Healthline VOLUME 22

Coram®* Continuing Education Program

Osteomyelitis

The term osteomyelitis comes from the Greek *osteon*, which means bone, *myelo*, which means bone marrow, and *itis*, which means inflammation. It is an infection of the bone and bone marrow. While any type of pathogen can lead to the development of osteomyelitis, bacteria are the most common causative organisms. Osteomyelitis is typically classified as acute (a first episode or an episode lasting less than two weeks), subacute (an episode lasting two to six weeks), and chronic (repeat episode or an episode lasting longer than six weeks). Persons at risk include those with diabetes, peripheral vascular disease, or compromised immune systems, as well as persons who are on hemodialysis or are intravenous drug users. While osteomyelitis is largely treatable, an insufficiently attended infection can become chronic, potentially leading to the development of ischemic bone tissue and permanent deformity, fracture, and disability. Treatment decisions include site of care, with a typical care plan incorporating long-term intravenous antibiotic therapy in the home setting.

Osteomyelitis can affect both adults and children, although anatomy, risk factors, and the most common sites of infection vary. In adults, osteomyelitis often affects the vertebrae and the pelvis. In children, osteomyelitis typically affects the adjacent ends of long bones.

Inoculation

The site of infection becomes inoculated via one of three major routes.

- ***Hematogenous*** seeding, in which the pathogens migrate from one infected site in the body to another via the bloodstream. Hematogenous osteomyelitis is more commonly seen in younger populations, typically involving the metaphyses of rapidly growing bones and affecting the tibia and femur predominantly.
- Spreading to nearby bone from a ***contiguous*** source of infection, such as from a diabetic foot ulcer, complex cellulitis, or deep burns. Contiguous infection may also be associated with vascular insufficiency.
- ***Direct inoculation*** of the bone, such as through puncture wounds, open fractures, or post-prosthetic joint replacement.

Approximately 20% of adult cases of osteomyelitis are hematogenous, with post-traumatic osteomyelitis accounting for about 47% of cases and vascular insufficiency, primarily in patients with diabetes, in about 34%.[1,2]

There are important anatomical differences between adults and children that can influence the risk and cause of osteomyelitis. In children, to support the needs of growth, circulation within the bones is different from that of adults, as illustrated in Figure 1. This results in a greater predisposition for hematogenous infection in children. In newborns and young infants, the nutrient artery ends at the epiphysis. At approximately 12 months, the growth plates form, but the nutrient artery does not cross the growth plate. Instead, it loops sharply back around and empties into the large venous sinusoids. Given the tight loops, blood flow is sluggish, providing an ideal environment for bacterial seeding. Once the growth plate closes, there is a re-anastamosis of what is called the transphyseal vessel across the growth plate, from which stems a more “normal” blood flow.

Causative Organisms

While the specific causative organism(s) is isolated in only about 35%–40% of osteomyelitis cases, there is some degree of predictability.[3] The most common causative organism is *Staphylococcus aureus,* which is implicated in approximately 80% of cases; it is followed by *Streptococcus pneumoniae* and *Streptococcus pyogenes.*[2] Community-associated methicillin-resistant *S. aureus* (CA-MRSA) continues to be a major cause in many regions of the United States.[4] In addition, there are pathogens associated with certain types of injuries or disease states. For

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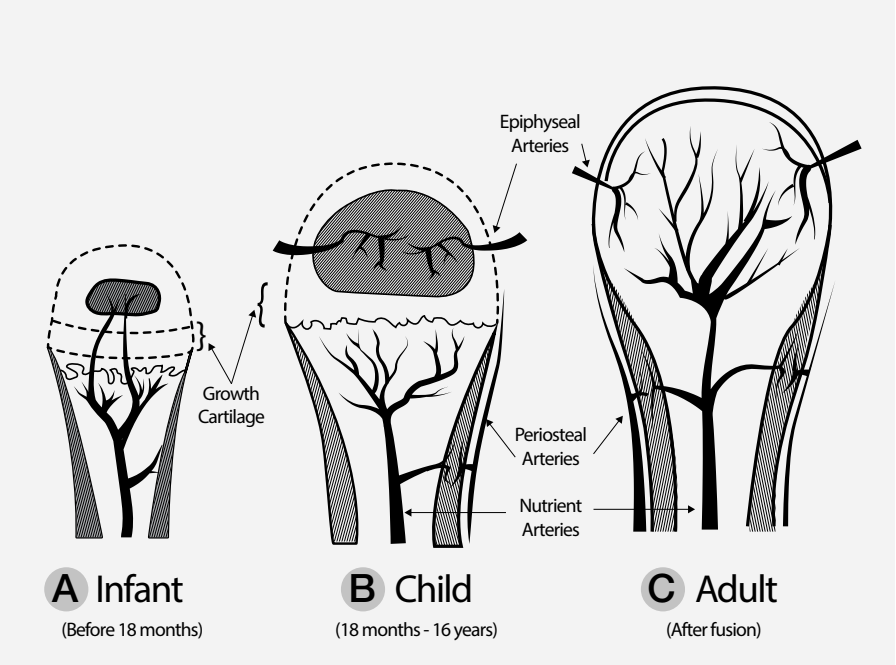

Figure 1. Long Bone Vasculature in Children and Adults

example, *Staphylococcus epidermis* may be associated with a post-operative or traumatic wound. Group B streptococci are common causative organisms in neonates. Other bacteria might be suspected depending on the cause or type of infection; for example, streptococci in bite injuries, diabetic foot ulcers or bed sores, and pseudomonas in cases of nail punctures, IV drug abuse, or in patients on dialysis. Salmonella is frequently the causative organism for osteomyelitis in patients with sickle cell disease.

A typical case of hematogenous osteomyelitis is caused by a single type of bacterium. Polymicrobial infection is more likely with infections such as those associated with diabetic foot osteomyelitis, post-traumatic osteomyelitis, chronic osteomyelitis, and chronic septic arthritis. Anaerobic bacteria can complicate polymicrobial infection and may be present more often than is commonly recognized. In chronic osteomyelitis, anaerobic bacteria may be present.

Pathophysiology

Bone is normally resistant to infection. However, when bacteria or other microorganisms are introduced into bone, regardless of route, they may enter the space of the bone marrow. As part of the normal inflammatory response, pus forms. The pus spreads in the limited space within the bone, resulting in increased pressure and decreased blood flow. Diminished blood flow leads to ischemia and bone necrosis, as well as a decreased ability of white cells to arrive at the site and phagocytize the infecting organisms. In advanced acute cases or in chronic osteomyelitis, pieces of the devascularized, necrotic segments of bone, called sequestra, can break away. Pathologic fractures may develop through the areas of devascularized bone. Additionally, unchecked chronic osteomyelitis can result in the development of fistulas that track out to the skin.

Small sequestra may be completely destroyed by granulation tissue from the surrounding living tissue. Large pieces of dead bone, however, cannot be completely destroyed. They may ultimately be reabsorbed, be eliminated through a sinus tract, or remain and provide a source of continued infection. Importantly, complete healing takes place only when all of the dead bone is gone, whether it has been destroyed, discharged, or excised.

In children, the spread of infection in the long bone can lead to formation of a subperiosteal abscess. The periosteum (the fibrous membrane that covers the bone) is then stimulated, resulting in formation of new periosteum beneath the elevated periosteum. When this new bone is encased around the sequestrum, the walled-off area provides an environment for pathogenesis.

The pathophysiology of osteomyelitis resulting from a contiguous source of infection follows the reverse order for hematogenous disease. Infection generally progresses from soft tissue to the periosteum, and ultimately into the bone itself.

Classification

Two primary classification systems are used to stage a patient's osteomyelitis. The Waldvogel system groups acute and chronic bone infections as either hematogenous or secondary to a contiguous focus. Contiguous-focus osteomyelitis is further delineated based on the presence or absence of vascular insufficiency.

The more commonly used Cierny-Mader classification system (Figure 2) involves anatomic staging that assesses both histology and the degree of bone involvement, but also considers the strong prognostic predictability of host factors. The Cierney-Mader system anatomically groups patients in stages one through four:

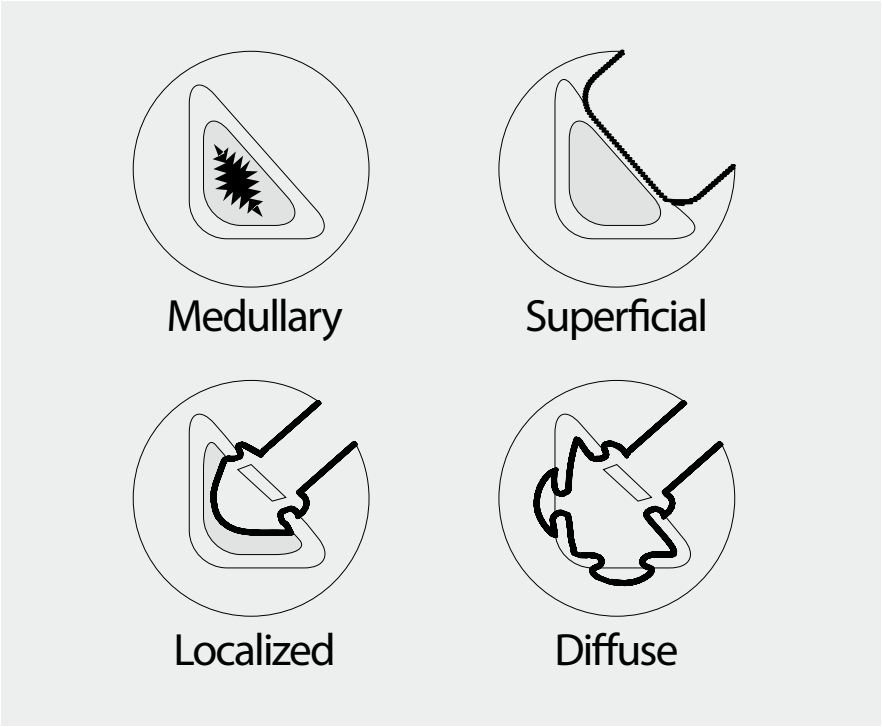

Figure 2. The Cierney-Mader Classification System

- Stage 1 disease, typically caused by a single organism, is confined to the medullary bone cavity.
- Stage 2 disease is a superficial osteomyelitis. Infection is limited to the bone surface, often in the presence of an adjacent soft tissue defect. The deeper cortical bone and medullary cavity remain intact.
- Stage 3 disease, often polymicrobial, is an advanced localized infection of bone and soft tissue.
- Stage 4 osteomyelitis represents diffuse disease involving multiple bony and soft tissue layers, and is often accompanied by instability of the bone or limb.

Host factors divide the patients further into three classes:

- Class A: Individuals have normal physiologic, metabolic, and immune functions.
- Class B: Patients are compromised with systemic or local factors that affect immune surveillance, metabolism, and local vascular integrity, such as concomitant diabetes mellitus, liver or renal disease, malignancy, use of steroids, extensive scarring, malnutrition, or use of tobacco products.
- Class C: Patients present with factors creating greater risk from treatment than from the osteomyelitis itself. These are typically patients with significant comorbidity.

Symptoms

The symptoms of osteomyelitis are influenced by such factors as site of infection, patient age, and severity. Symptoms may include:

- Pain, redness, and/or tenderness in the infected area
- Swelling and warmth in the infected area
- Fever, chills
- Nausea
- General discomfort, uneasiness, or ill feeling
- Drainage of pus through the skin
- Lower back pain (in the presence of spinal involvement)
- Lower extremity edema
- Changes in gait

In cases of vertebral osteomyelitis, patients may present with insidious, progressive back pain and abscesses. Fever is frequently absent. In approximately 10% to 15% of these patients, an infection leads to spinal cord depression and its associated symptoms.[3] It can be difficult to diagnose osteomyelitis in infants and young children because they often do not exhibit pain or specific symptoms in the infected area. Patients with diabetes and/or peripheral vascular disease may not experience pain at the site.

In the pediatric population, the diagnosis of osteomyelitis can be challenging as children often present with only nonspecific signs and symptoms, and clinical findings are extremely variable. Children may experience decreased movement and pain in the affected limb and adjacent joint, as well as edema and erythema over the involved area and fever, malaise, and irritability. Newborns with osteomyelitis may demonstrate decreased limb movement alone, without any other signs or symptoms.

Diagnosis

The first component of diagnosis is a history and physical, assessing for a potential triggering event as well as presenting signs and symptoms. Blood tests are ordered to assess for elevated white blood count, erythrocyte sedimentation rate, and/or C-reactive protein. In addition, blood cultures are drawn for potential identification of the causative organism(s). Any sources of draining are similarly cultured. A needle aspirate may be taken from the site, again for culture, via an

open, core-bone, or needle biopsy as appropriate.

A number of radiologic tests may be used to both diagnose and stage osteomyelitis, with varying degrees of usefulness. X-rays may rule out other causes of symptoms, such as a fracture, but x-rays are not highly diagnostic for early stage osteomyelitis because it takes a significant amount of bone loss for abnormalities to show up on plain film. An ultrasound may be helpful to identify soft tissue abnormalities, periosteal elevation, or the presence of an abscess.

However, ultrasound cannot image intraosseous abnormalities and is therefore infrequently used to diagnose or monitor osteomyelitis.

A radionuclide bone scan is highly sensitive for bony changes and, while not used to obtain a definitive diagnosis, it is useful in establishing suspicion for osteomyelitis. A computerized tomography (CT) scan is helpful in evaluating the integrity of bone or the presence of foreign bodies or necrosis. A CT may also be used to help guide needle biopsies. For diagnosis, however, magnetic resonance imaging (MRI) shows bone inflammation and is therefore the primary radiologic diagnostic tool. The MRI also provides excellent soft-tissue imaging, providing better visualization of tissue edema, abscess, and/or infectious tracts.

Ultimately, a diagnosis of osteomyelitis can be made if a patient meets at least one of the following criteria:

1. Has organisms that have been cultured from bone
2. Has evidence of osteomyelitis on direct examination of the bone during an invasive procedure or histopathologic examination
3. Has at least two of the following signs or symptoms:
    a. Fever (>38°C)
    b. Localized swelling
    c. Tenderness
    d. Heat
    e. Drainage at suspected site of bone infection

In addition, the patient must have at least one of the following:

1. Organisms that have been cultured from blood
2. Positive laboratory test on blood (such as an antigen test for *H. influenzae* or *S. pneumoniae*)
3. Imaging test evidence of infection (such as abnormal findings on x-ray, CT scan, MRI, or radiolabel scan [such as gallium or technetium])[5]

Treatment

The primary objective of treating osteomyelitis is to eliminate the acute infection and prevent the development of chronic infection and its potential for permanent deformity, fracture, and disability. Treatment combines both medical and surgical intervention, including IV and oral antibiotics, surgical debridement and, under certain circumstances, adjunctive therapies such as hyperbaric oxygen therapy.

Antibiotic selection should be based on the most likely pathogen(s), local antimicrobial resistance patterns, and intrinsic host factors. Given the risk of resistance and the necessary focus on antimicrobial stewardship, it is imperative that once culture or biopsy results are available, empiric antibiotic regimens be adjusted to an agent directed toward the specific causative organism(s). In adults, the standard duration of IV anti-infective therapy is four to six weeks, although length of therapy is significantly impacted by the source, type, and severity of infection, response to therapy, and numerous host factors. Younger patients typically require a minimum of four weeks of antibiotics, but increasingly, a switch to oral antibiotic therapy is considered. Many children with acute uncomplicated osteomyelitis can be successfully treated with a short course of intravenous antibiotic, followed by therapeutically equivalent oral therapy once appropriate cultures identify the cause and response to the IV antibiotic has been documented.[6]

Shorter courses of IV antibiotic therapy may also be prescribed following surgical debridement or reconstructive surgery depending on such factors as concomitant use of antibiotic-impregnated beads, the status of cultures at the time of surgery, and host factors that might impact immunity and/or healing.

Long-term IV antibiotic therapy requires the placement of a central line, often a peripherally inserted central catheter (PICC). Midline catheters may be an alternative with select drug therapies of less than four weeks' duration.

In some cases of osteomyelitis, particularly with contiguous or direct inoculation, antibiotic therapy alone will not cure the infection and the patient will require surgical debridement of the infected necrotic bone. Surgery may also be necessary if the affected limb is unstable secondary to bony destruction. In chronic infection, surgical removal of dead bone tissue is often indicated. Depending on the amount of bone removed, open space left by the removed bone tissue may require filling either with a bone autograft or allograft, held in place by pins, plates, or screws, or with packing material to promote the growth of new bone tissue. External fixators may be used to hold bones in place until healing is complete.

While adequate surgical debridement is often effective, for some patients with chronic osteomyelitis, successful treatment requires both surgical debridement and long-term, high antibiotic-

concentration materials placed within the bone at the site of infection. Devascularized bone diminishes the absorptiveness of systemic antibiotics, particularly in the face of peripheral vascular disease. Local insertion of antibiotic-impregnated materials may be used to supplement debridement and systemic antibiotics. Locally implanted antibiotics also minimize the potential for systemic side effects commonly associated with some IV agents.

Traditionally, the vehicle of choice for localized antibiotic administration has been polymethylmethacrylate (PMMA) antibiotic beads. PMMA is combined with a heat-stable antibiotic such as vancomycin or gentamycin and formed into beads that are surgically placed within the bony cavity. The beads provide a local depot for antibiotic administration and maintain space for subsequent bone grafting. However, PMMA is not bioabsorbable and thus requires surgical removal as well. Another option is a bioabsorbable formation bead, which has also been shown to have positive results.[7,8] These pellets are implanted and then are resorbed at a rate that is consistent with new bone growth. As pellets resorb, newly formed, woven bone forms within the debrided cavity. The antibiotic contained within the pellets is released at a predictable rate, allowing new bone formation within a bone defect.

Infection of an orthopedic prosthesis requires surgical removal with debridement of the infected tissue surrounding the area. Depending on the infection's severity and host factors, a new prosthesis may be implanted in the same operation, or delayed until the infection has resolved.

Hyperbaric Oxygen

The use of hyperbaric oxygen (HBO) may be considered as adjunctive treatment for refractory osteomyelitis. For HBO treatment, the patient is placed in a specialized chamber that allows intake of 100% oxygen at two to three times atmospheric pressure. The result is a systemic oxygen concentration of 10 to 15 times the normal amount, and increased tissue oxygenation. Increased oxygenation enhances peripheral vasoconstriction, allowing acute reduction in tissue edema; inhibits the growth of anaerobic organisms; improves leukocyte toxicity; stimulates fibroblast growth and collagen formation; induces the development of new blood vessels; and enhances antibiotic efficacy. HBO treatment is typically administered for 90 to 120 minutes per day for approximately 20 to 40 days.

Prognosis

With early and effective treatment, the prognosis for people with acute osteomyelitis is typically excellent. Chronic osteomyelitis, however, is more difficult to treat. Long-term antibiotic administration is needed, there is ongoing risk of recurrence, and amputation may ultimately be required. ♦

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Image Sources

1. Figure 1: http://1.bp.blogspot.com/-bEQwwU92NIs/UKU4hmUlr5I/AAAAAAAAAlw/g-AwPXKlY8o/s1600/epiphyseal+arteries.jpg
2. Figure 2: http://www.antimicrobe.org/new/images-Monographs/e12_classification.jpg

Self-Assessment Quiz: Osteomyelitis

LEARNING GOAL

To gain knowledge of the disease process and treatment options of osteomyelitis.

LEARNING OBJECTIVES

At the end of this program, the reader will be able to:

1. Describe the pathophysiology and risk factors associated with osteomyelitis.
2. Discuss the clinical presentation of osteomyelitis.
3. List diagnostic and treatment modalities for osteomyelitis.

SELF-ASSESSMENT QUESTIONS

In the Quiz Answers section on the next page, fill in the correct answer for each question. To obtain two (2.0) contact hours toward CE credit, the passing score is 100%. Return your Self-Assesment Quiz to Coram via email or fax. See the next page for details on how to return to your quiz. Please allow approximately seven days to process your test and receive your certificate upon achieving a passing score.

1. **In cases of vertebral osteomyelitis, patients may present with:**
   a. Insidious back pain
   b. Sudden back pain
   c. Progressive back pain
   d. All of the above
   e. A and C
   f. B and C

2. **Vertebral osteomyelitis is most common in adults.**
   a. True
   b. False

3. **Osteomyelitis of long bones is more common in:**
   a. Adults
   b. Children
   c. Neither A nor B; incidence is equal

4. **Which of the following is NOT a source of osteomyelitis:**
   a. Hematogenous spread
   b. Contiguous spread
   c. Direct inoculation
   d. Indirect inoculation

5. **The Cierny-Mader classification system incorporates:**
   a. Anatomic staging
   b. Histology
   c. Host factors
   d. All of the above
   e. A and C

6. **Symptoms of osteomyelitis are often non-specific, particularly in neonates and young children.**
   a. True
   b. False

7. **The specific causative organism(s) can be identified in the majority of bone infections.**
   a. True
   b. False

8. **Staphylococcus aureus is the most common causative organism for osteomyelitis.**
   a. True
   b. False

9. **The mainstay of osteomyelitis treatment today is:**
   a. Short-term antibiotics
   b. Long-term antibiotics
   c. Hyperbaric oxygen
   d. Surgery

10. **Potential treatment modalities include:**
    a. IV antibiotics
    b. Transition to oral antibiotics if/when appropriate
    c. Surgical debridement of necrotic bone
    d. Placement of antibiotic-impregnated beads
    e. Hyperbaric oxygen therapy
    f. All of the above

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Osteomyelitis

QUIZ ANSWERS

Fill in the key below with the correct answers to receive 2.0 Continuing Education credits.**

1. (a) (b) (c) (d) (e) (f)
2. (a) (b)
3. (a) (b) (c)
4. (a) (b) (c) (d)
5. (a) (b) (c) (d) (e)
6. (a) (b)
7. (a) (b)
8. (a) (b)
9. (a) (b) (c) (d)
10. (a) (b) (c) (d) (e) (f)

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