AV block
  - first-degree heart block when PR interval is prolonged to >30 milliseconds

# Treatment of Isolated Lyme Arthritis

- Doxycycline (100 mg twice per day)
- Amoxicillin (500 mg 3 times per day)
- Cefuroxime axetil (500 mg twice per day)
- For children, amoxicillin (50 mg/kg per day in 3 divided doses [maximum 500 mg/dose])
- Duration: 28 days

ΕΥΧΑΡΙΣΤΩ

# THANK YOU