UWTASP
tele-antimicrobial stewardship program

Osteomyelitis: Overview and Updates

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Project ECHO

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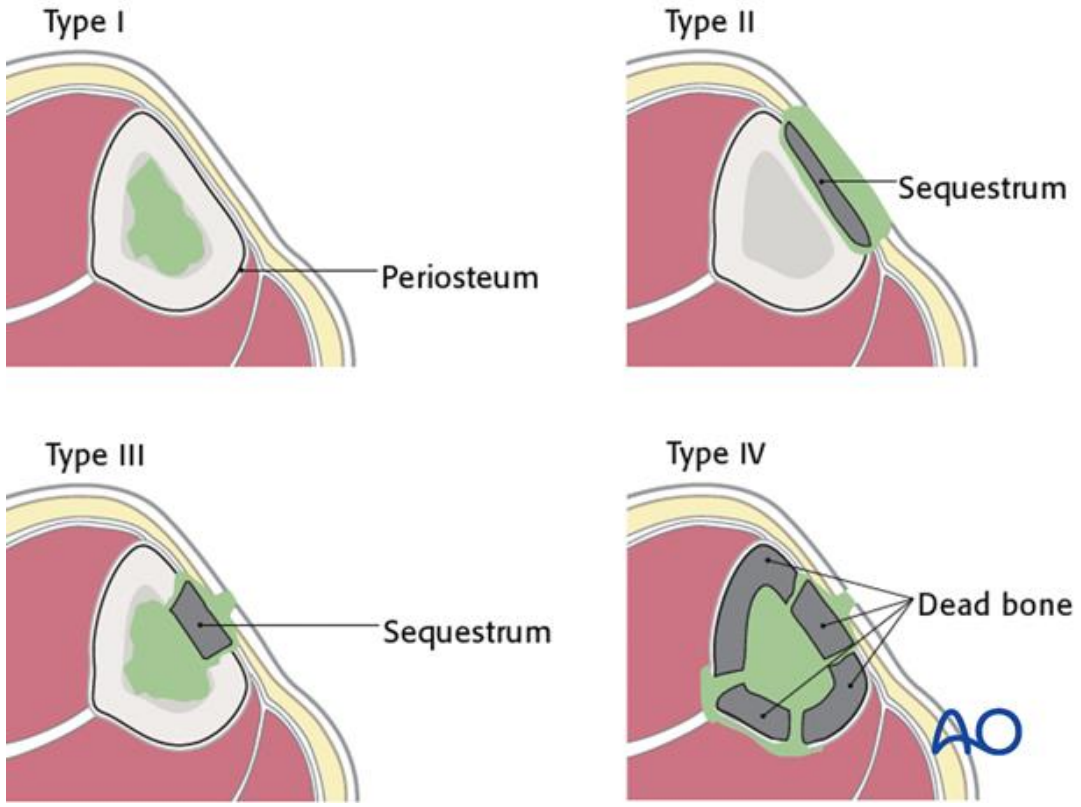
Sections

1. Classification
2. Pathophysiology
3. Microbiology
4. Diagnostic Approach
5. Treatment

OM: Classification

- By source: hematogenous vs contiguous
- By chronicity: acute vs chronic
- By location: Vertebral vs extremity vs other
- By presence or absence of hardware
- By anatomy: Cierny-Mader



Aofoudation.org

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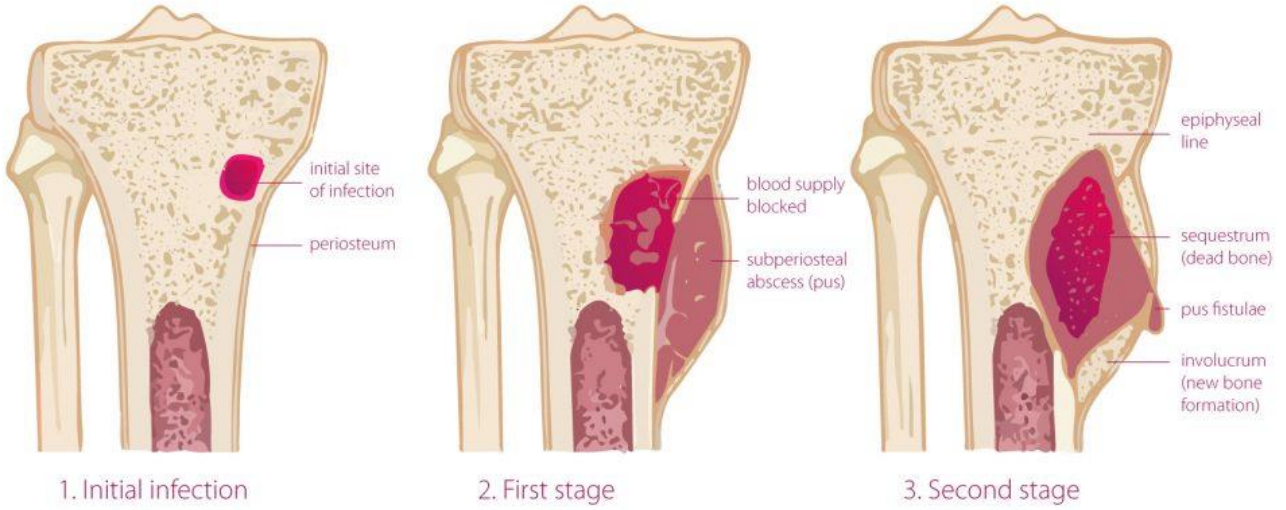
OM: Pathophysiology

- Introduction of bacteria to the marrow cavity: hematogenous, traumatic, or contiguous
- Pus in the marrow cavity->increased pressure->vascular compromise->bone necrosis



https://www.tobig.eu/bone-101/infection-osteomyelitis/

OM: Microbiology

- **Staph aureus** is the most common pathogen in all forms of OM
- Hematogenous OM is most often vertebral and most often monomicrobial
- Contiguous OM often polymicrobial including GNRs and anaerobes
- Skin flora (CoNS, Cutibacterium acnes) common in prosthetic joint infection

OM: Obtaining a Sample

- ID of the organism (s) should generally always be attempted
- If bacteremic and OM is hematogenous, generally no need for further sampling
- If contiguous, deep bone sample should be obtained after debridement
- **Hold antibiotics** prior to sampling unless unstable

OM: Diagnostic Approach

- When to suspect:

  --> Deep non-healing wound esp w/ worsening pain

  --> New MSK pain in someone with bacteremia (especially SA)

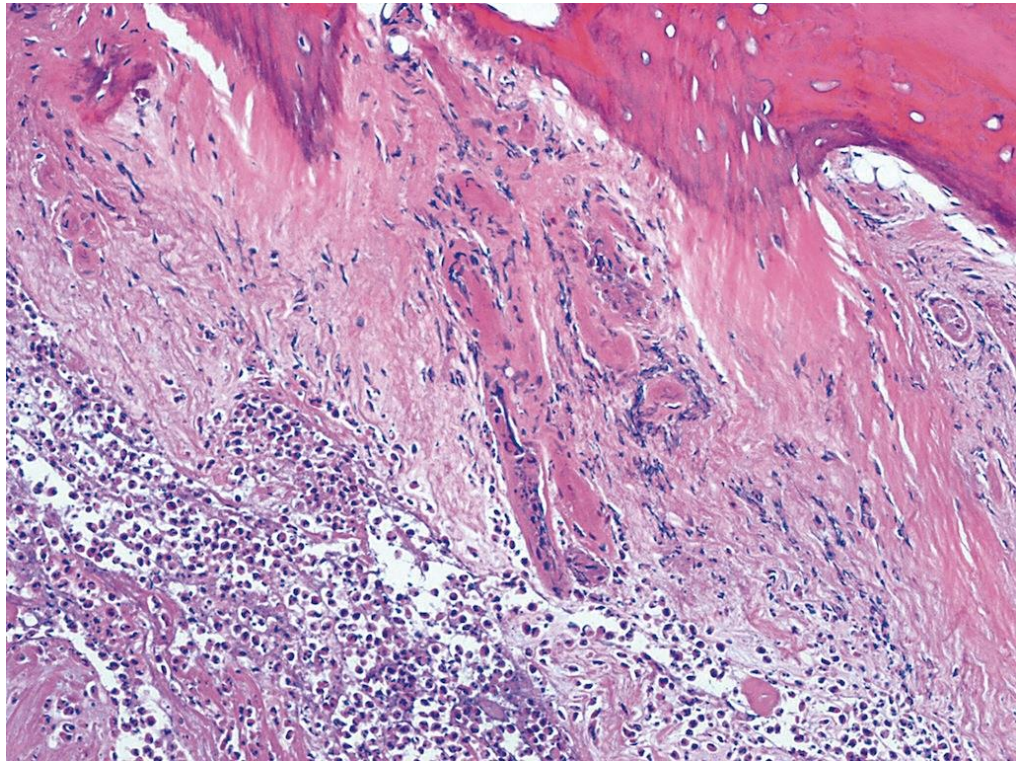
  --> Unresolving pain a/w prosthetic material

  --> Loosening of prosthetic material on XR

  --> Diabetic foot wound that probes to bone (cannot be extrapolated to other wounds)

OM: Diagnostic Approach

- Gold Standard: Bone histopathology (ideally with positive culture)
- Most OM is diagnosed empirically based on imaging and clinical context



https://www.pathologyoutlines.com/topic/bonebacterialosteomyelitis.html

OM: Diagnostic Imaging

- Plain XR: Low sensitivity but cheap and quick

  --> Takes about 2 weeks for any bony destruction to be visible
- CT: About 70% sensitive.

  --> Easier to see subtle bony changes, and sinus tracts
- MRI: Typical diagnostic modality

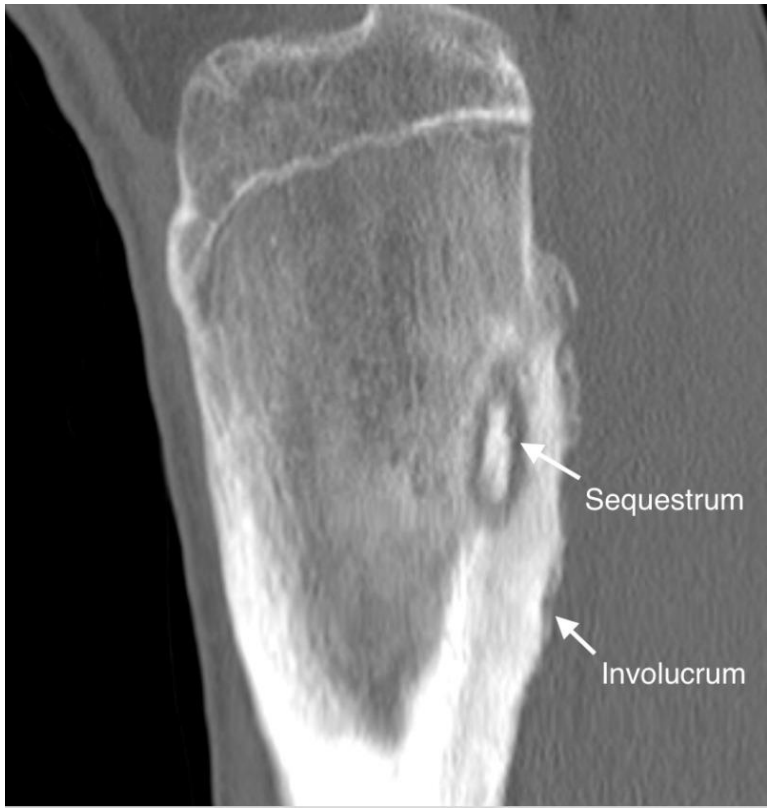
  --> About 96% sensitive, **81% specific**

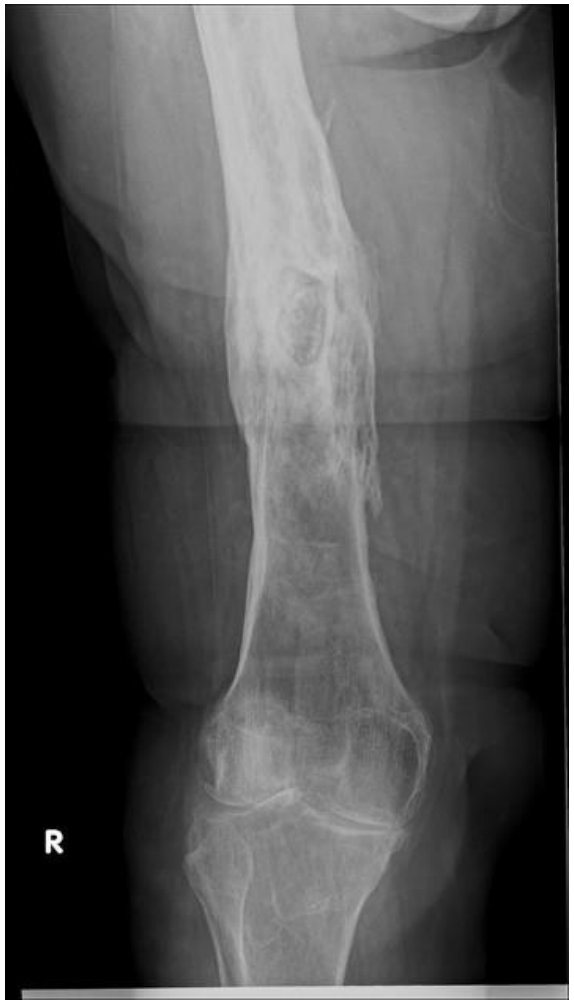
  --> Can see marrow edema which is the earliest sign

  --> Contrast not needed for marrow edema but helpful for seeing abscesses and fistulas

1. *Llewellyn A, Jones-Diette J, Kraft J, Holton C, Harden M, Simmonds M. Imaging tests for the detection of osteomyelitis: a systematic review. Health Technol Assess 2019;23(61):1–128.*

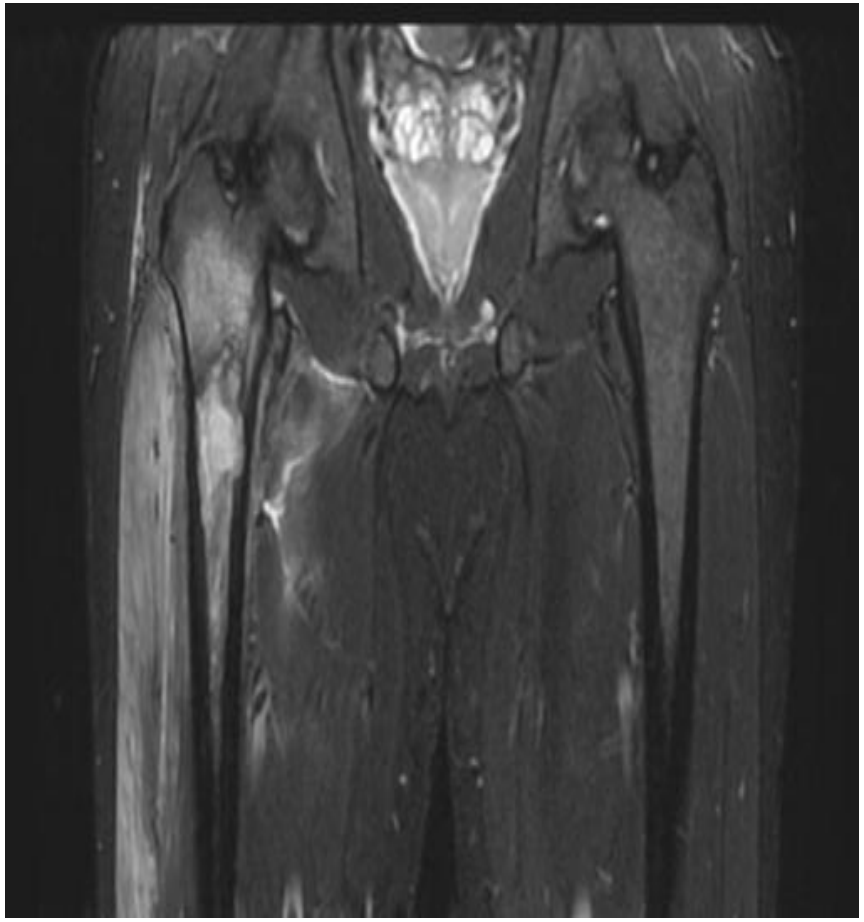
OM: Diagnostic Imaging

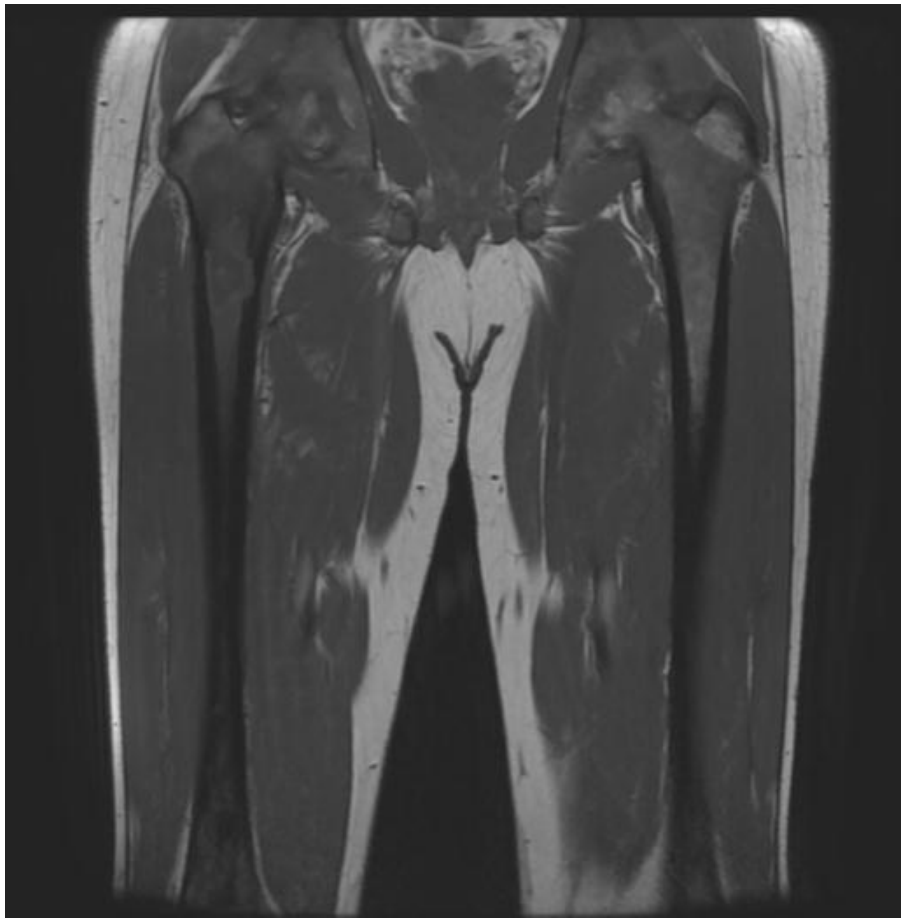




Radiopaedia

OM: Diagnostic Imaging

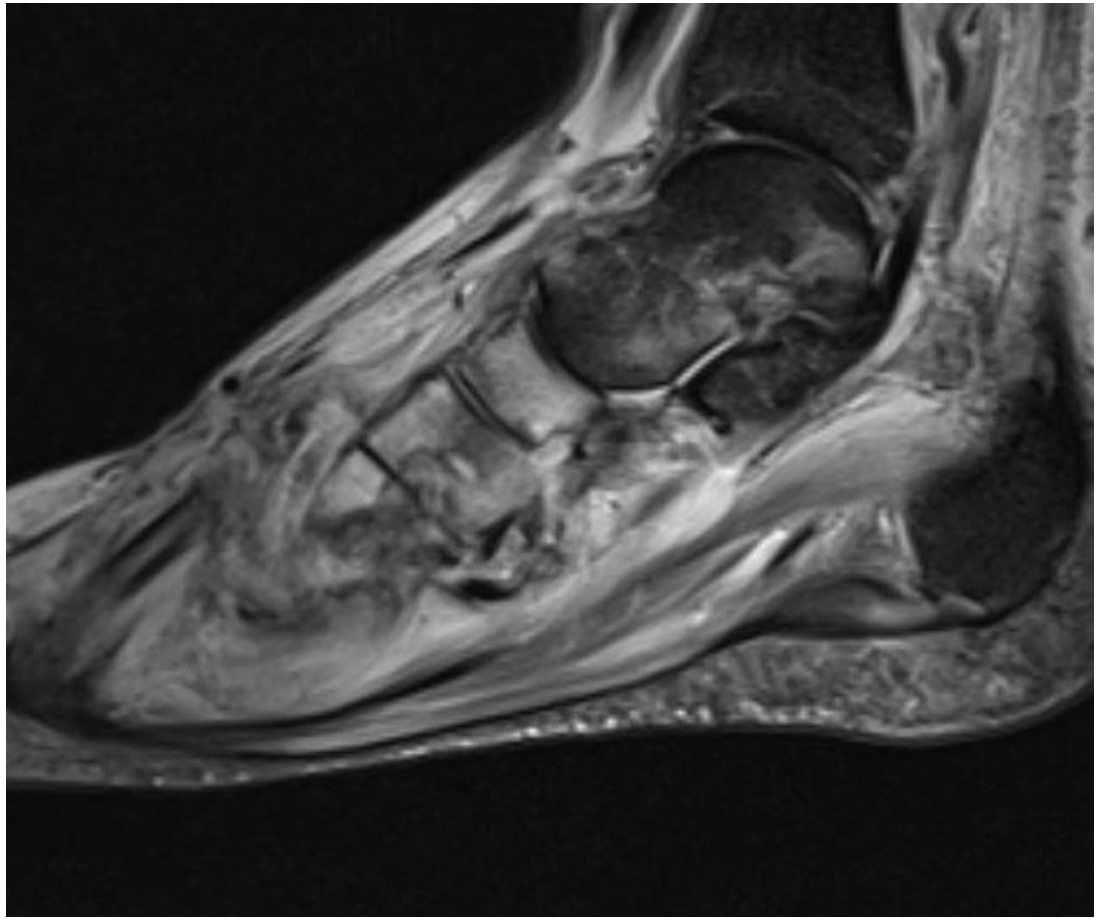




Radiopaedia

OM Mimics on MRI

- MRI is **not** 100% specific!
- Stress fracture or contusion
- **Charcot arthropathy**
- Bone tumors
- Severe OA or other inflammatory arthropathy
- Avascular necrosis



Radiopaedia

OM: Nuclear Imaging

- No clear benefit over MRI
- Possible option if MRI contraindicated
- Includes PET/CT, Scintigraphy
- PET/CT: 83% sensitive, 93% specific
- Scintigraphy (bone scans, tagged WBC, gallium): Two dimensional, relatively low sensitivity and specificity

Llewellyn A, Jones-Diette J, Kraft J, Holton C, Harden M, Simmonds M. Imaging tests for thedetection of osteomyelitis: a systematic review. Health Technol Assess 2019;23(61):1–128.

OM: Surgical Management (debridement)

- Surgical intervention is **usually** necessary for source control or bone coverage-without it, antibiotics are **not curative**
- Primary indications:

  -->Presence of necrotic bone or adjacent soft tissue

  -->Presence of abscess (in the bone or adjacent soft tissue)

  -->Coverage of exposed bone

  -->Essentially **always** required if curing chronic OM is to be attempted

To Be Continued....

- End of part 1
- Questions?

OM: Medical Treatment

- Empiric regimen for most patients: ceftriaxone + vancomycin
- Initial pathogen-directed treatment for MSSA: IV cefazolin 2 g q8h
- Initial pathogen-directed treatment for MRSA: IV vancomycin dosed by AUC (goal AUC of 400 to 600 mg ▪ hour/L)
- IV daptomycin 10 mg/kg daily (renally adjusted) is a reasonable alternative for MRSA
- Typical duration for OM without hardware: 6 weeks
- Typical duration for OM with hardware: 12 weeks? (extrapolated from PJI)*

**Bernard et al., 2021*

OM: Oral Antibiotics

The NEW ENGLAND JOURNAL of MEDICINE

Oral versus Intravenous Antibiotics for Bone and Joint Infection

Authors: Ho-Kwong Li, M.R.C.P., Ines Rombach, D.Phil., Rhea Zambellas, M.Sc., A. Sarah Walker, Ph.D., Martin A. McNally, F.R.C.S.(Orth.), Bridget L. Atkins, F.R.C.P., Benjamin A. Lipsky, M.D., +52 , for the OVIVA Trial Collaborators* Author Info & Affiliations

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OM: OVIVA Trial

- Published 2019
- Multicenter open-label RCT (performed in UK)
- Primary end-point: Definite treatment failure within 1 year after randomization
- 1054 participants
- 61% had hardware
- **92%** had surgical debridement
- ~40% Staph aureus in both groups, ~30% CoNS
- Only **10%** of SA was MRSA

OM: OVIVA Trial

- **15%** treatment failure in IV group, **13%** treatment failure in oral group
- Conclusion: PO therapy for OM is **non-inferior** to IV therapy!

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OM: Oral Antibiotic Regimens

	Participants randomized to IV Antibiotic* (N = 521)	Participants randomized to PO Antibiotic* (N = 523)	Total* (N = 1044)
Glycopeptides[a] (IV)	214 (41.1%)	22 (4.2%)	236 (22.6%)
Penicillins (IV)	38 (7.3%)	11 (2.1%)	49 (4.7%)
Cephalosporins (IV)	173 (33.2%)	8 (1.5%)	181 (17.3%)
Carbapenems (IV)	41 (7.9%)	5 (1.0%)	46 (4.4%)
Other single IV antibiotic	35 (6.7%)	2 (0.4%)	37 (3.5%)
Combination IV antibiotics	35 (6.7%)	6 (1.1%)	41 (3.9%)
Penicillins (PO)	8 (1.5%)	83 (15.9%)	91 (8.7%)
Quinolones[b] (PO)	33 (6.3%)	191 (36.5%)	224 (21.5%)
Tetracyclines[c] (PO)	4 (0.8%)	57 (10.9%)	61 (5.8%)
Macrolides / Lincosamide [d] (PO)	10 (1.9%)	68 (13.0%)	78 (7.5%)
Other single PO antibiotic (PO)	10 (1.9%)	54 (10.3%)	64 (6.1%)
Combination PO antibiotics (PO)	13 (2.5%)	87 (16.6%)	100 (9.6%)

1.

Li H-K, Rombach I, Zambellas R, et al. Oral versus Intravenous Antibiotics for Bone and Joint Infection. New England Journal of Medicine [Internet] 2019 [cited 2026 Feb 23];380(5):425–36. Available from: https://www.nejm.org/doi/full/10.1056/NEJMoa1710926

OM: Principles of oral therapy

- >80% of patients in the PO group in OVIVA had at least 1 week of IV lead-in (no good data for or against)
- Only in DFI has 100% PO therapy been well-studied (but it works!)
- Pick antibiotics with good oral bioavailability (high blood levels):

-->Quinolones

-->Linezolid

-->Metronidazole

-->TMP-SMX

-->Doxycycline

Caveats for Specific Drugs

- Linezolid and metronidazole:

  -->Increasing risk of toxicity after 2 weeks (neuropathy, thrombocytopenia)

- TMP-SMX

  -->Should given at higher dose (2 DS tabs BID)

  -->Needs regular lab monitoring for K and Cr

- Doxycycline

  -->*theoretically* a bad choice due to calcium binding (not proven clinically)[1]

1 Clinical Practice Guideline by the Pediatric Infectious Diseases Society and the Infectious Diseases Society of America: 2021 Guideline on Diagnosis and Management of Acute Hematogenous Osteomyelitis in Pediatrics | Journal of the Pediatric Infectious Diseases Society

Quinolones FTW

- Quinolones are the mainstay of oral OM therapy for susceptible organisms
- Ciprofloxacin was the most commonly-used oral drug in OVIVA
- Levofloxacin is **more** bactericidal for SA (Kang et al., 1994)
- Caveats: vascular aneurysms, tendinitis, C diff, QT prolongation

MRSA

- MRSA is a more challenging but curable with orals
- Unpublished HMC data: clinical failure >3x more likely with MRSA than MSSA OM (but still successful in majority of cases)
- Quinolone resistance common in MRSA (57% at HMC)
- Options:

  --> **TMP-SMX**

  --> Levofloxacin/moxifloxacin (if susceptible)

  --> Linezolid (limited by toxicity)

  --> Doxycycline (if you dare)

The Eternal Mystery of Rifampin

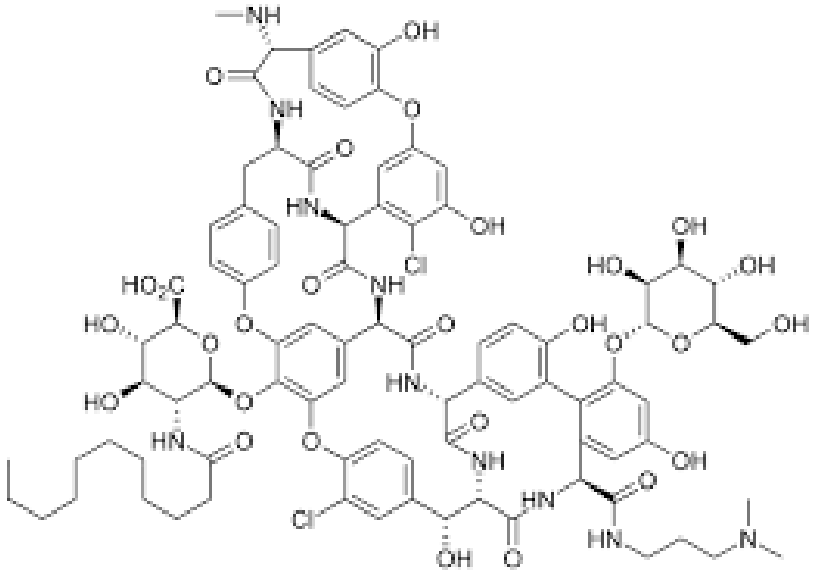
- Rifamycins are uniquely able to kill Staph in biofilms
- Barrier to resistance **very** low, should **never** be given alone
- Always confirm susceptibility if able
- Some evidence of benefit for HW-associated OM (Zimmerli et al. 1998)
- No proven clinical benefit in native-bone OM but commonly done (most patients in OVIVA who got cipro also got rifampin)
- Dose in OVIVA was 300 mg BID (we do 600 mg daily)

The next frontier: oral beta-lactams?

- Cephalexin commonly used for OM in children (but bones are more vascular and they seem to have less GI intolerance)
- Amoxicillin and amox-clav are **well-absorbed**
- Amox-clav has been well studied for DFI OM
- High-dose amoxicillin (1 g TID) reasonable for susceptible organisms (E faecalis, Streptococci)
- High-dose amox-clav (TID) comes with risk of hepatotoxicity!

OM: Dalbavancin

- Dalbavancin has a 14 day half-life
- A 2 dose regimen (days 0, 15) will maintain adequate levels for 6 weeks and a 3 dose regimen (days 0, 15, 42) for 12 weeks (Lin et al., 2026)
- Small studies show some promising results (no true RCT comparison) (PMID: 32273805, 30858217, 30396697)



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OM: Conclusions

- OM often requires surgical management with prolonged antibiotics
- Staph aureus is the most common cause
- Oral antibiotics can (and should) be used for treatment
- Primary regimen is fluoroquinolone +/- rifampin