Clinical diagnosis of Lyme and the major tick-borne diseases

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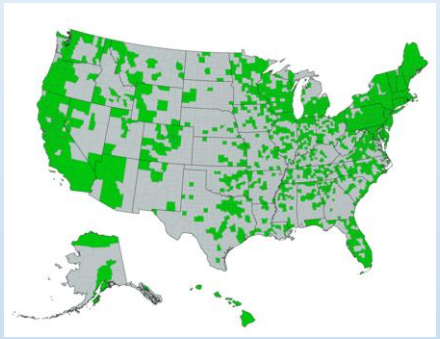
Lyme Bytes October 2024

Outline

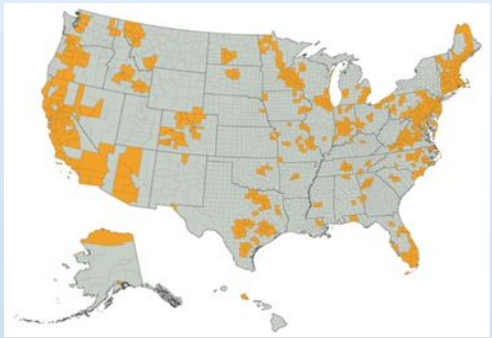
- Exposure, vector behavior, tick bites and tick saliva
- Non-tick transmission
- When to suspect TBDs
- Initial presentation and progression
  - Borrelia
  - Babesia
  - Bartonella
  - Rickettsias
- Clinical guide

It begins with potential exposure….

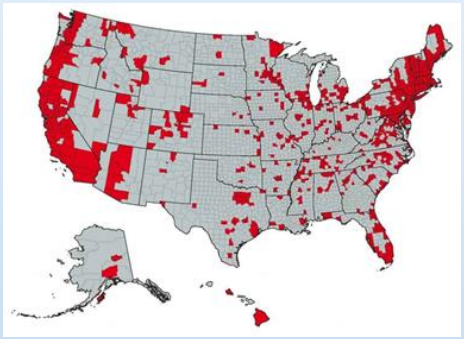
Where



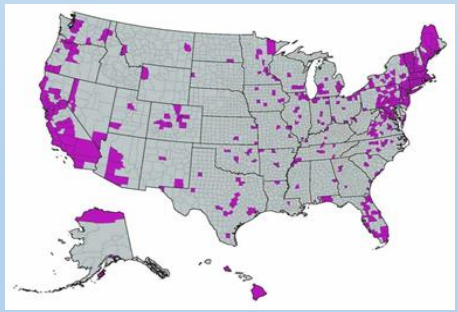
LYME



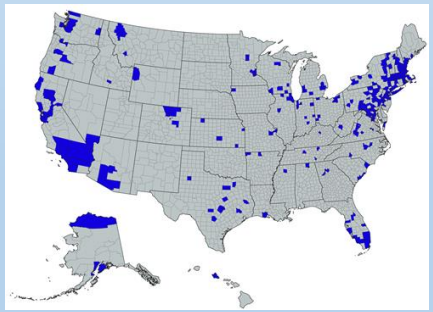
TBRF



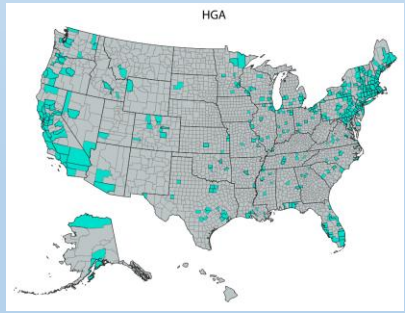
BABESIA



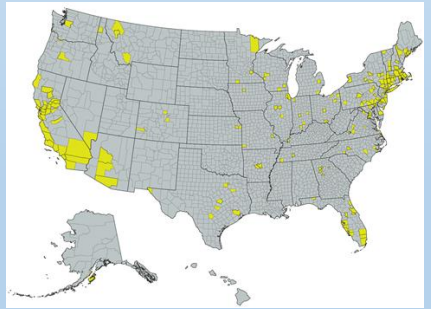
BARTONELLA



EHRLICHIA



ANAPLASMA



RICKETTSIA

It begins with potential exposure….

When:

- All year!
- April through October said to be highest but that applies mainly to the more northern states
- Southern states can have tick activity all year long

Don’t forget that people do travel and may pick up an infection from other countries

Vector behavior- questing vs. seeking

IXODES (deer tick) and DERMACENTOR (dog tick)

- **Questing**:
  - Climbs against gravity to the tips of vegetation with its barbed forelegs extended
  - Grabs onto passing people and animals

AMBYLOMMA (lone star tick) and ORNITHODOROS (relapsing fever tick)

- **Seeking**:
  - Can literally run quickly, like a spider, attracted to a host's heat and CO2

Functional properties of tick saliva

- “Ensuring attachment is maintained and nothing leaks out from the feeding site, is the role of a cement plug formed by polymerization of glycine-rich proteins secreted after initial attachment
- The attachment process severs tissues including nerves, causing pain and provoking host hemostatic responses (vasoconstriction, platelet aggregation, and fibrin clot formation)
- Host inflammatory and immune responses are induced
- Most of the constituents of tick saliva function to counter these host responses.”

TICK SALIVA- Complex chemistry

RESULT:

- Painless bites- often go unnoticed
- Pathogen transmission is enhanced
- Host defenses are circumvented
- Infections are more easily established

Constituent	Examples
Water	Excess water from host bloodmeal
Ions	Na^+, Cl^- (excess ions from host bloodmeal)
Non-peptidic molecules	Adenosine, prostaglandins, endocannabinoids, microRNAs
Tick peptides	Variegins, hyalomins, madanins
Tick proteins	Chitinases, mucins, ixostatins, cystatins, defensins, glycine-rich, hyaluronidases, Kunitz-type proteins, lipocalins, metalloproteases
Host proteins	Immunoglobulins, haptoglobin, transferrin
Exosomes	May contain microRNA, peptides, proteins

Tick saliva and its role in pathogen transmission. Wien Klin Wochenschr. 2023; 135(7-8): 165–176. 2019 May 6. doi: 10.1007/s00508-019-1500-y

Non-tick transmission

This has been seen in all the major tick-borne diseases

Can include:

- Maternal-fetal
- Transfusion
- Sexual transmission
- Iatrogenic (needle sticks)
- Animal bites/scratches in Bartonella

ALSO: Improper tick removal and handling

When to suspect TBDs

In the proper setting:

- “summer flu”, “atypical sinus infection”, “spider bite”, “ringworm”
- Unexplained persisting fatigue
- Decreased executive function- children and adults
- Unexplained or new onset of an anxiety disorder
- Personality change
- Signs of autonomic dysfunction
- “Atypical” anything! Arthritis, Lupus, MS, dementia, etc.
- Fever of unknown origin (culture-negative endocarditis)

Basically any unexplained or unusual multisystem disorder

Initial presentation of TBDs

BORRELIA (Lyme and TBRF)

- Gradual onset of nonspecific, viral-like symptoms that begin to target individual organs over several weeks
- Rash: painless, persisting red bump at bite site; ~50% go on to develop expanding rash

BABESIA

- Fairly rapid development of headache, fever, sweats and fatigue over several days

BARTONELLA

- Gradual onset of nonspecific symptoms that begin to target the nervous system, eyes and GI tract over days to weeks

RICKETTSIAS

- Fairly rapid onset of high fever, headache and muscle aches- hours to days
- Generalized vasculitic rash in 85% RMSF, <5% in others

Lyme disease - cardinal clinical features

MULTISYSTEM

- Joints, peripheral nervous system, central nervous system
- Skin, cardiac, GI and others possible
- MANY nonspecific symptoms

MIGRATORY

- Symptom location and organ type will vary
- The only infection known to cause migratory neuropathy and migratory arthritis

CYCLIC

- Classic 4-week cycle of symptoms in Lyme; may be shorter cycle in TBRF

Symptom development in Lyme

JOINTS:

- Joint pain is due to synovial inflammation- can swell, become tender, slightly warm and effusions occur in the larger joints
- Arthritis is usually NOT symmetric, and usually involves the larger joints
- Arthritis can wax and wane, and can migrate from one joint to another
- Stiff neck, nuchal headache, “Lyme shrug”

NERVOUS SYSTEM

- Peripheral- migratory, non-symmetric neuropathy. Tingles, numbness, decreased reflexes, etc.
- Also autonomic neuropathy with postural insufficiency, accelerated heart rate, vagal dysfunction, vasomotor signs and symptoms
- Central- cognitive impairment, delayed memory with slow retrieval, speech errors, etc.

CARDIAC- initially, AV conduction defects that usually clear. Later, cardiomyopathy affecting muscular function, ectopics and ventricular conduction defects

Erythema migrans

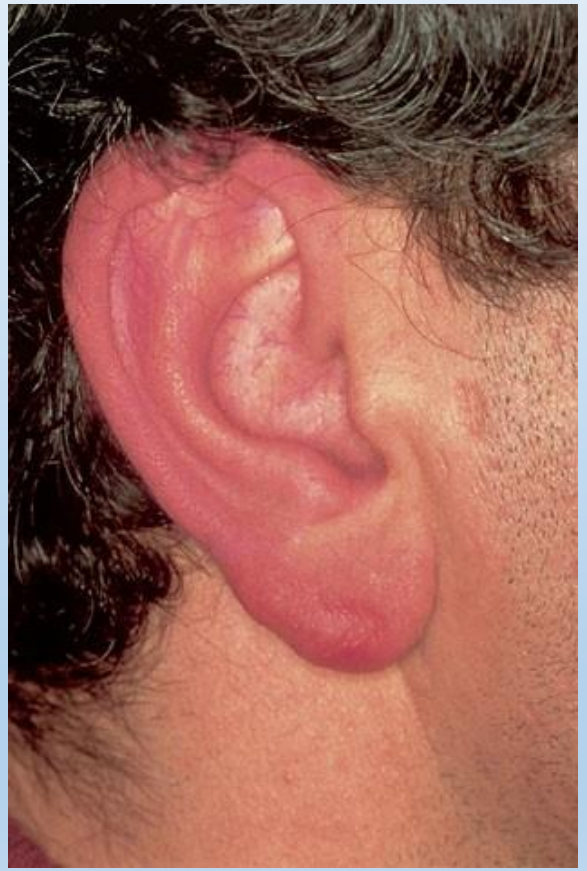
Classical “bullseye” rash is actually quite rare!

Uniform Rash

Not always circular- follows skin planes

Borrelia lymphocytoma

- Hot, red, swollen and tender
- Usually involves the ear; may also involve the nipple
- Site of active infection with *B. burgdorferi*



Acrodermatitis Chronica Atrophicans (ACA)

Appears late in the illness

- Usually associated with *B. afzelii* but some cases associated with *B. garinii* have been reported
- Inflamed skin slowly evolves into thinned, atrophic skin and sclerotic patches are possible
- Underlying neuropathy

All can improve with treatment!

Tick-borne relapsing fever often mimics Lyme

The classical description of acute presentation with rapid cycles of fever is probably rare!

- A Lyme-like presentation is probably more common
- IGeneX study: 543 US patients with suspected Lyme:
  - 32% were positive for antibodies to Lyme Borrelia
  - 22% were positive for Ab to Relapsing Fever Borrelia
  - 7% were positive for Ab to both LB and RFB
- Clinically, they ALL resembled Lyme patients, not “relapsing fever” patients, so when suspecting Lyme, also consider TBRF

Babesiosis- the most common co-infection in Lyme patients

- Fevers, day and night sweats
- Migraine-like headache- band-like and can respond to migraine medications
- Air hunger and/or dry cough
- Profound fatigue
- Balance issues- tippy and unsteady without vertigo or postural effects
- Cognitive dysfunction often more severe than that from Lyme
- Lyme patients co-infected with Babesia are more ill and more difficult to treat so suspect Babesiosis in your most-ill patients

Many other symptoms that overlap with Lyme and TBRF

Bartonella

- **CNS** - irritates and stimulates the CNS
  - Anxiety, insomnia, tremors, ataxia, seizures, panic attacks, rage attacks, antisocial behavior, depression, hallucinations, schizophrenia, dementia
- **Eyes** - uveitis, retinitis, retinal artery and vein thromboses
- **Regional lymphadenopathy**
- **Connective tissues**: tender nodules (sub-Q, along fascia), sore soles, tendonitis, bone pain
- **Painful joints** without synovial swelling- is ligament and tendon pain
- **Peculiar skin manifestations**
  - "Bartonella tracks" (like atypical stretch marks)
  - "Bacilliary angiomatosis" (red bumps that may scab)
- **GI involvement**
  - Gastritis (mimics H. pylori), mesenteric lymphadenitis (diffuse mid-abdominal pain)
  - Peliosis hepatis- hemorrhagic liver cysts (spectrum from asymptomatic to liver dysfunction, and rarely, cyst rupture and death)

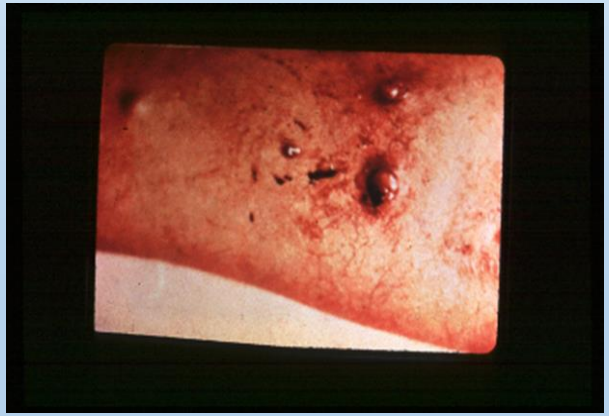
Bartonella clinical picture

Clue: unusual response to Lyme treatments

- Lyme treatments may not work at all, or
- Lyme treatments may only offer partial benefit
  - Most Lyme meds inhibit but do not kill Bartonella
- Rapid return of symptoms if treatment ends too soon
  - Lyme growth is measured in weeks; Bartonella growth is measured in days
  - Do symptoms decrease over several weeks and then flare (Lyme), or
  - Do symptoms increase in a matter of a few days (Bartonella)

Bartonella rashes

BARTONELLA TRACKS AND BACILIARY ANGIOMATOSIS



BACILIARY ANGIOMATOSIS

The Rickettsias

Anaplasma, Ehrlichia, Rocky Mountain Spotted Fever and other Rickettsias

- CAN BE FATAL!!
- Acute fever, severe headache, myalgias, malaise
- Here, pain is in muscles and not the joints
- Often associated with low WBCs, low platelets, and elevated LFTs
- Rash- vasculitic; blanches with pressure and refills from center; includes palms and soles
  - RMSF- 85%; Others ~5%

Rickettsial rashes

Rashes are vasculitic-

- Usually begin on extremities including palms and soles
- Red center with pink edges
- Blanch with pressure then refills from the center

Clinical guide

INFECTION	ONSET	CYCLES	SYMPTOMS	HEADACHE	FEVER	SWEATS	RELAPSE
LYME	Gradual	4 weeks	Multisystem Migratory, cyclic Joints	Nuchal "Lyme shrug"	Afternoon, Low-grade	No	Slow (weeks)
BARTONELLA	Gradual	No	Excitatory Soft tissues Lymphadenopathy	No	Morning- Low-grade	Light	Rapid (days)
BABESIA	Can be abrupt	5-7 days	Tippy, air hunger/cough Worsens everything	Band-like, Migraine-like	Any time, Can be high	Drenching	Slow (weeks to months)
RICKETTSIAS	Abrupt	No	Acute flu Muscles Low WBC, Plts	Knife in the eyes	Constant, High	Acutely	Gradual


Thank you!!