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REVIEW

Septic arthritis in Western and sub-Saharan African children - a review

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Abstract This article reviews what is known about the incidence, aetiology, presentation, bacteriology and management of septic arthritis in children. It compares where possible the different presentations and characteristics of this condition in the Western and sub-Saharan African regions.

Résumé Cet article est une revue de ce qui est connu sur l'incidence, l'étiologie, la présentation, la bactériologie et le traitement de l'arthrite septique chez l'enfant. Il compare les différentes caractéristiques de ces arthrites entre les pays de l'ouest et les pays sub-sahariens.

Incidence

Septic arthritis in children is rare in the West and common in sub-Saharan Africa. There is little more detail on the incidence or prevalence than this in the published literature. In 1990 Shaw [106] in a review of septic arthritis in infancy and childhood reported that it is approximately twice as common as osteomyelitis in this age group, but that its relative incidence decreases, so that by adolescence the two conditions occur with a similar incidence. There are several reported studies of septic arthritis from the West and from sub-Saharan Africa [56, 65, 66, 79, 86], which again suggests that it is much more common in Africa. These reports all discuss patients that presented at single institutions, and none of them has a denominator or source population so that no accurate estimate of incidence can be made.

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Aetiology and pathogenesis

A few cases of septic arthritis occur because of direct inoculation of bacteria into the joint, through injury or snake or animal bites in a rural community or by iatrogenic causes such as hip infection following femoral artery puncture [84], but the majority of cases are believed to occur by internal dissemination of bacteria [77, 95]. The bacteria may arrive in the joint via the blood stream as haematogenous spread or by direct spread from adjacent structures. In the hip and the shoulder, part of the metaphyseal shaft is intra-articular, and osteomyelitis of the femoral or humeral shaft may spread to the adjacent joint [85]. Trueta [119] in 1959 showed that neonates have small transphyseal blood vessels which allow direct spread from the bone to the epiphysis and thus to the joint. These vessels disappear at around 6 months. This may explain the different pattern of the clinical appearance of septic arthritis between neonates and older infants. With the former it is more common to have an associated osteomyelitis, indeed in some series 60–100% of cases of neonatal septic arthritis have adjacent osteomyelitis [106].

The presence of bacteria in a synovial joint either by direct or haematogenous spread does not necessarily cause septic arthritis. Many children have a severe persistant bacteraemia, but do not develop septic arthritis [40]. It is likely that there is a combination of other factors involved in addition to the presence of bacteria. It is also very likely

that trauma is one of these factors. In many cases of septic arthritis there is evidence of preceding trauma, and it is a plausible theory that capillary stasis as a result of this trauma causes a nidus of infection that may develop into septic arthritis. Microtrauma at the capillary level may also reduce oxygen tension locally and decrease the efficiency of the natural humoral and cellular defence response [95]. The joints of the lower limb in the West are more commonly involved in trauma than the upper limb and have correspondingly more septic arthritis. Olney's work on rabbits [92] supports this theory, that microtrauma in the presence of a co-existing bacteraemia renders joints susceptible to infection.

When a blood-borne pathogenic bacteria arrives at a susceptible synovial joint a cascade of events is set in motion. The synovium is extremely vascular and contains no basement membrane, with the result that bacteria and white cells leak into the joint space [106]. Polymorphonuclear leucocytes are activated by the presence of bacteria and produce both collagenase and neutral and acid proteases [20, 21]. The white cells are not the only source of destructive enzymes as the synovial lining cells also produce enzymes [29], as do some bacteria, especially *Escherichia coli* and *Staphylococcus aureus* [112]. These proteolytic enzymes destroy the mucopolysachcharide ground substance of articular cartilege and allow collagen fibres in the cartilege to be further destroyed by friction as the joint moves. William Hunter had no knowledge of the existence of enzymes but gave an apt description 300 years ago when he noted in 1743 the destructive effects of sepsis on articular cartilage, stating:

> When a cartilage is inflamed and soaked in a purulent material, the connecting fibres will be the soonest to give way and the cartilage will become soft and red [53].

Today we know a little more about the mechanism, but the basic pathological description remains valid. Phemister in 1924 was an early worker in the field of joint infection and found that incubation of cartilage with *Staphylococcus aureus* alone did not result in any cartilage breakdown, but the addition of staphyloccal pus to the ferment caused destruction of the cartilage [99].

Smith [108] showed that cartilage destruction starts to occur as early as 8 h after infection. Early administration of antibiotics helps to slow down the process, but even if intravenous antibiotic therapy is started within the first 24 h of infection, significant glycosaminoglycan destruction and collagen disruption occurs. Potent inhibitors of these proteolytic enzymes have been found in joint fluid, so it is likely that there is a complex interplay of enzymes within the joint [42].

In addition to enzymes from bacteria, white cells and synovium, the chondrocytes themselves may also play a part in the destruction of cartilage. Ultrastructural analysis of chondrocytes in experimentally produced septic arthritis has shown an increase in lysosomal electron-dense bodies, suggestive of the production of proteolytic enzymes in both superficial and deep layers of articular cartilage. Chondrocytes, in common with polymorphonuclear leukocytes, have both neutral and acid proteases and may be stimulated to release these either by bacterial lipopolysacharides or by interleukin 1 (IL-1) [38, 57, 78].

The source of IL-1 is generally thought to be the monocyte [46]. IL-1 acts as an inflammatory hormone rather than having any intrinsic enzymic or degrading activity itself. It can lead to increased amounts of prostaglandin E and collagenase from both the chondrocyte and synovial cells. In mature cartilage without sepsis, chondrocytes respond to IL-1 by breaking down the surrounding proteoglycan matrix.

Recent work on joint destruction in septic arthritis suggests that in addition to the acute inflammatory mechanism above, there is also a delayed immune response that does not require viable bacteria. Arthritis can be induced experimentally in animals by systemic injection of bacterial antigens, such as peptidoglycans [41, 60]. These antigens are preferentially deposited in the synovial tissue of remote joints and incite a sustained immune response resulting in arthritis. Laboratory work with mice shows that strains of *Staphylococcus* that produce exoproteins (i.e., enterotoxin) cause more severe arthritis in infected joints than do strains that do not produce exoproteins [3]. Following on from this, it was discovered that specific inhibition of T-lymphocyte proliferation decreases the severity of arthritis, while generalised inhibition of the immune system increases the severity of arthritis [1, 2]. This leads to the possibility that bacterial antigens and bacterial exotoxins stimulate T-lymphocyte proliferation and that this can occur even though the bacteria have been killed. T lymphocytes then degrade the ground substance and destroy articular cartilage, thus playing a similar role in infective arthritis to that which they play in non-infective chronic arthritis [12].

Predisposing causes

Joint infection is perhaps surprisingly uncommon in HIV positive adults, but where it is found it is often associated with intravenous drug abuse, haemophilia and a CD4 count in the region of 250 [120]. Children who are HIV positive have an increased risk of septic arthritis [51], and anaemic, malnourished, underweight children in sub-Saharan Africa are also at high risk [65, 66, 79]. In adults, *Salmonella* septic arthritis is associated with systemic lupus erythema-

tosis (SLE), liver disease, schistosomiasis and avascular necrosis [17]. It has also been reported after iguana bites [91]. Salmonellosis, osteomyelitis and joint infections are also common in sickle cell disease [5]. The cause for this is probably the fact that intravascular sickling causes capillary occlusion, which devitalises and possibly infarcts the gut, permitting salmonella invasion. Reduced function of the liver and spleen together with interference of reticuloendothelial system function due to erythrophagocytosis also suppresses clearance of *Salmonella* from the blood stream. Abnormal opsonisation and complement function probably also play a role [5].

Clinical features

A child with acute septic arthritis is typically unwell, with a fever. The joint is usually swollen, warm to the touch and acutely painful. The pain is exacerbated by movement, and the child holds the limb still. The position of most comfort varies with the joint, thus the septic hip is held in slight flexion, external rotation and abduction, the knee in slight flexion and the shoulder in internal rotation and abduction. These positions represent the position of maximum joint volume and therefore minimum pressure. If the condition is not treated then the infection may spread to cause local cellulitis and swelling of the whole limb. The child may also become toxic. Having outlined the typical case, however, the infant and neonate with a less well-developed immune system may present with much less severe symptoms and signs. The clinician must be alert to the possibility of septic arthritis in an infant with a swollen joint, minimal pain and no or mild fever [106]. In the author's Zambian series several of the children presented with so called 'pseudoparalysis' [66]. The affected limb was floppy and not actively used. If it was examined there did not appear to be significant pain. There are no comparative figures on the prevalence of pseudoparalysis in Western and sub-Saharan children with septic arthritis, but it is the observation of many clinicians that it is relatively more common in Africa. This may be due to the poor nutritional state of patients in sub-Saharan Africa and to the reduction in immune response [25].

Joints involved

There is a major difference in terms of the site of infection between septic arthritis in children in the West and children from sub-Saharan Africa. The main reason for this is the large number of infections of the shoulder that are seen in sub-Saharan Africa. Jackson and Nelson reviewed 514 infected joints in 471 Western children and found the knee to be the most commonly affected with 41%, followed by the hip with 23%, the ankle with 14%, the elbow 12% and the wrist and shoulder 4% each [56]. In Gillespie's series of 102 children the shoulder only represented 3% [33]. Molyneux's series from Malawi in 1982 reported the shoulder as being involved in 28% of cases, second only to the knee with 51% [79]. In the author's own series from Zambia the shoulder was involved in 19 out of the 34 prospectively studied cases, representing 56% of all infected joints [66]. Molyneux is the only author to have proposed a mechanism to explain why the shoulder is so commonly involved. She has observed that mothers in sub-Saharan Africa carry their children on their backs and swing them up by the arm. She has postulated the theory that microtrauma to the joint may make it susceptible to seeding of infection when there is a bacteraemia [79].

Boys are more commonly affected by septic arthritis than girls [33, 65, 87]. There is no obvious reason for this gender difference, but it may be that boys are more likely to be involved in activities that lead to repetitive minor joint trauma [109].

Complications

Untreated septic arthritis can cause cartilage destruction by the mechanisms outlined above. Infection can then spread to the underlying growth plate, causing destruction of the physis with consequent loss of growth or tethering of the plate causing deformity [96]. Epiphyseal separation can also occur [7, 76]. Joint infection can also spread to the adjacent bone and cause osteomyelitis [6]. The presence of infection in the joint can cause a reactive capsular thickening which may reduce movement and result in fibrous ankylosis and even joint fusion. It may also lead to the opposite, namely capsular stretching and joint laxity or dislocation. Long-standing joint sepsis can discharge to the outside and cause chronic sinus formation and subsequent superinfection [6].

Bacteriology

In the West, septic arthritis may be caused by a wide spectrum of bacteria, but there is a definite age relation to the common pattern [77]. In neonates less than 2 months old infected in the community the common organisms are group B *Streptococci*, followed by *Staphylococcus aureus* and gram-negative rods. If the infection was acquired in the hospital situation then *Staphylococcus* is more common and is reported as being the cause in up to 62% of cases [22]. In

the infant from 2 months to 4 years in the West *Haemophilus influenzae* has in the past been reported to be the most common cause of septic arthritis [106]; however, with increasing and effective vaccination campaigns the influence of this bacterium is diminishing [11, 50] and *Staphylococcus* and *Streptococcus* are again the common causes [77]. Some authors also report an increase in the incidence of joint infection by *Kingella kingae*, which mirrors the decline of *H. influenzae* [63, 64].

High prevalence of *Salmonella* infections in sub-Saharan Africa

The picture is completely different in sub-Saharan Africa where *Salmonella* has a very high prevalence. It was cultured in 26 out of 34 (59%) of the author's cases in Zambia [66]. All of these children were under 3 years of age. *Salmonella* was grown in 40% of the culture-positive cases in Molyneux's Malawi series [79] and in 60% of the cultures in Ndauti's series in Kenya [86].

The reason for the high prevalence of *Salmonella* in septic arthritis is probably because it is the single most prevalent organism found in the blood of sub-Saharan children [69, 73, 89, 122]. Most cases of *Salmonella* bacteraemia are found in children between 6 months and 5 years of age, with the highest incidence between the ages of 10 and 14 months [39, 40]. It is also strongly associated with anaemia, poor nutritional status and malaria [39, 40, 69, 73, 89, 122]. In the author's Zambian series all the 26 children with *Salmonella* septic arthritis were anaemic and all were underweight [66]. It is thus likely that the high incidence of *Salmonella* septic arthritis is secondary to the high prevalence of *Salmonella* bacteraemia, which is in turn secondary to the poor nutritional status of the children in this part of Africa. The argument is strong if not compelling that *Salmonella* septic arthritis in sub-Saharan children is a disease of poverty.

Diagnosis

The diagnosis of septic arthritis is essentially clinical. It has already been discussed above that in young children, and especially malnourished children, there can be a less acute clinical presentation and diagnosis is more difficult. In well-nourished children with a normal immune response there is typically an elevated ESR and white cell count, but, as with the clinical appearance, in the anaemic underweight child these parameters may be normal. The author's Zambian series had many cases where the ESR and neutrophil count were normal [66]. Where C reactive protein (CRP) can be measured it has been reported as being more sensitive in both diagnosis and monitoring [121].

The definitive diagnostic test is bacteriological examination of the joint fluid collected by aseptic needle aspiration of the affected joint. This should be performed with a wide-bore needle (at least 20 gauge) to ensure adequate aspiration. The fluid should be gram stained, cultured, and white cells, glucose and lactate should be measured. The gram stain alone may confirm the diagnosis in up to 50% of cases [80]. It can also give guidance for early antibiotic selection before culture and sensitivity results are available. Some series report positive culture rates of as low as 60% [86]. However, other reports have positive culture rates of 80% [47]. Ike [54] suggests that increased efficiency of joint fluid culture can be obtained by the immediate transfer of the joint aspirate to blood culture bottles. The synovial fluid white cell count in septic arthritis is variable, ranging from 25,000 to 250,000 cells per millilitre; however, the differential consistently reveals around 90% polymorphonucleocytes [37, 48, 61, 84]. Synovial fluid glucose levels in septic arthritis decrease relative to serum glucose levels and are often below 40 mg per decilitre [37]. Comparisons between serum and joint glucose levels are often made harder because of time differences in sample taking and intravenous infusions in seriously ill patients, which may alter serum levels. Lactic acid levels in synovial fluid may be elevated, except in gonococcal infections [114]. Immunoelectrophoresis may be performed to look for antigens to *Haemophilus*, *Meningococcus*, *Strep. pneumoniae* and other bacteria [114]. PCR (polymerase chain reaction) assay, where it is available, may also be used to detect remnants of bacteria in the face of negative culture [54].

Imaging of infected joints is not easy. Plain X-rays often show no bony changes in the first 10 days of an infection. There may, however, be evidence of a widened joint space relative to the uninvolved side [106]. This increased space, and the fluid that is causing it, can also be demonstrated with ultrasound scans. Radioisotope scanning using technetium or gallium- or indium-labeled white cell scans may be performed, but are not generally very helpful in the diagnosis as they can be positive in both septic arthritis and adjacent osteomyelitis. [9, 47, 117]. Some authors, however, are more optimistic about their usefulness [6]. Computerised tomography (CT) and magnetic resonance imaging (MRI) scans are seldom used in the diagnosis of septic arthritis, but if available can show the presence of fluid in the joint and early changes in the adjacent bone. They may also show reactive changes or spread of infection to the surrounding tissues. MRI can also differentiate between septic arthritis and transient synovitis [68].

Differential diagnosis

This includes chronic infections such as tuberculosis and fungal infections, trauma, juvenile chronic arthritis and other non-infective arthropathies, rheumatic fever, adjacent osteomyelitis, sickle-cell disease, haemophilia, neoplasi, and Henoch Schonlein Purpura [106]. Mechanical problems also need to be considered, including Perthe's disease and slipped femoral epiphysis in the hip, and cartilage problems or other causes of internal derangement in the knee.

Treatment

The above review of the literature shows that septic arthritis involves an inflamed joint that contains bacteria and pus. On purely empirical grounds it has long been felt that the treatment should involve removal of the pus as rapidly and as completely as possible and that this should be combined with the administration of antibiotics. Few authors would disagree with that outline. However, the method of draining the pus remains a matter of considerable debate [49]. The general principle of removing pus from an infected joint is not questioned and is usually assumed to be self evident, although as with many established ideas in medicine, there is no prospective study evidence that removal of the pus gives a better outcome than leaving it in the joint. As with many long-established ideas in medicine, it is now difficult to question and it would be hard to get ethical permission to conduct a study that compared removing pus to leaving it in the joint.

There are a number of possible ways of removing the pus, ranging from invasive surgery where the joint is formally opened via minimally invasive surgery such as arthroscopy [8], so-called tidal irrigation [55], where the joint is aspirated then saline or other lavage fluid is washed in and out of the joint through wide bore needles, and simple aspiration. There has never been a prospective comparison of all the above methods of removing pus, or even a prospective comparison between any of them. Different authors tend to favour their chosen method. Goldenburg [35] and Lane [63] have both observed that the method of pus removal offered to a patient with septic arthritis depends largely on the specialty of the clinician under whom the patient is admitted. Patients being looked after by paediatricians and rheumatologists tend to have needle aspiration, while patients looked after by surgeons have a surgical method of pus removal. Advocates of their own methods make claims for their particular technique; for example, Parisien [94] claims that arthroscopy "is the most reasonable alternative to repeated aspirations or arthrotomy in the management of pyarthrosis in accessible joints". Chung [18] also advocates arthroscopy and gives examples of successful treatment, but offers no control group.

Other authors have written case reports of successful treatment by one or another of the methods of pus removal [31]. Goldenburg in 1975 tried to throw light on the controversy and wrote a retrospective review comparing needle aspiration to surgery as modes of initial drainage [35]. Broy in 1986 returned to the same question and reviewed the literature from 1959 to 1984 to find the answer [15]. Neither paper was conclusive. In 1993 Ho entitled his editorial "How best to drain an infected joint. Will we ever know for certain?" [49]. Three years previously Shaw in a major review of acute septic arthritis [106] described open surgical drainage as the "gold standard" for removal of pus, against which all other methods are measured. Bertone in a study on septic arthritis in horses showed that arthrotomy eradicated joint infection more completely than arthroscopy, but that secondary wound infection was a problem [8]. Nord, in a study on septic arthritis in goats, showed that giving antibiotics with arthrotomy, or athroscopy, or needle aspiration or even just giving antibiotics on their own gave similar results [90]. These last two studies are interesting attempts to solve the problem, but they involve an animal model, and it is questionable as to whether their results hold for humans.

Some authors have concluded that aspiration is a satisfactory method for all joints except the hip, and others that the hip joint can be satisfactorily aspirated [123]. Many take the midline view that they will start with joint aspiration, and if it fails then move on to surgery [48]. It is hard to escape the observation that there is as yet no clear answer to this question.

How antibiotics are administered and for how long are two more questions for which there are no definitive studies. Most clinicians agree that intravenous antibiotics are advised in the early stages, with a change to oral when the patient is apyrexial. Many clinicians also give antibiotics for 4 to 6 weeks, but again there is no scientific backing for this period. There is animal evidence that steroids administered with antibiotics may have a protective effect in reducing cartilage damage [115].

After the pus has been removed and antibiotics have been given, most clinicians will allow the patient to move the joint as the pain allows. One of the fathers of British orthopaedics, Robert Jones, had a dictum that rest after infection of a joint should be "prolonged, uninterrupted and enforced" [104]. This has gradually been discarded as Salter in a seminal study on rabbits in 1981 showed that continuous passive motion gave improved clinical and pathological results after joint infection and injury [104]. The study has not been repeated in humans, but early movement has become the accepted practice. It will probably never be tested because

of the difficulty of restraining people, especially children, who want to move, and because of the many other advantages of being active.

Prognosis

Septic arthritis is a serious condition in any part of the world. The potential for major complications makes its diagnosis and early treatment an emergency. There is no doubt that the major factor in the improved management of septic arthritis in the last century was the discovery of antibiotics. In 1920 the mortality for a child with septic arthritis was around 10%, and this was reduced to less than 1% by 1970 [33]. There have been no prospective studies looking specifically for prognostic factors in septic arthritis; nevertheless, certain factors have regularly been associated with poor outcome. These are as follows:

- Age less than 1 year [49], which is probably due to immaturity of the immune system.
- Joint site, especially the hip and the shoulder, and polyarticular infections [24]. The shoulder and the hip both have an epiphysis that is completely contained within the joint and perhaps more vulnerable to infection and vascular embarrassment, and they both have intra-articular metaphyseal bone. Thus, the spread of infection from adjacent osteomyelitis is possible. The presence of infection in more than one joint may indicate a reduced host response to infection, which is itself likely to be linked to a worse prognosis.
- Underlying serious illness, e.g., renal failure, diabetes, cirrhosis and malignancy [49]. A poor outcome in this group is likely to be due to the combination of chronic disease and acute infection.
- Immunosuppressive drugs, e.g., corticosteroids and cytotoxic agents [24]. This is only to be expected as the drugs reduce the body's ability to resist infection.
- Long duration of symptoms and long delay in treatment [83, 108]. If the degree of damage to the joint by bacterial and other enzymes is related to the length of time these enzymes are in action, then delay in treatment is likely to be detrimental to the outcome.
- Virulent organisms, especially *Staphyloccus aureus* and gram-negative bacilli [34]. This may be due to associated cell-mediated immunity caused by bacterial exoprotein.

The above factors are taken from literature relating to patients from the West, but are likely to be of relevance also to the prognosis in septic arthritis in sub-Saharan Africa.

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