

1. Lyme Arthritis and the Seronegative Spondyloarthropathies

## **Lyme Arthritis and the Seronegative Spondyloarthropathies**

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2. Lyme Disease

## **Lyme Disease**

- 1975: Allen Steere and colleagues investigate cluster of children with arthritis
- 1976: Lyme arthritis described, arthropod vector proposed
- 1982: *Borrelia burgdorferi* identified as causative agent

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3. Lyme Disease - clinical stages

## Lyme Disease - clinical stages

- Stage 1 (Early localized): days
  - erythema migrans rash at tick bite site
- Stage 2 (Early disseminated): weeks
  - flu-like illness,
  - cardiac, neurologic
- Stage 3 (Late) - months to years:
  - Lyme arthritis
  - Encephalopathy or Neuropathy

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4. Lyme Arthritis and Spondyloarthritis: Slide 4

## *Ixodes scapularis* (deer tick)



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5. Lyme Arthritis and Spondyloarthritis: Slide 5

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6. Lyme Arthritis and Spondyloarthritis: Slide 6

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7. Lyme Arthritis

## Lyme Arthritis

- The only chronic inflammatory arthritis in which the etiology is known
- Perhaps the only chronic inflammatory arthritis that can be cured!
- Occurs in ~60% of untreated patients with *B.Burgdorferi* infection

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8. Lyme Arthritis Cont'd

## Lyme Arthritis Cont'd

- **Pattern:** intermittent, recurrent attacks of swelling and pain in one or a few joints at a time, especially the knee
- **Usually:** monoarticular or oligoarticular, large joint
- **Spectrum:** short episodes of mild joint pain, to intermittent attacks over years most commonly, to chronic arthritis in about 10% of patients

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9. Lyme Arthritis and Spondyloarthropathy: Slide 9

## Lyme Arthritis Affecting Knee

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10. Lyme arthritis is due to active infection

## Lyme arthritis is due to active infection

- Hypothesis - *B burgdorferi* avoids immune detection in synovium for months
- Arthritis occurs when T-cells activate against the bacteria
- Synovial lesion identical to RA
- PCR indicates presence of *B burgdorferi* in the joint of untreated Lyme arthritis patients

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11. Lyme Arthritis Cont'd

## Lyme Arthritis Cont'd

- Most patients can be cured with oral antibiotic therapy
- A small percentage of patients have persistent inflammation and negative PCR on synovial fluid testing, suggesting that the spirochete has been eradicated and that the ongoing inflammation is due to another process

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12. The Autoimmune Paradigm

## The Autoimmune Paradigm

- A trigger (?environmental antigen or infectious agent) in a genetically susceptible individual triggers an autoimmune process
- RA (unknown trigger +HLADRB1\*0401 = RA)
- Lyme Arthritis (*B. Burdorferi* + HLADR4B1\*0401) = chronic persistent arthritis)
- AS (unknown trigger + HLA B27 = AS)

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13. Lyme arthritis: Immunogenetic Susceptibility

## Lyme arthritis: Immunogenetic Susceptibility

- Treatment resistant Lyme arthritis: high frequency of HLA-DRB1\*0401 and related alleles
- Strong parallel to rheumatoid arthritis alleles
- Golden opportunity: study immune response in these patients
- However! *Borrelia burgdorferi* does not trigger RA

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14. Cellular Immunity in Lyme Arthritis - OspA protein

## Cellular Immunity in Lyme Arthritis - OspA protein

- OspA serves as “stealth” protein: early in the infection there is at most a weak immune response to it
- Lyme Arthritis: OspA recognized by >70%
- In HLA-DRB1 susceptible patients:
  - Reactivity with OspA is associated with chronic Lyme arthritis
  - T cells reactive to specific OspA antigens concentrate in the joint

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15.

## Molecular Mimicry

### **Molecular Mimicry**

- Aberrant immune activation against self antigen triggered by the presence of a foreign antigen that shares molecular or antigenic properties with self
- The arthritogenic antigen in *B. Burgdorferi* *has not been defined*
- Gross, Huber et al (1998): Possible antigen: human lymphocyte function associated antigen (hLFA-1)

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## Four Major Spondyloarthropathies

### **Four Major Spondyloarthropathies**

- Ankylosing Spondylitis (AS)
- Inflammatory Bowel Disease Related Arthritis (IBD)
- Psoriatic Arthritis (PsA)
- Reactive Arthritis (Reiter's Syndrome) (ReA)

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17. Seronegative Spondyloarthropathies

## **Seronegative Spondyloarthropathies**

- Seronegative (test negative for RF)
- Presence of HLA B27 (Class I)
- Inflammation of the sacroiliac joint and spine
- Enthesitis: Inflammation at insertion sites of tendon or ligament to bone
- Asymmetric Inflammatory Arthritis
- Extrarticular Disease

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18. Lyme Arthritis and Spondyloarthropathy: Slide 18

### **Anatomy of the Enthesis**

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19. Ankylosing spondylitis (AS) - HLA-B27 association

## **Ankylosing spondylitis (AS) - HLA-B27 association**

- AS patients: >95% HLA-B27 positive
- <5% chance of AS if are HLA-B27 +
  - But family history of AS increases risk
- How does HLA-B27 cause disease:
  - fails to eliminate organism?
  - presents arthritogenic peptide?
  - Answer is not known

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20. Ankylosing spondylitis - clinical features

## **Ankylosing spondylitis - clinical features**

- Men > women as much as 5:1 but some question this as possible bias
- mean age of onset in 3rd decade
- inflammatory pain - AM stiffness; *improves* with activity
- X-rays show gradual fusion of spine, other involved joints
- enthesitis common (in contrast to RA)

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21. Lyme Arthritis and Spondyloarthropathy: Slide 21

### **Normal sacroiliac joints**

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22. Lyme Arthritis and Spondyloarthropathy: Slide 22

### **Ankylosing spondylitis - fused sacroiliitis joints**

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23. Lyme Arthritis and Spondyloarthropathy: Slide 23

## Spinal fusion in ankylosing spondylitis

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24. Normal posture and posture in patient with ankylosing spondy...

## Normal posture and posture in patient with ankylosing spondylitis

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25. Lyme Arthritis and Spondyloarthropathy: Slide 25

## Ankylosing Spondylitis - typical postural changes

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26. Ankylosing spondylitis clinical features (cont)

## Ankylosing spondylitis clinical features (cont)

- Extraarticular features a hallmark:
  - acute anterior uveitis/iritis (33%)
  - aortitis (1%)
  - pulmonary fibrosis - upper lobes (1%)
  - oral ulcers

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27. Spondyloarthropathies - Other

## Spondyloarthropathies - Other

- Psoriatic arthritis
  - occurs in 5% of psoriasis patients
  - closest to RA in chronicity and pattern of joint distribution to RA but still distinct
  - minimal HLA-B27 association
- Reactive arthritis
  - follows urogenital (chlamydia) or GI infection
  - moderate HLA-B27 association

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28. Spondyloarthropathies - other

## Spondyloarthropathies - other

- Inflammatory bowel disease associated arthritis
  - spondylitic form associated with B27 and *independent of* bowel activity
  - peripheral arthritis form *not* B27 associated and *associated with* active bowel inflammation

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29. Lyme Arthritis and Spondyloarthritis: Slide 29

**Psoriatic or reactive arthritis - “sausage toe”**



**Shown Shaded**

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30. Pathogenesis - hypotheses

## **Pathogenesis - hypotheses**

- **Molecular mimicry**: *Klebsiella aeruginosa* and the HLA-B27 molecule share similar peptide sequence
- **Antigens in joint** - bacterial antigens found in synovium of ReA patients
- **Organism in joint** - chlamydia DNA found in synovium of patients with ReA.

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31.

## Treatment of spondyloarthropathies

### **Treatment of spondyloarthropathies**

- NSAIDS/COX2
  - symptomatic relief but do not halt disease
- DMARDs – (eg methotrexate)
  - some disease modifying effect but not against spinal progression
- Anti TNF agents
  - great promise

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