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## **Bone and joint infections: clinical forms, risk factors, prevention, etiology, diagnosis and treatment**

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**Abstract**

Bone and joint infections pose many threats to human life and health. The scope of knowledge and skills to deal with this problem has improved significantly in recent years. The chosen direction should be continued so that we can prevent and treat bone and joint infections with the highest possible effectiveness.

**Key words:** bones infection, joints infection, osteoarthritis, osteitis, arthritis.

## **Introduction**

Bone and joint infections are one of the most serious challenges of modern orthopedics. The fact that they can pose a threat to the life and functioning of the patient makes them a complication that raises concerns for both patients and orthopedists. The progress in the prevention, diagnosis and treatment of bone and joint infections over the last 35 years has been enormous. The effectiveness of treating these infections is currently around 90%, so the concerns associated with them have been relatively decreasing over the years. Based on research from previous years, thanks to the development of knowledge in the field of both implant placement and the use of antibiotics, orthopedists and entire teams taking care of patients affected by bone and joint infections have developed strategies to reduce the risk associated with it.(Babiak & Pędzisz 2019)

The methods used include systemic antibiotic therapy or treatment requiring the use of a local antibiotic carrier or antibacterial substance. The strategies chosen differ from each other and it is impossible to determine which one is the best, due to the insufficient number of patients who could be a control group, allowing comparing the effectiveness of individual methods on an appropriately large clinical sample. (Nowakowski & Mazurek 2017)

## **Clinical forms of bone and joint infections**

### **Bacterial arthritis**

Risk factors. The risk of developing bacterial arthritis increases when dealing with a patient who has undergone joint replacement surgery, especially at an older age, which in itself also promotes the occurrence of bacterial arthritis. Patients with immunodeficiencies, both congenital and acquired, resulting from alcoholism, diabetes, immunosuppressive treatment or HIV infection, as well as hematological diseases such as hemophilia. People suffering from rheumatic diseases such as rheumatoid arthritis, SLE or gout, as well as infections of the skin and soft tissues and kidney or liver failure. Patients with trauma, after joint punctures, extremely

emaciated, suffering from cancer, malnourished and drug addicts taking drugs intravenously also show increased susceptibility.

**Prevention.** Bacterial arthritis is most often caused by microorganisms from outside, so you should avoid situations where bacteria can get directly into the joint. In the case of injuries and after surgery, you should pay special attention to hygiene. You should also treat all infections that may be a source of infection.

**Etiological factors.** The most common causes of bacterial arthritis include *Staphylococcus aureus*, coagulase-negative staphylococci, *Neisseria gonorrhoeae*, Enterococci, Gram-negative rods, anaerobic bacteria, viruses, fungi, *Mycobacterium tuberculosis*. (Babiak & Pędzisz 2019)

**Diagnostics.** The diagnosis of infection is based on both the physical examination, subjective examination and on the test results. We notice symptoms of joint inflammation and in the subjective examination the patient informs us about the procedure, intra-articular injection or joint injury. In laboratory tests, we will most often see a large increase in ESR and CRP, leukocytosis, as well as a high level of PCT (although a low level does not rule out bacterial infection). The synovial fluid is usually turbid and yellow-green in color. It contains a large number of cells with a significant predominance of neutrophils >75%. In the case of suspected *N. gonorrhoeae* infection, a culture should be performed of both synovial fluid and blood.

**Treatment.** Depending on the stage of advancement according to Stutz and Gachter, we choose different methods of treatment. If we are dealing with the initial stage, i.e. 1 and 2, in which there is a clear purulent discharge, the fluid collected by performing a decompressive puncture should be examined. Then antibiotics are administered (never administered intra-articularly). Subsequent removal of the fluid should take place during arthroscopy or by joint drainage during open surgery. It is recommended to immobilize the joint for a short time during drainage and to perform passive and active joint exercises as early as possible. In stage 3, chronic, we perform synovectomy arthroscopically or on an open joint. We do not use flushing drainage in this case. The treatment of choice for stage 4 is arthrodesis or resection arthroplasty of the joint. (Hryniewicz et al. 2013)

## **Acute purulent hematogenous osteitis**

It is a condition that affects children much more often than adults. The bones are affected by the entry of microorganisms from primary foci, such as teeth or skin, via the bloodstream. It is accompanied by bone marrow involvement, which usually begins in the venous sinuses of the metaphyses of long bones. Especially the bends where the venous vessels branch off from the metaphyseal loops are susceptible to bacterial colonization, due to the slower blood flow in these places. (Babiak & Pędzisz 2019)

### **1. In newborns and infants**

It is characterized by easy transmission of infection from the metaphysis to the cartilaginous epiphysis, and then to the joint. The clinical picture of purulent arthritis dominates (this is due to the presence of transepiphyseal vessels, which disappear with age). The most common etiological factor is beta-hemolytic streptococci, less frequently *Staphylococcus aureus* and others.

### **2. Children**

In this case, purulent inflammation involves the shafts and metaphysis of the bones, without reaching the epiphysis or the joint. This is due to the growth cartilage, which separates the epiphysis from the metaphysis, effectively preventing the spread of infection. The joint can only be affected when the metaphysis of the bone is within the joint capsule, as in the hip or knee joint. The periosteum is strong and provides protection against the spread of infection outside the bone. Characteristic for this type is a bone necrosis surrounded by a "coffin", which can be seen on X-ray. The most common etiological factor is *S. aureus*.

### **3. Adults**

In this type, we usually deal with acute inflammation, which progresses to subacute, and later becomes chronic inflammation. As a result of the loss of growth cartilage, the infection through continuity, again similarly to neonates and infants, can spread to the epiphysis and joint. The most common occurrence is noted in patients with immune disorders and in those using immunosuppressive therapy.

**Risk factors.** Age below 16 years, this group comprises about 80% of patients. Boys are more often affected than girls. Patients who are malnourished, have impaired immunity and soft tissue damage are also at risk.

**Prevention.** Educating patients about the threat of microbial infections and informing them about the importance of reacting quickly if they notice any worrying symptoms. Earlier medical attention and prompt administration of antibiotics increase the chances of cure.

**Diagnostics.** The diagnosis should be based on laboratory tests, imaging tests and interview. The patient mentions difficulty moving and fever, and may mention an infection of another organ that he has recently had. Laboratory tests may show leukocytosis, elevated CRP, ESR and PCT. The most valuable imaging tests are USG and MRI, although it is also worth using an X-ray in two projections (note that in the first two weeks after infection the X-ray image may be normal).

**Treatment.** It is performed to stop the progression of bone tissue destruction caused by the inflammatory process. Intravenous antibiotic therapy can be used, followed by oral antibiotic therapy or combined treatment, a combination of surgery and antibiotic therapy. The type of treatment used depends on the time at which the CKD is diagnosed. If an abscess has not yet formed at the time of diagnosis, antibiotic therapy will be effective. However, if we are dealing with an intraosseous abscess, or antibiotic therapy applied for 48 to 72 hours is ineffective, surgical decompression will be indicated. (Nowakowski & Mazurek 2017)

## **Other forms of bone inflammation**

Other forms of bone inflammation are subacute osteomyelitis - Brodie's abscess, Chronic sclerotic osteitis - Garre's osteomyelitis and SAPHO: Syndrome and Chronic Recurrent Multifocal Osteomyelitis.

### **Subacute osteomyelitis - Brodie's abscess**

In Brodie's abscess we are dealing with a well-demarcated inflammatory process located in the metaphysis of long bones, most often in the tibia.

Risk factors. Brodie's abscess most often occurs in school-age adolescents.

Prevention. Early evaluation and treatment of pain and swelling that accompany inflammation are key to preventing permanent damage.

Etiological factors. Brodie's abscess is most often caused by staphylococci, sometimes also by streptococci.

Diagnostics. The dominant symptom is limb pain, mainly at night. Soft tissues in the area of the abscess may be warm. In laboratory tests, CRP and ESR may be slightly elevated, the remaining are diagnostically insignificant. In X-ray examination, an osteolytic focus with a reactive sclerotic envelope (differentiate with solitary bone cyst and fibrous dysplasia). MRI and CT are not useful in differential diagnosis. Blood cultures are often negative.

Treatment. During the surgical procedure, a biopsy should be taken for bacteriological and histological examination. Then, the focus should be cleaned with Ringer's solution and the purulent membrane should be removed. In the final stage of the operation, the defect should be filled with spongy bone chips mixed with an antibiotic. (Babiak & Pędzisz 2019)

### **Chronic sclerotic osteitis - Garre's osteomyelitis**

Ineffectively treated acute inflammation is the cause of chronic sclerotic osteitis, which is currently considered a minimally invasive form of inflammatory progression. Sclerosis involves the spongy bone and there is a superstructure of the cortex of the long bone shafts. There is no abscess.

Risk factors. It is most common in children and adolescents. In the face and neck, the risk of infection is often influenced by odontogenic infection.

Prevention. Be careful when overusing antibiotics, as their frequent use promotes the occurrence of this condition.

Etiological factors. The most common infection is caused by staphylococci.

**Diagnostics.** The most important changes are progressive bone sclerosis and an increase in its circumference, as well as visible overgrowth of the marrow cavity of long bones. The predominant symptoms are pain caused by pressure (this causes increased pressure in the marrow cavity) and thickening of the affected bone fragment. When changes occur in many places, the patient will have an increased level of CRP and ESR. The abscess is not visible on X-ray.

**Treatment.** Surgical treatment consists of cutting a longitudinal window in the cortical layer and the corresponding part of the overly calcified spongy bone in the diaphysis of a long bone, which will reduce the intraosseous pressure. NSAIDs are administered to alleviate symptoms. Sometimes, macrolides are effective in improving the patient's condition. (Reymond, J et al. 2004)

### **SAPHO: Syndrome and Chronic Recurrent Multifocal Osteomyelitis**

SAPHO- is a chronic rheumatic disease, one of the seronegative spondyloarthropathies. SAPHO is an acronym for the words: synovitis, which is inflammation of the synovial membrane of the joints, usually the sternoclavicular and sternocostal joints; acne, which is acne that occurs on the trunk; pustulosis, pustular psoriasis, affecting the palms and soles of the feet; hyperostosis, meaning overgrowth of bones; osteitis, which means inflammation of the bones.

**Risk factors.** More frequent cases are reported in girls. The peak incidence is at 10 years of age.

**Prevention.** Regular laboratory tests and, in the case of predisposition, specialist tests to detect the HLA-B27 antigen.

**Etiological factors.** It is suspected that chromosome 18 may have an influence on the occurrence of SAPHO. However, this is not a confirmed theory.

**Diagnostics.** Histologically, SAPHO in the chronic phase is like plasma cell inflammation. In addition, a patient with SAPHO has a constantly elevated ESR, while other



inflammation parameters have normal values. Differentiation is performed by performing imaging tests, i.e. X-ray, as well as scintigraphy and biopsy.

Treatment. NSAIDs are the mainstay of treatment for SAPHO. (Nowakowski & Mazurek 2017)

### **Purulent hematogenous arthritis**

These are conditions with an acute and rapid course. In them, the synovial membrane and joint capsule are affected by bacteria that enter with the blood. Sometimes it can also spread through continuity. Usually occurring symptoms are high fever, pain in the joint that limits its mobility, redness and swelling. The most common location is the joints of the lower limbs. Arthritis is divided according to the time of appearance of symptoms from contamination with microorganisms. We distinguish early, symptoms appear in less than 6 weeks, and late, over 6 weeks. In the case of late inflammation, it is not possible to restore the function of the joint to its pre-disease state. (Nowakowski & Mazurek 2017)

Purulent arthritis of hematogenous origin can be divided into those occurring in newborns, children and adults.

#### **1. Newborns and children**

Risk factors. Open fracture, injury that penetrates deep into the joint, joint surgery, and also a complication of joint puncture.

Prevention. Purulent hematogenous arthritis should be suspected in any child who has a fever, and whose arthritis had an acute onset.

Etiological factors. Most often it is a hematogenous infection from a focus that was located in other parts of the body. The usual infectious agent is *Staphylococcus aureus* and group B streptococci in infants and newborns up to 2 months of age, as well as *Streptococcus pneumoniae* in younger and older children.

**Diagnostics.** The patient's general condition is poor, there is fever, as well as nausea and vomiting. In laboratory tests, increased leukocyte count, predominance of polymorphonuclear cells, increased CRP levels and ESR. The synovial fluid is cloudy, yellow-gray, and septic. In imaging studies, X-ray and MRI are useful in differential diagnosis, while ultrasound can be used to assess the synovial membrane.

**Treatment.** It is absolutely necessary to perform a joint puncture. If we obtain purulent fluid, it is mandatory to perform an arthrotomy and lavage and to administer intravenous antibiotic therapy (for at least 2 weeks). (Le Saux 2019)

## 2. Adults

They occur rarely, usually in people with impaired immunity, i.e. oncology patients, taking immunosuppressive drugs, addicted to alcohol and drugs, HIV positive. The etiological factor is usually fungi, e.g. *Candida albicans*. (Nowakowski & Mazurek 2017)

### **Bursitis**

The most common location is the olecranon and prepatellar bursa. Initially, they are usually not bacterial inflammations. Initial symptoms include serous effusion, which leads to bursal distension and pain, as well as increased skin temperature in this area.

**Risk factors.** Minor, direct injuries that do not penetrate.

**Prevention.** You should take care of your health and not overload your joints with heavy physical work, excessive strength, lifting weights, etc.

**Pathomechanism.** Their formation is associated with overloading the joints or their injuries, in the vicinity of which the bursae are located.

**Diagnostics.** Ultrasound examination shows effusion in the bursa, which may have different echogenicity, depending on this, we may be dealing with a hematoma or purulent fluid.

Treatment. Puncture and evacuate the retained fluid. Then apply a steroid into the lumen of the bursa and apply a dressing that will compress the area. If we are dealing with purulent fluid,

we should incise the bursa, rinse with lavaseptic, insert a sterile drain and implement broad-spectrum antibiotic therapy. (Sułko, J. 2017)

## **Specific infections**

### **1. Osteoarticular tuberculosis**

It is a secondary infection resulting from the spread of tuberculosis bacilli, which in the body had its primary focus, e.g. in the lungs. The most common location is the vertebral bodies, the hip joint and the knee joint, although it can be found in virtually all bones and joints.

Risk factors. Residency in highly industrialized countries, such as China or Russia. Patients with acquired immune deficiencies and undergoing immunosuppressive treatment.

Prophylaxis. Tuberculosis vaccination (BCG), rapid molecular tests, airing of patient rooms, isolation of patients with diagnosed tuberculosis. Subjecting people who have had contact with tuberculosis patients to tests to exclude the disease.

Etiological factors. *Mycobacterium tuberculosis* complex is a factor responsible for the occurrence of this disease entity. (Zieliński et al. 2016)

Diagnostics should include X-rays of the affected joints and bones and places that could be the primary focus of infection. IGRA-type tests, which replaced the classic tuberculosis test and PCR tests. (Korzeniewska- Koseła 2014)

Treatment. Oral antibiotic therapy is used in combination with chemotherapeutics. The main uses are rifampicin, hydrazide, pyrazinamide and many other complementary and additional drugs. 4-5 combined drugs should be taken for a period of 6 to 18

months. It is also necessary to clean the focus in the bone and remove the pathologically changed synovial membrane. Then the place that was subjected to the procedure should be immobilized and relieved. (Korzeniewska- Koseła et al. 2021)

## 2. Brucellosis

It is a disease that affects many organs, including the spine, sacroiliac joints and knees. In the spine, it is usually located in the L4 vertebral body. It is a disease transmitted by animals.

Risk factors. Having animals at home and contact with wild animals. Consuming meat or milk of infected animals. Working as a farmer, butcher or veterinarian is also associated with a higher risk of contracting brucellosis.

Prevention. Avoiding drinking unpasteurized milk and its products or meat that has not been previously heat treated. It is also important to take care of personal hygiene, as well as frequent and thorough hand washing.

Etiological factors. It is caused by *Brucella* bacteria.

Diagnostics. Scintigraphy and MRI are useful tests in the early stages of the disease, because changes in X-ray are usually visible only after several months.

Treatment includes antibiotic therapy, in which tetracyclines, rifampicin and aminoglycosides are used. (Parfieniuk- Kowerda 2017)

## 3. Syphilis of bone and joints

We distinguish between congenital and acquired forms of syphilis. Painful thickenings around the joints in the neonatal period may indicate the presence of the congenital form. In acquired syphilis, however, characteristic is keloid bone inflammation in the tertiary period.

Risk factors. Most often, infection occurs sexually through damaged skin, mucous membrane, so casual sexual contact, unprotected sex, inadequate care for intimate hygiene are factors that increase the likelihood of infection. Addiction to psychoactive substances, alcohol, as well as living in a city are risk factors.

Prevention. Avoiding frequent changes of partners and casual sexual contact, using condoms, sexual education.

Etiological factors. The pale spirochete is responsible for causing this disease.

Diagnostics. The earliest changes on X-ray appear in the metaphyses of the bones of the knee and elbow joints. Osteolytic and osteosclerotic changes can be found in the nasal bone, collarbones and forearm bones on X-ray. In the knee joint, we usually deal with the so-called Clutton's joint, which is an exudative inflammation.

Treatment. Benzylpenicillins administered intravenously or intramuscularly are used here. (Korkosz 2017)

### **Chronic recurrent multifocal osteitis**

As the name suggests, it is characterized by the occurrence of multiple foci of bone inflammation, most often without the possibility of demonstrating the presence of bacteria. Today, it is more often classified as an autoimmune disease. Bone changes usually occur symmetrically, most often in the metaphysis of long bones, clavicle, sternum, vertebrae or mandible.

Risk factor is age from 4 to 15 years, because this is the age in which this disease occurs most often.

Prevention. There is no specific prevention that can be used to prevent the occurrence of this disease.

Etiological factors. They are unknown. It may probably be associated with congenital disorders of the immune system.

Diagnostics. The elimination method is used here. X-ray shows no characteristic changes in the initial period of the disease, in later stages osteoblastic and sclerotic changes in long bones occur. Biopsy is also often used.

Treatment involves the administration of NSAIDs and periodic X-rays. However, many patients need intensive treatment, including the use of steroids and sulfasalazine. Recently, treatment with bisphosphonates has been showing positive effects.(Babiak & Pędzisz 2019)

### **Chronic osteoarthritis**

The chronic process of bone inflammation develops when the infected patient has co-occurring immune system disorders or the microorganism responsible for the infection is antibiotic-resistant.

Risk factors. Diabetes, immunosuppressive drugs, hip surgery, malnutrition, advanced age, alcoholism, nicotine addiction. Untreated acute bone inflammation can develop into chronic and there is no strict time limit between them.

Prevention. Raising public awareness of the threats posed by microbial infections, how dangerous they can be. In the case of acute inflammation, rapid response, implementation of appropriate antibiotic therapy to prevent the development of chronic inflammation.

Etiological factors are often beta-hemolytic streptococci, *Staphylococcus aureus*, mycobacteria and others, which are also responsible for causing osteomyelitis.

Diagnostics. Biopsy is necessary to differentiate from musculoskeletal tumors. Microbiological examination is necessary to apply appropriate antibiotic therapy. In laboratory tests, ESR is elevated, while CRP, leukocytosis and blood smear are usually normal. In an X-ray examination after more than a month, sclerosis can be observed, as well as necroses in a characteristic "coffin".

Treatment. Surgical treatment includes resection of infected bone and surrounding soft tissue, biopsy for microbiological and histopathological examination, closing of dead space and reconstruction of bone defect, fixation of bone fragments and administration of antibiotics taking into account information after culture.(Hryniewicz et al. 2013)

### **Periprosthetic infections**

These are rare complications after orthopedic procedures. They can end in limb amputation or even death due to sepsis. The percentage of implant infections is small, but the total number of such infections is growing every year. Studies have shown that most infections revealed within 2 years of the procedure result from intraoperative infection of the endoprosthesis.

Risk factors. Advanced age, over 80 years, alcohol and nicotine addiction, chronic inflammation of the skin and subcutaneous tissue, liver and kidney failure, taking immunosuppressive drugs, chronic malnutrition, active infection for over 3 months, previous injury or fracture in the joint area, impaired blood supply to the limb.

Prevention. Ensuring sterile conditions during procedures during which prostheses are inserted into patients.

Etiological factors. Depending on the microorganism causing the inflammation, as well as on when the infection began and on the most common symptoms, we distinguish 3 types: type I - the etiological factor is highly virulent strains of *Staphylococcus aureus*, Gram-negative rods, coagulase-negative staphylococci; type II the etiological factor is less virulent strains of coagulase-negative staphylococci, *Propionibacterium acnes*; type III - the etiological factor is virulent strains of *S. aureus*, beta-hemolytic streptococci, Gram-negative rods.

Diagnostics. The diagnosis is made after analyzing the clinical, microbiological and histological examination. Usually, the patient reports fever and rest pain, and in the history also mentions a past surgery. Increased ESR and CRP levels. In imaging studies: X-ray - massive osteolysis and periostitis, USG - fluid collection.

Treatment. We can treat in two ways, depending on the patient's condition, the time of symptoms from prosthesis insertion, its stability, the presence of a fistula and infiltration, as well as the etiology of the infection. We distinguish repeated surgical interventions, in the place where the prosthesis insertion procedure or suppressive antibiotic therapy was previously performed. (Nowakowski & Mazurek 2017)

#### **Disclosure:**

##### **Author's contribution:**

Conceptualization: Paweł Arkadiusz Malmur, Aleksandra Romanowska, Mateusz Dobosz; Methodology: Jakub Maciej Pieniążek, Weronika Biaduń-Mućko; Software: Paweł Arkadiusz Malmur, Kinga Rogowska-Borettini, Klaudia Arciszewska, Aleksandra Padkowska; Check: Kinga Rogowska-Borettini, Aleksandra Romanowska, Aleksandra Padkowska; Formal analysis: Weronika Biaduń-Mućko, Mateusz Dobosz, Kinga Rogowska-Borettini; Investigation: Aleksandra Romanowska, Paweł Arkadiusz Malmur, Klaudia Arciszewska; Resources: Paweł Arkadiusz Malmur; Data curation: Aleksandra Romanowska; Writing - rough preparation: Weronika Biaduń-Mućko, Kinga Rogowska-Borettini, Jakub Maciej Pieniążek; Writing - review and editing: Aleksandra Romanowska, Jakub Maciej Pieniążek, Klaudia Arciszewska, Aleksandra Padkowska; Visualization: Mateusz Dobosz, Paweł Arkadiusz Malmur; Supervision: Aleksandra Romanowska; Project administration: Aleksandra Padkowska, Mateusz Dobosz, Paweł Arkadiusz Malmur, Weronika Biaduń-Mućko.

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