
In The Name of GOD The
Compassionate the Merciful

osteomyelitis

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Osteomyelitis

is categorized as acute or chronic based on histopathologic findings, rather than duration of the infection.

Acute osteomyelitis is associated with inflammatory bone changes caused by pathogenic bacteria, and symptoms typically present within two weeks after infection.

Necrotic bone is present in chronic osteomyelitis, and symptoms may not occur until six weeks after the onset of infection

Further classification of osteomyelitis is based on the presumed **mechanism of infection**:

- Hematogenous
- Direct inoculation: from contiguous soft tissue infection or a chronic overlying open wound

ETIOLOGY

- ✓***Staphylococcus aureus*** **is the most common cause of acute and chronic hematogenous osteomyelitis in adults and children.**
- ✓**Group A streptococcus, Streptococcus pneumoniae, and Kingella kingae are the next most common pathogens in children.**
- ✓**Group B streptococcal infection occurs primarily in newborns.**
- ✓**In adults, S. aureus is the most common pathogen in bone and prosthetic joint infections.**
- ✓**Fungal and mycobacterial infections have been reported in patients with osteomyelitis, but these are uncommon**

Clinical Features

➢ Acute hematogenous osteomyelitis:

- Bacteremic seeding of bone
- Most often in children
- Systemic symptoms, including fever and irritability, as well as local erythema, swelling, and tenderness over the involved bone.

➢ Chronic osteomyelitis:

- Generally secondary to open fractures, bacteremia, or contiguous soft issue infection.

- **Hematogenous osteomyelitis is much less common in adults than in children.**

- **It typically involves the vertebrae, but can occur in the long bones, pelvis, or clavicle.**
- **Patients with vertebral osteomyelitis often have underlying medical conditions (e.g., diabetes mellitus, cancer, chronic renal disease) or a history of intravenous drug use.**

- **Back pain is the primary presenting symptom.**

Chronic osteomyelitis from **contiguous soft tissue** infection is becoming more common because of the increasing prevalence of **diabetic foot** infections and peripheral vascular disease.

Clinical symptoms of osteomyelitis can be nonspecific and difficult to recognize. They include:

- Chronic pain
- Persistent sinus tract or wound drainage
- Poor wound healing
- Malaise
- Sometimes fever

Diagnosis

Acute osteomyelitis

- **Mostly in children**
- **Rapid onset and localization of symptoms.**
- **Systemic symptoms such as fever, lethargy, and irritability may be present.**

- **The physical examination should focus on identifying common findings, such as erythema, soft tissue swelling or joint effusion, decreased joint range of motion, and bony tenderness.**

Chronic osteomyelitis

Table 1. Diagnostic Criteria for Chronic Osteomyelitis

Imaging studies (e.g., plain radiography, magnetic resonance imaging, bone scintigraphy) demonstrating contiguous soft tissue infection or bony destruction
Clinical signs
Exposed bone
Persistent sinus tract
Tissue necrosis overlying bone
Chronic wound overlying surgical hardware
Chronic wound overlying fracture
Laboratory evaluation
Positive blood cultures
Elevated C-reactive protein level
Elevated erythrocyte sedimentation rate

NOTE: *Items listed in order of decreasing diagnostic ability for osteomyelitis. If osteomyelitis is suspected, a bone biopsy with bacterial culture should be considered for definitive diagnosis.*

ESR and/or CRP level may be helpful to guide response to therapy.

The physical examination should focus on locating a possible nidus of infection, assessing peripheral vascular and sensory function, and exploring any ulcers for the presence of bone.

If a contiguous infection with ulcer is present, such as in diabetic foot infections, the use of a sterile steel probe to detect bone may be helpful in confirming the presence of osteomyelitis

- **Microbial cultures** are essential in the diagnosis and treatment of osteomyelitis.
- The preferred diagnostic criteria for osteomyelitis are a positive culture from bone biopsy and histopathology consistent with necrosis.

- **Superficial wound cultures do not contribute significantly to the diagnosis of osteomyeliti**

IMAGING

Table 2. Diagnostic Imaging Studies for Osteomyelitis

Imaging modality	*Sensitivity (%)*	*Specificity (%)*	*Comments*
Computed tomography	67	50	Generally should not be used in osteomyelitis evaluation
Leukocyte scintigraphy	61 to 84	60 to 68	Combining with technetium-99 bone scintigraphy can increase specificity
Magnetic resonance imaging	78 to 90	60 to 90	Useful to distinguish between soft tissue and bone infection, and to determine extent of infection; less useful in locations of surgical hardware because of image distortion
Plain radiography (anteroposterior, lateral, and oblique views)	14 to 54	68 to 70	Preferred imaging modality; useful to rule out other pathology
Positron emission tomography	96	91	Expensive; limited availability
Technetium-99 bone scintigraphy	82	25	Low specificity, especially if patient has had recent trauma or surgery; useful to differentiate osteomyelitis from cellulitis, and in patients in whom magnetic resonance imaging is contraindicated

MRI with gadolinium is the imaging modality of choice, particularly for detection of early osteomyelitis and associated soft-tissue disease.

Treatment

- **Treatment of osteomyelitis depends on appropriate antibiotic therapy and often requires surgical removal of infected and necrotic tissue.**

- **Choice of antibiotic therapy should be determined by culture and susceptibility results, if possible.**
- **In the absence of such information, broad-spectrum, empiric antibiotics should be administered.**
- **False-negative blood or biopsy cultures are common in patients who have begun antibiotic therapy. If clinically possible, delaying antibiotics is recommended until microbial culture and sensitivity results are available.**

TABLE 106-3 Antimicrobial Therapy of Chronic Osteomyelitis in Adults for Selected Microorganisms

MICROORGANISMS	FIRST CHOICE*	ALTERNATIVE CHOICE*
Staphylococci		
Oxacillin sensitive	Nafcillin sodium or oxacillin sodium, 1.5-2 g IV q4h for 4-6 wk, *or* cefazolin, 1-2 g IV q8h for 4-6 wk	Vancomycin, 15 mg/kg IV q12h for 4-6 wk; some add rifampin, 600 mg PO qd, to nafcillin/oxacillin
Oxacillin resistant (MRSA)	Vancomycin,† 15 mg/kg IV q12h for 4-6 wk *or* Daptomycin 6 mg/kg IV q24h	Linezolid, 600 mg PO/IV q12h for 6 wk, *or* levofloxacin,† 500-750 mg PO/IV daily, plus rifampin, 600-900 mg/day PO for 6 wk if susceptible to both drugs
Penicillin-sensitive streptococci	Aqueous crystalline penicillin G, 20 x 10^6 U/24 hr IV either continuously or in six equally divided daily doses for 4-6 wk, or ceftriaxone, 1-2 g IV *or* IM q24h for 4-6 wk *or* cefazolin, 1-2 g IV q8h for 4-6 wk	Vancomycin, 15 mg/kg IV q12h for 4-6 wk
Enterococci or streptococci with MIC ≥0.5 μg/mL, *or Abiotrophia* or *Granulicatella* spp.	Aqueous crystalline penicillin G, 20 x 10^6 U/24 hr IV either continuously or in six equally divided daily doses for 4-6 wk, *or* ampicillin sodium, 12 g/24 hr IV either continuously or in 6 equally divided daily doses; the addition of gentamicin sulfate, 1 mg/kg IV or IM q8h for 1-2 wk is *optional*	Vancomycin,† 15 mg/kg IV q12h for 4-6 wk; the addition of gentamicin sulfate, 1 mg/kg IV *or* IM q8h for 1-2 wk is *optional*
Enterobacteriaceae	Ceftriaxone, 1-2 g IV q24h for 4-6 wk, *or* ertapenem 1 g IV q24h	Ciprofloxacin,† 500-750 mg PO q12h for 4-6 wk, *or* levofloxacin 500-750 mg PO q24h
Pseudomonas aeruginosa	Cefepime, 2 g IV q12h, meropenem, 1 g IV q8h *or* imipenem, 500 mg IV q6h for 4-6 wk	Ciprofloxacin,† 750 mg PO q12h for 4-6 wk, *or* ceftazidime, 2 g IV q8h

SA GUIDELINES

Clinical Practice Guidelines by the Infectious Diseases Society of America for the Treatment of Methicillin-Resistant *Staphylococcus aureus* Infections in Adults and Children

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MRSA bone infections

Surgical debridement and drainage of associated soft tissue abscesses is the mainstay of therapy and should be performed whenever feasible (A-II).

❖ **Antibiotics available for parenteral administration include:**

- **Vancomycin (B-II)**
- **Daptomycin 6 mg/kg/dose IV once daily (B-II)**

❖ **Some antibiotic options with parenteral and oral routes of administration include the following:**

- **TMP-SMX 4 mg/kg/dose (TMP component) twice daily in combination with rifampin 600 mg once daily (B-II)**
- **Linezolid 600 mg twice daily (B-II)**
- **Clindamycin 600 mg every 8 h (B-III)**

Some experts recommend the addition of rifampin 600 mg daily or 300–450 mg PO twice daily to the antibiotic chosen above (B-III).

MRSA bone infections

The optimal duration of therapy for MRSA osteomyelitis is unknown.

- **A minimum 8-week course is recommended (A-II).**
- **Some experts suggest an additional 1–3 months (and possibly longer for chronic infection or if debridement is not performed) of oral rifampin-based combination therapy with TMP-SMX, doxycycline-minocycline, clindamycin, or a fluoroquinolone, chosen on the basis of susceptibilities (C-III).**

Table 3. (*Continued*)

Manifestation	Treatment	Adult dose	Pediatric dose	Class[a]	Comment
Bone and joint infections					
Osteomyelitis	Vancomycin	15–20 mg/kg/dose IV every 8–12 h	15 mg/kg/dose IV every 6 h	BII/AII	Surgical debridement and drainage of associated soft-tissue abscesses is the mainstay of therapy. (AII). Some experts recommend the addition of rifampin 600 mg QD or 300–450 mg BID to the chosen antibiotic (BIII). For children ≥12 years of age, linezolid 600 mg PO/IV BID should be used. A single-strength and DS tablet of TMP-SMX contains 80 mg and 160 mg of TMP, respectively. For an 80-kg adult, 2 DS tablets achieves a dose of 4 mg/kg.
	Daptomycin	6 mg/kg/day IV QD	6–10 mg/kg/day IV QD	BII/CIII	
	Linezolid	600 mg PO/IV BID	10 mg/kg/dose PO/IV every 8 h, not to exceed 600 mg/dose	BII/CIII	
	Clindamycin	600 mg PO/IV TID	10–13 mg/kg/dose PO/IV every 6–8 h, not to exceed 40 mg/kg/day	BIII/AII	
	TMP-SMX and rifampin	3.5–4.0 mg/kg/dose PO/IV every 8–12 h	ND	BII/ND	
		600 mg PO QD			

TABLE 106-4 Surgical Principles in Osteomyelitis

Adequate drainage of all infected tissue
Extensive débridement of all infected tissue
Removal of all hardware
Management of dead space (flap)
Complete wound closure
Stability of infected fracture

Native vertebral osteomyelitis (NVO)

Native vertebral osteomyelitis (NVO) in adults is often the result of hematogenous seeding of the adjacent disc space from a distant focus, as the disc is avascular.

IDSA GUIDELINE

Infectious Diseases Society of America (IDSA) Clinical Practice Guidelines for the Diagnosis and Treatment of Native Vertebral Osteomyelitis in Adults[a]

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Diagnosis of NVO Be Considered in:

1. New or worsening back or neck pain and fever
2. New or worsening back or neck pain and elevated ESR or CRP
3. New or worsening back or neck pain and bloodstream infection or infective endocarditis
4. Fever and new neurologic symptoms with or without back pain
5. New localized neck or back pain, following a recent episode of Staphylococcus aureus Bloodstream infection

Diagnostic Evaluation

- Obtaining bacterial (aerobic and anaerobic) blood cultures (2 sets) and baseline ESR and CRP
- Spine MRI
- Combination spine gallium/Tc99 bone scan, CT scan or a PET scan in patients with suspected NVO when MRI cannot be obtained.
- Serologic tests for Brucella species in patients with subacute NVO residing in endemic areas for brucellosi
- PPD test or obtaining an interferon-γ release assay in patients with subacute NVO and at risk for Mycobacterium tuberculosis

- An image-guided aspiration biopsy in patients with suspected NVO (based on clinical, laboratory, and imaging studies) when a microbiologic diagnosis for a known associated organism (S. aureus, Staphylococcus lugdunensis Brucella species) has not been established by blood cultures or serologic tests.

- We advise against performing an image-guided aspiration biopsy in patients with suspected subacute NVO (high endemic setting) and strongly positive Brucella Serology.

TREATMENT

- **In patients with neurologic compromise with or without impending sepsis or hemodynamic instability, we recommend immediate surgical intervention and initiation of empiric antimicrobial therapy**

- **In patients with normal and stable neurologic examination and stable hemodynamics, we suggest holding empiric antimicrobial therapy until a microbiologic diagnosis is established**

Optimal Duration of Antimicrobial Therapy

- **Total duration of 6 weeks of parenteral or highly bioavailable oral antimicrobial therapy for most patients with bacterial NVO.**

- **We recommend a total duration of 3 months of antimicrobial therapy for most patients with NVO due to Brucella species**

Table 2. Parenteral Antimicrobial Treatment of Common Microorganisms Causing Native Vertebral Osteomyelitis

Microorganism	First Choice[a]	Alternatives[a]	Comments[b]
Staphylococci, oxacillin susceptible	Nafcillin[c] sodium or oxacillin 1.5–2 g IV q4–6 h or continuous infusion or Cefazolin 1–2 g IV q8 h or Ceftriaxone 2 g IV q24 h	Vancomycin IV 15–20 mg/kg q12 h[d] or daptomycin 6–8 mg/kg IV q24 h or linezolid 600 mg PO/IV q12 h or levofloxacin 500–750 mg PO q24 h and rifampin PO 600 mg daily [122] or clindamycin IV 600–900 mg q8 h	6 wk duration
Staphylococci, oxacillin resistant [123]	Vancomycin IV 15–20 mg/kg q12 h (consider loading dose, monitor serum levels)	Daptomycin 6–8 mg/kg IV q24 h or linezolid 600 mg PO/IV q12 h or levofloxacin PO 500–750 mg PO q24 h and rifampin PO 600 mg daily [122]	6 wk duration

Table 3. Selected Oral Antibacterial Agents With Excellent Oral Bioavailability Commonly Used to Treat Patients With Native Vertebral Osteomyelitis

Oral Agents	Comments
Metronidazole 500 mg PO tid to qid	Can be used in the intital course of NVO due to *Bacteroides* species and other susceptible anaerobes.
Moxifloxacin 400 mg PO once daily	Is not recommended for use in patients with staphylococcal NVO, but may be used in patients with NVO due to Enterobacteriaceae and other susceptible aerobic gram-negative organisms.
Linezolid 600 mg PO bid	Can be used in the intital course of NVO due to oxacillin-resistant staphylocci when first-line agents cannot be used.
Levofloxacin 500–750 mg PO once daily	Is not recommended for use in patients with staphylococcal NVO as monotherapy but may be used in patients with NVO due to Enterobacteriaceae and other susceptible aerobic gram-negative organisms.
Ciprofloxacin 500–750 mg PO bid	Is not recommended for use in patients with staphylococcal NVO but may be used in patients with NVO due to Enterobacteriaceae and other susceptible aerobic gram-negative organisms including *Pseudomonas aeruginosa* and *Salmonella* species.
TMX-SMX 1–2 double strength tabs PO bid	Is not recommended for use in patients with staphylococcal NVO but may be recommended as a second-line agent in patients with NVO due to Enterobacteriaceae and other susceptible aerobic gram-negative organisms. May need to monitor sulfamethoxazole levels.
Clindamycin 300–450 mg PO qid	Recommended as second-line choice for sensitive staphylococcal NVO.
Doxycycline and rifampin	Mostly used in patients with brucellar NVO.

IDSA GUIDELINES

Infectious Diseases Society of America Clinical Practice Guideline for the Diagnosis and Treatment of Diabetic Foot Infections[a]

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For mild to moderate infections in patients who have not recently received antibiotic treatment, we suggest that therapy just targeting aerobic GPC is sufficient.

For most severe infections, we recommend starting broad-spectrum empiric antibiotic therapy, pending culture results and antibiotic susceptibility data.

Consider providing empiric therapy directed against MRSA in a patient with a prior history of MRSA infection; when the local prevalence of MRSA colonization or infection is high; or if the infection is clinically severe.

We recommend that definitive therapy be based on the results of an appropriately obtained culture and sensitivity testing of a wound specimen as well as the patient's clinical response to the empiric regimen.

We prefer parenteral therapy for all severe, and some moderate, DFIs, at least initially, with a switch to oral agents when the patient is systemically well and culture results are available.

Clinicians can probably use highly bioavailable oral antibiotics alone in most mild, and in many moderate, infections and topical therapy for selected mild superficial infections

We suggest an initial antibiotic course for a soft tissue infection of about 1–2 weeks for mild infections and 2–3 weeks for moderate to severe infection

diabetic foot osteomyelitis

- Doing a PTB test for any DFI with an open wound.
- Plain radiographs of the foot: They have relatively low sensitivity and specificity.
- For a diagnostic imaging test for DFO: MRI but is not always necessary for diagnosing or managing DFO.

- We suggest that the most definitive way to diagnose DFO is by the combined findings on bone culture and histology.
- When bone is debrided to treat osteomyelitis, we suggest sending a sample for culture and histology
- For patients not undergoing bone debridement, we suggest that clinicians consider obtaining a diagnostic bone biopsy when faced with specific circumstances, eg, diagnostic

- **When a radical resection leaves no remaining infected tissues:**

Prescribing antibiotic therapy for only a short duration (2–5 days).

- **When there is persistent infected or necrotic bone:**

Prolonged (≥4 weeks) antibiotic treatment.

Table 10. Approach to Treating a Patient With Diabetic Foot Osteomyelitis

When to consider a trial of nonsurgical treatment
• No persisting sepsis (after 48–72 h if on treatment)
• Patient can receive and tolerate appropriate antibiotic therapy
• Degree of bony destruction has not caused irretrievable compromise to mechanics of foot (bearing in mind potential for bony reconstitution)
• Patient prefers to avoid surgery
• Patient comorbidities confer high risk to surgery
• No contraindications to prolonged antibiotic therapy (eg, high risk for *C. difficile* infection)
• Surgery not otherwise required to deal with adjacent soft tissue infection or necrosis
When to consider bone resection
• Persistent sepsis syndrome with no other explanation
• Inability to deliver or patient to tolerate appropriate antibiotic therapy
• Progressive bony deterioration despite appropriate therapy
• Degree of bony destruction irretrievably compromises mechanics of foot
• Patient prefers to avoid prolonged antibiotics or to hasten wound healing
• To achieve a manageable soft tissue wound or primary closure
• Prolonged antibiotic therapy is relatively contraindicated or is not likely to be effective (eg, presence of renal failure)

Table 6. Antibiotic Selection Overview: Questions a Clinician Should Consider

Is there clinical evidence of infection?
Do not treat clinically uninfected wounds with antibiotics
For clinically infected wounds consider the questions below:
- Is there high risk of MRSA?
Include anti-MRSA therapy in empiric regimen if the risk is high (see Table 7) or the infection is severe
- Has patient received antibiotics in the past month?
If so, include agents active against gram-negative bacilli in regimen If not, agents targeted against just aerobic gram-positive cocci may be sufficient
- Are there risk factors for *Pseudomonas* infection?[a]
If so, consider empiric antipseudomonal agent If not, empiric antipseudomonal treatment is rarely needed
- What is the infection severity status?
See Table 9 for suggested regimens for mild versus moderate/severe infections

Abbreviation: MRSA, methicillin-resistant *Staphylococcus aureus*.

[a] Such as high local prevalence of *Pseudomonas* infection, warm climate, frequent exposure of the foot to water.

MRSA	*Linezolid*[b]	Expensive; increased risk of toxicities when used >2 wk
	Daptomycin[b]	Once-daily dosing. Requires serial monitoring of CPK
	Vancomycin[b]	Vancomycin MICs for MRSA are gradually increasing
Pseudomonas aeruginosa	***Piperacillin-tazobactam***[b]	TID/QID dosing. Useful for broad-spectrum coverage. *P. aeruginosa*

Based on the available data, it appears that linezolid may be effective for the treatment of selected cases of osteomyelitis, particularly those caused by multi-resistant Gram-positive pathogens.

Septic Arthritis

- **It occurs most commonly during the first 2 yr of life and adolescence.**
- **Half of all cases occur by 2 yr and three fourths occur by 5 yr .**
- **Joints of the lower extremity constitute three fourth of all cases.**

etiology

S.aureus is the most common agent.

- **H.influ type b is the most common factor in 3 month to -4 yr .**
- **Streptococci , pneumococci, meningococci that may occure in the absence of sepsis or meningitis.**
- **Gonococcal arthritis most common cause of polyartheritis and monoarticular artheritis in adolecent.**

Risk Factors:

TABLE 105-1 Predisposing Factors in Bacterial Arthritis
Major Factors
Rheumatoid arthritis
Advanced age
Diabetes mellitus
Chronic renal failure
Previous joint surgery
Penetrating joint injury
Recreational intravenous drug use
Endocarditis
Immunosuppression Organ and bone marrow transplant Immunosuppressant therapy including systemic corticosteroids, DMARDs, and anti-TNF agents
Minor Factors
Joint disease Crystal induced arthritis (gout and pseudogout) Osteoarthritis Charcot's arthropathy
Chronic systemic disease Collagen vascular disease Malignancy Chronic liver disease Sickle cell disease Alcoholism
Hypogammaglobulinemia
Intra-articular injection (e.g., glucocorticoids)
Skin disease with or without infection
Low socioeconomic status

Clinical manifestation

Erythema , warmth , swelling, and tenderness with a palpable effusion and decreased range of movement . Toddlers demonstrate a limp .

Acute septic arthritis most often involves a single joint .

Multiple joints in 10% .

1. **The onset may be sudden with fever and chills**
2. **Insidious with symptoms noted only when the joint is moved .**

Clinical manifestation(con)

Often difficult to assess septic arthritis of the hip and may cause referred pain the knee .

The hip for minimize pain from pressure ,The limb may be positioned in external rotation and flexion .

The knee and elbow joints usually are in flexion .

diagnosis

- **Leukocytosis , elevated ESR or CRP are common .**
- **Arthrocentesis is the test of choice for rapid diagnosis .**
- **Blood or joint cultures are positive in 70%up to 85% in cases**
- **Ultra Sonography is helpful in detecting joint effusion and may guide localization for aspiration .**

treatment

Therapy is based on :

1. **Likely organism**
2. **Gram stain of joint fluid**
3. **Host immunologic status**
4. **Drainage or debridement of the joint space should always be performed.**

Parenteral antimicrobial agents.

TABLE 105-5 Recommended Empirical Therapy for Adult Native Joint Bacterial Arthritis

GRAM STAIN	PREFERRED ANTIBIOTIC[a]	ALTERNATIVE ANTIBIOTIC
Gram-positive cocci	Vancomycin, 15-20 mg/kg (ABW) daily every 8-12 hr[b]	Daptomycin, 6-8 mg/kg daily[c] or linezolid, 600 mg IV or PO every 12 hr[c]
Gram-negative cocci[d]	Ceftriaxone, 1 g every 24 hr	Cefotaxime, 1 g every 8 hr[e]
Gram-negative rods[f]	Ceftazidime, 2 g every 8 hr *or* Cefepime, 2 g every 8 hr *or* Piperacillin-tazobactam, 4.5 g every 6 hr	Aztreonam, 2 g every 8 hr *or* Fluoroquinolone[g] *or* Carbapenem[h,i]
Gram-stain negative[f]	Vancomycin *plus* Ceftazidime *or* Cefepime	Daptomycin[c] *or* linezolid[c] *plus* Piperacillin-tazobactam *or* Aztreonam *or* Fluoroquinolone[g] *or* Carbapenem[h,i]

management of MRSA bone and joint infections

		600 mg PO QD			
Septic arthritis	Vancomycin	15–20 mg/kg/dose IV every 8–12 h	15 mg/kg/dose IV every 6 h	BII/AII	Drainage or debridement of the joint space should always be performed (AII).
	Daptomycin	6 mg/kg/day IV QD	6–10 mg/kg/dose IV QD	BII/CIII	
	Linezolid	600 mg PO/IV BID	10 mg/kg/dose PO/IV every 8 h, not to exceed 600 mg/dose	BII/CIII	
	Clindamycin	600 mg PO/IV TID	10–13 mg/kg/dose PO/IV every 6–8 h, not to exceed 40 mg/kg/day	BIII/AII	
	TMP-SMX	3.5–4.0 mg/kg/dose PO/IV every 8–12 h	ND	BIII/ND	

- **For MRSA joint infections, vancomycin should be continued and therapeutic serum concentration monitoring performed to achieve a trough of 15 to 20 mg/L.**
- **Linezolid and daptomycin are an alternative for patients with MRSA native joint infection. In clinical practice, most clinicians have reserved their use for patients with cultures yielding vancomycin-intermediate *S. aureus*, vancomycin-resistant enterococcus, or who are allergic to, intolerant of, or not clinically responding after 3 to 5 days of vancomycin.**

➢ **A 3–4-week course of therapy is suggested.**

Linezolid(oxatent)

- **The mainstay of treatment for serious MRSA infections has until recently been the glycopeptides vancomycin and teicoplanin.**
- **However, concern about the gradual development of resistance and concerns about efficacy have turned attention to the development of new agents active against Gram-positive bacteria. Those that have been licensed for treating cSSTI are linezolid, daptomycin and tigecycline.**

On the basis of the evidence suggesting that *S. aureus* exposure to trough serum concentrations of <10 mg/L can produce strains with vancomycin-intermediately susceptible *S. aureus* (VISA)-like characteristics.

it is recommended that trough serum vancomycin concentrations always be maintained at >10 mg/L to avoid the development of resistance.

- To improve penetration, to increase the probability of optimal target serum concentrations, and to improve clinical outcomes of complicated infections, such as bacteremia, endocarditis, osteomyelitis, meningitis, and hospital-acquired pneumonia caused by *S. aureus*, trough serum vancomycin concentrations of 15–20 mg/L are recommended.
- To achieve rapid attainment of this target concentration for seriously ill patients, a loading dose of 25–30 mg/kg (based on actual body weight) can be considered.

The only new oral agent is linezolid.

There is, however, evidence to show that agents such as co-trimoxazole and tetracycline, which are cheap and reasonably well tolerated, have good efficacy against MRSA and the rate of therapeutic failure is low.

Clindamycin may also be clinically effective but the rates of resistance may be high and inducible resistance needs to be excluded with the 'D' test.

- **Linezolid is the first agent in a new class of synthetic antibiotics, the oxazolidinones.**

- **Bacteriostatic against enterococci and staphylococci, but bactericidal against most strains of streptococci.**

- ✓ **added advantages of early intravenous-to-oral switch with the oral preparation having 100% bioavailability and excellent tissue penetration.**
- ✓ **Linezolid use is also associated with significant reduction in the requirement for intravenous treatment and with the length of hospital stay.**

Efficacious in the treatment of cSSTIs (including diabetic foot infections) caused by Gram-positive organisms (including MRSA), with a well-defined safety profile and straightforward dosing.

It is also approved for:

- **Nosocomial pneumonia**
- **Community-acquired pneumonia**
- **Uncomplicated skin and skin structure infections.**

- The common adverse reactions indicated for vancomycin are nephrotoxicity and ototoxicity and Erythroderma (red man syndrome)

- When used for short periods, linezolid is a relatively safe drug.
- Long-term use of linezolid has been associated with bone marrow suppression, which is characterised particularly by thrombocytopenia.
- Thrombocytopenia appears to be the only adverse effect that occurs significantly more frequently with linezolid than with glycopeptides or beta-lactams

Linezolid has an oral and parenteral formulation, which are equivalent.

The oral formulation has the potential to offer economic benefits as compared with other therapies

FDA-approved indications for linezolid include:

- **Infections with vancomycin resistant *Enterococcus faecium*, including those with associated bacteremia**
- **Nosocomial pneumonia caused by *Staphylococcus aureus* (methicillin-susceptible and methicillin-resistant strains) and *Streptococcus pneumoniae***
- **Uncomplicated skin and skin structure infections caused by *S. aureus* (methicillin-susceptible strains only) and *Streptococcus pyogenes***
- **Complicated skin and skin structure infections, including diabetic foot infections (without osteomyelitis) caused by *S. aureus* (methicillin-susceptible and methicillin-resistant strains), *S. pyogenes,* and *Streptococcus agalactiae***
- **Community-acquired pneumonia caused by *S. aureus* (methicillin-susceptible strain) and *S. pneumoniae* (including cases with concurrent bacteremia)**

MRSA is rapidly replacing MSSA

Hematological Toxic Effects of Linezolid in Patients with Chorionic Osteomyelitis

Patients with chronic osteomyelitis were randomly divided into two groups (n= 40/each): the **intervention group** received vitamin B_6 tablets at a dose of 40 mg twice daily from the beginning of treatment with linezolid (600 mg intravenously) and the **control group** received placebo and linezolid (600 mg intravenously). Blood variables including hemoglobin (Hb), white blood cells (WBC) and platelets (PLT) will be measured at the beginning of treatment and in the first, second and third weeks (days 7, 14 and 21) after the intervention

Conclusion:

In the present study, although there was no significant difference in the hematological parameters of osteomyelitis patients (treated with linezolid) in the two groups receiving vitamin B_6 and placebo, but the trend of changes in people receiving vitamin B_6 showed better conditions.

What is certain is that in order to make a definite statement about the effect of vitamin B_6 on the hematological variables of patients, it is necessary to conduct a study with a larger sample size as well as more detailed studies.