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Medical Management of Osteomyelitis: 2024 Update

It's important to use the right antibiotic to achieve maximum efficacy.

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Objectives

1) Define osteomyelitis and briefly describe clinical presentation and diagnostics

2) Identify causative microbes based on osteomyelitis etiology

3) Interpret literature evaluating medical management of osteomyelitis, with a focus on oral antimicrobial therapy

4) Analyze factors affecting therapy choice and treatment duration

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Definitions and Epidemiology

Osteomyelitis (OM) is defined as an infection of the cancellous or cortical bone caused by any of three general etiologies—hematogenous seeding (blood borne), spread of contiguous infection, or associated with vascular insufficiency [Glaudemans 2019, Bevilacqua 2007]. Hematogenous seeding of the bone is often seen in pediatric and geriatric patients [Lew 2004]. Contiguous spread includes infections secondary to an adjacent soft tissue (e.g. cellulitis, ulceration) or joint infection, or an external source, including trauma (direct extension by penetration of bone with sharp object), fracture, or surgery [Bevilacqua 2007, Glaudemans 2019, Lew 2004]. Pyogenic OM rates are an estimated 20 cases per 100,000 person-years. Rates are increasing in older patients, those with prosthetic joints, and diabetics [Spellberg 2022]. Patients with uncontrolled diabetes often present with lower extremity ulcers secondary to peripheral neuropathy and vascular insufficiency [Lew 2004]. Ulcerations and persistent hyperglycemia allow bacteria to colonize and infect the bone [Glaudemans 2019, Bevilacqua 2007]. Patients with poorly managed diabetic foot infection (DFI) can experience progression to osteomyelitis [Bevilacqua 2007, Lew 2004].

Hematogenous seeding is generally considered the most common etiology of osteomyelitis in the pediatric patient.

Signs, symptoms, and presentation

OM can be characterized as acute or chronic [Lew 2004]. The immune response to infection leads to inflammation, bone destruction, and clini-

cal signs associated with OM [Bevilacqua 2007, Lew 2004]. Signs and symptoms of infection include fever, malaise, and pain [Bevilacqua 2007]. Chronic infection and inflammation can lead to bone necrosis and sequestrum or sinus tract formation [Lew 2004].

Diagnosis

Diagnostics of osteomyelitis begins with clinical examination and plain radiography. Assessment of vasculopathy and neuropathy can also be involved in the diagnosis. Magnetic resonance imaging (MRI), three-phase bone scan, white blood cell scan, and probe-to-bone test are additional components to elucidate the diagnosis. Although MRI can reveal edema and inflammation, positive bone histology and deep culture are required for definitive diagnosis and etiology identification [Bevilacqua 2007]. Single photon emission computed tomography (SPECT) scans, when paired with fluorodeoxyglucose, are also specific and accurate in diagnosing osteomyelitis. Blood cultures are recommended in patients with suspicion of or risk factors for hematogenous spread or systemic infection. Molecular diagnostic modalities are available in some institutions, and emerging data suggest possible utility in rapid identification of infecting organisms. Positive bone biopsy specimens or blood cultures and sensitivities are vital in selecting targeted antimicrobial therapy.

Monitoring laboratory parameter trends may aid in OM diagnosis and management. A study performed at our institution delineated C-reactive protein (CRP) greater than 3.2 and erythrocyte sedimentation rate (ESR) greater than 76 to be attributable to OM. Procalcitonin (PCT) is a novel hematologic marker used to aid in osteomyelitis diagnosis. PCT is a precursor peptide to calcitonin secreted by the thyroid gland. Levels are often elevated during an acute infective process and can predict soft tissue infection. Currently, data on routine use of serial biomarkers alone in OM management are mixed [Spellberg 2022].

Microbiology

The two most common pathogenic organisms in OM are Staphylococcus aureus followed by Streptococcus spp. S. aureus is hardy and particularly difficult to treat due to its predilection for intracellular persistence and ability to form biofilm and surface adherence [Lew 2004]. Post-traumatic and post-surgical infections may be polymicrobial or due to nosocomial Gram-positive or Gram-negative bacteria [Lew 2004]. Vertebral OM may be caused by either Gram-positive or Gram-negative species, or other geographic and exposure history-specific pathogens such as fungi, Brucella spp., or Mycobacteria. [Berbari 2015, Lew 2004]. Various Gram-positive, Gram-negative, or anaerobic organisms may be pathogenic in OM secondary to DFI [Lipsky 2012].

Increasing healthcare exposure and antimicrobial overuse has led to the propagation of antibiotic resistance in the healthcare and community settings. Methicillin-resistance among S. aureus isolates (MRSA) has risen dramatically. Community-acquired MRSA (CA-MRSA) is considered more virulent than healthcare-acquired species (HA-MRSA). Nevertheless, it is generally more sensitive to common antimicrobials, including doxycycline, clindamycin, and trimethoprim-sulfamethoxazole (TMP-SMX). Use of empiric anti-MRSA agents depends on local antibiogram data, risk factors, colonization status, and previous cultures [Spellberg 2022].

Coagulase-negative Staphylococci (CoNS), including S. epidermidis, β-hemolytic Streptococci, Enterococci, and Cutibacterium (Propionibacterium) acnes are also potential causative pathogens. S. epidermidis is increasingly resistant to methicillin (MRSE) and other common empiric antimicrobials, including fluoroquinolones and TMP-SMX [Lew 2004]. Penicillins and narrow-spectrum cephalosporins are first-line against Streptococci with linezolid and clindamycin considered alternatives. Oral treatment options against Enterococci, including vancomycin-resistant strains, include linezolid, tedizolid, and tetracyclines, though data is limited [Fraimow 2009].

Multi-drug resistant Gram-negative or polymicrobial infections may be encountered in susceptible patients, such as those with recent healthcare exposure, diabetes, trauma, or surgery. Limited oral options exist for treatment of Gram-negative infection and rising resistance rates to first-line agents increase relapse risk [Fraimow 2009]. Fluoroquinolones and TMP-SMX are mainstays in therapy against Enterobacterales. Ciprofloxacin is considered more active against Gram-negatives, including P. aeruginosa, compared to levofloxacin and moxifloxacin, which have greater efficacy against S. aureus [Fraimow 2009, Kim 2014]. Guidelines suggest avoidance of anti-pseudomonal agents unless patients are from tropical climates, have recent antimicrobial exposure or surgery, gangrene, or previous positive cultures [Spellberg 2022, Schaper 2023]. Clindamycin, metronidazole, beta-lactam/beta-lactamase inhibitor combinations, and moxifloxacin are effective against many anaerobes.

Bone histology and culture in addition to clinical judgment, are needed for a definitive diagnosis of osteomyelitis.

Treatment should be based on likely or proven causative pathogens, institutional antibiograms, severity of illness, treatment pathways, published clinical data, risk of adverse drug events, drug interactions, and cost [Schaper 2023]. In complex patients, co-management with infectious diseases specialists may be considered.

Treatment Options—General

Management of OM in adults often includes surgical intervention and antimicrobial therapy. Antibiotic beads and hyperbaric oxygen therapy (HBOT) can supplement therapy. Debridement and drainage of abscesses

should be performed to ensure source control and pharmacotherapy success. OM was traditionally thought to require long-term intravenous antimicrobials followed by highly bioavailable oral suppressive therapy upon symptomatic improvement and availability of culture and sensitivity reports [Lipsky 2012, Khan 2012]. An increasing body of literature questions the lengthy duration of intravenous drug administration and supports even earlier transition to active, highly bioavailable oral therapy [Li 2019, Spellberg 2022]. The landmark OVIVA study assessed 1-year treatment failure rates in 1054 patients with bone and joint infections treated with IV versus oral antimicrobials within 7 days of surgery or start of therapy. The authors demonstrated non-inferior rates of treatment failure, and patients in the oral treatment arm had reduced hospital length of stay compared to IV treatment (14 vs 11 days; $p < 0.001$) [Li 2019].

Treatment with oral medication increases patient convenience, decreases economic and societal burden, and prevents potential complications of long-term vascular access. Catheter occlusion and infection occur in up to 9% of patients [Li 2019, Khan 2012]. Some guidelines propose oral antimicrobial therapy in clinically stable patients after adequate source control with no psychosocial reasons affecting procurement and compliance [Spellberg 2022].

Half-life does not greatly impact choice of oral antimicrobials in treatment of osteomyelitis

Treatment Options—Oral

Drug-specific factors affecting oral antimicrobial choice include plasma protein binding, bioavailability, volume of distribution, lipophilicity, molecular weight, charge, and bone penetration. As Fraimow and colleagues highlight, interpretation of standard minimum inhibitory concentration (MIC) results are based on achievable serum concentrations and may not be reliable depending on active, free drug concentrations in the bone [Fraimow 2009]. A review by Thabit, et al. discusses cortical and cancellous bone concentrations compared to MIC breakpoints of commonly encountered pathogens in OM [Thabit 2019]. Drug distribution to the bone often may be unpredictable. Infected and inflamed bone may lead to hyperemia and increased drug presence. However, avascular and necrotic bone, presence of foreign material, and biofilm prevent adequate penetration to the site of infection due to lack of blood flow and distribution [Lew 2004, Kim 2014]. As such, decisions should be made on available clinical evidence, and consultation with infectious diseases physicians or pharmacists may be considered.

Highly bioavailable oral antimicrobials should be utilized in management of OM [Lipsky 2012]. The dose and frequency should be adapted to maximize pharmacokinetic and pharmacodynamic parameters of each agent. Potential adverse drug events (ADEs), including C. difficile infection, also affect treatment choice, especially at the high doses needed to effectively treat OM [Khan 2012, Fraimow 2009]. Lastly, it is imperative to determine whether monotherapy or combination therapy should be used. Especially in the cases of foreign-material associated bone and joint infection due to MRSA, monotherapy was associated with treatment failure [Kim 2014, Lew 2004].

TMP-SMX

TMP-SMX is a combination bactericidal antimicrobial that synergistically and sequentially inhibits bacterial folic acid biosynthesis [Khan 2012]. Spectrum of activity includes MSSA, CA-MRSA, and certain Gram-negative pathogens, including E. coli, Klebsiella spp., Enterobacter spp., and Proteus mirabilis [Fraimow 2009]. Treatment success rates in studies using TMP-SMX with or without rifampin approach 90% [Euba 2009, Nguyen 2009, Spellberg 2012]. The pharmacodynamic parameter associated with efficacy is time above MIC; however, achieving an adequate Cmax above MIC is vital. Dosing for management of MRSA OM ranges from 4–7 mg TMP/kg/dose every 12 hours orally. Higher doses of up to 10 mg/kg TMP q12h (approximately 2 TMP-SMX double-strength tablets (160 mg TMP/800 mg SMX) twice daily) may increase bone penetration and monotherapy treatment success [Kim 2014].

These doses, however, are likely to predispose patients to ADRs, including hyperkalemia, hemolysis in patients with G6PD deficiency, pancytopenia, nephrotoxicity, and gastrointestinal distress. Severe dermatologic reactions, including Stevens-Johnson syndrome may also occur with this agent. Plasma protein binding is estimated at 44% for TMP and 70% for sulfamethoxazole. Oral TMP-SMX is considered highly bioavailable—IV to oral dose conversion is 1:1 [Klepser 1996]. TMP-SMX distributes extensively into body tissues, making it an appealing choice in treatment of OM. Bone penetration is 50% and 15% of serum concentrations for TMP and SMX, respectively [Spellberg 2012].

Fluoroquinolones

Fluoroquinolones are bactericidal agents that inhibit bacterial topoisomerase IV and DNA gyrase, leading to disruption of DNA processing. Commonly employed agents in the class include ciprofloxacin, levofloxacin, and moxifloxacin. Spectrum of activity includes MSSA, Streptococci, E. coli, K. pneumoniae, S. marcescens, Enterobacter spp., and P. aeruginosa. The widespread use of fluoroquinolones in infectious diseases practice has led to promulgation of resistance to these agents. Monotherapy may be considered against susceptible Gram-positive and Gram-negative isolates. Co-administration with rifampin is recommended to curb resistance development and enhance bactericidal activity against Gram-positive pathogens. High doses of each oral agent are recommended for management of OM, such as ciprofloxacin 500 mg–750 mg every 12 hours, levofloxacin 750 mg once daily, and moxifloxacin 400 mg once daily. Clinicians should

monitor for musculoskeletal (tendonitis, muscle weakness), central nervous system (hallucinations, agitation), and cardiac (QT-prolongation) toxicities.

Potentially significant drug interactions exist with cations and antiarrhythmic drugs [Khan 2012]. Ciprofloxacin and levofloxacin protein binding range from 20 to 40% in. The pharmacodynamic parameters associated with efficacy are Cmax and AUC to MIC ratio. IV to oral dose conversion is estimated at 1:1 for levofloxacin and moxifloxacin and 1:1.25 for ciprofloxacin. Rapid absorption from the GI tract and high volumes of distribution allow appreciable drug concentration in deep tissues, including bone [Khan 2012]. Mean bone to serum ratios range from 27–120% for oral ciprofloxacin and 43–105% for oral moxifloxacin, generally exceeding the Staphylococci MIC90 [Spellberg 2012, Kim 2014, Landersdorfer 2009].

These agents are especially enticing for use against S. aureus due to their ability to penetrate osteoblasts where this pathogen often persists [Landersdorfer 2009]. Fluoroquinolone treatment success rates in OM trials have ranged from 50–77% [Greenberg 2000, Gentry 1990, Khan 2012, Zimmerli 1998, Spellberg 2012]. The US Food and Drug Administration (FDA) approved delafloxacin in 2017 for treatment of acute bacterial skin and skin structure infections (ABSSSI). This agent demonstrates in vitro activity against MRSA, in addition to the previously noted pathogens. Its role in OM management remains to be elucidated as data is limited to case reports [Vidwans 2023].

Clindamycin

Clindamycin is a bacteriostatic lincosamide that acts on the 50S ribosomal subunit inhibiting bacterial protein synthesis. Spectrum of activity includes CA-MRSA, Streptococcus spp., and anaerobes, including Peptostreptococcus spp. and Prevotella spp. Clindamycin has shown efficacy in treatment of pediatric and adult OM. Oral doses in treatment of OM range from 300–450 mg every 6 hours to 600–900 mg every 8 hours, with higher doses preferred, if tolerated. Adverse reactions associated with clindamycin include gastrointestinal distress, elevated liver function values, and dermatologic reactions. Clindamycin demonstrates greater than 90% plasma protein binding and a bioavailability of 90%. The pharmacodynamic parameter associated with efficacy is AUC to MIC. Of note, S. aureus may display inducible clindamycin-resistance that should be tested for using the erythromycin D-test [Fraimow 2009]. Traditionally, clindamycin bone penetration ranges were estimated 40 to 70% of serum concentrations, though recent literature suggest ratios closer to 21–45% [Spellberg 2012, Landersdorfer 2009].

Rifampin demonstrates greatest efficacy against biofilms and foreign material-associated osteomyelitis.

Oxazolidinones

Oxazolidinones inhibit bacterial protein synthesis by binding to the 23S ribosomal subunit. Linezolid is the most commonly employed agent in this class. Its spectrum of activity includes MRSA, Streptococcus spp., and Enterococci (including vancomycin-resistant isolates), and is indicated for treatment of ABSSSI, nosocomial pneumonia, and VRE infections. Oral and intravenous dosing are equivalent (100% bioavailability) at 600 mg every 12 hours. Bone to serum ratio of linezolid ranges from 37–51%, with bone concentrations exceeding Staphylococci MIC90 [Spellberg 2012, Kim 2014, Landersdorfer 2009].

Treatment success rates range from 55 to 100% in Gram-positive OM and is comparable to ampicillin-sulbactam for DFI [Nguyen 2009, Lipsky 2004, Kim 2014]. Linezolid has generally poor activity against biofilm and should be combined with a biofilm-active agent such as rifampin, if indicated. ADRs associated with linezolid include myelosuppression (anemia, thrombocytopenia), peripheral and optic neuropathy, and hypoglycemia. One study reported side-effects in over 50% of patients, especially in those with treatment duration greater than 2 weeks. Treatment discontinuation rates were up to 30% [Senneville 2006].

Dose adjustment or therapeutic drug monitoring may be required in patients at risk for toxicity and those with renal impairment. Linezolid's inhibition of monoamine oxidase can lead to drug-drug interactions with antipsychotics, antidepressants, and anxiolytic agents. Plasma protein binding of linezolid is approximately 30% and volume of distribution is 0.65 L/kg. The pharmacodynamic parameter associated with efficacy is time above MIC. The FDA recently approved a novel agent in this class, tedizolid, with reportedly lower incidences of ADRs. Increasing data demonstrate potential utility as oral treatment of OM [Park 2016, Launer 2018]. Limited information is available regarding tedizolid's bone penetration [Si 2017]. Labeled dosing is 200 mg once daily.

Metronidazole

Metronidazole is a bactericidal agent that inhibits nucleic acid synthesis by binding to DNA and electron-transport proteins. This agent possesses reliable activity against a myriad of anaerobic pathogens, including Bacteroides and Clostridium spp. Metronidazole is indicated for treatment of many anaerobic infections, including bone and joint infections caused by Bacteroides spp. Possible adverse reactions include convulsive seizures, peripheral neuropathy, dysgeusia, neutropenia, and a disulfiram-like reaction. The pharmacodynamic parameter associated with efficacy is Cmax above MIC. Plasma protein binding is minimal and dosing is equivalent for IV and oral (1:1) at 500 mg every 8 hours due to high bioavailability. Metronidazole bone concentration is similar to serum concentrations, making it an attractive option for oral treatment of anaerobic OM [Spellberg 2012].

Tetracyclines

Tetracyclines are bacteriostatic agents that inhibit bacterial protein

synthesis through 30S ribosomal subunit binding. Oral tetracyclines, including doxycycline and minocycline, are commonly employed in management of OM. These agents are active against CA-MRSA and are indicated in a variety of infections. Staphylococci generally have greater sensitivity to minocycline compared to doxycycline, although many isolates are sensitive to both [Fraimow 2009]. These agents have greater than 90% bioavailability allowing for equivalent IV to PO conversion. Both agents are highly protein-bound (greater than 90%) and each dosed at 100–200 mg every 12 hours. Tetracyclines' extremely high volumes of distribution make them effective in OM. The pharmacodynamic parameter associated with efficacy is AUC to MIC. Doxycycline's bone to serum concentration ranges from 2–86% and depends on the site of infection [Spellberg 2012].

Rifampin

Rifampin, a commonly employed agent in the rifamycin class, inhibits bacterial-specific DNA-dependent RNA polymerase. This agent is commonly an adjunct in managing OM due to its activity against MRSA, ability to penetrate biofilm, and retention of activity against stationary phase Gram-positive organisms [Kim 2014]. Resistance to rifampin can develop rapidly through polymerase mutations and, hence, should not be used as monotherapy. Co-administration of rifampin with another agent, such as a fluoroquinolone, can increase treatment success rates and prevent emergence of resistance to either agent [Fraimow 2009, Zimmerli 1998]. Combination treatment with rifampin achieved treatment success rates of greater than 80%, including foreign material-associated infections. Mixed data suggests the addition of rifampin reduces OM relapse rates thereby improving long-term outcomes [Spellberg 2022].

Rifampin has the potential for a myriad of drug-drug interactions due to its induction of drug metabolism and transport enzymes. Notable side-effects include flu-like symptoms, red-orange discoloration of body fluids, rash, and hematologic and hepatic toxicity [Khan 2012]. Rifampin bioavailability can vary depending on the duration of therapy. Single dose pharmacokinetic studies demonstrate a bioavailability of greater than 90% [Kim 2014, Agrawal 2005]. However, auto-induction of metabolizing enzymes decrease bioavailability to approximately 70% over time [Agrawal 2005]. The optimal dose of rifampin in managing OM is generally cited as 600 mg daily, although 450 every 12 hours has also been reported [Fantoni 2019]. Rifampin demonstrates a large volume of distribution, including penetration into bone and the central nervous system [Khan 2012]. Rifampin's bone to serum concentration ratio range from 20–57% according to some studies and approximate its serum levels in others [Spellberg 2012, Landersdorfer 2009].

Beta-lactams

The beta-lactam class, including penicillins, cephalosporins, carbapenems, and monobactams, are among the most effective and commonly prescribed anti-infectives. They exert bactericidal activity by inhibiting cell wall transpeptidation [Khan 2012]. Spectrum of activity varies inter- and intra-class. Of note, no currently approved oral beta-lactam in the U.S. possesses clinically relevant activity against MRSA or P. aeruginosa. Beta-lactam bioavailability is lower than previously reviewed antimicrobials, emphasizing the need to optimize pharmacokinetic and pharmacodynamic parameters. Commonly employed oral beta-lactams include amoxicillin, amoxicillin-clavulanate, (di)cloxacillin, and cephalexin/cefadroxil. The pharmacodynamic parameter associated with efficacy is time above MIC.

Plasma protein binding and bioavailability vary greatly depending on the agent. For example, bioavailability for ampicillin ranges from 37–39% compared to 80% for amoxicillin. Bone penetration of these agents relative to serum concentrations are estimated at 10–20% [Fraimow 2009]. Amoxicillin may achieve up to 30% of its serum concentration in the bone (range: < 10–31%) compared to 14% for clavulanate [Landersdorfer 2009]. Cephalexin and cefpodoxime achieve 18 and up to 30%, respectively. Maximally tolerated doses should be employed to ensure consistent bone concentrations above the MIC of the target pathogen. For example, amoxicillin 500–1000 mg every 8 hours, amoxicillin-clavulanate 875 mg every 12 hours to 1g every 8 hours, cephalexin 500–1000 mg every 6 to 8 hours, and cefpodoxime 400 mg every 12 hours may be used [Fantoni 2019]. More data are available indicating beta-lactam efficacy in pediatric, hematogenous OM compared to adult, chronic OM [Kim 2014].

No oral beta-lactam in the U.S. possesses clinically relevant activity against MRSA or P. aeruginosa.

Miscellaneous Agents

Data exist regarding utility of other oral antimicrobials, including fosfomycin, fusidic acid, and pristinamycin in treatment of Gram-positive OM. However, these agents were not reviewed due to limited or conflicting data or lack of availability in the U.S.

Combination Therapy

A variable amount of data exists for combination oral treatment of complex bone infections. Examples primarily include: fluoroquinolones, linezolid, TMP-SMX, clindamycin, fusidic acid, and tetracyclines each in combination with rifampin [Kim 2014, Lew 2004]. Please see individual sections above.

Treatment duration

Antimicrobial treatment duration is often dependent on outcome of surgical intervention. Intravenous therapy for 4–6 weeks had been traditionally recommended to ensure adequate serum and bone concentrations during the period of bone revascularization

after surgery [Kim 2014, Lew 2004, Mouzopolous 2011]. Current data, however, suggest initial, short-course intravenous therapy (1–2 weeks) during the period of highest bacterial burden followed by oral therapy is appropriate even in the setting of foreign material, assuming adequate surgical intervention [Li 2019, Mouzopolous 2011, Daver 2007, Spellberg 2022]. Success rates of less than 2 weeks intravenous therapy before switching, 2–4 weeks, 4–6 weeks, and greater than 6 weeks were 83%, 72%, 75%, and 66%, respectively (p = 0.68) [Daver 2007].

The Infectious Diseases Society of America (IDSA) recommends the following treatment durations: if infected soft tissue remain, continue treatment for 2–4 weeks. If infected bone remains or surgery is not performed, treatment for 6 weeks to greater than 3 months is recommended [Lipsky 2012, Bevilacqua 2007, Schaper 2023]. Vertebral OM secondary to MRSA, epidural abscesses, or in ESRD often necessitates treatment for 8 weeks or longer. Suppression therapy for months after initial management may also be required, especially in the setting of infected hardware or prostheses. In practice, treatment duration often depends on clinical response.

Conclusion

Medical management of OM is a constantly evolving landscape. An increasing body of data supports early conversion to oral antimicrobial treatment of osteomyelitis. Choice of agent should take in account patient, drug, and pathogen-specific factors. Optimization of pharmacokinetic and pharmacodynamic parameters may increase probability of treatment success. **PM**

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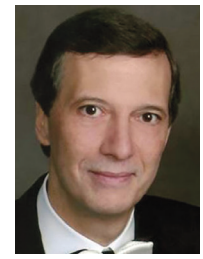

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CME **EXAMINATION**

1) What is generally considered the most common etiology of osteomyelitis in the pediatric patient?

- **A) Vascular insufficiency**
- **B) Hematogenous seeding**
- **C) Contiguous—adjacent soft tissue infection**
- **D) Contiguous—trauma**

2) Which of the following pathogens most commonly causes community-acquired osteomyelitis in adults?

- **A) Staphylococci**
- **B) Enterobacterales**
- **C) Cutibacterium (Propionibacterium) acnes**
- **D) Pseudomonas aeruginosa**

3) Which of the following are diagnostic tests, in addition to clinical judgment, needed for a definitive diagnosis of osteomyelitis?

- **A) Plain radiograph**
- **B) Magnetic resonance imaging**
- **C) Bone histology and culture**
- **D) Positive blood cultures**

4) Which of the following are potential complications of long-term venous access?

- **A) Access site infection**
- **B) Mechanical or thrombotic occlusion**
- **C) Increased cost**
- **D) All of the above**

5) Which of the following drug-specific characteristics does not greatly impact choice of oral antimicrobial in treatment of osteomyelitis?

- **A) Bioavailability**
- **B) Bone penetration**
- **C) Half life**
- **D) Volume of distribution**

6) Potential adverse drug reactions secondary to long-term linezolid therapy include which of the following?

- **A) Optic neuropathy**
- **B) Myelosuppression**
- **C) Nephrotoxicity**
- **D) A + B**

Continuing Medical Education

CME **EXAMINATION**

7) Which of the following agents demonstrates greatest efficacy against biofilms and foreign material-associated osteomyelitis?

A) Cephalexin
B) Doxycycline
C) Linezolid
D) Rifampin

8) Which of the following antimicrobials does not demonstrate a 1 to 1 IV to oral conversion?

A) Ciprofloxacin
B) Levofloxacin
C) Metronidazole
D) Minocycline

9) Against which of the following pathogens would oral TMP-SMX not be effective?

A) E. coli
B) P. aeruginosa
C) MSSA
D) CA-MRSA

10) Duration of intravenous antimicrobial treatment of acute osteomyelitis should be:

A) At least 6-8 weeks, irrespective of the pathogen
B) Based on patient-specific risk factors, clinical response, and evaluation of collateral impact of long-term venous access
C) Contingent solely on normalization of CRP and ESR
D) Length of hospital stay

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EXAM #2/24
Medical Management of Osteomyelitis: 2024 Update (Caputo, Fahoury, Beggs, and Raja)

Circle:

1.	A	B	C	D	6.	A	B	C	D
2.	A	B	C	D	7.	A	B	C	D
3.	A	B	C	D	8.	A	B	C	D
4.	A	B	C	D	9.	A	B	C	D
5.	A	B	C	D	10.	A	B	C	D

Medical Education Lesson Evaluation

Strongly agree [5]	Agree [4]	Neutral [3]	Disagree [2]	Strongly disagree [1]

1) This CME lesson was helpful to my practice ____

2) The educational objectives were accomplished ____

3) I will apply the knowledge I learned from this lesson ____

4) I will makes changes in my practice behavior based on this lesson ____

5) This lesson presented quality information with adequate current references ____

6) What overall grade would you assign this lesson?

A B C D

7) This activity was balanced and free of commercial bias.

Yes _____ No _____

8) What overall grade would you assign to the overall management of this activity?

A B C D

How long did it take you to complete this lesson?

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What topics would you like to see in future CME lessons ? Please list :

_____

_____

_____

_____

_____