Osteomyelitis

Learning Objectives.

At the end of this module, you should be able to :

1. **discuss the differences in the causes of endogenous and exogenous osteomyelitis**
2. **describe the pathological changes which occur in disease development**
3. **understand which individuals may be at risk of developing osteomyelitis, and why this is so**
4. **describe the clinical signs and symptoms of both acute and chronic osteomyelitis**
5. **give the management strategy for treating osteomyelitis**

Osteomyelitis is a bone infection usually associated with bacteria, although it should be remembered that fungi, parasites, and viruses also can cause bone infection. It is categorised according to the pathogen's mode of entry into bone tissue;

> **exogenous osteomyelitis** - enters from outside the body, e.g., through open fractures, penetrating wounds, or surgical procedures. The infection spreads from soft tissues into adjacent bone.
>
> **endogenous (haematogenous) osteomyelitis** – pathogens are transported in the blood from sites of infection elsewhere in the body. The infection spreads from bone to adjacent soft tissues, and this is more common in infants, children, and the elderly.

In infants, incidence rates of osteomyelitis amongst males and females are equal whereas in children and older adults, males are most commonly affected. Osteomyelitis is also a common complication of sickle cell anaemia, and low oxygen tension.

There is a UK incidence of 10-100/100,000 population per year for acute haematogenous osteomyelitis. Prevalence of osteomyelitis after a foot puncture is thought to be as high as 16%, rising to 30-40% in diabetic patients.

Risk factors commonly include:

- Trauma (orthopaedic surgery or open fracture)
- Prosthetic orthopaedic device
- Diabetes
- Peripheral vascular disease
- Chronic joint disease
- Alcoholism
- Intravenous drug abuse
- Chronic steroid use
- Immunosuppression
- Tuberculosis
- HIV and AIDS
- Sickle cell disease
- Presence of catheter-related blood stream infection

This disorder is difficult to treat, and often culminates in extensive physical disability. Several factors contribute to the difficulty in treating bone infection:

1. Bone contains multiple microscopic channels that are impermeable to the cells and substances of the body's natural defences. Once bacteria gain access to these channels, they are able to proliferate unimpeded.

2. The microcirculation of bone is highly vulnerable to damage and destruction by bacterial toxins. Vessel damage causes local thrombosis of the small vessels, which leads to ischemic bone necrosis.

3. Bone cells have a limited capacity to replace bone destroyed by infections. Initially, osteoclasts are stimulated by infection to resorb bone, which opens up isolated bone channels so that cells of the inflammatory and

immune systems can gain access to the infected bone. At the same time, however, resorption weakens the structural integrity of the bone. New bone formation usually lags behind resorption, and the haversian systems in the new bone are frequently incomplete.

Causative organisms

Staphylococcus aureus is the usual cause of haematogenous osteomyelitis. Other potential causative agents include group B streptococcus, *Haemophilus influenzae, Salmonella,* and gram-negative bacteria. Group B streptococcus and *H. influenzae* tend to infect young children; *Salmonella* infection is associated with sickle cell anaemia; and gram-negative infections are most common in older adults and immunocompromised individuals with impaired immunity. Mycobacterial, viral, and fungal infections occur in more severely immunocompromised individuals.

Cutaneous, sinus, ear, and dental infections are the primary sources of bacteria in haematogenous bone infections. Soft-tissue infections, disorders of the gastrointestinal tract, infections of the genitourinary system, and respiratory infections are also sources of bacterial contamination. In addition, infections that occur after total joint replacements are sometimes the cause. The vulnerability of specific bone depends on the anatomy of its vascular supply.

In adults, haematogenous osteomyelitis is more common in the spine, pelvis, and smaller bones such as those in hands and feet, microorganisms reaching these areas via the vascular and lymphatic system.

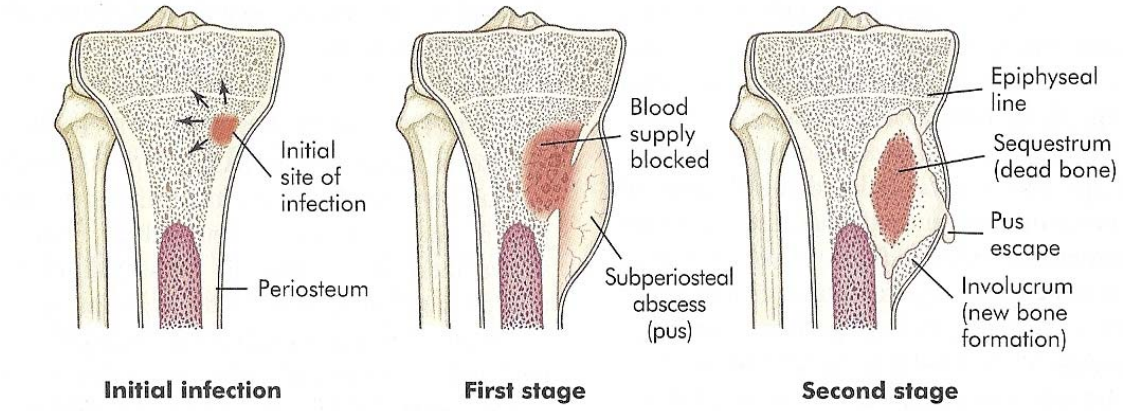
Exogenous osteomyelitis can be caused by human or animal bites or even traumatic injury to the mouth where mucosal tissues are damaged by the teeth. These injuries inoculate local soft tissue with bacteria that later spread to underlying bone. Deep bites can introduce micro-organisms directly onto bone. The most common infecting organism in human bites is S. *aureus,* whereas with animal bites the most common infecting organism is

Pasteurella multocida, which is part of the normal mouth flora of cats and dogs.

Direct contamination of bones with bacteria can also occur in open fractures or dislocations with an overlying skin wound. Intervertebral disk surgery and operative procedures involving implantation of large foreign objects, such as metallic plates or artificial joints, are associated with exogenous osteomyelitis. Local injections and venous punctures are significant causes of exogenous osteomyelitis. Exogenous osteomyelitis of the arm and hand bones tends to occur in those who abuse drugs, and again S. *aureus* is the most common pathogen.

In general, individuals who are chronically ill, have diabetes or alcoholism, or are receiving large doses of steroids or immunosuppressive drugs are particularly susceptible to exogenous osteomyelitis, or recurring episodes of this disease.

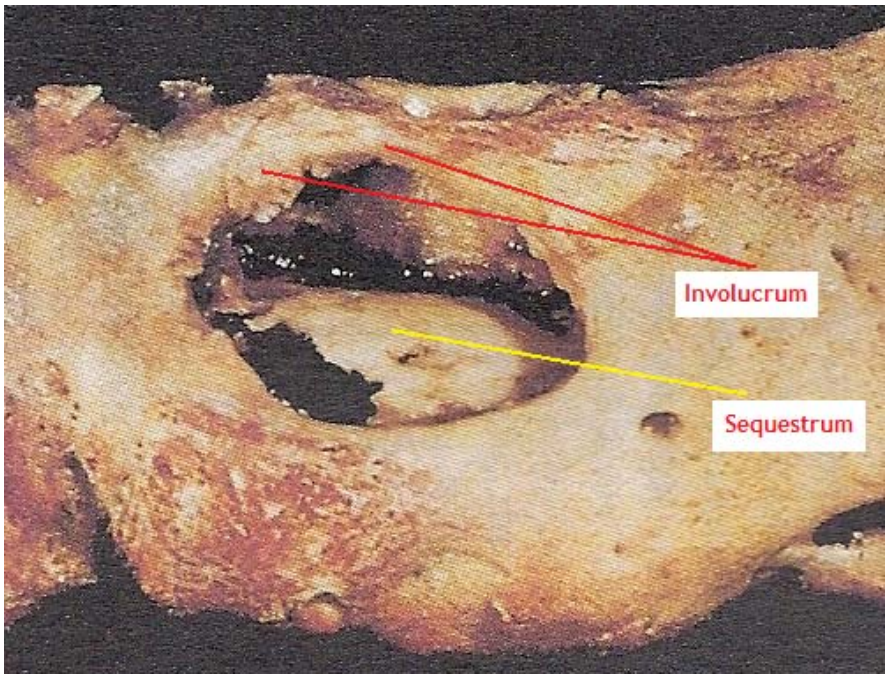
Pathological features



The pathological changes occurring in osteomyelitis are the same whether the source in endogenous or exogenous. The invading pathogen provokes an intense inflammatory response, with increased vascular activity, tissue fluid leakage, oedema, and white cell activity. Once the process has begun the terminal vessels in the bone thrombose, and exudate seals the bone

canaliculi. Inflammatory exudate extends into the metaphysis and the marrow cavity and through small metaphyseal foramina into the cortex. In children, exudate that reaches the outer surface of the cortex forms abscesses that lift the periosteum off underlying bone. This disrupts blood vessels that enter bone through the perisoteum, reducing the blood supply to the underlying bone. The end result of this is necrosis and death of the affected area, resulting in a sequestrum**,** an area of dead bone.

Lifting of the periosteum also stimulates an intense osteoblastic response, which results in the laying down of new bone around the infected areas, in some cases sealing off the sequestrum. This new layer of bone is known as the involucrum. If the wall of the involucrum is incomplete, then exudate from the sequestrum can escape, and due to the presence of collagenases within the exudate, a sinus track is formed, leading to the skin surface, allowing the discharge of exudate.

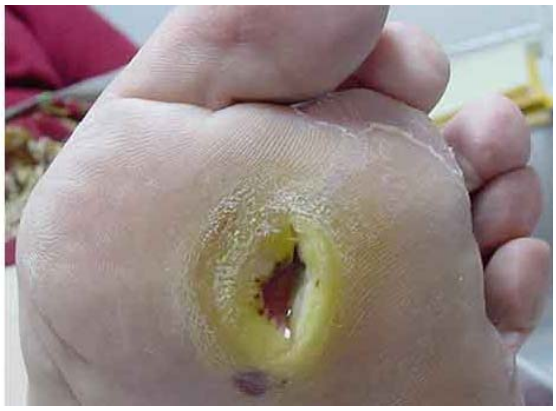


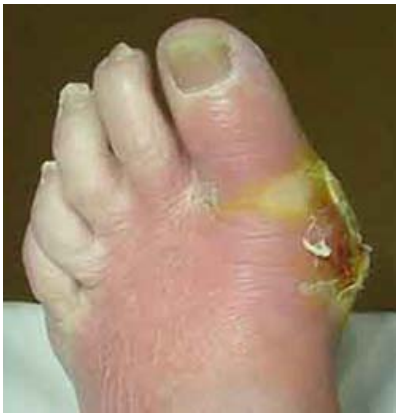
Involucrum development in adults is less common because the perisoteum is more firmly attached. What is more likely is that the cortex is disrupted and weakened, predisposing to the development of pathological fractures.

Clinical manifestations

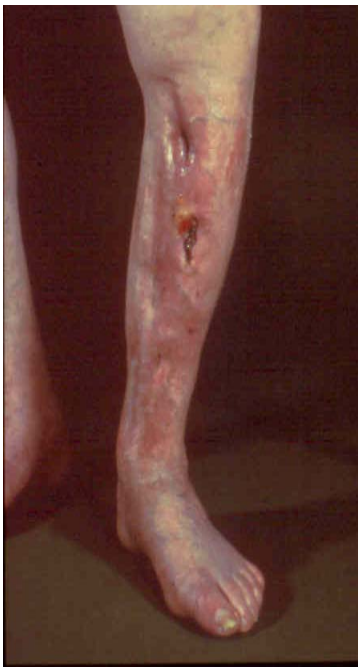
These vary depending on the age of the individual, the affected area, the initiating event, and the organism involved.

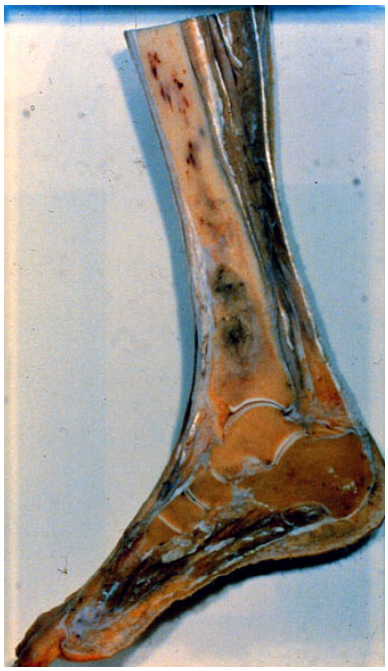
Acute :





Chronic :





Acute osteomyelitis causes abrupt onset of inflammation. If an acute infection is not completely eliminated, the disease may become sub-acute or chronic. In sub-acute osteomyelitis, signs and symptoms are often indeterminate, whereas in the chronic stage, infection is silent between

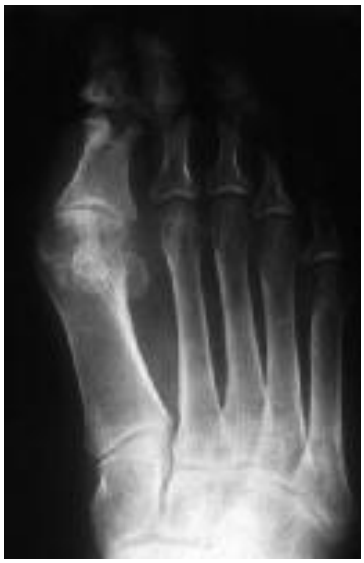
exacerbations. The micro-organisms persist in small abscesses or fragments of necrotic bone, resulting in intermittent episodes of acute osteomyelitis. The progression from acute to sub-acute osteomyelitis may be the result of inadequate or inappropriate therapy, or the development of drug- resistant microorganisms.

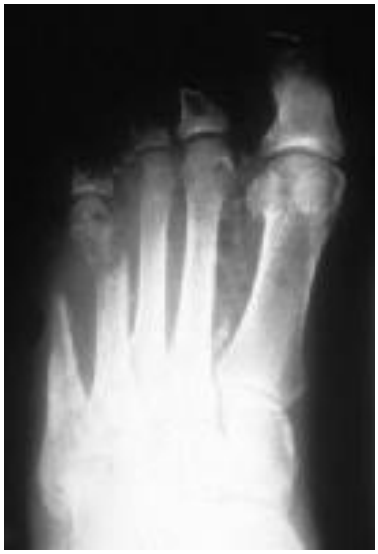
In the adult, haematogenous (endogenous) osteomyelitis has a slow onset. The symptoms are usually vague and include fever, malaise, anorexia, weight loss, and pain in and around the infected areas. Oedema may or may not be evident. Recent infection (urinary, respiratory, skin) or instrumentation (catheterization, cystoscopy, myelography, diskography) usually precedes onset of symptoms.

Single or multiple abscesses (Brodie's abscesses) characterise sub-acute or chronic osteomyelitis. Brodie's abscesses are circumscribed lesions usually localised in the ends of long bones and surrounded by dense ossified bone matrix. The abscesses are thought to develop when the infectious micro-organism has become less virulent, or the individual's immune system is resisting the infection somewhat successfully.

In exogenous osteomyelitis, the usual signs and symptoms of soft-tissue infection are common. Inflammatory exudate in the soft tissues disrupts muscles and supporting structures and forms abscesses. Low-grade fever, lymphadenopathy, local pain, and swelling usually occur within days of initiation.

Radiologically, evidence of acute osteomyelitis is first seen with overlying soft-tissue oedema at 3-5 days after infection. Bony changes are not evident for 2-3 weeks, and initially manifest as periosteal elevation followed by cortical or medullary lucencies ('thinner' areas of bone). Approximately 40-50% focal bone loss is necessary to cause detectable lucency on plain films. By 28 days, 90% of patients demonstrate some abnormality.





With laboratory results, the WBC count may be elevated, but it is more commonly seen as normal. C-reactive protein levels are usually increased but nonspecific, although this is a more useful marker than ESR as this takes longer to show elevation. Culture or aspiration findings in samples of the exudate are normal in 25% of cases, and blood culture results are positive in only 50% of patients with haematogenous osteomyelitis.

Diagnosis of osteomyelitis requires 2 of the 4 following criteria:

- Purulent material on aspiration of affected bone
- Positive findings of bone tissue or blood culture
- Localised classic physical findings of bony tenderness with overlying soft-tissue erythema or oedema
- Positive radiological imaging study

The Cierny-Mader staging system is used to determine the status of the disease process regardless of its aetiology, regionality or chronicity. It takes into account the state of the bone, the patient's overall condition and factors affecting the development of osteomyelitis.

Cierny-Mader Staging System :

Anatomical state of the bone

Stage 1: medullary osteomyelitis (infection confined to the bone surface)

Stage 2: superficial osteomyelitis (contiguous type of infection)

Stage 3: Localised osteomyelitis (full-thickness cortical sequestration which can easily be removed surgically)

Stage 4: diffuse osteomyelitis (loss of bone stability, even after surgical debridement)

Patient's general condition (physiological class)

A host: healthy patient

B host: there is systemic (Bs) or local (Bl) compromise, or both

C host: treatment morbidity outweighs morbidity of disease

Factors affecting immunity, metabolism and local vascularity

Systemic factors (Bs): malnutrition, renal or hepatic failure, diabetes mellitus, chronic hypoxia, immune disease, malignancy, extremes of age, immunosuppression or immune deficiency

Local factors (Bl): chronic lymphoedema, venous stasis, major vessel compromise (chronic local hypoxia), arteritis (chronic local hypoxia), small vessel disease (chronic local hypoxia), extensive scarring, radiation fibrosis, neuropathy, tobacco abuse

To determine disease stage;

anatomical state + physiological class = clinical stage

For example- Stage 4Bs osteomyelitis = a diffuse lesion in a systemically compromised patient.

Management

Generally, if there is early clinical suspicion, confirmation through imaging and microbiological tests and prompt treatment are the keys to a successful outcome. Analgesia (and limb splinting if a long bone is involved) may be necessary and is an important part of symptom control. Ultimately, surgery may be required to debride the bone and close any defects.

Treatment regimes

Empirical therapy in non high-risk patient:

- Flucloxacillin plus benzylpenicillin, plus either fusidic acid or rifampicin depending on the severity of infection.

Empirical therapy in high-risk patient:

- Flucloxacillin plus either an aminoglycoside (e.g. gentamicin) or a quinolone (e.g. ciprofloxacin) plus either fusidic acid or rifampicin, depending on severity of infection.
- Alternatively: a second-generation cephalosporin (e.g. cefuroxime) plus either fusidic acid or rifampicin depending on severity.

Empirical therapy in penicillin-allergic patient:

- Clindamycin plus a quinolone (e.g. ciprofloxacin).
- Alternatively: vancomycin plus a quinolone (e.g. ciprofloxacin).

Empirical therapy in MRSA positive suspected patient (also consult microbiology):

- Vancomycin should be used instead of flucloxacillin.
- Gentamicin or a quinolone (e.g. ciprofloxacin) can be added subject to local policies and the advice of your microbiologist.

Treatment for acute infection is usually for 4-6 weeks and chronic infection for at least 12 weeks. High doses are required to achieve suitable bone penetration in high enough concentrations in necrotic avascular bone.

Intravenous treatment is used initially and also to cover any surgical period, up to two weeks post surgery. The switch to oral therapy may happen once the clinical condition stabilises, the inflammatory markers are going down and there are reliable microbiology results.

Although treatment is guided by clinical response and the level of inflammatory markers, an early drop in C-reactive protein levels does not mean that antibiotic therapy should stop. Therapy should be for at least four weeks. Changes on plain X-ray lag at least 2 weeks behind normalisation of CRP.

Specifically consult a microbiologist if there is a risk of MRSA or if there is a prosthetic device in situ. Microbiologists will also be able to help in the case of polymicrobial infection. Rifampicin should not be used alone as antimicrobial resistance rapidly develops.

With chronic osteomyelitis it is usually appropriate to delay treatment until culture and sensitivity results are obtained, unless the infection is severe, in which case empirical treatment is started (see above). Surgical debridement is the mainstay of treatment in chronic cases as it removes the necrotic tissue and provides an infection-free scaffold for future healing. If surgery is not possible, indefinite antimicrobial therapy may be required but this is generally accepted to be less effective than surgery.

Prognosis

This depends on the number of risk factors and the patient's general condition, hence the use of a staging system during the patient assessment period. Outcomes are improved if treatment is started 3-5 days after onset of the infection. Timely diagnosis and intervention in an otherwise well patient should lead to full recovery, although follow-up over several months will be required to monitor for relapse.

KEY LEARNING POINTS.

1. **Osteomyelitis is infection of the bone, either from and external or internal source.**
2. **The commonest causative organism is *S.aureus.***
3. **The physical structure of bone makes osteomyelitis more difficult to treat because of the blocked canaliculi preventing blood flow through bone tissue.**
4. **Involucrum development is more common in children, whereas in adults the bone is more likely to develop pathological fracture.**
5. **Acute osteomyelitis has an abrupt onset with the signs of acute inflammation.**
6. **Chronic osteomyelitis symptoms are slower in onset, and are more non-descript.**
7. **A staging system is often used to clinically describe the severity of infection.**
8. **Management requires long-term use of anti-biotics, as well as pain management, and surgery.**