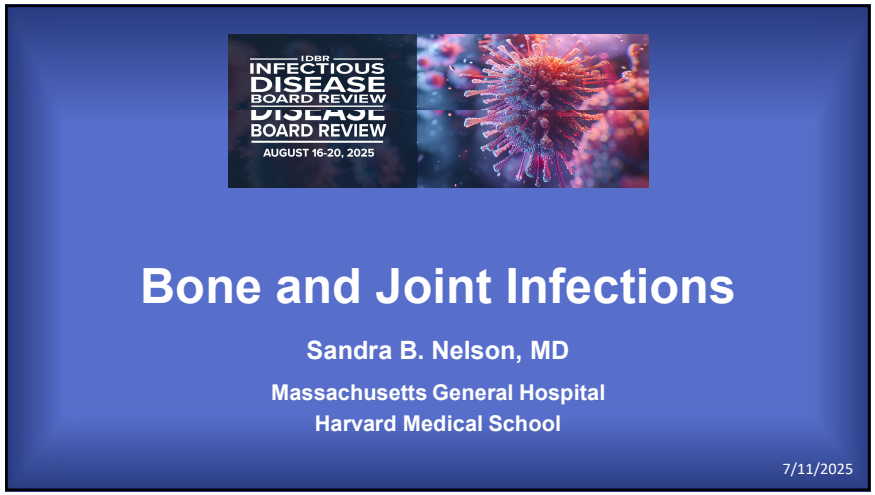
49 Bone and Joint Infections

Speaker: Sandra Nelson, MD



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Osteomyelitis: Unifying Principles

- Diagnosis can only be confirmed through bone histopathology and culture
- Imaging studies:
  - MRI is the most sensitive imaging study for diagnosis
  - Serial plain films and CT are more useful in subacute and chronic infection (bony erosion)
  - Bone scan is an excellent “rule-out” test; should never be used to confirm infection
  - Imaging studies not useful as a test of cure
- Optimal therapy remains an evolving target
  - 6 weeks of antimicrobial therapy commonly used
  - Oral therapy increasingly supported
  - Longer oral suppression in setting of retained hardware

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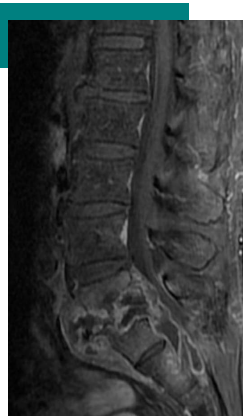
Question #1

- 57-year-old male presented with 3 months of progressive lower back pain.
- He denied fevers or chills, but his wife noticed 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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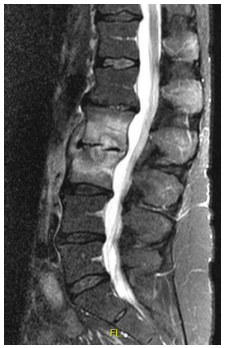
Vertebral Osteomyelitis: Diagnosis



- Imaging pearls
  - MRI most sensitive 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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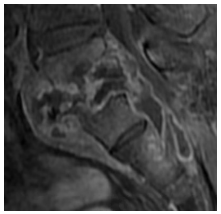
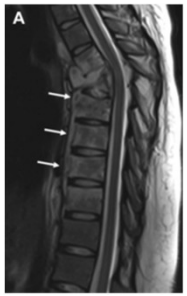
Pott's Disease

- 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





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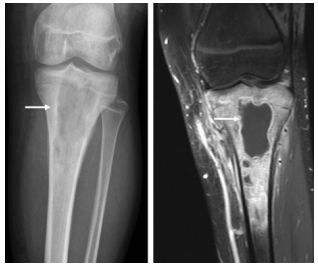
Brodie's Abscess: Subacute hematogenous osteomyelitis

- 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



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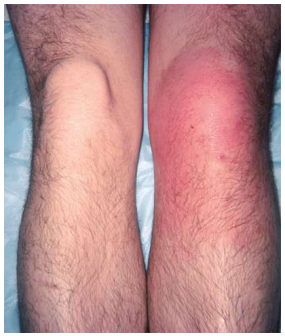
Septic Arthritis



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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 and presents to the ED.

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/μL (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 13

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Septic Arthritis: Clinical Pearls

- Synovial fluid cell counts: No diagnostic threshold
  - Higher probability of SA if WBC >50,000/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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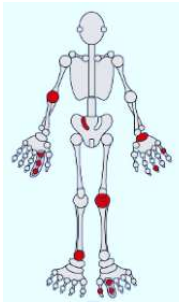
Joint Involvement



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 16

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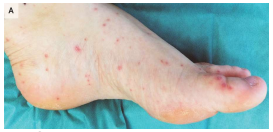
Rat Bite Fever

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



Giorgiutti NEJM 2019: 381:1762

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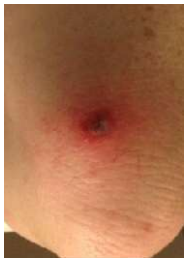
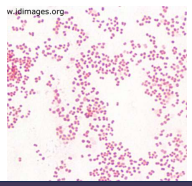
Gonococcal Arthritis

- 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 sampling (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

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

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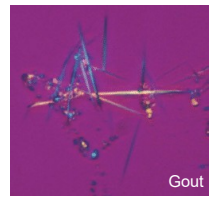
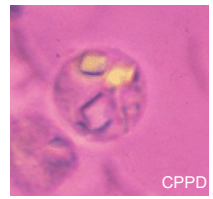
Crystalline Arthritis: Clinical Pearls

- 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^3
  - Needle-shaped monosodium urate crystals
- CPPD less likely to mimic septic arthritis
  - Crystalline disease and septic arthritis can coexist (esp. CPPD)
  - CPPD rarely has cell count >30,000
  - CPPD rarely associated with high fever
  - Rhomboid-shaped calcium pyrophosphate dihydrate crystals





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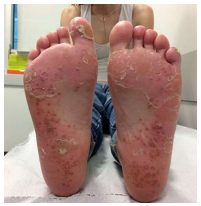
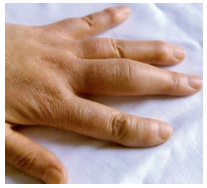
Masquerading as Infection…

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 blennorhagica)
- Still's disease
- Sarcoid (Lofgren's)
- Polymyalgia rheumatica ….





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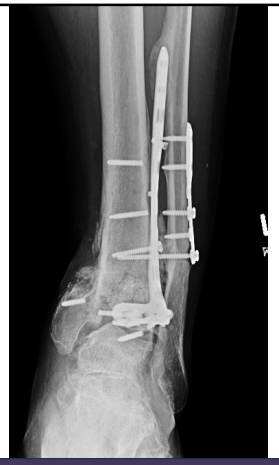
Fracture-related Infections



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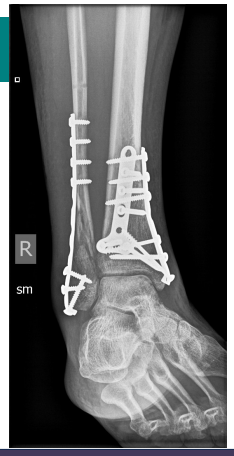
Question #3

- 44-year-old healthy woman suffered a right ankle closed pilon fracture and underwent open reduction and internal fixation (ORIF)
- Chronically discharging wound despite courses of cephalexin and trimethoprim-sulfamethoxazole
- Two months after ORIF, superficial wound culture grows methicillin-susceptible *Staph aureus*
- Plain films: Hardware intact; fracture not yet consolidated



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Question #3

What are your next steps?

A. No surgical debridement; cefazolin for 6 weeks
B. Surgical debridement with hardware removal; 6 weeks of cefazolin
C. Surgical debridement with hardware removal; 6 weeks of cefazolin and rifampin
D. Surgical debridement without hardware removal; 6 weeks of cefazolin and rifampin
E. Surgical debridement with hardware exchange; 6 weeks of cefazolin 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 stage
Antibiotic choice and duration not well studied

	Early infections prior to fracture union	Late nonunion	Late, healed fracture
Surgical Strategy	Debride and retain (assuming implants well fixed)	Hardware removal Revision or external fixation	Hardware removal
Antimicrobial Management	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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Oral Antibiotics for Bone and Joint Infections

- Now supported by a large body of literature for definitive therapy of bone and joint infection
  - Caution with life- or limb-threatening infections
- 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 and bacteremia)
  - Not well studied for drug-resistant bacteria (e.g. MRSA)
  - Concern for malabsorption
- Little data to support “bone-penetrating antibiotics”
  - Some advantage to quinolone + rifampin in Staphylococcal PJI

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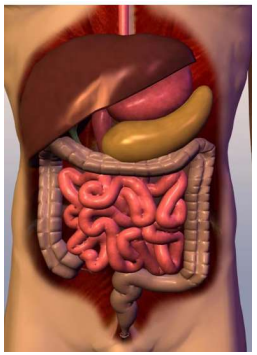
Highly Bioavailable Oral Therapy



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

*Oral cephalosporins and tetracyclines not as well studied in bone and joint infection

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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)
- Specifics
  - Never to be used in monotherapy of established infection
  - 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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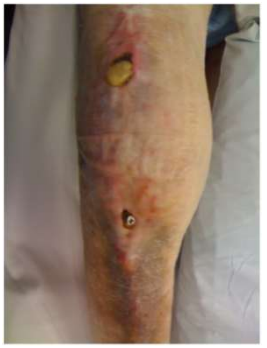
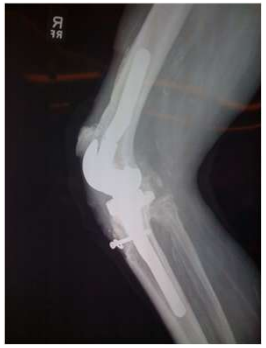
Prosthetic Joint Infection (PJI)





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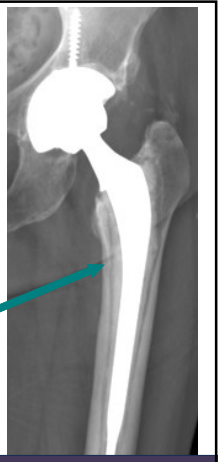
PJI: Diagnostic Pearls

- Diagnosis of early and late hematogenous PJI usually 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/μL % pmns > 90	WBC > 3000/μL % pmns > 70
Synovial fluid Alpha-defensin	Usually positive	Usually positive



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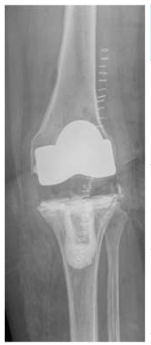
PJI: Management



Surgical Procedure	Indication	Antimicrobial Therapy
Debridement and implant retention (exchange of modular components)	Early surgical site infection Acute hematogenous Well-fixed components	6 weeks antibiotics (IV/PO) Continued oral antibiotics to complete 3-6 months Rifampin if Staph
1-stage exchange	Acute and subacute infections Healthy soft tissues Sensitive organisms	6 weeks antibiotics (IV/PO) Continued oral antibiotics to complete 3 months Rifampin if Staph
"2-stage" exchange Antibiotic spacer (With or without 2nd stage)	Chronic infections Sinus tracts Resistant organisms	6 weeks antibiotics (IV/PO)

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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?

A. Ampicillin in the cement; systemic vancomycin
B. Ampicillin in the cement; systemic ampicillin
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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Question #4

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

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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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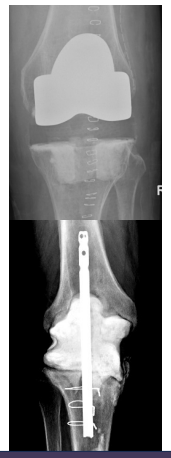
Antimicrobial Cement (PMMA)

- "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 β-lactams)
  - Osteocyte toxicity (avoid quinolones)
  - Vancomycin and aminoglycosides most common
  - Toxicity and allergy reported but rare



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Prevention of PJI

- Immunosuppressives:
  - Stop biologics, no need to stop DMARDs or low dose prednisone
- Surgical antibiotic prophylaxis: one dose prior to surgery
- Urinary tract infections:
  - Diagnose and treat symptomatic UTI
  - Do not screen for asymptomatic bacteriuria
- Dental prophylaxis: no more!
- *Staph aureus* decolonization reduces surgical site infection

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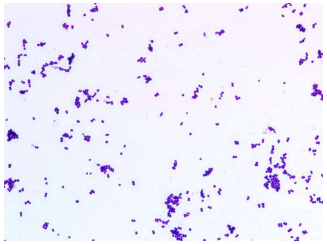
Microbiology of Musculoskeletal Infections



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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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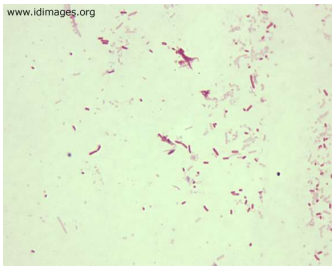
Question #5

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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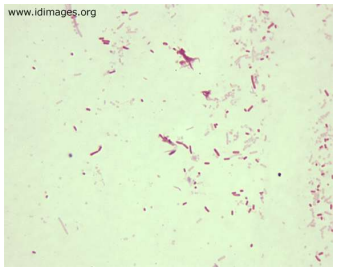
Question #5

Culture growth at 3 days incubation



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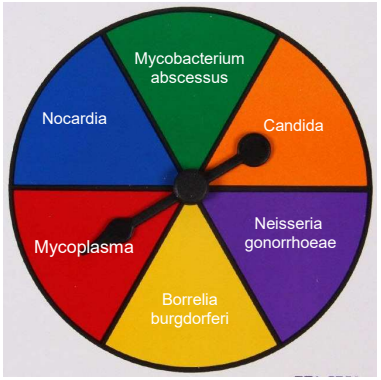
Guess the Bug

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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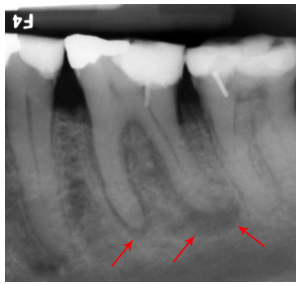
HACEK Organisms



- 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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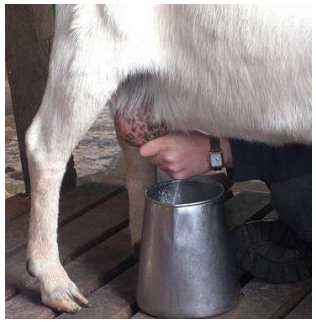
Brucella Species



- 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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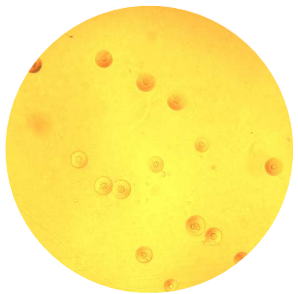
Mycoplasma hominis

- 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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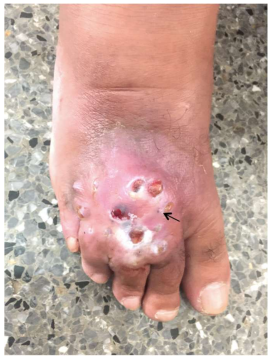
Yeasts and Molds

- 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



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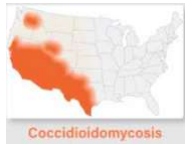
Endemic Mycoses

- Coccidiodes 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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