Osteomyelitis

(Treatment)

Nonvertebral osteomyelitis in adults

Nonhematogenous osteomyelitis

Absence of orthopedic hardware

Residual infected bone present

No residual infected bone

Presence of orthopedic hardware

Retained hardware

No retained hardware

Absence of orthopedic hardware

Operative debridement followed by ***antimicrobial therapy***

- **Surgical debridement:**

  1) Removal of necrotic material

  (drainage & debridement)

  2) Culture of involved tissue and bone

  3)A satisfactory soft tissue envelope

  overlying the site of infection, either via

  direct closure or flap coverage.

ANTIBIOTIC THERAPY

- Whenever possible, initiation of antibiotic therapy should be **delayed until bone cultures** can be obtained. Patients who have received antibiotics recently and do not have an acute need for surgical intervention should **discontinue antibiotics** for at least **two weeks** prior to debridement to **optimize microbiologic diagnosis**.

Empiric therapy

- Should consist of antimicrobial therapy with activity against methicillin-resistant *S. aureus* (**MRSA**) and **gram-negative organisms**.

Reasonable regimens include **vancomycin** in combination with a **third- or fourth-generation cephalosporin**.

- **Avoid** combined use of **vancomycin** with **piperacillin /tazobactam**,given the risk of nephrotoxicity with this combination .

- Antibiotic therapy **should be tailored** to culture and susceptibility data when available.

Definitive therapy

Staphylococcus aureus(MSSA)

- **Nafcillin**: 2 g IV every 4 hours
- **Oxacillin**: 2 g IV every 4 hours
- **Cefazolin**: 2 g IV every 8 hours
- **Flucloxacillin**: 2 g IV every 6 hours
- **Ceftriaxone**: 2 g IV every 24 hours

Staphylococcus aureus (MRSA)

Regimen of choice:

- **Vancomycin** Loading dose : 20 mg/kg

Then 15 to 20 mg/kg every 8 to 12 hours for most patients with normal renal function.

Alternative regimens:

- **Daptomycin**: 6 to 10 mg/kg IV once daily
- **Teicoplanin**: (where available) 12 mg/kg IV every 12 hours for 3 to 5 doses, followed by 12 mg/kg once daily

Adjunctive agents:

- **Rifampin**: 300 to 450 mg orally twice daily
- **Fusidic acid**: (where available) 500 mg orally 3 times daily

Staphylococcus aureus

- Antibiotic agents that warrant further study for treatment of **staphylococcal osteomyelitis** include **ceftaroline**, **telavancin**, and **dalbavancin.**

- It **is not favor** use of **trimethoprim-sulfamethoxazole**, **linezolid**, **tedizolid**, **clindamycin**, **fluoroquinolones**, **quinupristin-dalfopristin**, or **tigecycline** for definitive therapy of osteomyelitis due to ***S. aureus***.

Coagulase negative staphylococci (CONS)

- As the same as ***staphylococcus aureus*** according to methicillin susceptibility or resistance.

Gram-negative organisms

- **Ciprofloxacin**: 750 mg orally twice daily or 400 mg IV every 12 hours; if treating **Pseudomonas**, increase IV dose to 400 mg IV every 8 hours
- **Levofloxacin**: 750 mg orally or IV once daily
- **Ceftriaxone**: 2 g IV every 24 hours
- **Ceftazidime**: 2 g IV every 8 hours
- **Cefepime**: 2 g IV every 8 to 12 hours
- **Ertapenem**: 1 g IV every 24 hours
- **Meropenem**: 1 g IV every 8 hours

Enterococci

Monotherapy regimens

- **Ampicillin**: 12 g IV every 24 hours, either continuously or in 6 equally divided doses
- **Aqueous crystalline penicillin G**: 20 to 24 million units IV every 24 hours, either continuously or in 6 equally divided doses
- **Vancomycin**: 20 mg/kg loading dose, then 15 mg/kg IV every 12 hours, not to exceed 2 g per dose
- **Daptomycin**: 6 to 10 mg/kg IV once daily
- **Teicoplanin**: (where available) 12 mg/kg IV every 12 hours for 3 to 5 doses, followed by 12 mg/kg once daily

Combination therapy regimen

- **Ampicillin**: 12 g IV every 24 hours, given either continuously or in 6 equally divided doses

PLUS

- **Ceftriaxone**: 2 g IV every 12 to 24 hours

Streptococci

"penicillin sensitive"

One of the following:

- **Aqueous crystalline penicillin G:** 20 to 24 million units IV every 24 hours, either continuously or in 6 equally divided doses
- **Ampicillin:** 12 g IV every 24 hours, either continuously or in 6 equally divided doses
- **Ceftriaxone:** 2 g IV every 24 hours
- **Vancomycin:** 20 mg/kg loading dose, then 15 mg/kg/dose IV every 12 hours, not to exceed 2 g per dose, initially

Cutibacterium (formerly *Propionibacterium acnes*)

One of the following:

Aqueous crystalline penicillin G:	20 million units IV every 24 hours, either continuously or in 6 divided doses
Ceftriaxone:	2 g IV every 24 hours

Residual infected bone present

- A **prolonged duration** of **intravenous** or **highly bioavailable oral** antibiotic therapy, guided by antimicrobial susceptibility data

- The **optimal duration** of antibiotic therapy for treatment of osteomyelitis with residual infected bone is **uncertain.**

- Most experts favor continuing antimicrobial therapy at least **until debrided bone has been covered by vascularized soft tissue**, which is usually **at least six weeks** from the last debridement.

No residual infected bone

Short course of antibiotic therapy

- **In the absence of concomitant *soft tissue infection***, antibiotic therapy may be discontinued **as early as two** to **five days** after debridement.

- When **there is evidence of *soft tissue infection*** at the operative site, **10** to **14 days** of pathogen-directed **parenteral or highly bioavailable oral** therapy is reasonable.

Presence of orthopedic hardware

Surgical management strategies:

1) debridement with hardware **retention**
2) debridement with hardware **removal**

- Hardware **retention** may be attempted when the **"stability of the bone and hardware construct would be compromised" (such as in the case of fracture fixation hardware with unhealed fracture)** or when there is a **"clear anatomic separation between the osteomyelitis and hardware"**.

- Hardware should be **removed** if the hardware is **"no longer needed for bone stability"** or if **"adequate debridement of the infected bone cannot be achieved with hardware retention"**.

Retained hardware

- Patient should be treated with a **prolonged** duration of **intravenous antibiotic therapy**.
- The **optimal duration** is **uncertain**; most experts favor **six weeks** of therapy.
- While on parenteral antimicrobial therapy, patients should have **weekly blood work** for safety monitoring.
- Following completion of parenteral therapy, patients should receive **long-term antibiotic suppression** with an **oral** agent, guided by antimicrobial susceptibility data.

Retained hardware

- **Regimens for antibiotic suppression:**

Staphylococci, methicillin susceptible:

Rifampin	300 to 450 mg twice daily
plus one of the following:	
Levofloxacin	500 to 750 mg once daily
Ciprofloxacin	500 to 750 mg twice daily
Fusidic acid (where available)	500 mg three times daily
Clindamycin	300 to 450 mg three times daily

Staphylococci, methicillin resistant:

Rifampin	300 to 450 mg twice daily
plus one of the following:	
Levofloxacin	500 to 750 mg once daily
Ciprofloxacin	500 to 750 mg twice daily
Fusidic acid (where available)	500 mg three times daily
Clindamycin	300 to 450 mg three times daily
Linezolid	600 mg twice daily

Gram-negative organisms:

Ciprofloxacin	500 to 750 mg twice daily
Levofloxacin	500 to 750 mg once daily
Trimethoprim-sulfamethoxazole	1 double-strength tablet twice daily

Penicillin-sensitive streptococci:

Amoxicillin	750 to 1000 mg three times daily
Clindamycin	300 to 450 mg three times daily

Retained hardware

- In general, **oral antimicrobial** suppression **should be continued until fractures are united**. Once fracture healing is demonstrated radiographically, the timeframe for discontinuation of oral antimicrobial suppression should be determined carefully.

- **Factors influencing the duration of therapy:**
  - The **microbiology** of infection,
  - The **duration** of infection prior to debridement,
  - The **tolerability** of the antimicrobial suppression regimen,
  - The **status** of the orthopedic hardware (if present) at the site of infection,
  - **Individual** patient circumstances.

The benefit of continuing suppressive treatment for longer than six months is uncertain.

Retained hardware

Antimicrobial suppression after fracture union :

If:

- **hardware removal could be performed** in the event of infection **relapse** (such as healed long-bone fracture),
- **The infection appears to be well suppressed**,

and

- The **patient is comfortable with the small possibility of further surgery**

we offer **discontinuation** of suppression.

If:

small possibility of surgery is **unacceptable**,

we **continue** suppression indefinitely

No retained hardware

- Patients with no retained hardware should complete a **prolonged duration of intravenous antibiotic therapy**.

- Most experts favor continuing antimicrobial therapy **at least until debrided bone has been covered by vascularized soft tissue**, which is usually **at least six weeks from the last debridement**

Hematogenous osteomyelitis

- **In adults**, hematogenous osteomyelitis most commonly involves the **vertebral bones**.

- **Treatment** of nonvertebral hematogenous osteomyelitis consists of **parenteral antibiotics**; in some circumstances, **surgical debridement** is also warranted.

- In general, patients with infection confined to the **medullary canal of the bone** may be treated with **antibiotics alone**.

Hematogenous osteomyelitis

- **Surgical debridement** is warranted in patients with:
  - * **subperiosteal collection or abscess**,
  - * **necrotic bone**,
  - * **concomitant joint infection**.

- Depending on the scope of the debridement, **bone grafting** or **other orthopedic reconstruction** may be required.

- **A critical component of surgical management** is **adequate soft tissue coverage.**

Hematogenous osteomyelitis

- In all patients, **blood cultures** should be obtained **prior to initiation of antibiotic therapy.** If blood cultures are negative, a **bone biopsy or aspirate of subperiosteal abscess** for culture should be performed.

- **Emprical** and **definitive antibiotic therapy** and **evaluation** of treatment are the same as **nonhematogenos osteomyelitis**

- **The optimal duration of antibiotic therapy** for treatment of hematogenous (nonvertebral) osteomyelitis is **uncertain**. In general, **at least four weeks** of parenteral therapy from the last major debridement (if performed) are warranted.

Monitoring during treatment

- **Laboratory monitoring** is needed to evaluation of :
  1) adverse drug effects
  2) control of infection
- Evaluation during **parenteral antimicrobial** therapy:
  1) weekly CBC and chemistries

  2) serum inflammatory markers [ESR] and [CRP]) at the **beginning** and **end** of parenteral therapy and at the time of **transition to** oral suppressive therapy (**if used**).

- We do not routinely monitor **weekly** serum inflammatory markers during parenteral antimicrobial therapy. However, if there is **clinical suspicion for treatment failure**, we use inflammatory markers (in conjunction with clinical examination and radiographic studies such as magnetic resonance imaging or plain radiograph) to guide further management.

- Evaluation during **oral suppressive antimicrobial** therapy:
  CBC , creatinine, and ALT at **2**, **4**, **8**, and **12** weeks and **then** every **6** to **12** months thereafter

Evaluation at the end of treatment

1) Clinical evaluation:

Examinnation of the site of infection for healing of the wound and soft tissue envelope.

Question regarding systemic symptoms of infection as well as pain (type and severity).

2) Evaluation of serum inflammatory markers (**ESR** and **CRP**):

Are useful to confirm response to antimicrobial therapy as well as to serve as a new baseline for future evaluation.

- **Routine radiographic imaging** not recommended :

  Frequently, residual inflammatory changes may be mistaken for persistent infection.

The ***decision to*** pursue ***radiographic imaging*** should be guided by clinical suspicion for relapsing infection : (worsening symptoms **and/or** rising inflammatory markers).

- **Persistently elevated inflammatory markers two weeks following completion of antimicrobial therapy (without an alternative explanation) should prompt concern for persistent osteomyelitis :**

- Ensure that a **thorough and complete debridement** has been performed.
- The **microbiologic diagnosis** and **susceptibility data** should be reviewed**.**