CLINICAL MANAGEMENT extra

Osteomyelitis: A Context for Wound Management

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GENERAL PURPOSE:

To provide an overview of osteomyelitis.

TARGET AUDIENCE:

This continuing education activity is intended for physicians, physician assistants, nurse practitioners, and nurses with an interest in skin and wound care.

LEARNING OBJECTIVES/OUTCOMES:

After completing this continuing education activity, you should be able to:

1. Distinguish the pathogenesis of osteomyelitis in children and adults.

2. Identify practical considerations for diagnosis and evidence-based treatment of osteomyelitis.

ABSTRACT

This educational activity reviews the pathogenesis of osteomyelitis and discusses practical considerations for diagnosis, treatment, and functional rehabilitation of pediatric and adult patients with osteomyelitic wounds. Antibiotic, surgical, and adjunctive treatments will be addressed. Emphasis is placed on consulting with infectious disease specialists and using evidence-based guidelines for antibiotic prescribing.

KEYWORDS: antibiotics, bone probing, bone sequestration, debridement, diabetes, excision, infectious disease, osteomyelitis, surgery, tuberculosis

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INTRODUCTION

Osteomyelitis is a bone infection that can cause permanent functional impairment and disability in affected patients.[1] It is essential to understand the medical terminology used in describing osteomyelitis, owing to conflations of taxonomy. Osteomyelitis is a noun referring to the inflammation of bone and bone marrow found in the medullary canal of bones. The term combines the prefix osteo- (bone) and the suffix –myelo (related to the myeloid tissue that exists in the bone marrow). Anatomical sites with blood marrow–laden tissue are susceptible to the hematogenous spread of bacteria, collectively leading to osteomyelitis.[1–3]

The first evidence of osteomyelitis was discovered in the vestiges of the fractured spine of a *Dimetrodon*, a Permian reptile that lived 291 to 250 million years ago.[2,3] This remnant contains evidence of perifracture inflammation and infection at points where the bone appeared roughened and swollen in and around the fracture.[2] Osteomyelitis is among the oldest histopathologic diseases known, dating from Hippocrates (460–370 BCE) with later microbial flora studied by Louis Pasteur.[2,3]

Pathophysiology

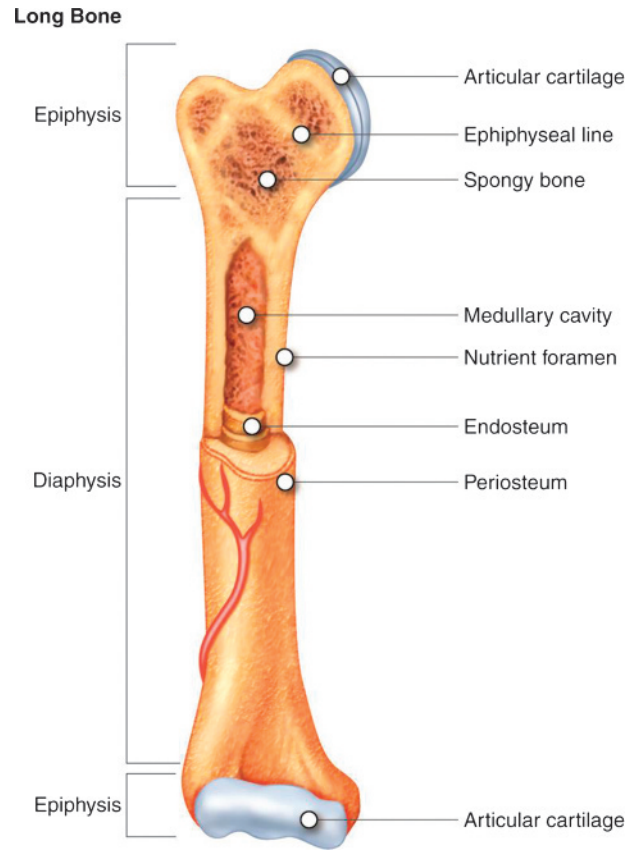
Areas of susceptibility to osteomyelitic infections are the long bones, vertebral bodies, and adjacent soft tissue and local infections.[2–4] Contiguous osteomyelitis tends to occur in younger individuals after trauma—either open fracture or minor closed trauma and related surgery.[5,6]

The femur and tibia are most commonly and equally affected in children (50% of cases) followed by long bones in the upper extremities in children. An exception is neonates, where 2 or more bones may be involved. In the pediatric population, acute osteomyelitis infections are primarily hematogenous in origin.[3–6]

In contrast, osteomyelitis in the adult patient is relatively rare in long bones. However, patients with hip replacements may have a higher susceptibility to infection because of the practice of implanting prosthetic hardware in the medullary canal (intramedullary rods).[7–9] The anatomical areas of osteomyelitic predisposition in adults are the feet, spine, and hips, with the spine being more common in hematogenous osteomyelitis.[4,9]

When considering the anatomy and histology of the bone, the most common site of infection is in the metaphysis (Figure 1). The major vascularization feeding the long bones usually penetrates the metaphysis (midway between the epiphyses) of the bone and subsequently through metaphyseal vascular loops that feed the epiphyseal plates (Figure 1). Intrinsic diminished blood flow in these circles (together with the absence of basement membranes) predisposes this site to osteomyelitis. In older adult patients, osteomyelitic infections have points of ingress and penetration related to pressure injury, diabetic foot ulcers, and total joint arthroplasties.[3,4,7,8]

Figure 1.
COMPONENTS OF LONG BONES



Osteomyelitis associated with vascular insufficiency usually occurs among individuals with diabetes mellitus.[8,9] The infection at the cortex is absorbed into the bone instead of sequestrating. Pieces of necrotic bone (sequestrum) can separate and can contain pus (Figure 2). New bone can begin to form over the injured periosteum; this is known as an involucrum and may partially surround a sequestrum with ongoing drainage.[3] As a consequence, the entire bone may be invaded and frequently remains chronically infected (Figure 2). Patients on prolonged bed rest or who rely on a wheelchair for mobility are subject to pressure-related skin ulceration and necrosis, most commonly in the sacral and buttock areas. These ulcerations are frequently invaded by polymicrobial flora emanating from the skin and gastrointestinal tracts, with soft tissue infection spreading to the bones of the pelvis and lower extremities.[3]

Microbial factors and biofilms[7] are significant cofactors in osteomyelitis pathogenesis. *Staphylococcus aureus* adhesions, including microbial surface components identifying adhesive matrix molecules, recognize polysaccharides related to fibronectin, fibrinogen, collagen, and heparin, promoting adherence to the bone matrix.[3,7] *Staphylococcus aureus* digested by osteoblasts persists and can become more resistant to antimicrobials. It is also thought to block the inhibition of proteolysis in musculoskeletal structures.[3,7]

Once the appropriate diagnosis is established, focused antibiotic treatment in adequate doses in consultation with an infectious disease specialist and surgeon is paramount. Multimodal treatment should be implemented as soon as possible, and this includes joint range-of-motion and progressive, dynamic cyclic loading of the joints as tolerated.[3–7,9,10]

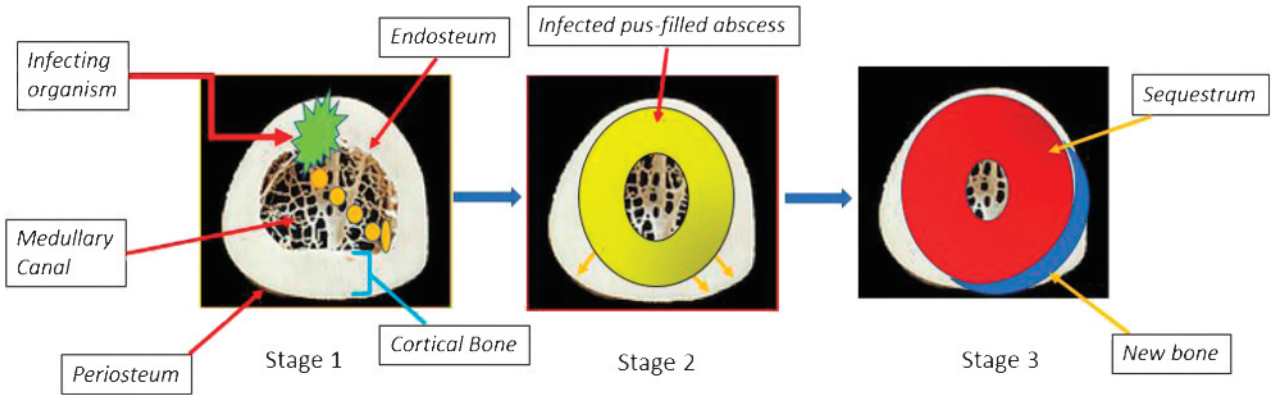
Classification

Osteomyelitis is classified by duration (acute or chronic), pathogenesis (trauma, contiguous spread, hematogenous, surgical), site, extent, or patient characteristics.[11] Osteomyelitis is a complex clinical and pathologic heterogeneous entity, with multiple diagnostic and treatment options. Although several classification systems for the diagnosis and treatment of osteomyelitis have been described, the Cierny-Mader classification system[12] (Table 1) is most prevalent in the medical literature and clinical practice, despite being 3 decades old. While other investigators have modified the classification systems for academic and research purposes, more work is needed in categorizing the evaluation and treatment options aligned with contemporary treatment options. Recent attempts to rectify the system's shortcomings in physiological class characteristics, treatment options, and rehabilitation outcomes have appeared in the literature.[11]

To this end, 10 osteomyelitis classification systems were recently evaluated Hotchen et al.[11] The authors used an evidence-based systematic review that concluded a heterogeneity of variables used for classification systems of long bone osteomyelitis. While some variables are used to guide management and rehabilitation after surgery (eg, bone defect), others were hypothesized to provide prognostic information (eg, host status; Table 2).[11] As a final point, some variables were used for descriptive purposes only (etiopathogenesis). In consideration of contemporary clinical practices, the authors concluded that 4 factors are essential to consider in any osteomyelitis classification schema[11]:

1. bone involvement,
2. antimicrobial resistance patterns of causative microorganisms,
3. the need for soft tissue coverage, and
4. host status.

Figure 2.
THE SEQUENCE OF OSTEOMYELITIS



Stage 1. The pathogenic sequence of osteomyelitis: the infecting organism, most commonly a *Staphylococcus aureus* inoculum, invades the medullary canal and becomes a nidus of infection. Stage 2. In the acute stage, the infected abscess results in infected pus from the inflammatory response and spreads to the vascular channels. Stage 3. In the chronic stage, the vascular channels are obliterated by the inflammatory process, with a resultant ischemia contributing to bone necrosis.

Table 1.
CIERNY-MADER CLASSIFICATION TYPE[12]

Type	Characteristics
I	Medullary osteomyelitis
II	Superficial osteomyelitis
III	Localized osteomyelitis
IV	Diffuse osteomyelitis

Etiology

There exist numerous typologies of osteomyelitis, including acute hematogenous osteomyelitis (AHO), vertebral osteomyelitis, osteomyelitis secondary to contiguous infection, and osteomyelitis secondary to vascular insufficiency. Acute posttraumatic osteomyelitis is secondary to external contamination and infection from the sequelae of open fractures, trauma,[9,11] and open (contaminated) war wounds that can become chronic.

Other related disorders are chronic recurrent multifocal osteomyelitis and tuberculous osteomyelitis.[13] The particular microbial flora causing infection is identified based on the clinical etiology. For example, *S aureus* (susceptible or resistant to methicillin) is the most frequent microorganism in any type of osteomyelitis, as compared with pathogens such as Enterobacteriaceae, *Pseudomonas aeruginosa*, and candidal species. Osteomyelitis-related *Mycobacterium tuberculosis* commonly presents in endemic populations and in patients with human immunodeficiency virus because of their susceptibility to opportunistic infections.[13]

OSTEOMYELITIS IN CHILDREN

Epidemiology

In children, the reported incidence rate of AHO ranges between 1:5000 and 1:10,000, with mean patient age of 6 years. The disease occurs in boys at a rate twice that of girls.[14] Hematogenous osteomyelitis is more common in children than in adults. More than half of pediatric cases occur in children younger than 5 years and in a quarter of children younger than 2 years.[3,15] However, osteomyelitis is uncommon in young infants (<4 months)[15,16] without underlying risk factors. The risk in this age group is related to complications at birth and the susceptibility of the host. In older infants and children, AHO is assessed and is routinely managed in a hospital setting. Acute hematogenous osteomyelitis is attributable to bacterial seeding that is thought to develop because of transient bacteremia resulting from otitis media, pharyngitis, minor lacerations, and minor trauma. The presentation of AHO can be acute or subacute and progress to chronic osteomyelitis.[17] As mentioned previously, osteomyelitis most often affects long bones (femur, 36%; tibia, 33%; humerus, 10%; and pelvis, 2.8%).[5] A single site of infection is most common. However, 5% to 20% of children are diagnosed with multifocal osteomyelitis.[5]

Musculoskeletal infections in the pediatric population represent a complex, heterogeneous grouping of conditions that may be concomitant with osteomyelitis, including discitis, septic arthritis, pyomyositis, abscesses, cellulitis, and necrotizing fasciitis.[14,17,18] In parallel, these infections may involve the lymphatic system and include palpable lymphangitis and lymphadenitis. Deep vein thrombosis is always of concern in the presentation of osteomyelitis.[14,17,18]

Osteomyelitis and septic arthritis are categorized according to the underlying nidus of infection: (1) hematogenous, (2) contiguous, and (3) direct inoculation. Concomitant septic arthritis may be the presenting diagnosis; it is an acute infection of the synovial membrane of the joints resulting in acute painful synovitis that can significantly limit activities of daily living. Septic arthritis is usually secondary to bacteremia. In younger children, the capsule of the joint often extends to the metaphysis because it is contiguous. Therefore, the cortex can be easily damaged and lead to septic arthritis secondary to osteomyelitis; conversely, septic arthritis can predispose patients to osteomyelitis. The epiphyseal growth plate can also be affected, causing growth discrepancies and chronic functional impairments and long-term disability or

Table 2.
PHYSIOLOGIC CLASS

Class	Characteristics
A	Good immune system and delivery
B	Compromised locally or systemically
C	Localized osteomyelitis
D	Diffuse osteomyelitis
Factors Affecting Physiologic Class	
Systemic Factors	**Local Factors**
Malnutrition	Chronic lymphedema
Renal or hepatic failure	Major-vessel compromise
Diabetes mellitus	Small vessel disease
Chronic hypoxia	Vasculitis
Malignancy	Venous stasis
Extremes of age	Extensive scarring
Immunosuppression	Radiation fibrosis
	Neuropathy
	Tobacco abuse

permanent joint destruction if the acute infection is not treated promptly.[11–14]

Etiology

The microbiologic epidemiology of AHO has remained relatively consistent over time, with *S aureus* accounting for a majority of cases. Regional variation in the antibiotic resistance of *S aureus* has occurred within the United States. In south Texas, the rates of methicillin-resistant *S aureus* and methicillin-sensitive *S aureus* in children who are diagnosed with AHO are 30.4% and 28.6%, respectively. Identifying a causative organism may be a challenge, with rates of culture-negative osteomyelitis ranging from 16% to 42%.[15] It is essential to attempt to identify the causative organism whenever possible to efficiently guide antibiotic therapy.[15,19,20]

In older infants and children, there are other known risk factors for an osteomyelitic infection such as sickle cell disease (SCD), immunodeficiency, sepsis, bacteremia associated with minor trauma, and chronic indwelling catheters. The relationship of SCD to osteomyelitis is of particular interest to wound care practitioners owing to the high incidence and prevalence of ulcerations related to SCD; the wounds are points of infection and contamination.[16,19,20] The prevalence of leg ulcers in patients with SCD varies greatly geographically, with frequencies as high as 75% in Jamaica and as low as 1% in Saudi Arabia. Healing times are measured in months to years, and ulcers often have a characteristic healing-relapsing course.

Despite improvements in the management of SCD over the past decade, AHO continues to be a serious infection in children with SCD and is associated with significant morbidity. The majority of patients with SCD are treated for a presumed diagnosis of AHO without definitive confirmation.[20,21] In a 10-year retrospective review by Weisman et al,[20] 30 children with SCD were studied. In this study, 18 males (median age, 12 years) were concomitantly diagnosed with and treated for osteomyelitis. Sites of involvement included lower extremities (n = 11), upper extremities (n = 10), pelvis (n = 2), vertebrae (n = 2), scapulae (n = 1), clavicles (n = 1), hands (n = 1), ribs (n = 1), and mandibles (n = 1). Leukocytosis (>15,000/μL) was observed in 13 patients (43%) at presentation. Baseline erythrocyte sedimentation rate (ESR) was elevated (>20 mm/h) in 29 patients (97%), but marked elevation (>100 mm/h) was present in 3 patients (10%). Baseline C-reactive protein was elevated (>10 mg/L) in 13 patients (43%). Bacteremia was present in 6 patients (20%). In the full study group of 30 patients, magnetic resonance imaging (MRI) findings were suggestive of osteomyelitis in 18 (60%) and indeterminate in the remaining patients. Osteomyelitis was confirmed in 3 patients (bone biopsy), probable in 6 patients (organism isolated from blood or abscess), and presumed in the remaining cases based on clinical, laboratory, and MRI findings. All patients were treated with prolonged antibiotic therapy. Six patients required surgical drainage/debridement, and 2 patients developed chronic osteomyelitis. There were no mortalities, and complete resolution was achieved in all patients.

Nontyphoidal *Salmonella* osteomyelitis seeding was isolated from cultures in 9 of the 30 patients (30%), whereas no organism was found in the remaining 21 patients (70%).[20] Interestingly, *Salmonella* osteomyelitis is thought to be seeded from the colon. While nontyphoidal *Salmonella* is a well-known cause of gastroenteritis, it is a rarer cause of extraintestinal infections such as osteomyelitis. That said, when *Salmonella* is identified as the causative organism for AHO, it is usually found in children with hemoglobinopathies such as SCD. It is postulated that children with hemoglobinopathies may be more susceptible to infection with *Salmonella* because of microscopic infarctions that occur along the intestinal mucosa and in bone.[21,22]

Clinical Manifestations

Acute hematogenous osteomyelitis may present acutely or subclinically and is defined as an infection diagnosed within 2 weeks of the onset of signs and symptoms.[15,17,18] The earliest symptoms of AHO in children can be subtle and dependent on the age of the patient. In neonates, pseudoparalysis of the affected extremity can occur, although many neonates will not show physical signs or mount a fever. In older infants and children, presentation of AHO follows a more typical pattern with focal tenderness, swelling, or difficulty with weight-bearing activities, particularly in the lower extremities.

Diagnosis

Acute hematogenous osteomyelitis remains a clinical diagnosis that is supported by acute inflammatory serum studies (white blood cell count, ESR, C-reactive protein) and radiological studies. Early in the course of the disease, findings from MRI studies are more sensitive and specific than plain films or computed tomography scans, and radionuclide studies (technetium 99m bone scan) are very sensitive and can be valuable early in the course of disease. In general, the diagnostic framework in children with suspected osteomyelitis is the recognition that the diagnosis is initially clinical, with a high index of suspicion.

The essentials of the diagnosis include an initial presentation with pain at a knee or hip joint and tenderness over the vertebral bodies. While there is a common finding of increased ESR, keep in mind that sedimentation rate is nonspecific and highly sensitive for a multitude of inflammatory processes. A definitive diagnosis can be made with biopsies. Leukocyte count is often elevated in acute diseases but may be at the high end of normal in more chronic infections. The C-reactive protein (an indirect marker of inflammation) is also elevated but is not necessarily

specific enough to rule out osteomyelitis. Plain x-rays may not demonstrate the severity of the disease until 10 to 14 days after the onset of signs and symptoms. The earliest visible x-ray changes are adjacent soft tissue swelling and bone reaction. There may be demonstrable lytic lesions and areas of sclerosis. If there are no plain film x-ray changes, a bone scan and an MRI should be considered. If the culture is obtained, it should be directly from the bone using needle aspiration or surgical biopsy. Blood cultures are often positive in more than 50% of the cases in patients with AHO.

Treatment

The mainstay of therapy for AHO is the use of systemic antibiotics and surgery if needed to drain abscesses or for debridement of necrotic tissue. The use of systemic antibiotics that are specific to *S aureus* should be considered in collaboration with an infectious disease specialist and your institution's pharmacy and therapeutics board. Surgery for acute osteomyelitis should be limited to the biopsy for diagnosis drainage of summative areas and debridement of necrotic bone. Involvement of the spine in the vertebral bodies should include collaboration with the neurosurgeon, owing to the potential for significant neurologic involvement. Patients should be assessed and treated by a physical therapy and habilitation team.[10,16,19–22]

Pediatric patients are characteristically treated with specific antibiotics directed at the most likely pathogen based on clinical presentation, age of the child, and the results of Gram stain if available with excellent outcomes. Because of the risk of disability to the growing child, care should be coordinated with a team of infectious disease specialists, pediatricians, orthopedic surgeons, and habilitation specialists. Of concern, however, are the patients who proceed to develop chronic osteomyelitis who may need more coordinated postacute services. This subset of patients is at risk of complications and recurrent infections.[14]

There remains a paucity of high-quality evidence to guide care for the pediatric patient with osteomyelitis. Moreover, there are substantial regional variations in the incidence, prevalence, severity of illness, and treatment outcomes of children with osteomyelitis; further research is required.

OSTEOMYELITIS IN ADULTS

Adult osteomyelitis most commonly arises from open fractures, diabetic foot infections, the surgical treatment of closed injuries,[4] and bone infections from implanted hardware (endoprosthesis). Patients usually have a history of prolonged debilitation and multiple surgical procedures. While complete amelioration and functional restoration are the treatment goal and the preferred outcome, there may be recurrences, depending on new or repeated trauma or decrease in the host's immune competence.[23]

The general typologies of osteomyelitis were briefly mentioned in the context of pediatric infections earlier in the article. What follows is a more in-depth framework concerning the various subtypes.

Acute Hematogenous Osteomyelitis

As previously discussed, AHO is a bone infection that has been seeded through the bloodstream. It makes up approximately 20% of cases of osteomyelitis in adults, although it is more common in children.[12] The infection is more common in males, irrespective of age, perhaps because males are more likely to engage in intense physical activity and are therefore more prone to injury of the spinal axis at the vertebrae and the load-bearing "3-joint complexes" in the lumbosacral spine. The vertebrae are the most common sites of spinal infection in adults, although hematogenous osteomyelitis also occurs in the long bones, pelvis, and clavicle.[9]

Vertebral Osteomyelitis

Vertebral osteomyelitis primarily affects adults older than 50 years, with age-related increases. Men are affected about twice as often as women. Before the development of antibiotics, vertebral osteomyelitis was fatal in about a quarter of all patients; now, mortality is uncommon. However, a delay in diagnosis can lead to devastating complications.

Pyogenic vertebral osteomyelitis usually is hematogenous in origin, with the arterial supply the most likely path of infection.[4] The redundant vertebral blood supply from the segmental arteries supplies the adjacent spinal segments, and consequently, the infection commonly involves a superior vertebra, the inferior vertebrae, and the intervertebral disk. The lumbar region is affected in approximately 45% of patients, followed by the thoracic spine (35%) and the cervical spine (20%).[4]

The nidus of infections is skin and soft tissue, the respiratory tract, infected intravenous sites, endocarditis, dental infections, and the genitourinary tract.[4] *Staphylococcus aureus* is the most common causal organism, except in the case of intravenous drug users, in whom *P aeruginosa* is most commonly isolated.[4]

Nongeneralized Vascular Contiguous-Focus Osteomyelitis

In this scenario, bacterial organisms may be directly inoculated into the bone at the time of trauma or surgery with subsequent spread from an adjacent soft tissue infection or facility-related contamination. Common factors in this form include surgical reduction and internal fixation of fractures, prosthetic devices, open fractures, and chronic soft tissue infections.

Although *S aureus* is the most commonly isolated organism, multiple pathogens are usually isolated from infected bone, frequently including gram-negative bacilli and anaerobic organisms. The

infection usually occurs about 1 month after inoculation from trauma, surgery, or soft tissue infection. Patients present with low-grade fever, drainage, pain, and loss of bone stability. Necrosis and soft tissue damage are frequent, leading to significant challenges in treatment.[4]

Generalized Vascular Insufficiency Contiguous-Focus Osteomyelitis

Patients with diabetes mellitus are most vulnerable to this type of osteomyelitis, and the small bones of the feet are most commonly infected. This is because inadequate tissue perfusion caused by perturbations in arteriolar and arterial blood flow that negatively moderates the local tissue response and chemotaxis predisposes patients to infection, most often caused by minor trauma to the feet.[10,23–26]

Multiple organisms are usually isolated from bone, most commonly coagulase-positive and gram-negative staphylococci, *Streptococcus* species, *Enterococcus* species, gram-negative bacilli, and anaerobic organisms.

The diagnosis of osteomyelitis can be challenging in patients with dysvascular disease. Patients may present with a seemingly unrelated problem, such as an ingrown toenail, cellulitis, deep space infection, or perforating foot ulcer, and the pain response pain may be muted by peripheral neuropathy. The examination may demonstrate decreased dorsalis pedis and posterior tibial pulses, poor capillary refill (rubor of dependency and pallor of elevation), and decreased sensation. Osteomyelitis is clinically present when bone remains exposed in an ulcer bed before or after debridement, or if a probe of a foot ulcer encounters bone.[10,24–26] The radiological evidence is a late finding.

The goal of treatment is generally to suppress infection and maintain the limb's integrity, keeping in mind that recurrent or new bone infections occur in most patients. Resection or amputation of the affected area is almost always needed.

Chronic Osteomyelitis

Both hematogenous and contiguous-focus osteomyelitis can become chronic. Chronic osteomyelitis is apparent when it reoccurs in a patient with a history of osteomyelitis who experiences a recurrence of pain, erythema, and swelling in association with a draining sinus.

Diagnosis is more challenging in patients with a painful orthopedic prosthesis, a pressure injury, a foot ulcer, or Charcot foot associated with peripheral vascular disease or diabetes.[10,24–26] The infection usually does not begin to regress until the nidus of the persistent contamination is removed.

Unfortunately, antibiotic therapy alone is usually insufficient, although empiric or culture-directed antibiotics remove many of the symptoms. Arresting the infection is particularly challenging when the integrity of surrounding soft tissue is poor, the bone is unstable secondary to an infected nonunion, or there is an adjacent septic joint.

Patients typically present with chronic pain and drainage and sometimes a low-grade fever. The sedimentation rate is usually elevated, and the leukocyte count is normal. The patient may present with a localized abscess, a soft tissue infection, or both if a sinus tract becomes obstructed. Rare complications of chronic osteomyelitis include squamous cell carcinoma at the site of tissue drainage and amyloidosis.[4]

Diagnosis in Patients with Diabetes

Osteomyelitis can be challenging to diagnose.[10,23] The intensity of inflammation, infection duration, site, vascularity, the presence or absence of a foreign body, and the presence or absence of associated pathology all affect the accuracy of any test. No noninvasive test can definitively establish or exclude osteomyelitis in complicated cases.

In the practice of evidence-based medicine, a prior probability of osteomyelitis should be assessed in all patients with diabetic foot ulcers.[27] Foot problems in patients with diabetes are common, but infections with osteomyelitis are extremely serious as they lead to an increased probability of amputation or death from complications. Among patients with diabetic foot ulcers, about 15% have osteomyelitis.[13,23–31]

The difficulties with diagnosis in patients with diabetes are amply illustrated in the literature.[4] In one study, as determined by bone biopsy and culture, osteomyelitis was found to underlie 28 of 41 diabetic foot ulcers (68%). Only 9 of the 28 cases had been diagnosed clinically by the referring physician. Most occurred in ulcers not exposing bone, and 64% had no evidence of inflammation on physical examination.[4]

Diagnosis of long bone osteomyelitis rests on the isolation of the pathogen from the bone lesion or blood culture. In the case of hematogenous osteomyelitis, positive blood cultures often can eliminate the need for a bone biopsy, provided there is radiographic evidence of osteomyelitis. Sinus tract cultures are reliable for confirming *S aureus*, but they do not predict the presence or absence of gram-negative organisms that cause osteomyelitis.[4,10,23] Antibiotic treatment must be based on meticulous cultures taken during debridement surgery or from deep bone biopsies[10,23] and antibiotic susceptibility tests.

Sedimentation rates and leukocyte counts often are elevated before therapy in acute disease, but the leukocyte count only rarely exceeds 15,000/μL, and the count is usually normal in patients with chronic osteomyelitis. Although a sedimentation rate that returns to normal in response to therapy is a favorable development, this laboratory determinant is not reliable in patients who are immunocompromised.[12,15]

Osteomyelitis of the lower extremity (ankle, heel, forefoot, and metatarsals) is a common challenge for patients with diabetes and is an important cause of amputation and admission to the hospital. The diagnosis of lower limb osteomyelitis in patients with diabetes remains a challenge and must be approached systemically. Patients with diabetes mellitus frequently have complications of ischemic vascular disease and peripheral neuropathy. In this setting, patients may be insensate and have concomitant diminished proprioception. Patients are often unaware of pressure phenomena related to footwear fit, with subsequent callus formation and breakdown of normal cutaneous barriers to infection. In addition, patients with neuropathy fail to recognize trauma, increasing the risk of skin breakdown.

Once organisms breach the skin barrier, the establishment and spread of infection are promoted by hyperglycemia, decreased chemotaxis, and decreased vascular supply. The infection then spreads to the contiguous underlying bone, which may be visible in the ulcer, and this bone can become the "basement" of the ulcer.[10,29] Approximately 25% of all nonhealing ulcers contain contiguous bone infection,[10] and osteomyelitis should be considered and ruled out on the initial presentation.[10]

Testing and Imaging Studies

Osteomyelitis of the foot causes significant morbidity in patients with diabetes, with a substantial financial burden to patients and institutions. Although there is no substitute for a detailed history, its utility in the diagnosis of osteomyelitis in patients with diabetes has not been well studied.[26,27,29,32]

The available evidence suggests that an ulcer that measures more than 2 cm^2 or a positive "probe-to-bone test" finding may be helpful to establish the diagnosis but has been challenged by Lavery et al.[33] The probe-to-bone test, that is, palpation of bone with a sterile blunt metal probe in the depths of infected pedal ulcers, was thought to be highly correlated with osteomyelitis. In later studies, however, it had a relatively low positive predictive value.[33]

An ESR greater than 70 mm/h or positive plain radiograph findings appear to be helpful in increasing the suspicion of osteomyelitis. Magnetic resonance imaging results should be interpreted in the context of the pretest probability.[29,32] Temperature, ulcer inflammation, white blood cell count, and swab culture do not appear to be helpful in establishing the diagnosis or directing therapy in patients with diabetes and a lower extremity ulcer.[27,29,32]

Although bone biopsy is 96% sensitive,[10] surgeons are often reluctant to perform one unless there is some other compelling indication to operate.[10] In the outpatient setting, osteomyelitis is most easily diagnosed by imaging studies.[10]

Plain films are positive for osteomyelitis if they show reactive bone formation and periosteal elevation. Plain films are the least expensive imaging study but have a sensitivity of 78% and specificity of only 50%. Because of the deficiencies of plain films, test combinations have been suggested. A combination of the leukocyte count, ESR, and plain films provided a combined sensitivity of 89% and specificity of 88%. If all 3 test results are positive, the positive predictive value of this combination is 69%. If all are negative, the negative predictive value is 96%.[10]

A conventional 3-phase bone scan is more sensitive for osteomyelitis than plain films, but specificity is still only 50%. Specificity is low because bone scans are ineffective for differentiating osteomyelitis from soft tissue infection contiguous to bone.[10] Indium leukocyte scanning has been reported to overcome this deficiency, with a sensitivity of 89%. When combined with a 3-phase bone scan, the sensitivity of indium white blood cell scanning is 100%, and the specificity is 81%.[31] Radionuclide tests either singly or in combination have the drawback of not revealing anatomic detail.

An MRI reveals anatomic detail and is extremely sensitive to the presence of marrow edema on the T2-weighted image. An analysis of 11 studies investigating the diagnosis of osteomyelitis by MRI showed a sensitivity of 95% and a specificity of 88%. One study that used histopathologic findings as the criterion standard found excellent predictive value, with a sensitivity of 98% and specificity of 75%.[10] Because the specificity rating of MRI is not 100%, other entities that cause marrow edema, such as resolving fracture or recent surgery, must be considered.

Adjunctive Treatment for Osteomyelitis

After a surgical evaluation, with or without surgical debridement and biopsy, management of osteomyelitis requires 6 weeks of antibiotics. Such treatment for up to 12 weeks has been suggested as hard-hitting treatment for osteomyelitis in persons with diabetes. For recurrent osteomyelitis or an initial presentation of osteomyelitis in an immunosuppressed patient (eg, transplant recipient), hyperbaric oxygen therapy may be considered in parallel with intravenous antibiotics.[10] An oxygen-rich environment enhances leukocytic killing and is synergistic with antibiotics.

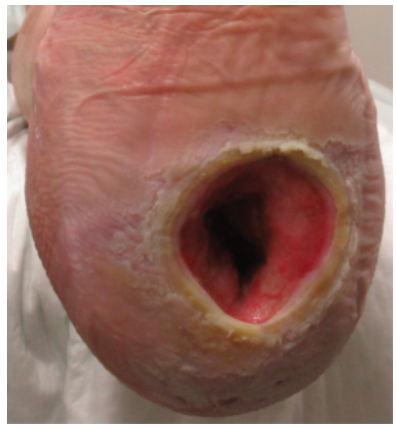
Surgical Management

Wound practitioners know that many, if not most, chronic wounds heal with conservative care. Although the physiatrist focuses on the functional aspects of medical management, the physical medicine and rehabilitation services must have access to consultants to effectively manage infections.[10]

The surgeon's role is critical in the scenario of a wound with frank tissue invasion, abscess, open purulence, fistulae, or acute osteomyelitis, any of which might lead to sepsis (Figure 3). These infections require early operating room debridement and culture.

Figure 3.

A 62-YEAR-OLD WOMAN WITH A 12-MONTH HISTORY OF LEFT CALCANEAL DIABETIC FOOT ULCER



The patient's wound treatments included ultrasonic debridement and offloading with total contact casting. The wound demonstrated early improvement but then retrogressed with flattened healing trajectory. Examination of wound probed to bone. Magnetic resonance imaging T2-weighted images revealed calcaneal osteomyelitis.

Images and case compliments of Jeffrey Niezgoda, MD, AZH Wound and Vascular Centers, Milwaukee, Wisconsin.

Soft Tissue Reconstruction. Musculocutaneous flaps are usually the best choice treatment of Stage 4 pressure injuries of the buttocks[10] in patients with SCI or when the concomitant loss of muscle function does not contribute to comorbidity or deficits in functional status. Tissue expanders serve to optimize wound coverage.[10] Musculocutaneous flaps are also occasionally used for well-vascularized pressure injury of the heel. Musculocutaneous flaps can ameliorate osteomyelitis and limit the further damage caused by shearing, friction, and pressure. Split-thickness skin grafts can also be used to repair recalcitrant venous ulcers and neuropathic ulcers.[10]

In older adults or patients with chronic illness, the benefits of reconstructive surgery might be outweighed by the risks. In addition to the risks of surgery, musculocutaneous flaps have a significant rate or ulcer recurrence, with short-term failure rate (most commonly the result of suture line dehiscence) from 5% to 36%. The long-term recurrence rate can be as high as 61%.[10] Recurrence can be minimized by careful attending to pathomechanical factors. If the biomechanical defect that led to the ulcer in the first place is not corrected (by means of specialty shoes, orthoses, stockings, seating systems, or beds), the ulcer is likely to recur postoperatively.[10]

Bone Repair and Reconstruction. The diabetic foot has deformities that predispose to ulceration. If the ulcer heals and then recurs several times, the orthopedic or podiatric surgeon should evaluate the patient for foot reconstruction, osteotomies, or tendon recessions to relieve the source of pathomechanical risk factors.[10]

Amputation. Major amputation secondary to significant dysvascular disease can be done at the digital, transmetatarsal, Symes, transtibial, or transfemoral level for rapidly expanding gangrene or overwhelming infection or chronic osteomyelitis. Amputation should be performed if tissue loss has progressed beyond the point of salvage, if surgery is too risky, if life expectancy is very low, or if functional limitations obviate the benefit of limb salvage.[34]

The wound care specialist should be involved in "staging" the amputation. The team approach should to take into account the patient's function, ambulation, the cardiopulmonary burden arising from increased energy expenditure, and oxygen consumption associated with periprosthetic gait training.[10,25,29]

CONCLUSIONS

This educational activity reviewed the pathogenesis of osteomyelitis and discussed practical considerations for the diagnosis, treatment, and functional rehabilitation of adult and pediatric patients with an osteomyelitic wound. An ulcer area greater than 2 cm^2, a positive probe-to-bone test result, and an ESR of more than 70 mm/h, coupled with abnormal plain radiograph results, are helpful in diagnosing the presence of lower extremity osteomyelitis in patients with diabetes.[31–33] An MRI that is not demonstrative of infection of the bone is enough to exclude the diagnosis of osteomyelitis. Traditional clinical history and physical examination of the wound is not specific or sensitive enough to reliably include or exclude osteomyelitis. However, the examination may create a high index of suspicion for its exclusion. A high index of suspicion and high pretest and posttest probability should initiate a comprehensive evaluation and an interdisciplinary treatment strategy.[31–33]

PRACTICE PEARLS

- Areas of susceptibility to osteomyelitis infections are the long bones, vertebral bodies, and adjacent soft tissue.
- Wound care management for children with AHO is inherently a multidisciplinary and collaborative process driven by clinical practice guidelines and evidence-based protocols.
- Osteomyelitis associated with vascular insufficiency usually occurs among individuals with diabetes mellitus.
- The microbiologic epidemiology of AHO has remained relatively consistent over time, with *S aureus* accounting for a majority of cases.
- Approximately 25% of all nonhealing ulcers contain contiguous bone infection,[22] and osteomyelitis should be considered and ruled out on the initial presentation.

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