Osteoarticular infections in young children: what has changed over the last years?

Dimitri Ceroni, Georgios Kampouroglou, Rebecca Anderson della Llana, Davide Salvo

Paediatric Orthopaedic Unit, Department of Child and Adolescent, University of Geneva Hospitals and University of Geneva Faculty of Medicine, Switzerland

Summary

Osteoarticular infections remain a significant cause of morbidity worldwide in young children. They can have a devastating impact with a high rate of serious and long-lasting sequelae, especially on remaining growth. Depending on the localisation of infection, they manifest as osteomyelitis, septic arthritis, a combination of both (i.e., osteomyelitis with adjacent septic arthritis) or spondylodiscitis. Osteoarticular infections can be divided into three types according to the source of infection: haematogenous; secondary to contiguous infection; or secondary to direct inoculation. During the last few years, many principles regarding diagnostic assays and the microbiological causes of these infections have evolved in a significant manner. In the present current-opinion review, we discuss recent concepts regarding epidemiology, physiopathology, and the microbiology of bone and joint infections in young children, as well as clinical presentations, diagnosis, and treatment of these infections. Clinicians caring for children need to be especially well versed in these newer concepts as they can be used to guide evaluation and treatment.

Key words: osteoarticular infection; osteomyelitis; acute; sub-acute; chronic; arthritis; spondylodiscitis; Kingella kingae; PCR assay; treatment

The respiratory tract: the breeding ground of pathogenic agents?

Direct inoculation into the bone or joint by bacteria via trauma, surgical reduction and internal fixation of fractures, spread from soft tissue infection, or nosocomial contamination are unusual occurrences in young children. Most osteoarticular infections (OAI) are primarily haematogenous in origin and result from symptomatic or asymptomatic bacteremia [1]. It is therefore important to recall the main portal of entry into the bloodstream for pathogens causing OAI in young children. Among all portals of entry, the respiratory tract is probably the most favourable to pathogens. Microorganisms can be found on droplets of moisture in the air and even in dust particles, and many diseases use this portal of entry.

The normal flora of the oropharynx contains a large population of common bacterial inhabitants. The most important group of microorganisms includes Streptococcus mitis, S. mutans, S. milleri, and S. salivarius. It is believed that these bacteria act as antagonists against invasion by potentially pathogenic microorganisms such as S. pneumoniae, S. pyogenes, Haemophilus influenzae type b (Hib), Neisseria meningitidis, or even Staphylococcus aureus. In addition, cultures from this region also show the presence of large numbers of diphtheroids, Moraxella catarrhalis, Neisseria species, and HACEK organisms (a group of gram-negative bacilli comprising Haemophilus spp., Actinobacillus actinomycetemcomitans, Cardiobacterium hominis, Eikenella corrodens and Kingella spp.) [2].

Invasive infections in young children are thus frequently caused by organisms carried asymptomatically in the respiratory tract [3, 4]. S. pneumoniae, Hib, N. meningitidis, S. aureus, and K. kingae may reside in the mucosal surface and are able to penetrate the bloodstream, disseminate, and invade distant organs [3, 5, 6]. Therefore, colonisation of the respiratory tract by these organisms is a prerequisite for later invasion, and human populations with high rates of carriage of these pathogens are also at increased risk of acquiring disease [3, 5–7]. However, oropharyngeal carriage of pathogens does not imply the subsequent development of invasive OAI, but it suggests that other co-factors may play a role in the
pathogenesis of invasive infections [8]. In addition, available evidence suggests that interactions occur with viral infections. Concomitant upper respiratory tract infection and stomatitis, including varicella-induced oral ulcers, are frequently present in affected patients, especially for *K. kingae* [2]. It appears that microorganisms colonising the oropharynx penetrate a mucosal layer previously damaged by a viral disease [9] and then progress throughout the airways, causing lower respiratory tract infection and/or invasion of the bloodstream [9]. Transient benign bacteremia may follow and the bacterium might be seeded in the joint space, bone, or intervertebral discs, resulting in a focal suppurative infection [9].

**Pathogens responsible for OAI**

The type of infecting pathogens for OAI depends on the age of the child and any associated medical problem. Apart from *S. aureus*, OAI with gram-negative organisms, Group B *Streptococcus*, and *Candida* are common in neonates. In children younger than 4 years, the reported number of cases of *K. kingae*-associated OAI has markedly increased since the 1980s. Indeed, several studies have demonstrated that *K. kingae* has been revealed to be the major bacterial cause of OAI in children aged between 6 and 48 months (30% to 93.8% of all culture-positive OAI) [8–14]. This now brings a coherent explanation to the fact that prior to the use of polymerase chain reaction (PCR) assays, 20 to 70% of OAI cases were culture-negative, despite the collection of blood, joint fluid, and bone for standard cultures [1, 15]. Although *S. aureus* is no longer considered as the most common cause of OAI in children aged less than 5 years, methicillin-sensitive *S. aureus* (MSSA) remains the most common pathogen responsible for OAI in older children. Since the use of penicillin in the early 1940s, OAI caused by methicillin-resistant *S. aureus* (MRSA) has become an increasingly common problem in the USA [15–18], even if MSSA is still the most common pathogenic organism. In addition, the emergence of Panton-Valentine leukocidin-positive (PVL+) community-acquired (CA-) MRSA and MSSA infections has been observed. OAI caused either by CA-MRSA or by MRSA/MSSA PVL+ have a more serious presentation, more complications, and require a more aggressive treatment than those due to MSSA [18–20]. Apart from *K. kingae* and *S. aureus*, other organisms causing OAI in young children include *S. pyogenes* and *S. pneumoniae*. Children with OAI due to *S. pyogenes* often have a previous history of varicella infection and usually present with a higher fever and white blood cell (WBC) count compared with those infected with *S. aureus* [1]. Children with OAI caused by *S. pneumoniae* are younger than those infected with *S. aureus* and *S. pyogenes* [1, 21, 22]. They are more likely to have joint involvement, spread of infection into the epiphysis, and thus subsequent disturbed epiphyseal growth (fig. 1) [1, 21, 22]. The incidence of Hib as a pathogen for OAI in young children has decreased noticeably as a result of an effective immunisation programme against this organism [1]. Hib invasive infections, such as OAI, are now rare in completely immunised children, but the onset of OAI due to Hib is not exceptional (fig. 2), considering on the other side that other serotypes are reported to cause bone and joint infections [1]. Young children with sickle cell disease have been reported to be particularly susceptible to OAI [1]. Causative organisms include *Salmonella*, *S. aureus* and, less commonly, *Escherichia coli*, *Shigella*, and *S. pneumoniae*.

**Osteomyelitis**

Osteomyelitis is an inflammation of the bone caused by infection involving bone and/or bone marrow with bacterial or fungal organisms. Osteomyelitis may take diverse forms and several classification systems have been developed to describe this condition. One of these focuses on the source of infection and distinguishes between osteomyelitis arising from haematogenous seeding and osteomyelitis secondary to spread of a contiguous focus of infection or vascular insufficiency [23]. However, osteomyelitis caused by contiguous spread of infection is rare in young children and those secondary to vascular insufficiency remain exceptional. A second system distinguishes between acute,
sub-acute, and chronic osteomyelitis based on the elapsed time between the onset of symptoms and diagnosis, irrespective of the underlying source of the offending pathogen [23, 24].

Acute haematogenous osteomyelitis

Acute haematogenous osteomyelitis (AHO) is defined as an infection diagnosed within two weeks of the onset of symptoms [23]. The incidence of AHO in children is 0.2–1.6/1000 children/year [25]. Approximately 50% of cases of AHO occur in the first 5 years of life [1]. Osteomyelitis in young children is generally of haematogenous origin and acute in most cases. Boys are more likely than girls to be affected and acute haematogenous osteomyelitis typically arises in the metaphysis of long tubular bones, with approximately two-thirds of all cases involving the femur, tibia, or humerus [1, 23, 26]. A seasonal variation can be observed with the hospital admission rate for osteomyelitis peaking in late summer and autumn. Clinically, trauma to the affected part can be observed in up to 50% of children who have AHO [27] and injury probably has an effect on decreasing resistance to infection.

Dysfunction of the immune system is another factor that has been observed to be associated with AHO. This is well illustrated by the increased susceptibility to infection in children with diseases characterised by deficient or altered immune function, in the neonate with an immature immune function, or during specific situations that may cause temporary and transient depression of the immune function (e.g., intercurrent viral illness, surgery, or malnutrition). Due to its rich vascular supply in young children, the metaphysis of the bone is most often involved. Two vascular characteristics contribute to the translocation of germs through the capillaries at this location. First, vessels beneath the physeal plate are small arterial loops that empty into venous sinusoids, resulting in a turbulence of the blood flow [28]. In addition, the endothelium wall of the metaphyseal capillaries has gaps that allow the passage of bacteria. Translocated pathogens then find locally favourable conditions to proliferate as they are not phagocytised, due to the absence of phagocytic cells in this region of the bone.

Once on site, the microorganism replicates and causes suppurative inflammation. Various inflammatory factors, bacterial toxins, and leucocytes themselves, contribute to tissue necrosis and the destruction of bone trabeculae and bone matrix [23]. Vascular channels are compressed and obliterated by the inflammatory process and the resulting ischemia also contributes to bone necrosis [23]. As a result, antibiotics and inflammatory cells cannot reach this vascular area; for this reason, surgical incision and drainage should be considered, especially when an abscess is present in the bone, sub-periosteally, or in the soft tissue [26]. Surgical intervention may enhance treatment as it may halt the phenomenon responsible for bone necrosis. It permits removal of devitalised bone and debridement of affected soft tissue, whereas surgical irrigation probably decreases the bacterial load. Thus, a surgical procedure should be considered not only when a child does not respond to empiric antibiotic therapy, but each time when pyogenic pathogens are thought to be responsible for AHO.

Sub-acute haematogenous osteomyelitis

Primary sub-acute haematogenous osteomyelitis (PSAHO) is an infectious process characterised by insidious onset, moderate localised bony pain, mild or no systemic manifestations, non-contributory laboratory results, negative blood cultures, and positive radiologic findings [29–39]. According to King and Mayo, any osseous infectious process of more than two weeks duration without acute symptomaticity can be referred to as sub-acute osteomyelitis [36]. PSAHO is most likely due to an atypical host-pathogen relationship that may comprise any combination of increased host resistance, decreased virulence of the causative organism, and/or prior antibiotic exposure [31, 32, 38, 40, 41]. The primary form of sub-acute HO, which occurs mainly in children, must be distinguished from osteomyelitis modified by inadequate or partial treatment with antibiotics and from other forms of the condition, such as chronic recurrent multifocal osteomyelitis and the SAPHO syndrome (synovitis, acne, pustulosis, hyperostosis, and osteitis) [42]. In many cases, cultures fail to identify the causative organism, especially when fine-needle aspiration is performed. Surgical drainage may yield positive cultures in 40% to 75% of patients. Some reports have suggested an increasing incidence of this form of osteomyelitis [35] and a higher prevalence in certain countries [34]. PSAHO can be divided into two main clinical forms according to the age of the child and its bacteriological aetiology. The first form, the infantile form, affects children aged between 6 months to 4 years. Approximately 90% of all PSAHO affect patients in this age group with K. kingae as the main observed microorganism (personal data to be published). In these young children, the clinical course of PSAHO is most likely explained by the natural low virulence of K. kingae. K. kingae osteoarticular infection is characterised by a mild-to-moderate clinical and biologic inflammatory response to infection with few (if any) criteria evocative of OAI. Many children in this age group are usually recognised late as having an osteoarticular infection, and an accurate diagnosis is generally delayed until after a bony lytic lesion has occurred (fig. 3). The second

Figure 3
Magnetic resonance imaging (MRI) of the distal femur of a 17-month-old boy, which showed a normal appearance on plain radiographs. MRI demonstrated a lytic lesion of the distal femoral epiphysis with an important abscess of the soft surrounding tissues. Specific cultures confirmed tuberculosis.
form, the juvenile form, affects children older than 4 years and *S. aureus* appears as the main bacteriological aetiology. In this situation, PSAHO is most likely the result of an increased host resistance and it can be hypothesised that the children who develop this resistance against *S. aureus* become able to contain the bone infection. Indeed, colonisation is recognised to be more frequent among children [43]. Remarkably, 20% of individuals are persistently colonised by *S. aureus* in the nares and 30% are transiently colonised [44]. Although colonisation predisposes an individual to *S. aureus* infection, colonised individuals may have less severe *S. aureus* disease compared with non-colonised individuals [45]. This raises the question as to whether colonisation could induce low level, adaptive immunity and subsequent milder infections [44].

PSAHO in children follows a benign course and the recommended treatment for sub-acute osteomyelitis with radiographic evidence of lucent lesions or nidus is currently curettage, biopsy, and culture followed by antibiotics [9–11, 46]. Many authors even suggest that antibiotics alone may be adequate and that surgery should be considered only for “aggressive lesions”, as well as those that do not respond to antibiotics [6, 41]. However, it is generally agreed that treatment should not be initiated until proper drainage and bacteriological samples have been obtained [9–11, 46]. In children less than 4 years, antibiotic therapy should be directed above all against *K. kingae*, whereas *S. aureus* is the bacteria most often associated with PSAHO in older children.

**Chronic osteomyelitis**

Osteomyelitis is considered chronic if the duration of the illness has been more than 3 months [26]. Chronic osteomyelitis is defined by the presence of residual foci of infection, which give rise to recurrent episodes of clinical infection. Chronic osteomyelitis is therefore a persistent infection of bone and bone marrow due to the presence of intracellular bacteria [47], which allows the pathogens to escape to the immune system and invade adjacent bone cells [48]. In developing countries, the disease usually results from untreated acute HO. In developed countries, chronic osteomyelitis remains fortunately a rare condition generally encountered after open traumatic injuries or as a complication of surgical procedures, such as open reduction and internal fixation of fractures. Chronic osteomyelitis may also result from specific medical disorders, such as immunodeficiency or sickle cell disease. Finally, chronic osteomyelitis may be part of the characteristics of other forms of the condition, such as chronic recurrent multifocal osteomyelitis and the SAPHO syndrome. Eradication of the infection is often very difficult and complications associated with both the infection and treatment are frequent.

**Septic arthritis**

Septic arthritis is an infection of the joint space by means of haematogenous dissemination of bacteria into the vascular synovium. Rates of septic arthritis are estimated to be between 5.5 and 12 cases per 100,000 children with a peak incidence in the early years of the first decade [1]. However, most cases of septic arthritis occur in children 3 years old or younger. Again, boys are affected twice as much as girls as they are probably more likely to be involved in activities leading to repetitive minor joint trauma. The hip and knee are the most common sites of septic arthritis and symptoms include acute onset of joint pain, fever, irritability and limp.

An acute inflammatory response follows bacterial spreading of the joint, resulting in the migration of polymorphonuclear WBCs, production of proteolytic enzymes, and cytokine secretion by chondrocytes. If the infection is not quickly cleared by the host, the potent activation of the immune response, in association with high levels of cytokines and reactive oxygen species, increase the release of host matrix metalloproteinases and other collagen-degrading enzymes, which in conjunction with bacterial toxins lead to joint destruction [49]. The polymorphonuclear response with subsequent release of these proteolytic enzymes can initiate degradation of articular cartilage 8 h after the onset of infection and lead to permanent destruction of the intra-articular cartilage and sub-chondral bone loss in as little as three days [49]. In addition, metalloproteinases and the antigen-induced inflammatory response may persist and continue to damage the joint architecture even after the infection has been cleared [50, 51]. To ensure a good prognosis, treatment of septic arthritis not only requires prompt recognition and rapid and aggressive antimicrobial therapy, but primarily surgical irrigation of the joint in order to clear the factors responsible for the potent activation of the immune response.

**Septic osteoarthritis**

There are a few situations in which an infectious process affecting the metaphysis can spread into the joint and result in osteoarthritis. In certain anatomical sites, the bony metaphysis is intracapsular and any bone infection may potentially lead to osteoarthritis, with concomitant osteomyelitis and septic arthritis. Osteomyelitis of locations, such as the upper end of the femur, proximal humerus, proximal tibia, and distal fibula, are more prone to spread sub-periosteally into the joint space. By contrast, the epiphyses of children younger than 18 months are vascularised by transphyseal vessels [52]. As these vessels enter the epiphysis and thus potentially the joint space, young children are more prone to have a higher risk of joint space infection complicating osteomyelitis [1]. Clinicians caring for children less than 18 months should keep in mind these anatomic characteristics as they must be used to guide evaluation and treatment. As an example, a very young child with an AHO of the proximal femur must be suspected to have a spread of the infection into the joint space. In this case, surgical treatment must not only focus on the bone treatment – irrigation of the joint is probably the most important surgical procedure as it will decrease the potent activation of the immune response responsible for the joint damage. By contrast, AHO must be considered when facing a situation of septic arthritis as treating only the septic arthritis will expose these very young children to recurrence of the infection.
**Spondylodiscitis**

Childhood spondylodiscitis remains an uncommon and often missed ailment in young children from 6 to 48 months of age. The diagnosis should be considered in toddlers who present with refusal to walk, gait disturbances, back pain, or even abdominal pain [53–55]. The pathophysiology remains controversial. Some authors regard it as an infective process of the intervertebral disc or endplates [56–59], whereas others consider it as a self-limiting inflammatory condition [60–65]. Childhood spondylodiscitis represents a continuum of spinal infections ranging from discitis to vertebral osteomyelitis, with occasional associated soft tissue abscess [54]. These entities likely fall within a broad spectrum of manifestations of a single disease with varying severity. A few studies highlighted a triphasic age distribution with varying signs and symptoms according to age. Thus, spondylodiscitis in childhood should be classified according to three separate age groups, namely neonates, infants, and older children [56, 57, 60, 61, 63, 66, 67]. The form affecting neonates (less than 6 months) is the most serious manifestation of the disease and is often associated with septicemia and multiple infectious foci. The vertebrae are classically severely damaged and sometimes entirely destroyed, leading to major kyphosis, especially when the thoracic spine is involved [66–68]. Neurologic findings are most likely to occur in this age group. Approximately 80% of spondylodiscitis in neonates are due to *S. aureus* [66, 67]. The second infantile form affects children from 6 months (end of maternally-derived immunity) to 4 years of age. This age group represents 60% of childhood spondylodiscitis [53, 56–60, 62, 63, 65, 67, 69–75]. When performed, the vast majority of biopsies come back sterile [57, 60, 64, 72, 74] or positive for *K. kingae* [53, 67]. Finally, in the third form affecting children older than 4 years, patients are more prone to sustain vertebral osteomyelitis [57, 59, 70]. This age group is also likely to be febrile and ill-appearing, and *S. aureus* is the predominant pathogen. Laboratory findings in spondylodiscitis, such as WBC count, C-reactive protein, and erythrocyte sedimentation rate, often provide non-specific information [54, 70, 73]. Blood cultures are usually the only means available to direct antimicrobial therapy, but unfortunately yield a high percentage of negative results [54, 60, 70, 73, 75]. The indication for more invasive procedures, such as biopsy or needle aspiration, is currently not established, especially in young children [53]. The literature reports success rates for the identification of the causative organism ranging from 0% to 63% for needle aspiration and open biopsy, respectively, [64, 67, 75–77]. However, these interventions are still not regarded as standard diagnostic procedures for most authors due to surgical and anaesthetic risks.

**Osteoarticular tubercular infections**

The incidence and prevalence of paediatric tuberculosis worldwide varies significantly according to the burden of the disease in different countries. Europe and North America are traditionally considered as low burden regions, and paediatric incidence rates vary from 1 to 15/100,000/year [78]. Tuberculosis of bones or joints occurs in around 5% in cases of paediatric extrapulmonary tuberculosis and, classically, tubercular OAs occur one to three years after pulmonary infection. Vertebral lesions (thoracic>lumbar>cervical) are probably the most common involvement and 80% of these affect more than one vertebrae. In decreasing order, other common sites are: hips; knee; ankle and foot; hand and wrist; elbow; shoulder; bursal sheaths; and other bones [79]. Tubercular OAI is rare, but not exceptional in Switzerland (fig. 4) and it must be considered when a very young child presents a clinical picture of subacute osteomyelitis with a mild-to-moderate clinical and biologic inflammatory response to infection. In general, contamination is intra-familial due to close proximity with elderly individuals from regions where the prevalence of tuberculosis is high (e.g., Balkans, Africa, India). Finally, immunocompromised children and those seropositive for human immunodeficiency virus (HIV) are supposed to be at high risk of exposure, as well as manifesting tubercular disease. The synergy of HIV and tuberculosis and the emergence of multidrug-resistant *Mycobacterium tuberculosis* have further complicated the issue.

**Culture detection of pathogens**

The yield of cultures has been significantly improved by inoculating clinical specimens into aerobic blood culture vials [80, 81] from a variety of automated or manual blood culture systems, such as BACTEC (Becton Dickinson, Cockeysville, MD, USA), Bact/Alert (Organon Teknika Corporation, Durham, NC, USA), Isolator 1.5 Microbial Tube (Wampole Laboratories, Cranbury, NJ, USA), or Hemoline DUO (bioMérieux Lyon, France). However, no controlled study has been performed to identify the best blood culture system for this purpose [9]. The primary isolation of any fastidious pathogens such as *K. kingae* from joint, bone, or blood samples appears strongly dependent on the methodology used [46]. Indeed, the recovery of *K. kingae* from purulent specimens seeded onto solid culture media is suboptimal and mostly results in a frustrating proportion of negative cultures [8–11, 46].

![Figure 4](image-url)

**Figure 4**

Sub-acute transphyseal osteomyelitis of the distal radius due to *K. kingae* in a 5-year-old boy who suffered from a chickenpox (varicella) infection three weeks before bone infection. This viral infection was considered as a predisposing factor for the development of osteomyelitis due to *K. kingae* resulting from a modulation of the immune system function.
Detection of pathogens by PCR assay

PCR is a biochemical technology in molecular biology to amplify a single or a few copies of a piece of DNA across several orders of magnitude, generating thousands to millions of copies of a particular DNA sequence (Wikipedia). Recognition of pathogens responsible for OAI by PCR assays has now become a common procedure, especially for fastidious microorganisms. There are currently two different nucleic acid amplification approaches. Broad-range 16S rRNA gene assay involves extracting DNA from clinical samples, incubating the DNA with broad-range oligonucleotide primers that anneal to constant regions of the 16S ribosomal RNA gene, and amplification of the intervening sequence, which varies according to the bacterial species [82]. The resulting amplification products are either sequenced and compared with sequences in the GenBank database or hybridised with organism-specific probes [83]. The use of the broad-range 16S rRNA gene assay offers the tremendous advantage of not requiring any a priori knowledge of the causative bacteria. However, this method is hampered by an insufficient sensitivity to detect all agents directly from clinical samples as the analytical sensitivity of the broad range 16S rRNA gene PCR is only 300 colony-forming units (cfu) [84]. In recent years, real-time PCR assays that amplify specific targets for most osteoarticular pathogens have been developed. Currently, real-time PCR assays that amplify K. kingae-specific targets, such as cnp60 or RTX toxin genes, have been developed and are associated with high reliability [8, 10–13, 84]. Real-time PCR assays specific to K. kingae targets, such as the RTX toxin, are 10–fold more sensitive than the broad-range 16S rRNA gene PCR (30 cfu vs 300 cfu) [84].

Antibiotic selection and treatment’s modalities

Successful treatment of osteoarticular infections depends on the appropriate selection and administration of antibiotic therapy and surgical procedure as needed [1]. Empiric therapy is usually selected to cover the most likely pathogens, which are determined above all by the age of the child, by local prevalence of specific infectious agents, and early laboratory results such as stain if available. When the culture’s results are then available, the antimicrobial therapy is modified depending on the organism and the susceptibility pattern. Absorption and penetration into the bony tissue, the joint, or the intervertebral disk should be satisfactory, and time-dependant antibiotics with a short circulating half-life are more likely to require frequent dosing [85]. Infants less than 6 months old with osteoarticular infections should be treated with antibiotics that have excellent coverage against S. aureus, S. agalactiae, and enteric gram-negative bacteria. In children aged between 6 months and 4 years, most of OAI are due to K. kingae. In Switzerland, as in Europe and Israel, there are very few beta-lactamase-producing clones of K. kingae and thus, beta-lactams are the drugs of choice for OAI due to this microorganism, as well for those due to S. aureus, S. pyogenes or S. pneumoniae. Finally, most of OAI in children are still exceptionally due to MRSA in our country and thus, the decision to cover empirically for MRSA is currently controversial due to concerns over developing resistances, costs, and potential complications with use of vancomycin. For spondylodiscitis, the situation is some confusing since there is no agreement in the literature regarding the antibiotics’ ability to enter discs in an active form. In fact, the antibiotic’s ability to spread through all parts of the disc is not only influenced by the vascular supply and structure of the disc (size and health), but also by the properties of the drug (size, solubility, binding and charge) [86]. The antibiotic’s charge in particular has been discussed in the literature, since the nucleus pulposus is rich in glycosaminoglycans and has a high density of negative charge [86]. Thus, it has been postulated that positively charged antibiotics (gentamicin or vancomycin) can enter the IVD, whereas negatively charged antibiotics (penicillin and cephalosporins) have limited [87–89] or poor penetration [90] because of repellant charges.

The length and route of treatment depend above all on the pathogen’s virulence, as well as the clinical and laboratory response to treatment (decreases of pain, fever, CRP, and ESR). Most of OAI in children could be converted to oral antibiotics between 3 or 5 days, and there are currently probably few advantages with antibiotic courses that are prolonged for more than 3 weeks. In countries such as the United States, where MRSA is a common pathogen and when the clinical setting is suggestive for an OAI due to MSSA PVL+, a more cautious conservative approach is probably well founded.

How to recognise K. kingae OAI

If K. kingae is currently considered as the most common cause of OAI in young children, most of these infections still remain unrecognised. Diagnosis requires a high index of suspicion since the presentation of K. kingae OAI is often characterised by a mild-to-moderate clinical and biologic inflammatory response to infection, with the consequence that these children present few, if any, criteria evocative of OAI [2]. Improving recognition of infection due to K. kingae is thus the next problem to resolve and there is a need for new diagnostic tests to improve their diagnosis. For example, a simple technique to detect K. kingae RTX toxin genes in the oropharynx might provide strong evidence that this microorganism is responsible for the OAI [91]. The positive predictive value of PCR detection in a pharyngeal sample is around 90%; however, the negative predictive value of this test is very high and failure to detect RTX gene sequences in the pharynx practically excludes the bacterium as the aetiology of the OAI [91, 92]. Such a non-invasive approach to diagnosis improves patient safety and comfort and reduces healthcare costs by reducing the need for invasive diagnostic procedures. A recent paper has also demonstrated that magnetic resonance imaging was useful in differentiating OAI due to K. kingae from those due to gram-positive cocci. In this study, epiphyseal cartilaginous involvement and modest soft tissues and bone reactions were suggestive for AHO due to K. kingae. There is also the need to have a criterion for distinguishing quickly OAI due to K. kingae than those due to pyogenic pathogens. A model to allow the differenti-
ation of K. kingae OAI from those due to typical pathogens in children aged less than 4 years, has been described and consists of the following four parameters: T° at admission <38°; C-reactive protein <55 mg/L; WBC count <14,000 leucocytes/mm³, and band shift <150 forms/mm³ [10]. This model is a subject of controversy, but it underlines the need for prospective studies to better define the clinical presentation according to the children’s age and causative organisms.

Conclusion

During these last years, the use of PCR assays has completely changed the microbiological ecology for OAI in young children. More than 50% of cases of OAI occur in the first 5 years of life and K. kingae has become the major bacterial cause of infection in this age group. The clinical presentation of K. kingae OAI is often subtle and may be associated with normal acute-phase reactants. Treatment of OAI is usually instituted empirically before the causative agent and its resistance pattern is known. The timing of surgery depends on the suspected pathogen and on the extent of the OAI. Trepanning an infected bone, draining an abscess, or washing the joint space might speed up the healing process. Aggressive debridement should be considered in difficult-to-treat cases of MRSA or when MSSA/MRSA is producing PVL. Any less virulent microorganisms, such as K. kingae, usually do not require a surgical procedure. There is also the need to have criteria for distinguishing quickly OAI due to K. kingae than those due to pyogenic pathogens.

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Correspondence: Dimitri Ceroni, MD, Paediatric Orthopaedic Unit, Department of Child and Adolescent, Children’s Hospital, 6 Rue Willy Donzé, CH-1211 Geneva 14, Switzerland, dimitri.ceroni[at]hcuge.ch

References

Figure 1
An 8-month-old boy sustained osteoarthritis of the left hip due to Streptococcus pneumoniae. Six months after the infection, the epiphysis had completely disappeared, confirming that children with osteoarticular infection due to S. pyogenes are more likely to have joint involvement, spread of infection into the epiphysis, and thus subsequent disturbed epiphysial growth.
Figure 2

Acute pendiaphysitis of the right humerus with an important sub-periosteal abscess in a 16-month-old girl. The osteomyelitis was due to Haemophilus influenzae type B despite the child being completely immunised.
Figure 3

Magnetic resonance imaging (MRI) of the distal femur of a 17-month-old boy, which showed a normal appearance on plain radiographs. MRI demonstrated a lytic lesion of the distal femoral epiphysis with an important abscess of the soft surrounding tissues. Specific cultures confirmed tuberculosis.
Figure 4

Sub-acute transphyseal osteomyelitis of the distal radius due to *K. kingae* in a 5-year-old boy who suffered from a chickenpox (varicella) infection three weeks before bone infection. This viral infection was considered as a predisposing factor for the development of osteomyelitis due to *K. kingae* resulting from a modulation of the immune system function.