

Osteomyelitis

Michael Allen, DO
Gerard Chang, MD

Objectives

- Define osteomyelitis
- Review classification systems
- Review workup
- Discuss treatment options
- Clinical case examples

Definitions

- Osteomyelitis: Infection of the bone, with infection or inflammation of surrounding soft tissue
- Acute
 - Infection of short duration
 - Characterized by suppuration (ie. abscess) but not Biofilm
 - Often hematogenous osteomyelitis
 - No osteonecrosis yet
 - Systemic symptoms common

Definitions

- Chronic
 - Long lasting infection- Months to years
 - Characterized by **necrotic bone** and bacterial colonies in protein/polysaccharide matrix (biofilm)
 - Often no systemic symptoms
- Occurs along spectrum with no clear time cutoff to separate acute vs chronic infection

Etiology

- Hematogenous seeding from remote source
 - Most common form in young children
 - Sluggish metaphyseal capillaries
- Contiguous spread from soft-tissue or joint infection
 - Common in older adults near arthroplasty
 - Lower extremity infections related to diabetes or vascular disease
- Direct inoculation from penetrating trauma or surgery
 - Common in young adults

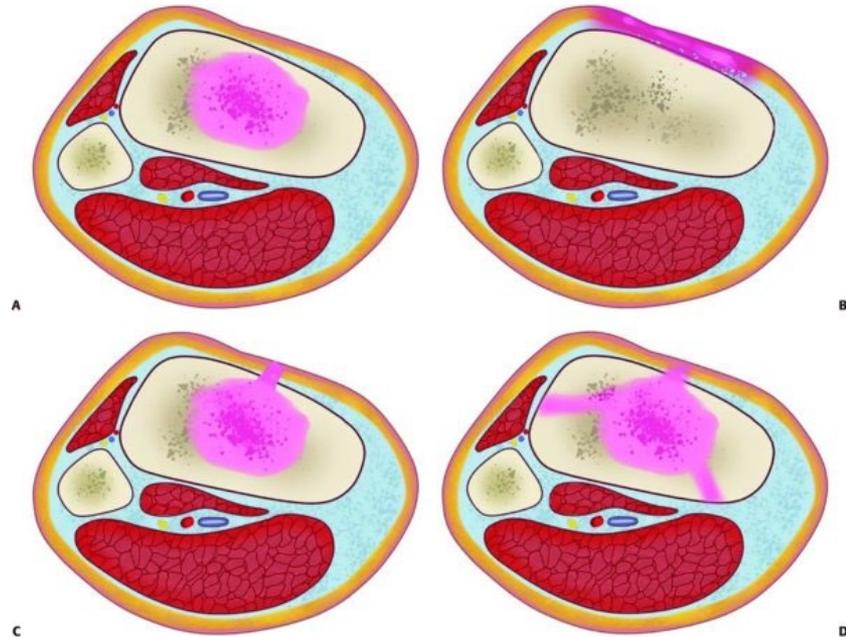
Classification schemes

- Waldvogel in 1970 proposed three groups:
 - Hematogenous
 - Secondary to a contiguous focus of infection
 - post op wound, direct puncture, superficial infection
 - Associated with vascular disease

New England Journal of Medicine, 1970, 282(4), 198–206

Classification schemes

- Cierny-Mader based on location in the bone and the host comorbidities
- 12 clinical stages (4 types x 3 host class)
 - A: Type I: medullary osteomyelitis.
 - B: Type II: superficial osteomyelitis.
 - C: Type III: localized osteomyelitis.
 - D: Type IV: diffuse osteomyelitis.
- Host
 - A - Healthy
 - B - Compromised locally (BL) or systemically (BS)
 - C - Requires suppressive or no treatment, Minimal disability, Treatment worse than disease, Not a surgical candidate



Paul Tornetta III, William M. Ricci, Robert F. Ostrum, Margaret M. McQueen, Michael D. McKee, Charles M. Court-Brown. *Rockwood and Green's Fractures in Adults*. Wolters Kluwer Health, 2019

Classification schemes

- Local and systemic factors
 - Address along with infection for best chance of resolution
- In CM staging, the stage helps determine treatment

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Anatomic Type	
Type	Characteristics
I	Medullary osteomyelitis
II	Superficial osteomyelitis
III	Localized osteomyelitis
IV	Diffuse osteomyelitis
Physiologic Class	
Host	Characteristics
A	Good immune system and delivery
B	Compromised locally (B ^L) or systemically (B ^S)
C	Requires suppressive or no treatment Minimal disability Treatment worse than disease Not a surgical candidate
Factors Affecting Physiologic Class	
Systemic Factors (S)	Local Factors (L)
Malnutrition Renal or hepatic failure Diabetes mellitus Chronic hypoxia Immune disease Extremes of age Immunosuppression Immune deficiency Tobacco abuse Alcohol abuse Malignancy	Chronic lymphedema Venous stasis Major vessel compromise Arteritis Extensive scarring Radiation fibrosis Small-vessel disease Neuropathy

Hematogenous Pathophysiology

- Bacteremia seeds long bones commonly around epiphyseal endplates
 - Slow capillary metaphyseal blood flow deposit bacteria
- Local inflammatory response increases intramedullary pressure
 - Occludes normal blood flow causing necrosis
 - Forces infection to break through cortex and form subperiosteal abscess
- Erosion through periosteum compromises bone blood supply further, worsening necrosis

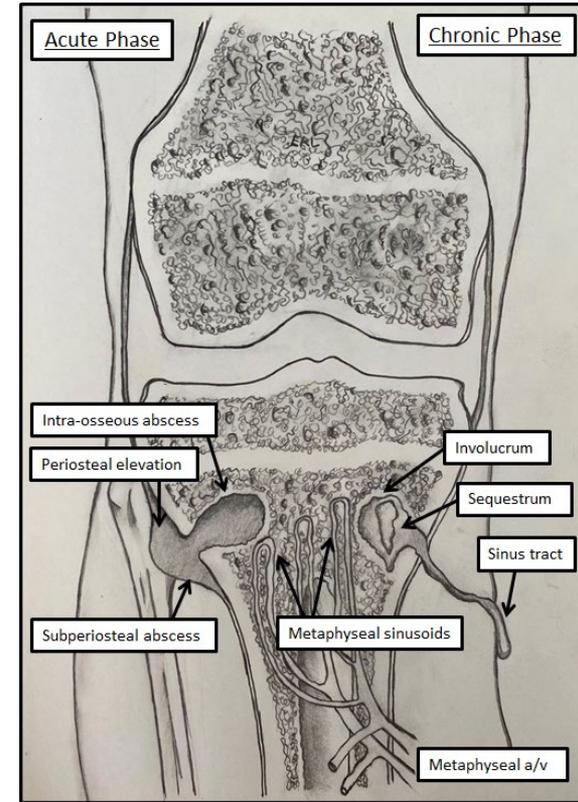
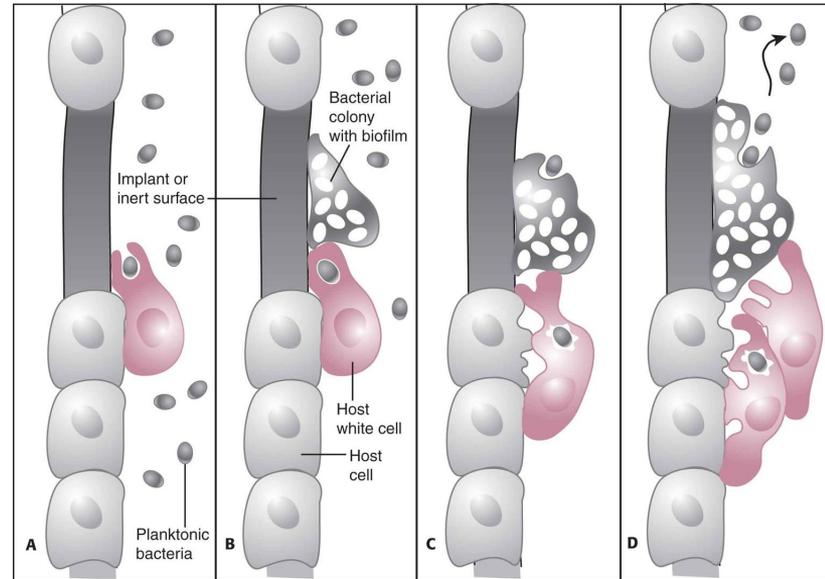


Image courtesy of Ezra Levy, DO

Core Curriculum V5

Hematogenous Pathophysiology

- Bacteria bind to cell surface receptors and extracellular matrix
 - Create local microcolonies and biofilm
 - *S. aureus* forms Staphylococcal abscess communities (SACs)
- Recruitment of phagocytes occurs creating metaphyseal abscess
 - Proteolytic enzyme release from phagocytes
 - Oxygen free radicals, cytokines
 - Decreased O₂ tension, pH
- Leads to osteolysis



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Hematogenous Pathophysiology

- SAC form in center of abscess surrounded by fibrin deposits
- *S. aureus* releases coagulase and von Willebrand factor-binding protein
 - Activates prothrombin
 - Polymerizes fibrin network around SAC
 - Protects from immune clearance
 - Immune cells unable to penetrate network
- Bacteria binding to sequestrum release extracellular polymeric substance matrix
 - Forms biofilm glycoalyx
 - Reduced O₂ tension and metabolic activity of bacteria
 - Barrier prevents immune clearance and penetration of antibiotics

Pathophysiology

- *S. aureus* and *epidermidis* can become intracellular inside osteoblasts
 - Further perpetuates chronic infection by limiting clearance by host immune system
- Staphylococcus surface-associated material (SAM) stimulates osteoclast activity
 - release of IL-1, IL-6, TNF- α .
- *S. aureus* protein A (SpA) binds to osteoblasts affecting metabolic activity and proliferation.
 - Induces RANKL secretion leading to osteolysis

Pathophysiology

- Necrotic bone separates to form the Sequestrum
 - Mixture of bone and purulence
- Reactive bone may form around the sequestrum, termed Involucum
 - May not completely surround sequestrum
 - Drainage from sequestrum may still occur through incomplete involucrum

Vertebral Osteomyelitis

- Bacteria seeded in metaphysis of vertebral bodies
- Infection spreads through endplate into disc
- Spread from disc space to adjacent vertebrae
- Vascular structures between vertebrae allow communication with distant vertebral bodies
 - Batson's venous plexus



Images courtesy of Michael Allen, DO

Microbiology

- Organisms vary based on age, type of osteomyelitis and location
 - Hematogenous commonly monomicrobial
 - Contiguous or direct inoculation can be monomicrobial or polymicrobial
- Children - *S. aureus* > *S. pneumoniae* > *K. kingae*
 - Sickle cell predisposes to *Salmonella* but *S. aureus* still more common
- Adults - *S. aureus*, coag-neg Staph
 - Kremers et. Al, reviewed 41 years of osteomyelitis cases in Minnesota
 - *S. aureus* overall most common
 - Incidence of osteo increased with incidence of diabetes in population

J Bone Joint Surg Am. 2015 May 20; 97(10): 837–845.



Local microbiomes

- Garcia del Pozo et. Al., Spanish series from 1994 - 2015, 344 cases
 - *S. aureus* 29.6%, ***P. aeruginosa* 4.1%**, MRSA 4.1%
 - Polymicrobial infection 35.4%.
- Jiang et. Al., Chinese series 2010-2015, 394 cases
 - *S. aureus* 34.91%, ***P. aeruginosa* 17.16%**, *E. coli* 6.51%
 - Diabetic foot most common monomicrobial organism was ***P. mirabilis* 20%**
- Hogan et. Al, German series 2008-2014, 401 cases
 - *S. aureus* NOT the most common in this location
 - *S. epi* 30%
 - *S. aureus* 29%
 - MRSE 13%
 - MRSA 6%

Rev Esp Quimioter. 2018 Jun; 31(3): 217–225.

Medicine (Baltimore). 2015 Oct; 94(42): e1874.

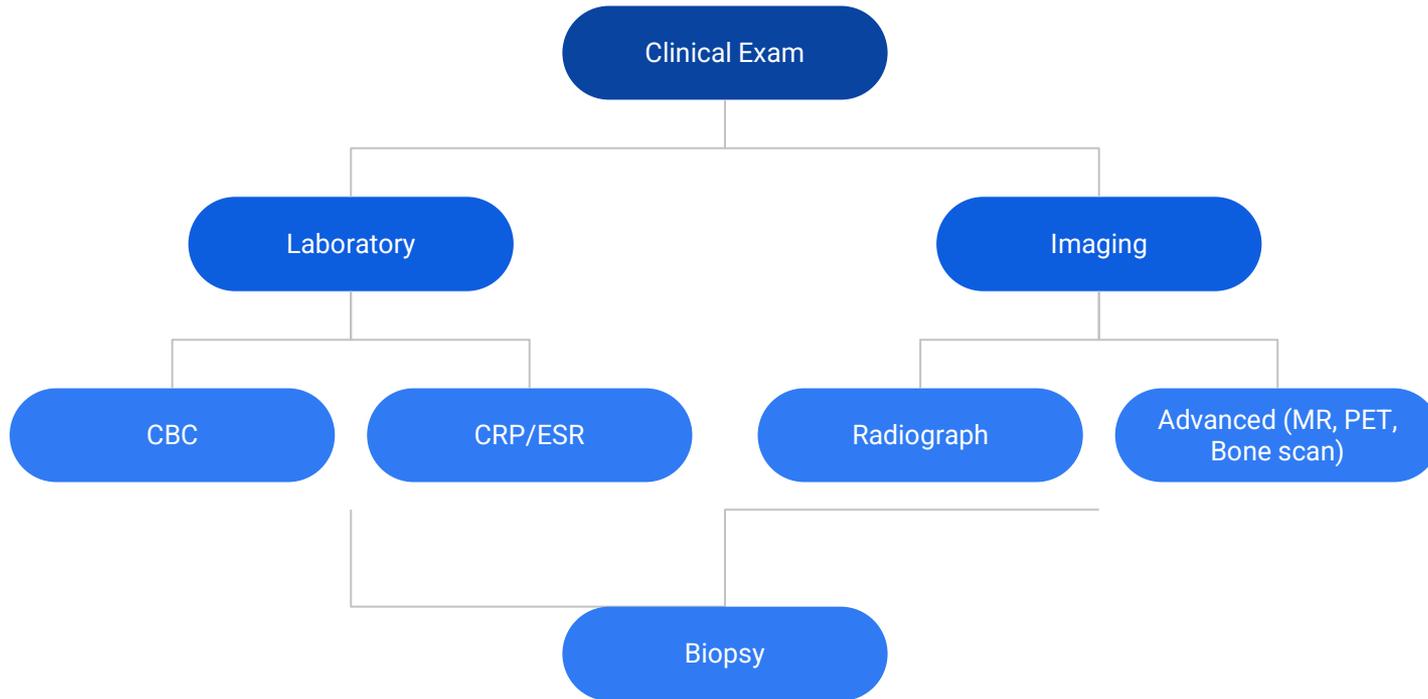
Arch Orthop Trauma Surg. 2013 Sep;133(9):1183-96



Clinical Presentation

- Acute
 - Pain
 - Erythema
 - Edema
 - +/- Fever (more common in pediatric)
 - Associated wound or sinus tract if direct/contiguous source
- Chronic
 - Generalized/systemic signs less common
 - Localized pain and edema
 - Sinus tract, non-healing ulcerations in vasculopath
 - Vertebral may present with neurological symptoms

Workup



Imaging

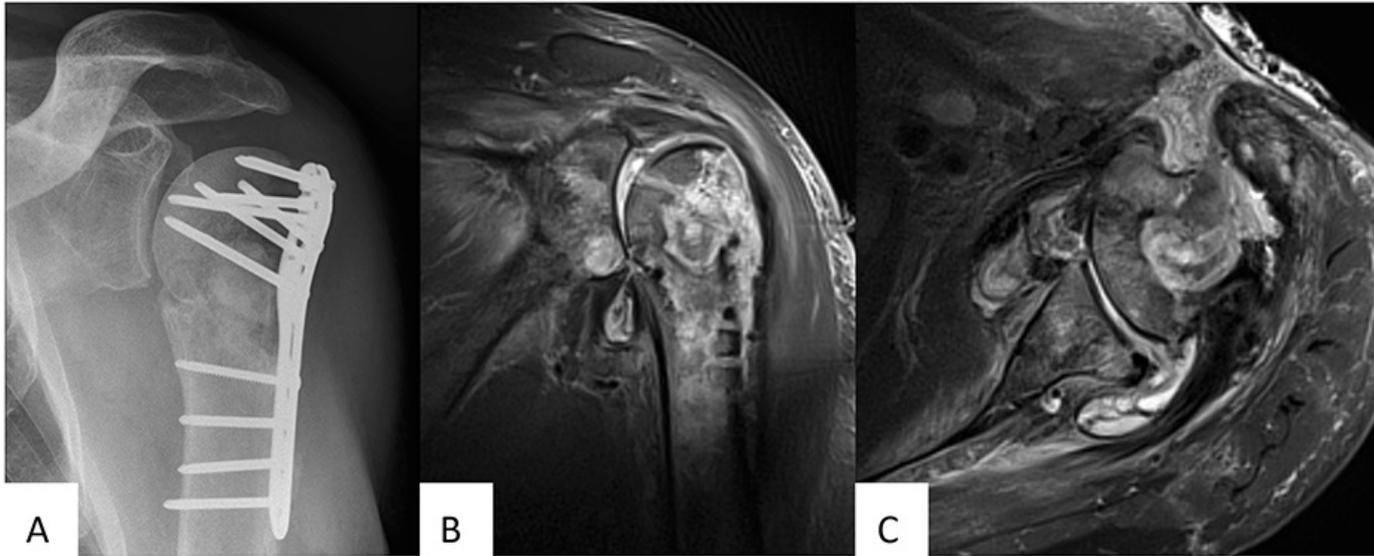
- First step is plane radiograph (sensitivity 28-75%)
 - Soft tissue swelling after a few days of onset
 - Look for ulceration and subcutaneous gas
 - 10-21 day lag before radiographic bony changes (osteopenia, periosteal reaction)
 - Cortical destruction later on with medullary lucency
- CT often obtained in ED
 - Not as sensitive as preferred modalities acutely
 - Can show cortical destruction and soft tissues well (with contrast)
 - Useful in chronic cases to visualize involucrum and sequestrum
- MR considered most useful when readily available

Magnetic Resonance

- High sensitivity and specificity
 - 90% sens, 79% spec (Clin Infect Dis. 2008 Aug;47(4):519-27.)
 - 93% sens, 75% spec (Diabetes Care. 2017 Aug;40(8):1111-1120.)
- Contrast is beneficial → soft tissue abscess, non-enhancing bone necrosis)
- T2/PD fat suppressed/STIR will show enhancement
 - Presence of edema is non-specific
- T1 decreased marrow intensity
- The combination of T2 enhancement and decreased T1 signal is suggestive of osteomyelitis in the right clinical context

Magnetic Resonance

MR demonstrating T2 enhancement, sinus tract to anterior skin



Govaert GAM, Kuehl R, Atkins BL, Trampuz A, Morgenstern M, Obrebsky WT, Verhofstad MHJ, McNally MA, Metsmakers WJ; Fracture-Related Infection (FRI) Consensus Group. Diagnosing Fracture-Related Infection: Current Concepts and Recommendations. J Orthop Trauma. 2020 Jan;34(1):8-17. Figure 1

Further imaging

- **Tchnetium 99 phosphate bone scan**
 - 81% sens, 28% spec (Clin Infect Dis. 2008 Aug 15;47(4):519-27.)
 - 91% sens, 92% spec (Diabetes Care. 2017 Aug;40(8):1111-1120.)
- **Indium 111 leukocyte scan**
 - 74% sens, 68% spec (Clin Infect Dis. 2008 Aug 15;47(4):519-27.)
 - 92% sens, 75% spec (Diabetes Care. 2017 Aug;40(8):1111-1120.)
- **18-FDG PET scan**
 - 89% sens, 92% spec (Diabetes Care. 2017 Aug;40(8):1111-1120.)
- **Overall, the sensitivity and specificity across studies is inferior to MRI and these are adjunctive modalities, not first line**
 - PET helpful in low grade spondylitis/discitis (Clin Radiol. 2016 Jul;71(7):632-46)



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Core Curriculum V5

Labs

- CRP and ESR (Clin Orthop Relat Res. 2019 Jul; 477(7): 1594–1602)
 - ESR >60 mm/h (74% sens, 56% spec) and CRP >7.9 mg/dL (49% sens, 80% spec) in predicting osteomyelitis of the diabetic foot
 - ESR *AND* CRP above cutoff = 36% sens and 91% spec
 - ESR *OR* CRP above cutoff = 87% sens and 45% spec
- CRP >3.2 mg/dL or ESR >60 mm/hr and associated ulcer depth >3 mm had 100% sens for osteomyelitis in diabetic foot (J Foot Ankle Surg. Jan-Feb 2009;48(1):39-46.)

The key is recognizing elevated inflammatory markers and interpreting along with imaging and clinical presentation!

Combined imaging and labs

- Tornetta et. Al investigated labs and imaging to diagnose infections in nonunions
 - Retrospective review of 95 nonunions who had preoperative serum WBC, CRP, ESR and nuclear med scan (In-111 WBC scan, Tc-99m scintigraphy, or combined)
 - Infection confirmed by positive by gross purulence intraop, positive intraop culture, gross infection immediately postop
 - Elevated CRP >1 mg/dL (OR=4.2, p=0.002), ESR >30 mm/hr (OR=5.2, p=0.0006) significant predictors of infection
 - WBC count >11k (OR=2.5, p=0.12) and In/Tc scanning (OR=2.5, p=0.29) not significant predictors

Tornetta et. Al continued

- When positives on these 4 tests, combined score predictive of infection:
 - 0 = 18.3%
 - 1 = 23.5%
 - 2 = 50.0%
 - 3 = 85.7%
- Nuclear scan had high specificity (92%) but low sensitivity (19%) and costly
- Just labs without nuclear scan:
 - 0 = 19.6%
 - 1 = 18.8%
 - 2 = 56.0%
 - 3 = 100.0%

Biopsy and culture

- Blood culture can isolate hematogenous seeding organism
 - More common in pediatric, less useful in adult
- Superficial wound swab not reliable → lack of concordance with bone culture
- Bone biopsy considered diagnostic “gold standard”
- Targeted biopsy can guide medical therapy
 - Highest yield before antibiotics or after 14 day holiday.

Treatment strategies

- Initial questions to guide therapy
 - What is the host type? Have they been medically optimized?
 - Is there osteomyelitis around retained hardware?
 - If so, is the hardware critical to stability?
- Treatment requires team approach with surgeon, ID, PCP, wound care AND PATIENT all on board

Treatment strategies

- Cierny-Mader Host
 - A → limb salvage, antibiotic therapy, surgery if indicated
 - BL → limb salvage, antibiotic therapy, likely surgery adjunct
 - BS → limb salvage, medical optimization first, address comorbid conditions, antibiotics and surgery
 - C → palliative, suppressive antibiotics vs amputation
- Type
 - I → intramedullary debridement (removal of hardware if present)
 - II → debride soft tissue and bone until healthy base
 - III → excision of involved bone with medullary debridement
 - IV → complete segmental excision and reconstruction

Empiric antibiotics

- Dudareva et. Al reviewed 223 chronic osteo patients undergoing definitive surgery from 2013-2017 compared with 157 from 2001-2004.
 - MRSA and VRE actually decreased, overall multi drug resistant organisms remained the same
 - Least resistance demonstrated to empiric combination of meropenem with vancomycin, followed by Piperacillin/Tazobactam with vancomycin
 - 32.3% of patients were culture negative demonstrating the importance of selecting empiric antibiotics which have least rate of resistance in the local microbiome.

Empiric antibiotics – vertebral osteo

- 358 cases of microbiologically proven hematogenous vertebral osteo 2005-2012
- MSSA (33.5%), MRSA (24.9%), *Enterobacteriaceae* (19.3%), *Streptococcus* species (11.7%)
- Oral regimens
 - 73.5% of isolated pathogens susceptible to levofloxacin plus rifampicin
 - 71.2% to levofloxacin plus clindamycin
 - 64.5% to amoxicillin-clavulanate plus ciprofloxacin
 - Susceptibility rates were better for community acquired vs hospital acquired!
- IV Vanco regimens
 - 93.0 % combined with ciprofloxacin
 - 94.1% with ceftriaxone
 - 95.8% with ceftazidime or cefepime





Antibiotic therapy

- Treatment success depends on adequate penetration of antibiotic into infected bone
- Different drug classes have variable bone penetration rates
 - **β -Lactam** bone levels range from 5-20% of parenteral serum level -> **Oral only reach ~10% of parenteral serum levels and are unlikely to reach MIC in bone**
 - Vancomycin/Daptomycin also poor bone penetration but serum levels are high
 - Oral fluoroquinolone, linezolid, TMP-SMX reach up to 50% of serum level in bone
 - Clindamycin reaches 40-70% of serum level
 - Metronidazole may reach serum levels in bone, useful for anaerobic infections
 - Rifampin reaches or exceeds serum levels, useful as adjunct therapy

Clin Infect Dis. 2012 Feb 1; 54(3): 393–407.

Antibiotic therapy

- Nonrandomized trials -> chronic osteo treated for 4–6 weeks with parenteral β -lactam antibiotic shown to cure 60%–90% of cases
 - Studies are not consistent in terms of surgical debridement, length of follow up etc...
- For long bone osteo, Vancomycin achieves low cure rates compared to β -lactams -> Odds ratio of recurrence 2.5 when vanco used
- Daptomycin shows cure rates of 65%–75% in chronic osteo

Clin Infect Dis. 2012 Feb 1; 54(3): 393–407.

Antibiotic therapy: Oral fluoroquinolones

- Oral fluoroquinolones are the most studied class for oral only therapy
- Spellberg and Lipsky review up to 2012 demonstrates:
 - Cure rates 60-80%
 - Therapy usually 12-16 weeks and usually higher dose than for other infections
 - Not enough data to conclude that the longer duration and high dose is required
 - Most failures due to *Pseudomonas* and to a lesser extent *S. aureus*



Antibiotic therapy: TMP-SMX

- TMP-SMX next most commonly studied after fluoroquinolones
- 7 mg/kg/d of trimethoprim, with rifampin 600-1200 mg/day, and debridement cured 100% of Staph osteo (Enferm Infecc Microbiol Clin. 1997 Jan;15(1):10-3)
- TMP-SMX for 6 months with debridement, 59/60 (98%) cured -> dose unclear (Rev Soc Bras Med Trop. Oct-Dec 1992;25(4):235-9)
- TMP-SMX BID at 10mg/kg TMP and 50mg/kg SMX BID for infected hardware/PJI (Antimicrob Agents Chemother. 1998 Dec;42(12):3086-91.)
 - Intention to treat success 66.7% (26/39) and per protocol success 86.7% (26/30)
- TMP-SMX (8 mg/kg/d) or linezolid, combined with rifampin cured 79%–89% of patients with infected orthopedic implants or chronic osteomyelitis. (Clin Microbiol Infect. 2009 Dec;15(12):1163-9)

Antibiotic therapy: Oral agent summary

- Oral fluoroquinolone and TMP-SMX at high doses are very successful for treating osteomyelitis
- Multiple studies confirm the importance of concurrent surgical debridement and removal of hardware if necessary.
- Rifampin may be useful as an adjunct
- Longer duration regimen may be required but there is not enough data on this to state unequivocally

Antibiotic therapy

- Cochrane review from 2013 concludes “The main finding of this review is the lack of evidence to guide practice.”
 - 4 trials compared oral quinolones with parenteral antibiotic
 - No difference in rate of remission at the end of therapy (RR 1.04, 95% CI 0.92 to 1.18; four trials, 150 participants)
 - Most of the included studies were >20 years old as of 2013
- There is no strong evidence supporting 4-6 weeks of IV therapy which is standard, or supporting longer courses of oral therapy
- These durations are mostly historical and ongoing studies are needed to compare short durations

Cochrane Database Syst Rev. 2013 Sep 6;(9):CD004439
Clin Infect Dis. 2012 Feb 1; 54(3): 393–407.



The OVIVA trial

- Oral versus Intravenous Antibiotics for Bone and Joint Infection published in NEJM 2019
 - Multicenter UK trial -> 1054 patients randomized to either 6 weeks of IV or oral therapy (527 in each group)
- Infections included: native appendicular osteo, native joint infection requiring excision arthroplasty, PJI, fixation device infection, or vertebral osteo
- Antibiotic selection left up to local specialists based on appropriate biogram

The OVIVA trial

- Median duration therapy 78 days IV, 71 days oral (P = 0.63)
- Treatment failure at 1 year primary endpoint
 - 74/506 (14.6%) for IV, and 67/509 (13.2%) for oral
- **Oral therapy was non-inferior to IV therapy**
- Most common antibiotics
 - IV: glycopeptides 41.1%, cephalosporins 33.2%
 - Oral: quinolones 36.5%, combination therapy 16.6%, penicillins 15.9%
- Nonsurgical costs £2,740 cheaper for PO with no difference in quality adjusted life years and similar rates of adverse events on both groups

Antibiotic therapy summary

- Multiple studies including large RCT from 2019 support oral therapy being as successful as IV therapy
- Antibiotic choice needs to be determined based on culture sensitivities and local resistance rates
- Most common oral regimens include fluoroquinolone or TMP-SMX
- Most common IV regimens include Vanco and β -Lactam
- Oral Rifampin is a useful adjunct to both oral and IV regimens
- Surgical debridement/removal of hardware must be considered

Surgical treatment principles

1. Excise ALL devitalized/infected bone and soft-tissue
2. Manage the dead space
3. Address soft-tissue envelope
4. Reconstruct the bone defect
 - Reconstruction always the last stage

Debridement

- Removal of nonviable soft-tissue surrounding infection site
 - Excise sinus tracts
 - Chronic infected tissue risk for Marjolin ulcer and future cancer
- Systematic removal of all necrotic and/or infected bone
 - Be methodical without skipping around
 - High speed burr, rongeur
- Debride to bleeding bone (“Paprika sign”)





Dead space management

- Tissue dead space needs to be occupied to prevent reaccumulation of infection
- Open space + poor vascularity = infection breeding ground
- Antibiotic beads
 - PMMA + antibiotic
 - Antibiotic should be heat stable and hydrophilic
 - Commonly Vancomycin and Tobramycin/Gentamicin
 - Open wound with beads plus occlusive dressing = bead pouch
- Bioactive glass -> forms hydroxyapatite like surface which bonds to bone and can fill defects and provide antimicrobial effect as well (altered pH, Ag⁺ ion release)

Dead space management: abx + PMMA

- Choose heat stable antibiotics -> exothermic polymerization
- Combined abx often used for synergistic effects -> both in increased elution and increased activity
- Most common choices are gentamicin, vancomycin, tobramycin, clindamycin
 - Gent + vanco covers most pathogens including MRSA/MRSE
- Maximum elution concentration at day 2-3, then drops from week 1-2
 - Smaller/more beads with greater surface area than larger bead/spacer -> higher elution rate and concentration
 - Spacer useful if attempting to maintain anatomic space



Dead space management: abx + PMMA

- Increasing abx concentration in PMMA may reduce structural integrity
 - Theoretical problem in PJI revision, not as much in beads/spacers which are not structural/load bearing
 - Variability in hand mixed formulations [J Orthop Surg (Hong Kong). May-Aug 2019;27(2)]
- Cacciola et. Al found that PMM retains minimum compressive strength of 70 MPa until loaded with 12 g of abx per 40 g PMMA (J Orthop. 2018 Sep 6;15(4):1004-1007)
 - Increasing Tobramycin and Gentamicin increases Vancomycin elution in triple antibiotic formation
- Hand mixing results in more air trapping which may increase elution rates (which also decreases structural integrity) [J Biomed Mater Res B Appl Biomater. 2009 Jul;90(1):467-75]

Dead space management: abx + PMMA

- There is a paucity of data for prospective trials of different antibiotic concentrations
- Many studies in arthroplasty literature for PJI
 - Most show good eradication with 2-4 g Vanco and 1.2-4.8 g Tobra/Gent per 40 g PMMA (Clin Infect Dis. 2012 Dec;55(11):1474-80)
 - Support in arthroplasty literature for achieving acceptable intraarticular concentrations with 4 g Vanco and ≥ 3.6 g Tobra
- Retrospective group of 40 infected tibia defects treated with premixed gentamicin PMMA with 2 g vanco, as beads or spacer (BMC Musculoskelet Disord. 2017 Jun 12;18(1):256)
 - 88.9% control with beads, 90.9% with spacer and induced membrane

Dead space management

- Bead pouch used in initial debridement in 84 lower extremities (tibia to foot) [Injury. 2010 Mar;41(3):285-93]
 - Exchanged after 48-72 hours
 - Followed with bone and soft tissue reconstruction as indicated
 - Success without amputation in 69/84 cases (82.1%)
- 15 infected tibia fractures treated with debridement and bead pouch with temporary porcine graft covering. (J Trauma. 1997 Aug;43(2):268-74)
 - 1 week IV abx, definitive surgery 2-6 weeks later
 - 15/15 eradicated infection prior to second stage fibula vascularized grafting

Dead space management

- Negative pressure wound therapy (NPWT)
 - Can temporize a wound but not ideal when trying to achieve high antibiotic concentrations
 - Vac system may have ability to instill with antibiotic solution
- Pelvis/LE osteo cases treated with debridement and NPWT instillation, 3/30 (10%) had recurrence at 8 months compared to historic control 55/94 (58.5%) [Wound Repair Regen. Mar-Apr 2009;17(2):278-86]
- In goat contaminated wound model, bead pouch alone had 6x less bacteria than bead pouch with NPWT. (J Orthop Trauma. 2012 Sep;26(9):512-8)
 - High levels of antibiotic eluent in the NPWT drainage as expected

Dead space management: Bead pouch



Soft-tissue reconstruction

Reconstructive ladder:

1. Healing by secondary intention
2. Primary closure
3. Delayed primary closure
4. Split thickness graft
5. Full thickness skin graft
6. Tissue expansion
7. Random flap
8. Axial/Pedicle flap
9. Free flap

Defects often requires local or free-tissue transfer
Must have skilled Microsurgeon available

Example: medial gastroc flap



Example: Anterolateral thigh free flap



Bone reconstruction

- Non-segmental defects
 - Additional stability may not be needed if there is cortical support
 - If large enough defect with structural concern, bone grafting 6-8 weeks after infection eradicated
- Segmental defects
 - Shorten bone to fill defect or replacing lost bone
 - Need provisional stability (most commonly external fixator)
 - Plan for bone defect
 - Masquelet technique
 - Bone transport
 - Structural autograft (fibula)

Masquelet technique (Induced membrane)

- Antibiotic spacer placement and soft-tissue coverage
 - Pseudomembrane forms around spacer
- Staged Bone grafting (4-6 weeks later)
 - Membrane secretes BMP-2, VEGF and other growth factors
 - Peak at 4 weeks after membrane induction then decreases rapidly (Aho et al. JBJS 2013)
- Reported success ~80% for implant dependent union
- 10-12 months for union, weight bearing



Bone transport

- Corticotomy made on one side (or both) distant to the infection site to create a segment
 - Segment is fixed to IM rod, Ring fixator, etc., that allows for controlled movement
- Segment is transported gradually towards the void, up to 1mm/day until original defect site is closed
- New bone formed by distraction osteogenesis at the corticotomy site



Circular fixation

- Advantages
 - Many options for pin placement
 - Excellent stability
 - Allows multiplanar deformity correction in addition to lengthening/transport
- Disadvantage
 - Pin site issues common
 - Technically demanding
 - Psychologically long process for patients



Acute Shortening

- Acute shortening >3cm may cause arterial flow impairment
- Results in limb length discrepancy and muscle shortening/dysfunction if length is not concurrently restored
- Reasonable definitive option for small bone defects and/or resources limited

Shortening/Lengthening

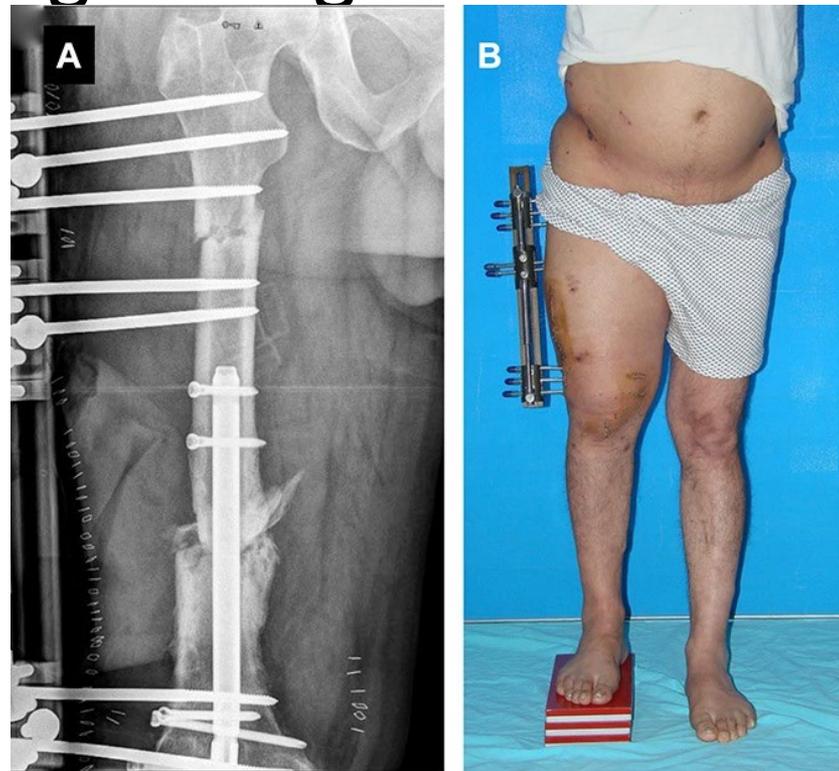
- Acute shortening of defect with concurrent lengthening of the bone through distraction osteogenesis distant to the infection defect
- Tetsworth et al, successfully treated infected tibial nonunions with 5.8 cm average defect with acute shortening and lengthening through ex-fix
 - No reported vascular complications with acute shortening in this series
 - Injury. 2017 Oct;48(10):2276-2284
- Sen et al, shortened 23 distal femur defects up to 7 cm acutely over supracondylar nail and lengthened with ex-fix
 - 100% union rate
 - No vascular complications after shortening
 - J Orthop Trauma. 2020 Sep;34(9):476-481

Shortening/Lengthening

Distal femur osteo and necrotic bone debrided

Distal femur retrograde nail

Proximal femur osteotomy gradually lengthened to eliminate discrepancy



Sen C, Akgül T, Tetsworth KD, Balci Hİ, Yildiz F, Necmettin T. Combined Technique for the Treatment of Infected Nonunions of the Distal Femur With Bone Loss: Short Supracondylar Nail-Augmented Acute Shortening/Lengthening. J Orthop Trauma. 2020 Sep;34(9):476-481. Figure 2.

Osteomyelitis around orthopedic implants

Three scenarios:

1. Stable hardware, fracture healed
2. Stable hardware, fracture not healed
3. Unstable hardware, fracture not healed

Stable hardware, fracture healed

- Treat with I&D, removal of hardware
- Follows Stage 3 treatment principles
 - Curette when possible, any remaining defect, hardware holes, pseudomembranes, etc.
- If fracture is united and stable, without segmental defect, then no further instrumentation needed for stability

Stable hardware, fracture not healed

- Stability is required to eradicate infection
- For acute infections attempt I&D, retain hardware, suppress with antibiotics until fracture healing
- Goal to convert from Stage 4 to Stage 3 osteomyelitis
- 71% success in achieving fracture healing with antibiotic suppression (Berkes et al. JBJS 2010)
 - Requires eventual hardware removal in ~30% cases
 - Hardware removal less likely in proximal (e.g. pelvis) vs. distal locations (e.g. tibia)
- If fracture healing achieved, principles follow Stage 3 treatment

Unstable Hardware, Fracture Not Healed

- I&D, removal of hardware
- Equivalent to Stage 4 Osteomyelitis (i.e. Segmental Defect)
- Requires strategy for bone stability (e.g. ring fixator, antibiotic nail, etc.) and management of segmental bone defect

Results (of Comprehensive, Multidisciplinary Treatment Protocol)

- 2207 cases from 1981 through 2007
 - 1898 limb-salvage protocols
 - 230 amputations (as primary treatment)
- 85% overall success (infection-free, functional reconstruction at 2 years)
 - A-hosts 96%
 - B-hosts 74%
 - Limb-salvage 84%
 - Amputation 91%

Plast Reconstr Surg. 2011 Jan;127

Results

- Treatment failures (n=319)
 - 43% aseptic nonunions
 - 28% wound sloughs
 - 15% unanticipated impairment
 - 12% recurrent sepsis
 - 2% deaths
- 82% success with retreatment
- Overall 2 year success rate of 95%
 - 99% A hosts
 - 90% B hosts

Plast Reconstr Surg. 2011 Jan;127

Results of limb salvage for tibial osteomyelitis

- 67 patients with 3.9 year follow up
 - Debridement with abx beads/rods and plastic closure if needed
 - 54 had fracture non-union with infection
 - 61 patients ultimately had their infection controlled by limb salvage
 - 48/54 non-unions achieved union
 - 5 patients required amputation
 - 1 patient on daily chronic antibiotics
- Failure associated with
 - Diabetics with neuropathy
 - Increasing surgeries

J Bone Jt Infect. 2019 Dec 10;4(6):306-313

Summary

- Commonly hematogenous or direct inoculation
 - Most common organism *S. aureus*
- Assess modifiable patient risk factors like glucose control, comorbid conditions optimization
- Cierny-Mader classification based on location in the bone, and comorbidities of the patient
 - Host type helps determine treatment options -> treatment may be worse than the disease
- Standard therapy includes debridement and IV abx for 4-6 weeks
 - More research needed, current concept that oral abx may be as good as IV abx

Summary

- Options for dead space management include antibiotic cement spacers, beads, pouches, wound vac.
 - Common abx regimen for cement is 2-4 g Vanco +/- 4 g Tobra/Gent
- Soft tissue reconstruction follows a stepwise ladder, useful to have help of Plastic surgery for complex closures/flaps
- Bone reconstruction options include transport, shortening/lengthening, induced membrane techniques
- Selecting a patient specific treatment regimen can result in high success rates with eradication of infection, demands team approach between Orthopedics, Infections Disease, PCP!

Case 1

26M MVA, treated at outside facility 3 months ago for pilon and ipsilateral platuea

Presenting with drainage from medial ankle, pain, fever.

Has had debridement, wound vac medially, PICC line with 6 weeks IV ceftriaxone.

Medial wound had closed and began draining a few days after completing abx



Images courtesy of Michael Allen, DO

Case 1



Case 1

- 26M with anxiety/depression, 1ppd smoker
- Draining medial wound with positive inflammatory labs
- Retained hardware, not in functional alignment
- Fracture is not healed
- CM Type 4, BL host → Discussion should include serial debridements, definitive fusion vs amputation, tobacco cessation, psychiatric comanagement
- First step: infected hardware, dead bone, and compromised soft tissues need to come out

Initial debridement

- Excise medial soft tissue tract and necrotic tissues
 - Closed primarily
- Remove all necrotic bone -> currette/rongeur to healthy bone
- Antibiotic spacer created to fill dead space
 - 2 g Vanco per 40g cement
 - Spacer used to help preserve length
- Initially on Vanco/Ceftriaxone until cultures result for MSSA -> switched to Ancef IV for 6 weeks



Images courtesy of Michael Allen, DO

Core Curriculum V5

Clinical course

- 2 months later, continued minimal drainage
 - CRP 0.475 mg/dL, ESR 26
- 6 weeks Ancef finished, transitioned to doxycycline 100 mg PO BID
- CRP/ESR normalizing but persistent drainage
- Underwent repeat I&D, abx spacer exchange (2 g Vanco per 40g cement)
 - Spacer used instead of beads to help minimize shortening in preparation for definitive fusion



Images courtesy of Michael Allen, DO

Clinical course

- 4 months after initial ROH
- Continuing oral Doxy
- CRP/ESR normal
- Skin healed and no further drainage or fluctuance
- Definitive ankle fusion planned



Images courtesy of Michael Allen, DO

Definitive surgery

Fibula osteotomy

Spacer removed, nonviable bone removed

Viable fibula morselized and mixed with 1 g Vanco powder and used as graft

Hindfoot fusion success, plan for lifelong suppressive oral doxy



8 months post op

Case 2

- 48M MVA with open tibia fracture treated 18 months prior
- Medial tibia skin defect never fully closed
- Draining from sinus



Images courtesy of Michael Allen, DO



Case 2

- 48M, 1ppd smoker
- Healed fracture on radiograph, retained IMN
- Overlying cellulitis/sinus

- CRP 18.9 mg/L, ESR 14

- CM Type III, BL host

- Fracture is healed and stable → remove hardware, debride bone and tissue
- How do you close the soft tissue defect?



- Plastic surgery consultation
- Preop CT angio to assess circulation
- Anterior tibial artery is occluded near wound
- Normal peroneal and posterior tibial artery
- Plan for reverse sural flap



- Nail removed → soft tissue sinus and necrotic tissue excised
 - Cortical window made under sinus tract and debrided back to healthy bleeding bone
 - Reamer Irrigator Aspirator used to debride canal
- Wound covered with vac until delayed flap 2 weeks later
- Cultures were polymicrobial including *E. faecalis*, MSSA, *S marcescens*, anaerobes
 - 2 weeks IV vanco with PO moxifloxacin 400 mg QD, then 4 weeks of PO doxy 100 mg BID with moxifloxacin



Delayed reverse sural fasciocutaneous flap two weeks later



- 2 months post op
- Healed and returned to work



- 2 months post op
- Healed and returned to work



Images courtesy of Michael Allen, DO