

# Bone and Joint Infections

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## Disclosures of Financial Relationships with Relevant Commercial Interests

- None

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## Osteomyelitis

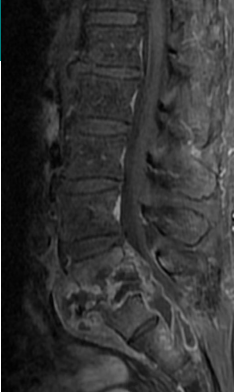


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## Question #1

- 57-year-old male presented with 3 months of progressive lower back pain.
- He denied fevers or chills, but reported weight loss
- Born in Cambodia, emigrated to U.S. as a child
- ESR 84 CRP 16
- MRI with discitis and osteomyelitis at L5-S1
- Blood cultures grew *Staph epidermidis* in 2 of 4 bottles



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## Question #1

What is the best next step in management?

- A. Repeat 2 sets of blood cultures
- B. Obtain interferon gamma release assay
- C. Percutaneous biopsy of disc space
- D. Initiate vancomycin; place PICC for six-week treatment course
- E. Empiric treatment with rifampin, isoniazid, ethambutol, and pyrazinamide

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## Vertebral osteomyelitis: diagnosis



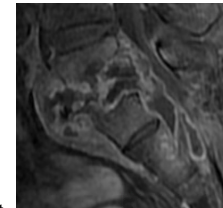
- Imaging pearls
  - MRI the most sensitive test in early infection
  - Infection almost always involves two contiguous vertebral bodies
- Blood cultures often positive in early infection
  - No further diagnostics if *Staph aureus* or *Staph lugdunensis*
- Brucella serologies, PPD/IGRA when appropriate epidemiology
- Percutaneous biopsy when blood cultures negative
  - Hold antibiotics 1-2 weeks prior if no sepsis or neurologic compromise

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## Pott's disease

- Clinical:
  - More indolent than pyogenic osteomyelitis
  - Constitutional symptoms common
- Radiographic:
  - Thoracic>lumbar with anterior involvement
    - Anterior collapse may lead to gibbus deformity
  - Relative sparing of the disc space until late
  - Multi-level disease, large paraspinal abscesses
- Treatment:
  - Conventional TB therapy, 6-12 months
  - Surgery often not necessary



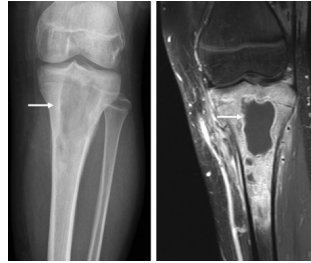
Simpfendorfer Infect Dis  
Clin N Am 2017;31:299

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## Brodie's abscess: Subacute hematogenous osteomyelitis

- More common in children and young adults
- Bacteria deposit in medullary canal of metaphyseal bone, become surrounded by rim of sclerotic bone → intraosseous abscess
- "Penumbra sign" on MRI
  - Granulation tissue lining abscess cavity inside bone gives appearance of double line
- *Staph aureus* most common



Simpfendorfer Infect Dis Clin N Am 2017;31:299

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## Hematogenous osteomyelitis: testable points

- Imaging studies:
  - MRI is the most sensitive imaging study for diagnosis
  - Plain films and CT are useful in subacute and chronic infection
  - Bone scan is an excellent "rule-out" test; should not be used to confirm infection
  - Imaging studies not useful as a test of cure
- Diagnosis can only be confirmed through bone histopathology and culture
  - Treatment for osteomyelitis in the absence of proven diagnosis may be acceptable
  - Limited role for molecular diagnostics
- Optimal therapy remains an evolving target
  - 6 weeks of antimicrobial therapy commonly used
  - Oral therapy supported in many circumstances

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## Diabetic foot osteomyelitis: testable points



- Probe to bone test is sufficiently specific to confirm diabetic foot osteomyelitis
  - but not other forms of osteomyelitis
- Superficial culture should not be used to inform microbial etiology
- No need to empirically target *Pseudomonas* unless:
  - Moderate to severe presentation with macerated ulcer and/or tropical humid climate
- Antibiotic duration (IWGDF guidelines)
  - 2-5 days if infected bone fully resected
  - 1-2 weeks if residual soft tissue infection after resection
  - 3 weeks if residual osteomyelitis following bone resection
  - 6 weeks if no surgical debridement or nonviable bone

IWGDF: International Working Group on the Diabetic Foot

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## Septic Arthritis



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## Question #2

A previously healthy 29-year-old woman developed acute right thumb pain followed by bilateral ankle pain and swelling, leading to inability to ambulate. She had no relief with NSAIDs.

On exam, she is afebrile. The right thumb MCP joint was erythematous and warm, and there were bilateral ankle effusions. She guards against movement of the thumb and ankles.

Plain films showed bilateral tibiotalar effusions

### Laboratory Studies

WBC 13,000 (72% pmns)  
ESR 62 CRP 47.7 mg/L  
ANA 1:40, speckled pattern

### Synovial Fluid Sampling (right ankle):

34,500 WBCs/ $\mu$ L (83% neutrophils)  
Negative gram stain  
No crystals

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## Question #2

**While synovial fluid cultures are pending, what is the next best step?**

- A. Measure anti-citrullinated peptide antibody
- B. Obtain HLA-B27 test
- C. Initiate treatment with systemic glucocorticoids
- D. Obtain blood cultures, cervical NAAT testing, and initiate vancomycin and ceftriaxone
- E. Bilateral ankle arthrotomy and debridement procedures

NAAT: Nucleic Acid Amplification test

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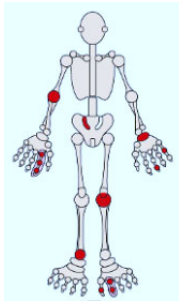
## Septic arthritis: clinical pearls

- Synovial fluid cell counts: no diagnostic threshold
  - Higher probability of septic arthritis if WBC  $>50,000/\text{mm}^3$
  - Lower cell counts do not exclude septic arthritis
- More subtle presentations in immunocompromised hosts and with indolent organisms
  - Subacute history
  - Lower synovial fluid cell counts
- Negative cultures and/or delayed culture positivity:
  - think Gonococcus, HACEK, Lyme, Mycoplasma

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## Joint involvement



Majority of septic arthritis is monoarticular

- Knee in 50%
- Axial joints (e.g. sternoclavicular); think PWID
- Sacroiliac joint: think PWID, Brucella

10-20 % of septic arthritis is oligo- or polyarticular

- Associated with bacteremia/sepsis
  - Staph aureus most common (look for endocarditis)
- Also seen in immunocompromised hosts

Other causes of polyarthritis

- Rat bite fever
- Disseminated gonococcus
- Viral infection
- Non-infectious

PWID: Persons who inject drugs 17

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## Rat bite fever

- Seen in children, pet store employees, laboratory technicians
- Polyarthritis (usually symmetric, often migratory)
- Associated with fever, maculopapular and/or pustular rash
- *Streptobacillus moniliformis*
  - in Asia *Spirillum minus*
- Rx: penicillin



Giorgiutti NEJM 2019; 381:1762

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## Gonococcal arthritis

- Tenosynovitis, arthralgias, skin lesions
  - Especially extensor surface tenosynovitis
  - Migratory arthralgias
- Purulent arthritis
  - May be polyarticular; knees most common
  - Lower synovial fluid cell counts more common
- Asymptomatic mucosal phase predisposes
  - Dissemination more common in women
- Dx: mucosal site (cervical, urethral) is highest yield
  - Blood (<30%) and synovial fluid (<50%) cultures lower yield
  - Compatible clinical syndrome



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## Viral arthritides

- Symmetric polyarthritis, often involving small joints
- Often associated with fever and rash
- Diagnose serologically (+IgM or 4-fold rise in IgG titer) or by viral pcr

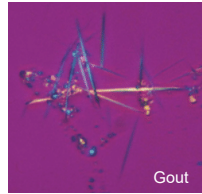
Viral causes of polyarthritis	Clinical and Epidemiologic Clues
Parvovirus B19	History of exposure to children (often a teacher or parent); more common in women. Hands most common; can be severe.
Rubella	Non-immune (non-US born). Cervical lymphadenopathy, fever, rash.
Hepatitis B Virus	Serum-sickness like reaction, resolves with development of jaundice; associated with polyarteritis nodosa (PAN)
Hepatitis C Virus	Immune complex arthritis associated with cryoglobulinemia
Alphaviruses (esp. Chikungunya)	Travel to or residence in endemic areas

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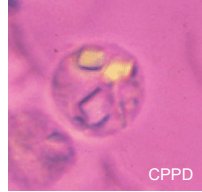
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## Crystalline arthritis: clinical pearls

- Acute gout mimics septic arthritis
  - Fever common
  - Monoarthritis and polyarthritis forms
  - Clues: rapid onset (hours), history of prior gout, alcohol, CKD, diuretics, elevated uric acid
  - Synovial WBC 10,000-100,000/mm<sup>3</sup>
  - Needle-shaped monosodium urate crystals
- CPPD less likely to mimic septic arthritis
  - CPPD and septic arthritis can coexist
  - CPPD rarely has cell count >30,000
  - CPPD rarely associated with high fever
  - Rhomboid-shaped calcium pyrophosphate dihydrate crystals



Gout



CPPD

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## Masquerading as infection...

### Many noninfectious causes of arthritis:

- Reactive arthritis
  - Following enteric or genitourinary infection
  - Asymmetric mono or oligo-arthritis affecting knees/ankles
  - Associated features: enthesitis (tendon insertion), dactylitis (sausage digits), mucosal lesions, urethritis, conjunctivitis/uveitis, skin lesions (keratoderma blennorrhagica)
- Still's disease
- Sarcoid (Lofgren's)
- Polymyalgia rheumatica ....



Coelho BMJ Case Reports 2017-222475

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## Implant Infections

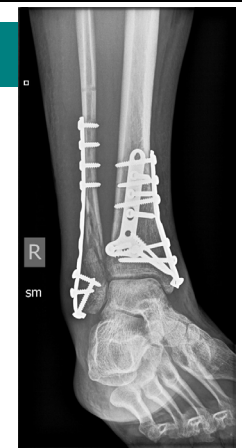


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## Question #3

- 44-year-old healthy woman suffered a closed right ankle pilon fracture and underwent open reduction internal fixation (ORIF)
- Chronically discharging wound despite courses of cephalexin and trimethoprim-sulfamethoxazole
- Two months after ORIF, deep wound culture grows *Staph aureus*
  - Sensitive to ciprofloxacin, clindamycin, levofloxacin, erythromycin, gentamicin, methicillin, rifampin, tetracycline, trimethoprim-sulfamethoxazole, vancomycin
- Plain films: hardware intact; fracture not yet consolidated
- She is hospitalized and started on IV cefazolin



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### Question #3

What do you recommend next?

- A. No surgical debridement; cefazolin for 6 weeks
- B. Surgical debridement with hardware removal; 6 weeks of trimethoprim-sulfamethoxazole
- C. Surgical debridement with hardware removal; 6 weeks of trimethoprim-sulfamethoxazole and rifampin
- D. Surgical debridement without hardware removal; 6 weeks of levofloxacin and rifampin
- E. Surgical debridement with hardware exchange; 6 weeks of levofloxacin and rifampin

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## Fracture-related infections

Goals include both fracture consolidation and infection eradication  
 Removal of hardware depends upon fracture healing and timeline  
 Antibiotic choice and duration not well studied

	Early infections prior to fracture union	Late nonunion	Late healed fracture
<b>Surgical Strategy</b>	Debride and retain (assuming implants well fixed)	Hardware removal Revision fixation	Hardware removal
<b>Antimicrobial Management</b>	Pathogen-directed therapy Addition of rifampin if Staph Duration often 12 weeks or until fracture heals	Pathogen-directed therapy Duration often six weeks	Pathogen-directed therapy Duration often two weeks following hardware removal

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## Antimicrobial treatment of bone and joint infection

- Few drugs are FDA approved for bone and joint infection
- Comparative studies are limited
- Duration of therapy an evolving target
- Suppression is commonly employed with infection in setting of retained hardware, but highly variable
  - decision to suppress (and how long to suppress) unlikely to be on boards

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## Oral antibiotics for bone and joint infections

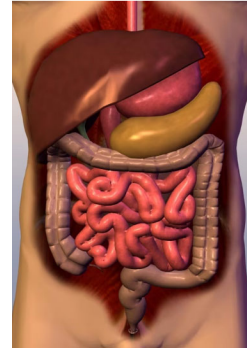
- Now supported by a large body of literature for definitive therapy of bone and joint infection
- Usually after an IV lead-in and after clinical response
- Relative contraindications/exclusions:
  - Lack of suitable oral option
  - Other indication for IV treatment (e.g. endocarditis / bacteremia)
  - Malabsorption
  - Not well studied for drug-resistant bacteria (e.g. MRSA)



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## Highly bioavailable oral therapy



Amoxicillin / amoxicillin-clavulanate  
Cefadroxil / cephalexin  
Ciprofloxacin / levofloxacin / moxifloxacin  
Clindamycin  
Doxycycline / minocycline  
Linezolid / tedizolid  
Metronidazole  
Rifampin  
Trimethoprim-sulfamethoxazole

\* No preferred regimen; most data to support quinolone + rifampin in Staphylococcal PJI

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## Rifampin in Orthopedic Infections

- Considered a “biofilm active” agent
- Best studied for Staphylococcal PJI in setting of hardware retention
  - Data extrapolated for other hardware infections (osteofixation, spinal implant)
  - Not as well established for other bacterial pathogens
- Specifics
  - Never to be used in monotherapy of established infection
  - Evidence supports quinolones as the best partner drug, but acceptable alternatives
  - Should not be used prior to surgical debridement and until partner drug therapeutic
  - Multiple drug interactions (primarily via Cyp 3A4 pathway)



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## Periprosthetic Joint Infection (PJI)



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## PJI: diagnostic pearls

- Diagnosis of early and late hematogenous PJI straightforward
- Multiple diagnostic algorithms have been developed for chronic PJI
- Diagnosis of chronic PJI confirmed if:
  - Sinus tract to the joint
  - Two synovial fluid or tissue cultures positive with the same organism

	Early PJI and Late hematogenous	Delayed (chronic) PJI
ESR/CRP	High	Normal or moderately elevated
Plain films	May be normal or show effusion	May be normal or show periprosthetic lucency
Synovial fluid cell counts	WBC > 10,000/ $\mu$ L % pmns > 90	WBC > 3000/ $\mu$ L % pmns > 75
Synovial fluid Alpha-defensin	Usually positive	Usually positive



SEE ENLARGED SLIDE FOLLOWING ENTIRE PRESENTATION

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## PJI: management



Surgical Procedure	Indication	Antimicrobial Therapy*
Debridement and implant retention (exchange of modular components)	Early surgical site infection Acute hematogenous Well-fixed components	12 weeks antibiotics (IV/PO) Rifampin if Staph
1-stage exchange	Acute and subacute infections Healthy soft tissues Sensitive organisms	12 weeks antibiotics (IV/PO) Rifampin if Staph
"2-stage" exchange Antibiotic spacer (With or without 2 <sup>nd</sup> stage)	Chronic infections Sinus tracts Resistant organisms	6 weeks antibiotics (IV/PO)

SEE ENLARGED SLIDE FOLLOWING ENTIRE PRESENTATION

\*2013 IDSA Guidelines; modified based on DATIPO study

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## Question #4

A 57-year-old woman underwent total hip arthroplasty

- She never achieved a pain-free state after surgery

Eighteen months postoperatively, she was diagnosed with delayed periprosthetic infection due to *Enterococcus faecalis*

- Sensitive to ampicillin, vancomycin, linezolid, daptomycin, gentamicin

Her orthopedist plans a two-stage exchange procedure utilizing a temporary spacer comprised of polymethylmethacrylate (PMMA)

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## Question #4

You are asked to provide recommendations about systemic and local antimicrobial therapy for the spacer. She has no antimicrobial allergies.

### What would you advise?

- Ampicillin in the cement; systemic vancomycin
- Ampicillin in the cement; systemic ampicillin
- Gentamicin in the cement; systemic ampicillin
- Tobramycin in the cement; systemic daptomycin
- Ceftriaxone in the cement; systemic linezolid

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## Question #4

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- C. Gentamicin in the cement; systemic ampicillin**
- D. Tobramycin in the cement; systemic daptomycin
- E. Ceftriaxone in the cement; systemic linezolid

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## Antimicrobial cement (PMMA)

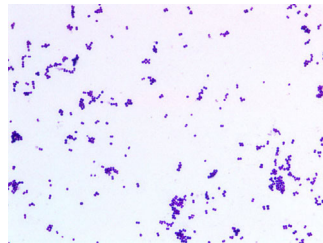
- “Spacer” serves mechanical role
  - Joint stability, allows mobility, prevents contractures
- Elution: high levels within the first few days
  - Local tissue concentration exceeds systemic delivery
  - May elute for months or longer
- Antimicrobial considerations
  - Known or suspected organisms
  - Thermal stability (avoid most  $\beta$ -lactams)
  - Osteocyte toxicity (avoid quinolones)
  - Vancomycin and aminoglycosides most common
  - Acute kidney injury seen in important minority
  - Allergy reported but rare



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## Microbiology of Musculoskeletal Infections



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## Question #5

A 56-year-old man with poorly controlled diabetes presents to ED with a one-week history of low-grade fevers and gradually progressive right knee pain and swelling. He traveled to the Dominican Republic one month ago and had no illnesses while traveling. He last saw a dentist six months ago and denies tooth pain. There is no history of injection drug use.

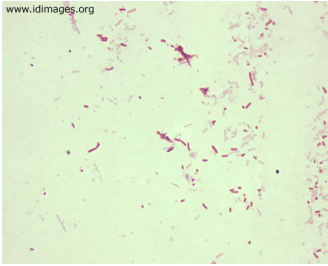
On exam he has a moderate effusion and pain with passive range of motion of the knee. His ESR (68) and CRP (17 mg/dL) are elevated, and synovial fluid is inflammatory (45,000 WBCs, with 82% neutrophils) with a negative gram stain.

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## Question #5

Culture growth at 3 days incubation



What is the most likely organism?

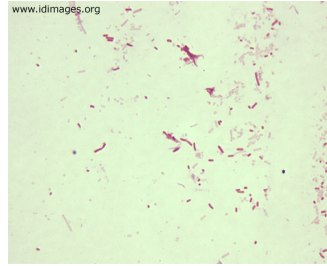
- A. *Serratia marcescens*
- B. *Salmonella heidelberg*
- C. *Staphylococcus aureus*
- D. *Kingella kingae*
- E. *Pasteurella multocida*

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## Question #5

Culture growth at 3 days incubation



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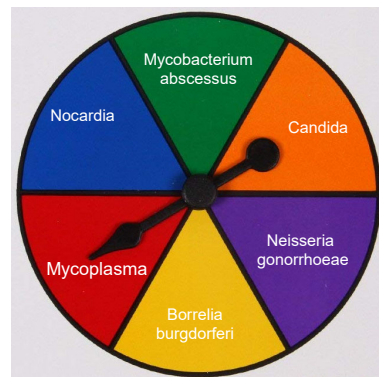
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## Guess the Bug

Musculoskeletal Edition



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## Salmonella species

- Clinical
  - Seen in sickle cell disease, immunocompromised, diabetes
  - Hematogenous infection (septic arthritis, spondylodiscitis, long bone infection)
- Epidemiology
  - Reptile exposure
  - Travel to developing world
  - Unsafe food hygiene



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## Serratia and Pseudomonas

- Risk Factors
  - Injection drug use (tap water)
  - Immunocompromised host
  - Indwelling lines
- Clinical factors
  - Usually hematogenous
  - Predilection for sacroiliac and sternoclavicular joints in injection drug use



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## HACEK organisms

- Clinical
  - Usually hematogenous
- Epidemiology
  - Antecedent mouth trauma, gum or dental infection, or dental procedure
  - Odontogenic infection may be silent
- Microbiology
  - Late growth in culture, may be culture negative
- *Kingella kingae*
  - Most common cause of osteoarticular infection in young children; diagnosed by PCR



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## Brucella species

- Clinical
  - Fevers often precede musculoskeletal symptoms
  - Septic arthritis with predilection for sacro-iliac joint
  - Also causes spondylodiscitis
- Epidemiology
  - Endemic in Latin America, Mediterranean, Middle East, parts of Asia
  - Consumption of unpasteurized dairy most common
- Microbiology
  - Small gram-negative coccobacillus; grows late in culture
  - Laboratory biohazard
  - Serologies helpful in non-residents of endemic areas



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## Pasteurella species

- Clinical
  - Direct inoculation (bite)
  - Hematogenous spread
  - Rapid clinical onset
- Epidemiology
  - Exposure to cats/dogs
  - Bite history not always elicited in hematogenous infection



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## *Mycoplasma hominis*

- Host factors
  - Immunodeficiency, especially humoral (CVID, XLA)
  - Postpartum women
- Clinical factors: hematogenous infection
- Microbiology
  - Difficult to grow in routine culture
  - “Fried egg” morphology in culture



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## *Borrelia burgdorferi* (Lyme)

- Clinical
  - Large effusions; some resolve over weeks but may recur
  - Warmth and swelling out of proportion to pain
  - Mono-arthritis of the knee most common
- Epidemiology
  - Northeast U.S. and upper mid-west with tick exposure
- Micro: culture-negative
  - Diagnosed serologically or with synovial fluid *Borrelia* PCR



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## Non-tuberculous mycobacteria



- Clinical
  - Slowly progressive tenosynovitis; can spread to bones and joints
  - May be accompanied by nodular lymphangitis
  - May cause polyarthritis in immunocompromised hosts
- Epidemiology
  - Environmental sources of water
  - Marine injury/trauma
  - Fish-tank exposure
  - Medical tourism
- Microbiology
  - Some organisms (marinum) grow better in cooler temperatures

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## Yeasts and molds

- Clinical
  - May be contiguous inoculation or hematogenous spread
  - Often more indolent than bacterial organisms
  - In the spine may mimic tuberculosis
- Epidemiology
  - Candida: injection drug use, indwelling lines, immunocompromise, antibiotic exposure
  - Molds: soil contamination (trauma), barefoot walking (Madura foot), immunocompromise (neutropenia), medical tourism



Karrakhouch BMC Dermatology 2020

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## Endemic mycoses

- Coccidioides and Blastomyces > Histoplasma
- Clinical
  - Subacute septic arthritis and long bone osteomyelitis
  - May see draining sinuses adjacent to osteomyelitis
  - In spine, may also mimic tuberculosis
  - Host immunocompromise more common in coccidioides
  - May see concomitant pulmonary infection



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**Thank you!**

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