

Infectious Diseases: Take-Home Messages and Clinical Pearls

James H. Maguire, MD
Senior Physician
Division of infectious Disease and Department of Medicine
Brigham and Women's Hospital
Professor of Medicine
Harvard Medical School

James H. Maguire, MD



- Harvard Medical School
- Internal Medicine Residency and Infectious Disease Fellowship, Peter Bent Brigham Hospital
- Professor of Medicine, Harvard Medical School; Senior Physician, Brigham and Women's Hospital
 - Focus: parasitic disease, musculoskeletal infections

Disclosures

- I have no financial disclosures

Differential diagnosis: fever vesicular rash

- Varicella
- Enterovirus (hand, foot mouth disease)
- Herpes simplex
- Impetigo
- Rickettsialpox
- Monkeypox
- Smallpox
- Cowpox
- Orf
- Molluscum contagiosum
- Noninfectious



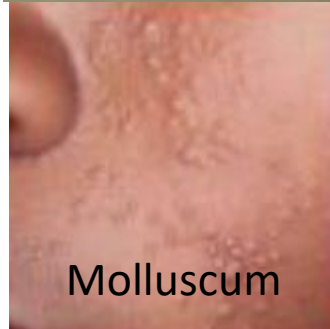
Eczema herpeticum



Varicella



Coxsackievirus A16



Molluscum



Smallpox



Bullous impetigo

Rickettsialpox

- *Rickettsia akari*
- Eschar at site of mite bite
- Tops of papular lesions develop vesicles, pustules
- Rash follows systemic symptoms by 2-3 days



J Am Acad Dermatol 2004;51:S137-42



CDC

Monkeypox

- Monkeypox: remote parts of central and West Africa
- Milder than smallpox, fatality 1-10%
- Transmitted primarily from rodents > nonhuman primates, pet prairie dogs (USA outbreak 2003)
- 2022 outbreak: close person-to-person contact , sexual networks implicated
- Diagnosis: real-time PCR of skin lesion material, serology
- Rx: antivirals (tecovirimat, brincidofovir), ?vaccinia immune globulin
- Prevent: infection control, attenuated smallpox vaccine

Infections and immunodeficiency

<u>Organism</u>	<u>Humoral</u>	<u>Complement</u>	<u>Phagocyte</u>	<u>Cellular</u>
Bacteria	Pneumococcus, meningococcus, <i>H. influenzae</i>	Meningococcus gonococcus (terminal components)	<i>S. aureus</i> , <i>enterics</i> , <i>P.</i> <i>aeruginosa</i>	<i>Salmonella</i> , <i>Listeria</i> , <i>Legionella</i>
Viruses	Enterovirus	-	-	Herpesviruses Hepatitis B,C
Fungi	-	-	<i>Candida</i> , <i>Aspergillus</i> , <i>Mucor</i>	<i>Cryptococcus</i> , endemic fungi, <i>Candida</i> , <i>Pneumocystis</i>
Mycobacteria	-	-	-	TB, atypicals
Protozoa	<i>Giardia</i>	-	-	<i>Toxoplasma</i> , <i>Cryptosporidium</i> , <i>T. cruzi</i> , <i>Leishmania</i>
Helminths	-	-	-	<i>Strongyloides</i>

Opportunistic infections in HIV

- Previously undiagnosed HIV, not taking antiretroviral therapy (ART) for financial, psychosocial or medical reasons
 - CD4 200-500: pneumococcal and other respiratory infections, tuberculosis, lymphoma zoster, thrush, AIDS-related complex (“ARC”)
 - CD4 <200: PCP, toxoplasmosis, endemic fungi, cryptococcosis
 - CD4 <50: *M. avium* complex, CMV
- Recently started on (effective) ART (immune reconstitution inflammatory syndrome -- IRIS)

Immune reconstitution inflammatory syndrome (IRIS)

- Recommend initiation of ART within 2 weeks of diagnosis of opportunistic infection (exception=CNS infections)
- IRIS: paradoxical worsening of infection or disease process following initiation of effective ART and restoration of immune response
- Most common with mycobacterial, viral and fungal infections; incidence 10-20%

Immune reconstitution inflammatory syndrome (IRIS)

- Fever, adenopathy common; localized symptoms and signs
- Usually occurs within a week to a few months after starting ART
- Continue ART and directed therapy for opportunistic infection in most cases
- NSAIDs, steroids

Infections and immunodeficiency

- Neutrophils
 - Decreased numbers
 - Impaired function
- Neutropenia
 - Cytotoxic chemotherapy, drug hypersensitivity, marrow disorders, other
 - Severe: ANC ≤ 500 ; profound < 100
 - Signs of infection often masked
 - Infections can progress rapidly, life-threatening

Neutropenia and infections

- Common pathogens
 - Gram-negative enterics (*E. coli*, *Klebsiella*, *Enterobacter*) > *Pseudomonas aeruginosa*
 - Gram-positive organisms (intravascular catheters): *S. aureus*, coagulase-negative staphylococci, enterococci
 - Fungi (prolonged neutropenia, antibiotics): *Candida* spp., *Aspergillus*, Zygomycetes

Neutropenia and infections

- High risk patients-empirical therapy:
 - Antipseudomonal β -lactam (cefepime, others)
 - Vancomycin – only when indicated
 - Prolonged fever : echinocandin (e.g., micafungin)
- Low risk: oral therapy (e.g., amoxicillin-clavulanate/ciprofloxacin; moxifloxacin)

Impaired neutrophil function

- Genetic: Chronic granulomatous disease, hyper-IgE (Job) syndrome, others
- Acquired: steroids, diabetes
- Infections in diabetics
 - Impaired phagocytosis
 - Vascular insufficiency
 - Neuropathy
 - Colonization (*S. aureus*, *Candida*)
 - (Impaired cellular immunity (TB, *Coccidioides*))

Infections in diabetics

- *S. aureus*-skin and soft tissue, pneumonia, bacteremia
- *Pseudomonas aeruginosa*: malignant otitis externa
- Rhinocerebral mucormycosis (acidosis)
- Candidiasis: cutaneous, mucosal, urinary
- Enteric organisms: UTIs, emphysematous cystitis/pyelonephritis, papillary necrosis
- Diabetic foot infections
- Necrotizing soft tissue infections

Skin and soft tissue infections

- Erysipelas (superficial): β -hemolytic streptococci > *Staphylococcus aureus*
- Cellulitis: β -streptococci, *S. aureus*
- Necrosis, purulence, abscess: *S. aureus*, especially MRSA
- Recurrent cellulitis (β -streptococci)
 - Lymphedema
 - Strategy: edema control, antifungals, foot care, prophylactic penicillin

Skin and soft tissue infections: special cases

Dog/cat bites	<i>Pasteurella multocida</i> , <i>Capnocytophaga canimorsus</i>
Saltwater	<i>Vibrio vulnificus</i>
Freshwater	<i>Aeromonas</i> , <i>Pseudomonas</i>
Hot tubs	<i>Pseudomonas</i>
Human bites	Skin and mouth flora
Fish, raw meat, poultry	<i>Erysipelothrix rhusiopathiae</i>

Treatment of MRSA skin and soft tissue infections

- Incision and drainage
- Oral antibiotics
 - TMP-SMX
 - Doxycycline
 - Clindamycin if susceptible
 - Linezolid, tedizolid
- Intravenous antibiotics: vancomycin, daptomycin, ceftaroline, linezolid
- Attempt decolonization for recurrences

Necrotizing soft tissue infections

- Necrotizing fasciitis
 - Group A β -hemolytic streptococci
 - Polymicrobial including anaerobes
 - Marine *Vibrios*, *Aeromonas*, rare MRSA
- *Clostridium perfringens* necrotizing cellulitis, myonecrosis
- Pain → erythema, edema → necrosis
- Treatment: antibiotics, surgical debridement, supportive therapy

Toxic shock syndromes

- *S. aureus*: menstrual, non-menstrual
- Group A streptococci: skin, soft tissue infections, other
- Exotoxin, super-antigen
- Hypotension, diffuse erythematous rash, end organ failure
- Treatment
 - Clindamycin plus beta-lactam antibiotic or vancomycin +/-IVIG (Streptococcal)
 - Source control: remove foreign body, surgery
 - Supportive care

Respiratory infections

- 22-year-old: 6-day history sore throat, difficulty swallowing admitted to ICU with fever, shortness of breath, hypotension, leukocytosis with left shift , ↑creatinine
- CXR/CT of chest: nodular opacities, effusion
- CT of neck: paratonsillar abscess, thrombosis of right internal jugular vein
- Cultures: *Fusobacterium necrophorum*
- Diagnosis: Lemierre syndrome
- Pressors, surgery, antibiotics, anticoagulation

The Clinical Presentation of *Fusobacterium*-Positive and Streptococcal-Positive Pharyngitis in a University Health Clinic

A Cross-sectional Study

Robert M. Centor, MD; T. Prescott Atkinson, MD, PhD; Amy E. Radtke, MLS; Li Xiao, PhD; Donna M. Crabb, MT (ASCP); Carlos A. Estrada, MD, MS; Michael B. Faircloth, MD; Lisa Oestreich, DO; Jeremy Hatchett, MD; Walid Khalife, PhD; and Ken E. Walters, MD

Ann Int Med 2015;162:2412

- Young adults with pharyngitis
 - 21% *Fusobacterium necrophorum*
 - 10% group A streptococcus
- *Fusobacterium* is resistant to macrolides
- Recommend: treat severe sore throat (3 or 4 of following: fever, no cough, tender anterior nodes, tonsillar exudate) with penicillin not azithromycin

Extrapulmonary tuberculosis

- Seen in 50% or more of patients with HIV/TB coinfection but also in not HIV-infected
- Clues
 - Sterile pyuria
 - Chronic lymphadenopathy (especially cervical)
 - Monoarthritis, spinal osteomyelitis (esp thoracic)
 - Lymphocytic predominant ascites
 - Chronic lymphocytic meningitis
 - Exudative pleural effusion
 - Pericarditis

Nontuberculous mycobacterial infection

- Acquired from environment
- Immune compromised; immune competent often with risk factor (lung disease, trauma, surgery)
- Sensitivity testing helpful, but not always predictive of response
- Treatment: combination therapy, prolonged, may require surgery

Nontuberculous mycobacterial infection

Disseminated (esp. HIV)	<i>M. avium-intracellulare</i> (MAC) <i>M. kansasii</i>
Pulmonary	MAC <i>M. kansasii</i> <i>M. abscessus</i>
Skin and soft tissue	<i>M. marinum</i> <i>M. abscessus, fortuitum, chelonae</i>
Catheter-associated	<i>M. abscessus, fortuitum, chelonae</i>
Cervical lymphadenitis	MAC, <i>M. scrofulaceum</i>
Leprosy	<i>M. leprae</i>
Buruli ulcer	<i>M. ulcerans</i>

Fungal infections of the lungs

- “Endemic” mycoses (dimorphic fungi)
 - Histoplasmosis: river valleys, guano in soil
 - Coccidioidomycosis: SW USA, Latin America
 - Blastomycosis: USA (south, south central)
 - South American blastomycosis (CA, SA)
 - Sporotrichosis (sphagnum moss, thorns)
 - Talaromycosis [penicilliosis] (China, SE Asia)
- Cryptococcosis (soil contaminated with bird droppings; *C. gatti* in Pacific Northwest)

Tick-borne infections in the USA

Bacteria

- *Borrelia burgdorferi*
- *Anaplasma phagocytophilum*
- *Ehrlichia chafeensis*
- *Rickettsia rickettsii*
- Rickettsia 364D, others
- STARI
- *Francisella tularensis*

- Relapsing fever

Borrelia

- *Borrelia miyamotoi*

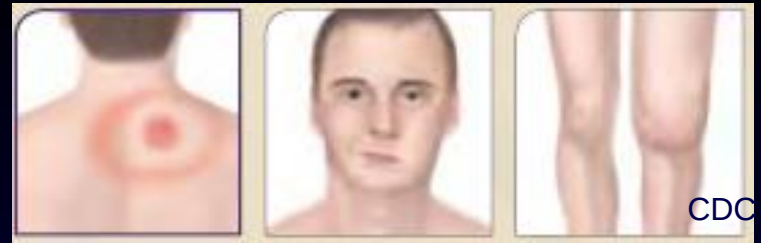
Viruses

- Colorado Tick Fever
- Powassan virus
- Heartland virus
- Bourbon virus

Protozoa

- *Babesia* spp

Lyme disease

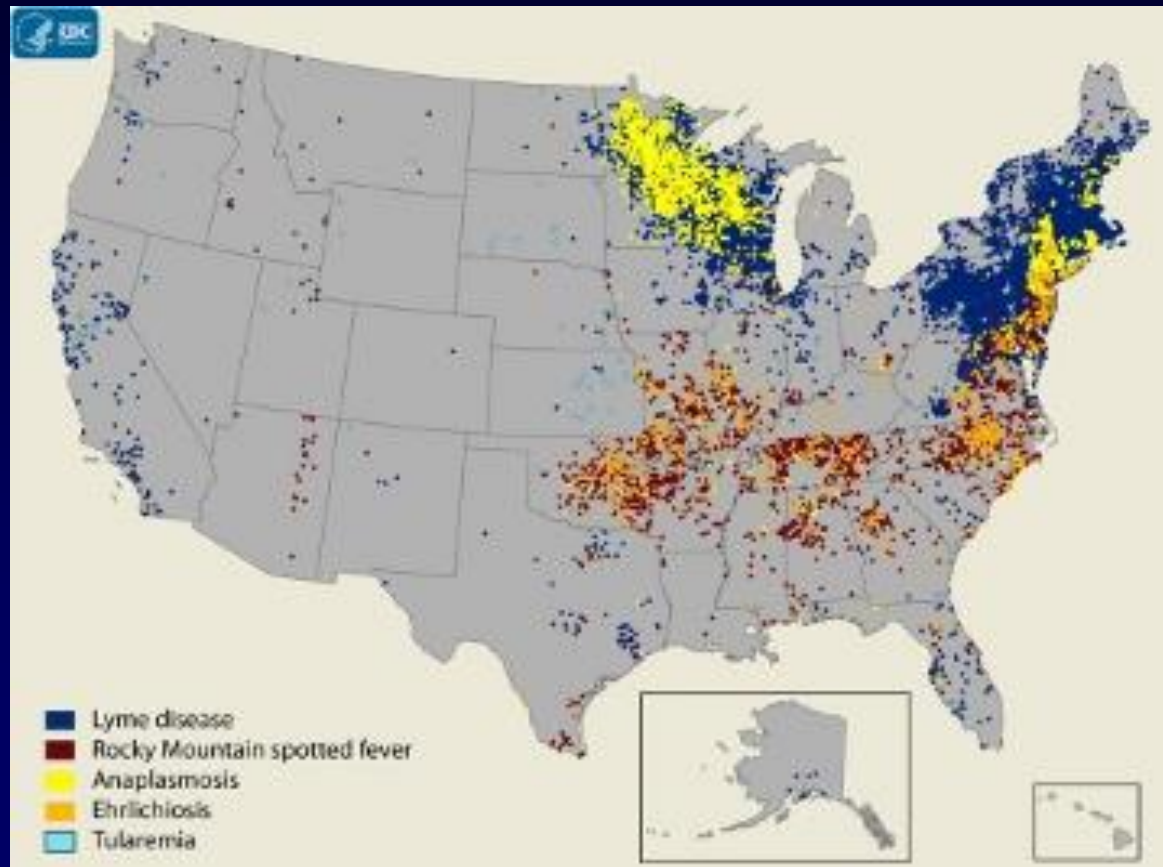


- Suspect in persons with possible exposure
- Most do not report tick bite
- Early Lyme disease
 - Diagnose clinically (serology often negative)
 - Erythema chronicum migrans
 - Fever, myalgia, Bell's palsy, meningitis, heart block, arthralgia
- Late Lyme disease: arthritis, neurological (encephalitis, neuropathy, radiculitis)

Lyme disease

- Diagnosis: two step testing: screening (immunoassay), second tier (immunoblot, immunoassay)
APHL 2021 guidelines <https://www.aphl.org/>
- Treatment
 - Oral doxycycline, amoxicillin or cefuroxime
 - Intravenous ceftriaxone: certain syndromes
 - Treatment > 28 days not indicated for chronic Lyme
 - No antibiotics for post-Lyme syndrome
- Prophylaxis for attached tick in Lyme-endemic area: doxycycline 200 mg PO x1

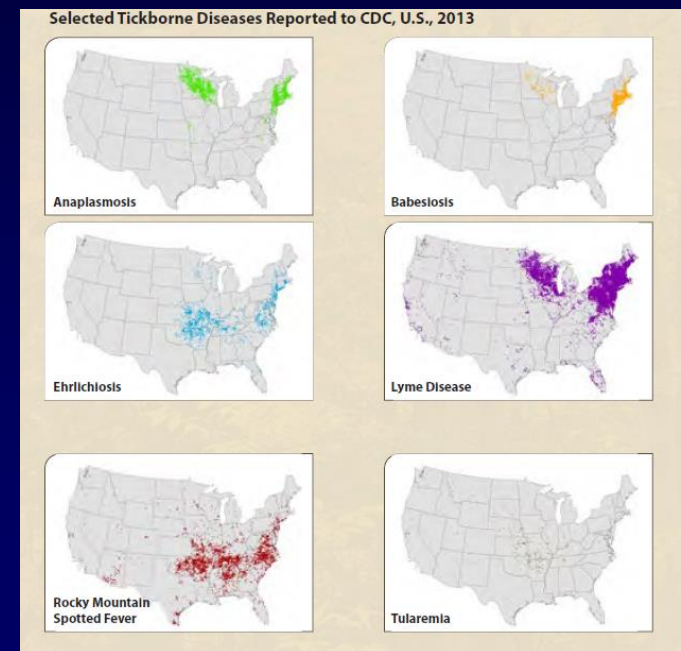
Ticks may carry and transmit multiple pathogens to same host (e.g., *Ixodes scapularis* (Lyme, anaplasmosis, babesiosis, Powassan virus, *Borrelia miyamotoi*)



Distribution of tick-borne infections (CDC)

Clinical approach to tick-borne infections

- Tick-borne infections can be rapidly fatal (e.g., Rocky Mountain Spotted Fever)
- Unexplained fever, chills, headache, fatigue, myalgia, arthralgia, rash, neurologic symptoms
- Consider place, season, activities, pets
- Rapid diagnostic testing often not available
- Early, empirical treatment can be life-saving (doxycycline)



Salmonella bacteremia

- Typhoid and other enteric fevers
- Transient bacteremia with gastroenteritis
- Endovascular infections
 - Atherosclerosis-aneurysms
 - Heart valves, especially prosthetic
 - Schistosomiasis
- Persistent infection, localized infections:
immune deficiency: AIDS, transplant, etc;
hemoglobinopathies,
- Usually do not treat salmonella gastroenteritis
unless at risk of localized or persistent
infection

Thank you!