

Infection & Arthritis

What to Consider...

Jennifer K. May MD
Rheumatology
Black Hills Orthopedic & Spine Center

Objectives

- To understand reactive arthritis and the clinical presentation
- To review other infectious arthritides
 - Lyme
 - Gonococcal
- To understand the the multisystem nature of reactive arthritis and develop the differential diagnosis

Definition: Reactive Arthritis

- A sterile joint inflammation that develops after a distant infection
- Triggering infections most commonly originate in the throat, urogenital, or GI tracts
- Process may occur without obvious preceding infection
 - Inflammatory bowel disease

Epidemiology

- Commonly effects young adults
- Males = females
- Incidence 30-40/100,000
 - RA: annual incidence rate per 100,000 population was 35.9 for females and 14.3 for males
 - AS: 7.3/100,000 person years
- Genetic association
 - Family clustering
 - Strongly associated with HLA-B27
- Frequency with associated infection varies

History

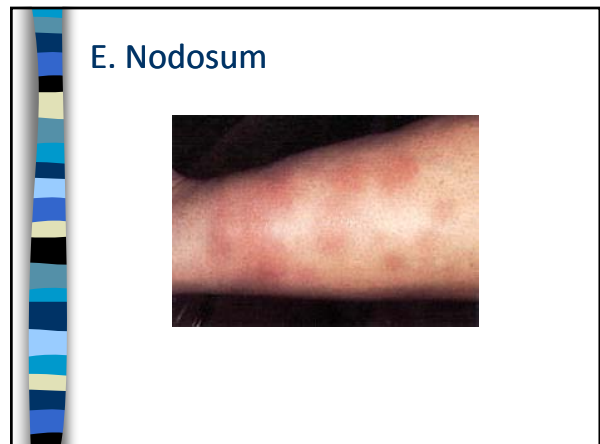
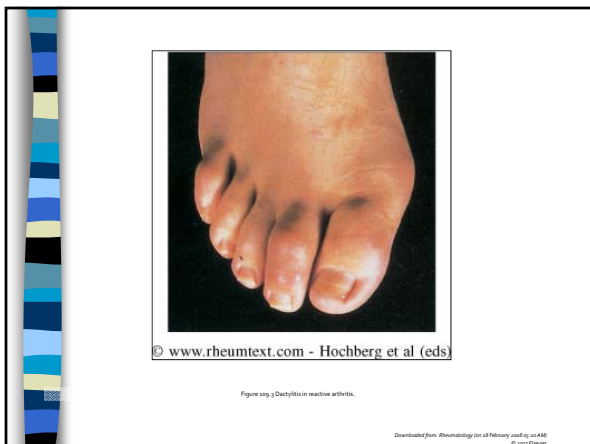
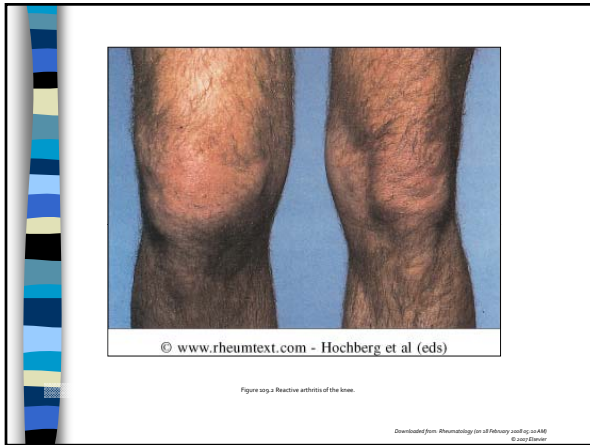
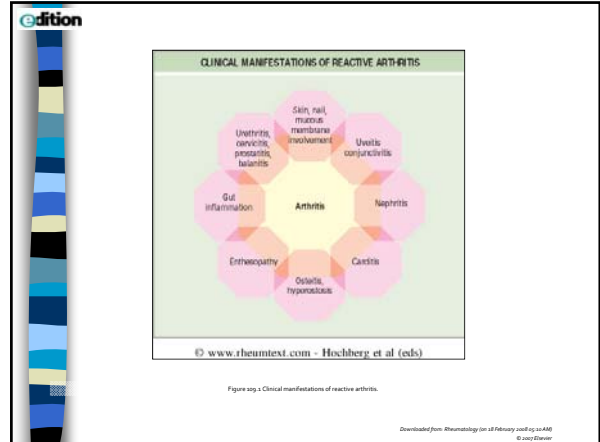
- Infections most commonly preceding reactive arthritis:
 - *Salmonella*, *Shigella*, *Yersinia*, *Campylobacter*, *Chlamydia trachomatis* or *C. pneumoniae*, *Borreliae*, *Neisseria*, & streptococci.
 - Viruses implicated:
 - Rubella, hepatitis, and parvovirus
- Not unusual that triggered infections can not be identified

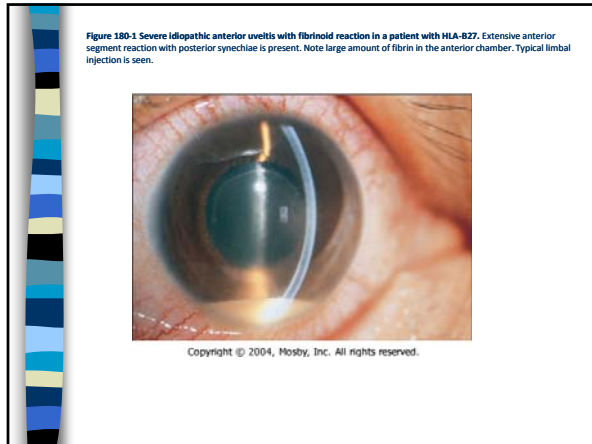
Clinical features

- Malaise, fatigue, fever
- Arthritis, enthesopathy, tendinitis, tenosynovitis, osteitis, and muscle pain
- Arthritis most common symptom
 - Asymmetric
 - Large joints of lower extremities most common
- Inflammation may vary from day to day

Clinical Features

- Skin and mucous membranes may be involved
 - *Erythema Nodosum*
 - *Keratoderma blenorrhagicum (pustulosis palmoplantaris)*
 - Painless shiny patches on palate, tongue, cheek mucosa ,and lips
- Eyes
 - Uveitis – unilateral or bilateral
 - Conjunctivitis
 - Strong tendency to recur
 - Recommend ophthalmologic exam
- Severity of disease variable





- ### Investigation
- ESR/CRP
 - CBC
 - Liver function
 - Urine analysis
 - Culture, Chlamydia PCR- 1st void urine
 - Joint aspiration if possible
 - Cell count, Gram stain/culture, Synovial fluid analysis
 - Rheumatoid factor- negative
 - ECG may be considered

- ### Investigation cont.
- Antibody assays:
 - *Salmonella*, *Yersinia*, *Campylobacter*, *Chlamydia*, *Neisseria gonorrhoeae*, *Borrelia burgdorferi*, and beta-hemolytic streptococci.
 - List of agents that lead to reactive arthritis is growing
 - Negative serologies does not exclude diagnosis
 - HLA-B27

- ### Imaging
- Do not need x-ray for diagnosis
 - MRI may be helpful
 - Joint effusions, Enthesitis/tendinitis
 - Benefits in routine clinical practice limited
 - Bone scan
 - Sensitive study
 - Better at detecting enthesopathy or periostitis
 - Colonoscopy
 - Tagged white blood cell scan

Treatment

- Antibiotics if infection is still present
- Rest
- NSAID
- Intra-articular steroids
- Systemic steroids
- Rarely, DMARD

Prognosis

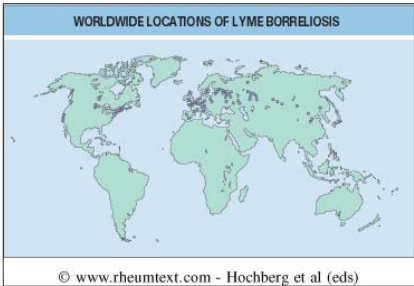
- Good prognosis
- Spontaneous recovery common
- Susceptibility to disease is strongly linked to HLA-B27 antigen

Summary of Reactive Arthritis

- Multisystem disease process “triggered” by infection
- Typically monoarticular, asymmetrical, arthritis, but severity of symptoms can vary greatly
- Exam abnormal...look at eyes, skin, GU system carefully to make a diagnosis
- Generally the arthritis resolves with conservative/supportive care

Lyme Disease

- First described as a separate entity 1976, clustering of disease in children of Lyme, Connecticut
- Multisystem illness that may effect skin, nervous system, heart, or joints
- Monitored by CDC since 1982
- Occurs 3 distinct areas: (90% of all cases in US)
 - North east- Maine to Maryland
 - Central- MN, WI
 - West- CA, OR

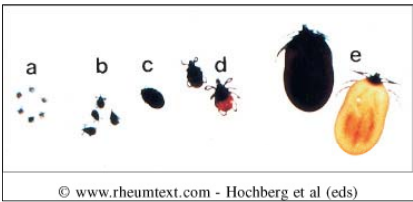


WORLDWIDE LOCATIONS OF LYME BORRELIOSIS

© www.rheumtext.com - Hochberg et al (eds)

Figure 9f-1 Worldwide locations of Lyme borreliosis. The yellow dots show affected locations in North America, Europe and Asia.

Downloaded from Rheumatology on 18 February 2008 by 141.146.135.100
© 2008 Elsevier



© www.rheumtext.com - Hochberg et al (eds)

Figure 9f-2 The life-cycle stages of Ixodes scapularis, the tick that transmits Lyme disease in the northeastern and north central USA. (a) Tiny larval ticks, which are 1 mm in diameter. (b) Overgrown nymphal ticks, which are only 2 mm in diameter. This stage of the tick is primarily responsible for transmission of the spirochete to humans during the late spring and early summer. (c) An engorged nymphal tick. (d) Overgrown adult male (black) and female (orange) ticks. (e) Engorged adult male and female ticks.

Downloaded from Rheumatology on 18 February 2008 by 141.146.135.100
© 2008 Elsevier

Lyme Disease

- Stage 1 (days after tick bite)
 - Erythema migrans, lymphadenopathy
 - ~15% go onto develop further symptoms
- Stage 2 (days- months after tick bite)
 - Disseminated infection, heart, nervous system, joints
 - Severe fatigue & malaise
 - Symptoms will resolve even if untreated in wks-months in 95% of patients
- Stage 3 (months-years)
 - Chronic axonal polyneuropathy
 - EMG abnormal- proximal and distal nerve segment

Lyme Manifestations

- Carditis- only 5% of infected untreated patients
 - AV block, myopericarditis, CHF
 - Duration usually brief...3 days- 6 weeks
- Joint involvement- 60%
 - Occurs months after onset of illness
 - Gradually improves over years
 - Migratory, large lower extremity joints
 - May effect other joints...TMJ

Acute Lyme





Figure p6.4 Erythema migrans of Lyme disease. Lyme disease usually begins with a slowly expanding skin lesion, erythema migrans, that occurs at the site of a tick bite. (a) Classic erythema migrans skin lesion (2 cm in diameter) on the back. The lesion has a white outer border, with slight central clearing. (b) Pale lesion (2 cm in diameter) with several vesicles in the center, near the groin. (c) Pale lesion (5 cm in diameter) with a target center over the iliac crest. In each instance, B. burgdorferi was isolated from a skin biopsy sample of the lesion. (Courtesy of Dr. Vijay Sikand, East Lyme, CT, USA)

Downloaded from Rheumatology on 18 February 2008 at 11:46 AM © 2007 Elsevier



© www.rheumtext.com - Hochberg et al (eds)

Figure p6.5 The swollen knee of a 3-year-old child with Lyme arthritis. In the USA, affected knees may be very swollen and warm, but not particularly painful. In Europe and Asia, the amount of joint swelling is often less.

Downloaded from Rheumatology on 18 February 2008 at 11:46 AM © 2007 Elsevier

Lyme Disease

- 10% of untreated patients develop chronic lyme arthritis:
 - 1 year or more of continuous joint inflammation
 - Even chronic lyme eventually remits spontaneously
- Serodiagnosis is insensitive during the first few weeks
 - 70-80% have seroreactivity (IgM) 2-4 wks after infection, even after antibiotic treatment
 - After 1 month, most are IgG positive
 - In persons with illness>1 month, +IgM alone is likely to be false positive

Criteria for positive Western Blot Analysis

First few weeks of infection	IgM	<u>2 of the following 8:</u> 18,21,28,37,41,58,93 kDa OR <u>2 of the following 3:</u> ospC (23), 39, 41b kDa
After first weeks of infection	IgG	<u>5 of the following 10:</u> 18,21,28,30,39,41,45,58,66,93 kDa

Treatment

- Antibiotics in early disease usually prevents progression & is curative
- No evidence to suggest need for oral Tx in follow-up to IV Tx, nor for prolonged high dose abx
- Intra-articular steroid injections
- There may be persistent non-specific complaints for many months following adequate treatment.
- Best treatment is prevention

Current Treatment Recommendations

Oral therapy

Adult Drug	Dosage	Duration
Doxycycline	100mg bid	3-4 wks
Tetracycline	250-500mg qid	3-4 wks
Amoxicillin	250-500mg qid	3-4 wks

IV therapy

3 rd generation cephalosporin:		
Ceftriaxone	2gm qd	2-4 wks
Cefotaxime	3gm bid	2-4 wks
Penicillin	20 million U 6 divided doses	2-4 wks
Chloramphenicol	50mg/kg/day divided doses	2-4 wks

Lyme Disease Summary

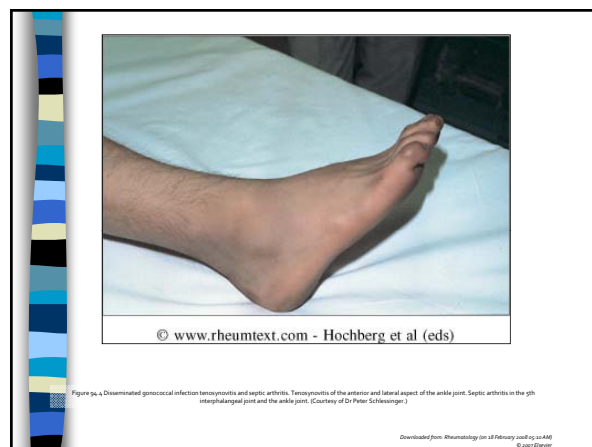
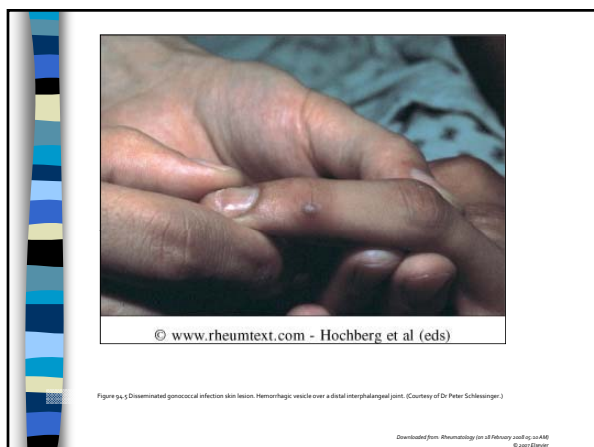
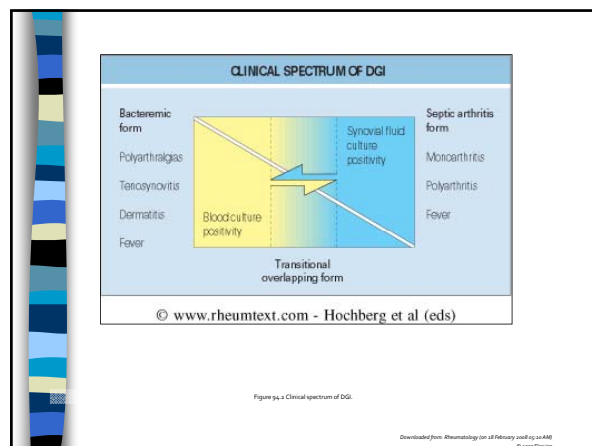
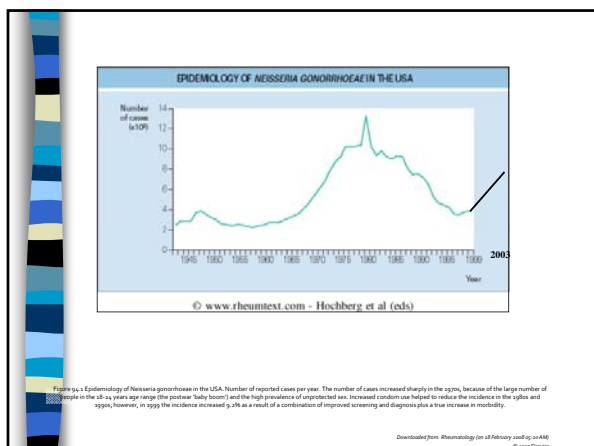
- South Dakota not an endemic area for Lyme
- Be selective with use of Lyme serologies
- No indication for prolonged or repeated antibiotic therapy
- Be aware that patients with later stages of Lyme may have nonspecific musculoskeletal complaints for many months. No indication for immunosuppressive therapy. Provide reassurance

Disseminated Gonococcal Infection

- Young, healthy adult
- Women more susceptible than men
- Genitourinary cultures positive for GC in 86%
- Cultures from joint fluid/blood often negative

Disseminated Gonococcal Infection

- PCR from joint fluid sensitive but expensive
- Prompt Antibiotic treatment resolves joint problems
- Penicillin resistance high, so 3rd generation Cephalosporin recommended.
- An estimated 600,000-800,000 cases of gonorrhea occur annually in the US



Summary of DGI

- Think of this always, but especially when seeing younger, sexually active patient with one swollen joint (knee).
- If suspicious of DGI: culture anything you can to confirm diagnosis and treat empirically
- Symptoms resolve with treatment and no effect on morbidity
- GC is very common. We have all seen this and missed it!

West Nile Virus

Goetz, Angella M. RN, MNES, CIC; Goldrick, Barbara A. MPH, PhD, RN, CIC West Nile virus: A primer for infection control professionals. AJIC: American Journal of Infection Control. 32(2):103-105, April 2004

- "In 1999, an outbreak of human West Nile encephalitis occurred in New York City. During the outbreak, 62 cases of human West Nile virus (WNV) infection were diagnosed, with 7 deaths. This was the first time that human WNV infections were detected in the Western Hemisphere. By 2002, the total number of human cases of WNV that year alone reached 4156, with 284 fatalities. In addition, investigations have shown that WNV can be acquired through organ transplantation, blood transfusion, breast milk, transplacental transmission, and occupational exposure."

General Overview

- Mosquito-borne flavivirus infection first reported in NA in 1999
- Infection is usually asymptomatic; however, can result in a sudden onset, febrile, flu-like illness with rare meningitis, encephalitis, meningoencephalitis, or acute flaccid paralysis
- Prognosis:
 - Mortality is uncommon
 - advanced age = worse prognosis and increases risk for neurologic morbidity and mortality

- Diagnosis: positive IgM on enzyme-linked immunosorbent assay (ELISA) of serum or cerebrospinal fluid (CSF)
- Treatment: primarily supportive
 - ribavirin and interferon alfa-2b have been used with mixed results
- West Nile virus infection should be reported to the local health department
- Mosquito repellent and lifestyle modification help to prevent infection

West Nile Virus

Jeha, L. E. MD; Sifa, C. A. MD; Lederman, R. J. MD, PhD; Prayson, R. A. MD, PhD; Isada, C. M. MD; Gordon, S. M. MD West Nile virus infection: A new acute paralytic illness. Neurology. 61(1):55-59, July 6, 2003.

- Mean age 74y/o (N=23)
- 74% men
- Fever (100%), AMS (74%), GI complaints (43%), back pain(35%), & rash(26%).
- Meningitis with flaccid weakness, proximal, asymmetric
- No mention of inflammatory arthritis

West Nile Virus

- Lab abnormalities
 - Hyponatremia
 - CSF neutrophilic pleocytosis
- EMG/NCS
 - reduced motor amplitude
 - active denervation
- MRI changes
 - cauda equina enhancement
 - parenchymal spinal cord signal abnormalities
 - leptomeningeal signal changes in the brain.

West Nile and Arthritis

- Local reports and some patient reports of an inflammatory arthritis presentation with West Nile.
- No case reports or clinical data to support observation
- No good data to suggest checking West Nile serologies in patients without neurologic symptoms.

Clinical Pearls: West Nile Virus

- High index of suspicion is required in flu-like illness with or without CNS manifestations, especially during late summer and early fall
- High index of suspicion is required in elderly patients with sudden onset CNS changes or paralysis; West Nile virus may present like a stroke in an elderly person
- Consider the diagnosis in patients following blood transfusion or organ transplant recipients who develop fever, headache, or myalgia within one week of blood transfusion in summer months in endemic regions



West Nile Summary

- This vector born illness is primarily neurologic.
- Do not check West Nile serologies on patients with non-specific complaints due to local fears.
- Inflammatory arthritis has been suggested by some but not in isolation...patient should have systemic complaints
- Care is supportive