

Pathophysiology of osteomyelitis

- Blood flow highly vascularized → developing vasculature = sluggish flow; trauma causes the formation of “blood lakes”
- Bacterial seeding: trauma to area causes spread
- Periosteum raised by pus & new layer of bone grows over pus
- Ischemia (blood flow stops) → necrotic cortical bone

Goals of therapy

- Cure infection
- Minimize morbidity (loss of limb or joint function); prevent recurrent
- Prevent progression to chronic osteomyelitis

Sources of bone infection

- Hematogenous: infection spreads through blood
 - Most common
 - Predominant in children
 - Usually long bones & joints; vertebrae affected (>50 yo)
- Contiguous: spread to bone from adjacent site of infection
 - Most commonly femur, tibia, mandible
 - More common in > 50 yo
- Penetrating trauma: puncture wound
- Vascular insufficiency: poor perfusion/circulation to area
 - Bones in feet & toes (diabetic foot infection)
 - Most common in > 50 yo

S/S: fever, pain, redness, swelling, limping or other loss of function or movement, tenderness over affected bone or joint

Lab tests

- Both:
 - WBC + diff (left shift)
 - ESR/CRP: non-specific markers of inflammation
 - Blood culture
- Bones
 - X-ray (lags behind 10-14 days)
 - Bone scan: early dx (1 day after onset of sx)
- Joint
 - Synovial fluid – purulence
 - WBC > 50 and/or 75% neutrophils
 - Crystal analysis
 - Gram stain (1/3 +ve)
 - Culture (90% +ve)

Sources of joint infection

- Bone infection adjacent
- Trauma over joint
- Prosthetic joint
- IV drug abuse
- Gonococcal infection
- RA-associated

Risk for poor outcomes

- Inadequate initial debridement
- Prosthetic material
- Duration of infection (>48h after abx started)
- Previous txt failure

Factors of abx selection

- Host: severity of illness; allergies; immune system; renal/liver function; age; adherence; site/source of infections
- Drug: spectrum of activity; penetration to site of infection; cidal vs. static; oral absorption; formulations; SEs; tolerability; interactions; cost
- Bug: likely pathogens; single or multi pathogen; sensitivities; resistance patterns/development; toxin producer; slow/fast grower

General treatment principles

- Surgical aspiration/exploration
- Early initiation of antibiotics (w/in 48h of onset of symptoms)
- IV drug therapy (initially) & long duration of therapy
- Empiric coverage of likely pathogens → targeted abx therapy once pathogen identified

Difficult penetration: brain/CSF, eye, bone, sinuses, joints, lungs, prostate, abscess, ascites, vegetation/clot, finger & toe nails

Duration of therapy

- Osteomyelitis: 4-6 weeks
- Septic arthritis: 2-4 weeks
- Prosthetic joint infections:
 - One-stage exchange (debridement & retention): 3-6 mos (2-4 weeks IV → PO)
 - Two-stage exchange: 4-8 wk + ≥ 2 weeks abx free and culture negative

Evidence for bone penetration:

- Concentrations in diseased bone >> healthy bone
- Penetration differs depending on type of bone
- No-long term studies and study methodology not standardized

Hematogenous osteomyelitis treatment		
Neonates	Staph aureus ; Group B strep; Gram –ve enterics	Cloxacillin + cefotaxime
		MRSA: Vancomycin + cefotaxime
Children	Staph aureus ; Group A strep; [rare: H. influenza, S. pneumoniae, Gram –ve enterics]	Cloxacillin
		MRSA: Vancomycin
		Not immunized against H. flu: add cefotaxime
Adults	Staph aureus ; [rare: Gram –ve enterics]	Cloxacillin or cefazolin
		MRSA: Vancomycin

Contiguous osteomyelitis treatment		
Head/neck	MIXED INFECTION ; Staph aureus ; anaerobes; gram –ve	Clindamycin +/- Gentamicin (gram –ve)
Soft tissue	Staph aureus ; Streptococci	Cloxacillin or cefazolin
		MRSA: Vancomycin

Penetrating trauma treatment		
Pseudomonas ; Staph aureus; bacillus; anaerobes	Children	Cloxacillin + ceftazidime + gentamicin
	Adult	Ciprofloxacin + cloxacillin or cefazolin
	MRSA	Vancomycin

Vascular insufficiency (diabetic foot ulcer) treatment	
Staph aureus ; Streptococci; gram –ve bacilli; anaerobes	Carbapenem or piperacillin/tazo or clindamycin + ciprofloxacin
POLYMICROBIAL INFECTION	MRSA: add vancomycin

Septic arthritis treatment	
Staph aureus ; Streptococci; [rare: candida species; pseudomonas; enterobacteriaceae]	Cloxacillin or cefazolin +/- ciprofloxacin or gentamicin
	MRSA: vancomycin

Prosthetic joint infection treatment		
Early (<3 months)	Staph aureus ; Coagulase negative staph (CoNS); enterobacteriaceae	Vancomycin +/- rifampin +/- ciprofloxacin or gentamicin
Delayed (3- 24 mos)	CoNS ; Propionibacterium; other anaerobes; Staph aureus	

Definite abx therapies	
MSSA	Cloxacillin 2g IV q4-6h Cefazolin 2g q8h Clindamycin 600 mg IV q8h
MRSA	Vancomycin* 20 mg/kg IV q8-12h +/- rifampin 600 mg PO daily *target trough 15-20 mg/L
CoNS	Vancomycin* 20 mg/kg IV q8-12h *target trough 15-20 mg/L
Group A or B Streptococcus	Penicillin G 4 million units IV q4h
Enteric gram -ve bacilli	Cefotaxime 2g IV q8h
Pseudomonas	Ceftazidime 2g IV q8h + gentamicin* 1-2.5 mg/kg/dose Also can use carbapenems or ciprofloxacin *target peak 8-10 mg/L
Mixed aerobic/ anaerobic	Imipenem 500 mg IV q6h Piperacillin/tazo 4.5 g IV q6h = 4g pip + 0.5 g tazo

Step down from IV → oral therapy

- IV continued until pt is:
 - Systemically better
 - Afebrile
 - Signs of inflammation & tenderness improved

Contraindications for IV → PO stepdown

- Neonates
- Not expected to attend follow-up appointments
- Immunocompromised
- MRSA if resistant to clindamycin
- Poor adherence
- Recurrent or chronic osteomyelitis
- No oral formulation or poor oral absorption of

Safety monitoring of abx

- Vancomycin:
 - Red neck syndrome with each dose
 - Urine output daily
 - SCr & urea 2-3 times/wk
 - Vestibular testing q2-4 wks
 - Beta-lactams:
 - Rash daily
 - SCr 1-2 times/wk
 - Urinalysis q1-2 wks
 - CBC weekly
 - Gentamicin:
 - SCr & urea 2-3 times/wk
 - Audiology testing
 - Fluoroquinolones: rash; blood glucose & CBC weekly
 - Rifampin:
 - Rash
 - urinalysis q2 weeks
 - LE if signs of jaundice, liver failure
 - CBC + diff weekly
 - Drug interactions
 - Orange/red staining of tears, urine, feces
- Clindamycin: rash, diarrhea

Effectiveness monitoring

- Vital signs & temperature q6h
- Local tenderness, pain, erythema, movement/function daily
- Blood cultures daily until negative (s/b negative for 2 days)
- WBC + diff twice weekly
- ESR/CRP weekly (controversial)
- Vancomycin trough levels once weekly
- Gentamicin peak & trough levels once weekly
- Adherence