

Septic arthritis in children

L'artrite settica in età pediatrica

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Abstract

Osteoarticular infections are a form of diagnostic and therapeutic emergency in infants and children, even if relatively rare.

Despite decades of experience with different protocols, and multiple clinical trials, today it is still difficult to determine what kind of antibiotics is really effective, what kind of associations are required, which is the optimal time range of a treatment, when and on which subjects to base the transition from a parenteral treatment to an oral one.

Current philosophy aims more and more at reducing hospitalization and costs, and wants to decrease the discomfort in the family. The purpose of these guidelines is to promote a reasoned clinical and therapeutic approach, in a context of diagnostic probabilities that offer the best chance of success in reducing hospitalization with a rapid transition to an oral treatment, and then outpatient, and thus educing totally the processing time.

Introduction

Osteoarticular infections are a form of diagnostic and therapeutic emergency in infants and children, even if relatively rare. Without a precocious and properly aimed antibiotic treatment there is the risk of a local and general septic expansion, and the possibility of some serious articular outcomes. The more the articular involvement is precocious, the more we can run risks of some adverse outcomes.

Despite decades of experience with different protocols, and multiple clinical trials, today it is still difficult to determine what kind of antibiotics is really effective, what kind of associations are required, which is the optimal time range of a treatment, when and on which subjects to base the transition from a parenteral treatment to an oral one.

In literature there are only a few studies reporting the incidence of septic arthritis in childhood (S.A.).^{9, 14, 27, 39, 40}

As for the frequency, based on age, Lechevalier reports that AS is present for 63% to <5 years, 49% <3 years and for 31% <2 years; on the contrary Valdiserri³⁸ for 80% < 4 years and 50 <1 year.

The most frequently affected sites are knee and hip with a variable incidence, according to various authors^{9, 13, 25, 27, 30, 38, 39, 40} (Table 1). The pathogenesis of SA has been not yet totally clarified, despite the numerous histological and histochemical studies (Schenk,²⁹ Whallen,⁴² Tudisco, Ippolito, and others³⁶). There were some hypohthesis concerning the vascular tissular osteo-articular anatomy during the period of children's growth, the main mechanism of inoculation, the virulence of the pathogen agent, the epidemiology in nursing infants and young children, bacteremia and, finally, concerning the role of trauma during this age.³² In infants and young children the location is typically epiphyseal and, while in older children metaphyseal. These different locations are the consequence of the special blood vessels at the extremity of long bones. Thanks to their studies concerning the vascularization of the proximal femoral epiphysis, Trueta³¹⁻³⁵ and Chung⁸ show how, before the appearance of the proximal epiphyseal ossification nucleus, epiphyseal vessels originate directly from metaphysis, while after the appearance of the ossification nucleus, a vascular autonomous epiphyseal net develops, while vascular vessels disappear.³⁵ Metaphysis of long bones, in

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Table 1

EPIDEMIOLOGY OF SEPTIC ARTHRITIS

Frequency of septic arthritis

Stott 2001	0,06/1.000/year
Wang 2003	0,05/1.000/year
Rasmont 2008	0,12/1.000/year
Lechevalier 1996	0,63/1.000/year

young children and infants, is almost entirely made up of spongy bone extremely rich in vessels tissue, with fetal-type circulation and voluminous capillary loops and large venous lakes, that are connected with the epiphyseal .

An infection of blood in the first months of life may propagate to the epiphyseal cartilage and quickly destroy the nucleus, whose subsequent development may be definitely compromised. Therefore acute arthritis in infants constitutes a separate chapter because of its anatomical peculiarities. For example the capsule, in the hip, is eccentrically inserted and the epiphyseal plate, and a part of the metaphysis, are intra-articular. In this way an infectious process, localized in the metaphysis, may spread to the epiphysis and become intra-articular or may invade directly the articular environment.

Table 2

CLINICAL SIGNS AND RELATIVE PERCENTAGE

Fever	40% – 90%
Articular pain	81% – 93%
Hydrarthrus	72% – 85%
Limping (knee, hip)	43%
Painful limitations of joint mobility	64% – 75%
Pseudoparalysis	90% newborn
Flush	86 %
Erythema	55 %

Table 3

BLOOD PARAMETERS

Marked polynucleosys +++	40%
ESR +++	89%
PCR +++	89%
Prealbumin	

Table 4

INTRAVENOUS ANTIBIOTICS TREATMENT

Empirical treatment using broad spectrum intravenous antibiotics (Gram positives + Gram negatives)	
Monotherapy	Association
beta-lactam (Cloxacillin)	Amoxicillin + Clavulanic acid
Cephalosporin II (Cefamandolo o Cefuroxime)	Vancomycin + Rifampicin (for MRSA)
Cephalosporin III (Ceftriaxone)	Monotherapy + Gentamicin (age < 3 months)

Table 5

MOST COMMON ISOLATED GERMS

	Newborn	Children
Stafilococcus Aureus	+++	+++
Stafilococcus Coag neg	-	++
Stafilococcus Methicillin resistant	Acquired in community	
Streptococcus pneumonia	++	-
Haemophilus influenza b	-	++
Group b Streptococci	+	++
Pseudomonas aeruginosa	-	++
Escherichia Coli	+	-
Klebsiella Kingae	-	+++
Enterobacter	+	+
Salmonellae	+	++

The immuno-biological fragility of newborn and infants is a facilitation factor.

The carrier of germs is essentially hematogenous, rarely cutaneous or by maternal infection.

Guidelines (Table 1): It is well known that AS heals in most cases with antibiotic therapy, but an antibiotic treatment should be implemented in high doses, intravenously and for prolonged periods (4-8 weeks).¹⁶ Current philosophy aims more and more at reducing hospitalization and costs, and wants to decrease the discomfort in the family. The analysis of recent literature shows us that we can rationalize the therapeutic approach in infants and children to osteo-arthritis through the help of what is current knowledge in epidemiology, bacterial sensitivity to major antibiotics, while the most recent clinical results have shown the same efficacy of a parenteral antibiotic therapy longer or inferior to the duration of 7 days.¹⁷ Current guidelines refer to common acute osteo-articular infections, not complicated in healthy infants and children, of hematogenous origin, with usual not well-identified bacteria or, as it often happens, not identified, excluding unusual germs of complex inoculation routes such as post-operative infections, or direct inoculation after bites and trauma, in chronic or complicated forms, or special situations such as severe host immunocompromise.^{13,16} The purpose of these guidelines is to promote a reasoned clinical and therapeutic approach, in a context of diagnostic probabilities that offer the best chance of success in reducing hospitalization with a rapid transition to an oral treatment, and then outpatient, and thus educing totally the processing time.

These recommendations are based on these essential points:

Rapidity in diagnosis

Knowledge of commonly involved bacteria, and their response to antibiotics

The results of clinical studies published in literature

The evaluation of the effectiveness of general and local treatment.^{13, 20}

Materials and methods

In front of a baby or a child with a suspected septic arthritis, the criteria for a correct diagnosis are clinical, laboratory and instrumental.

The *clinical data* are represented by fever, articular pain, hydrarthrus, painful limitations of joint mobility, pain on palpation of the limb, pseudoparalysis of the interested limb in newborn (Table 2).⁵

In *blood parameters* (Table 3) is always present:

marked polynucleosys

ESR level greatly increased

PCR level already and early increased. This parameter is crucial to follow the evolution of the infection: its decrease is indicative of the efficacy of the therapy; in absence of a decrease, a modification of the antibiotic therapy is required. Normalization is not a sufficient

criterion of recovery.^{6, 7}

Finally it may be useful to test the Prealbumin to study the nutritional status of the newborn. In Table 3 there are reported the percentages of positive results, keeping in mind that the association of at least two clinical and blood signs gives a 91% in sensitivity and a 95% in specificity.^{10, 30}

At the same time before moving to a deeper bacteriological understanding it may be useful to perform an *ultrasound instrumental examination*. Ultrasonography increases in importance because of its safety and repeatability, even though it requires an experienced operator for its performance. Ultrasound may influence the presence and type of endoarticular collection (Fig. 1) and permits to follow the evolution of the infection in the newborn and to understand the damage to the epiphyseal nuclei, especially that of the upper femur.^{15, 19, 24, 28} At a metaphyseal level it shows the presence of eventual subperiosteal abscesses. Later on it shows the periosteum far from the bone with a slight intermediate zone for the presence of an anechoic abscess. It finally allows to guide properly, specially in the less superficial areas, the evacuating puncture.

In special cases a bone scan can be performed but its use is still very controversial because some false negatives have been described that can be interpreted as indicative of a more serious index due to some important local circulatory disorders, that prevent the penetration of the tracer.¹

After ultrasound it becomes essential to isolate the responsible germ of the infection.

It can be done through:

systematic peripheral sampling (navel, urine, ENT)

blood cultures (positive in 40-60% of cases)

evacuating puncture: it is practiced in emergency and permits to collect liquid for cell culture and to decompress the joint. The germ is isolated in only 50-60% of cases.

An evacuating puncture must be repeated every 48 hours to evacuate the joint and to decrease the endoarticular pressure and doing like this the buffering effect it can have on the capsular vessels, with a possible consequent epiphyseal necrosis. It also allows to inject an antibiotic directly into the joints.

However, if the ultrasound shows the presence of pus in the articulation, we must effect an *arthrotomy* above all in neonates and young children, as most authors suggest.

In this way it can be done an articular wash too, that can get away all the articular bacterial toxic products that cause a fall in the rate of collagen necessary to maintain a good mechanical strength of the cartilage.

In more recent years arthroscopy is being considered more and more useful, especially for knee and shoulder because it grants a more rapid functional recovery. Postoperatively we need to leave a redon-drainage, and also to practice a restraint for analgesic aim.¹¹ After articular lavage, we can start an empirical treatment using broad spectrum intravenous antibiotics (Table 4) while expecting to know the responsible germ. It should be noted that if we start an antibiotic treatment late the risks for serious possible osteo-cartilaginous damages are higher.^{3, 37}

Table 6

WHEN THE RESPONSIBLE GERM IS IDENTIFIED, AN INTRAVENOUS ANTIBIOTIC THERAPY WILL BE CONTINUED FOR 4-7 DAYS

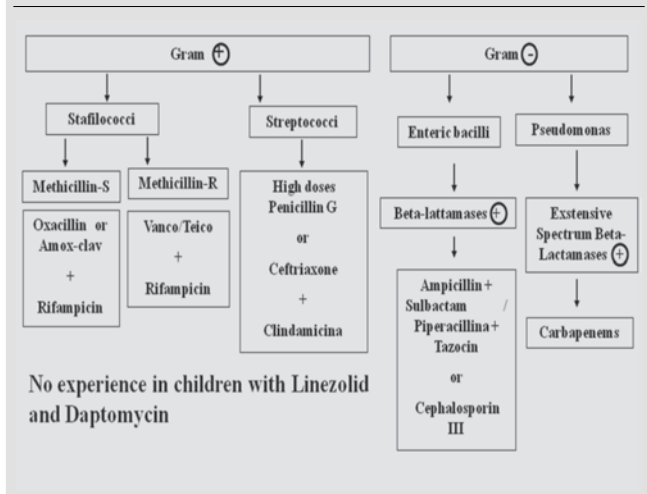


Table 7

WHEN THE GERM IS NOT ISOLATED

Not isolated germs

we will continue an intravenous broad-spectrum antibiotic therapy enhanced or modified if we don't get a positive response

Monotherapy	Association
beta-lactam (Cloxacillin)	Amoxicillin + Clavulanic acid
Cephalosporin II (Cefamandolo o Cefuroxime)	Vancomycin + Rifampicin (for MRSA)
Cephalosporin III (Ceftriaxone)	Monotherapy + Gentamicin (age < 3 months)

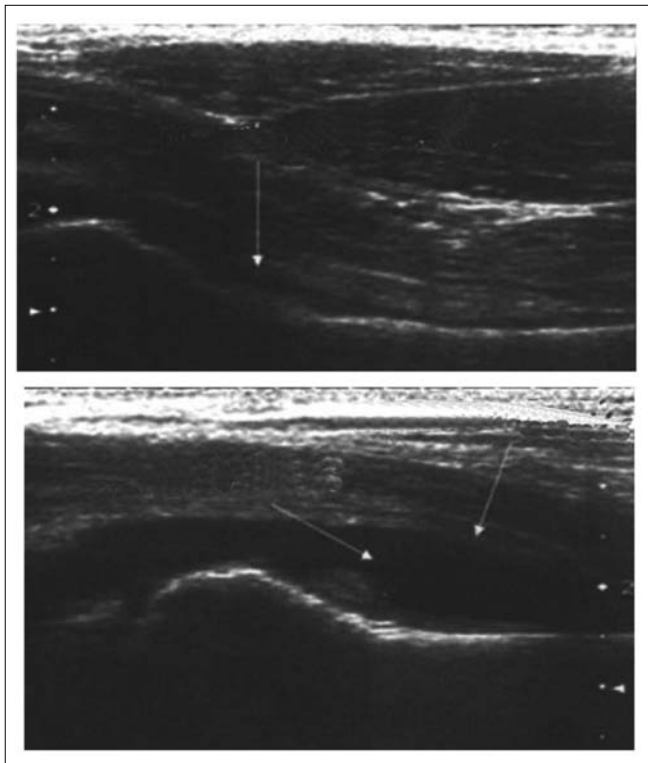


Figure 1.

the image above shows a normal hip ultrasound, the lower showing the presence of an abscess

The most common isolated *germs* are:

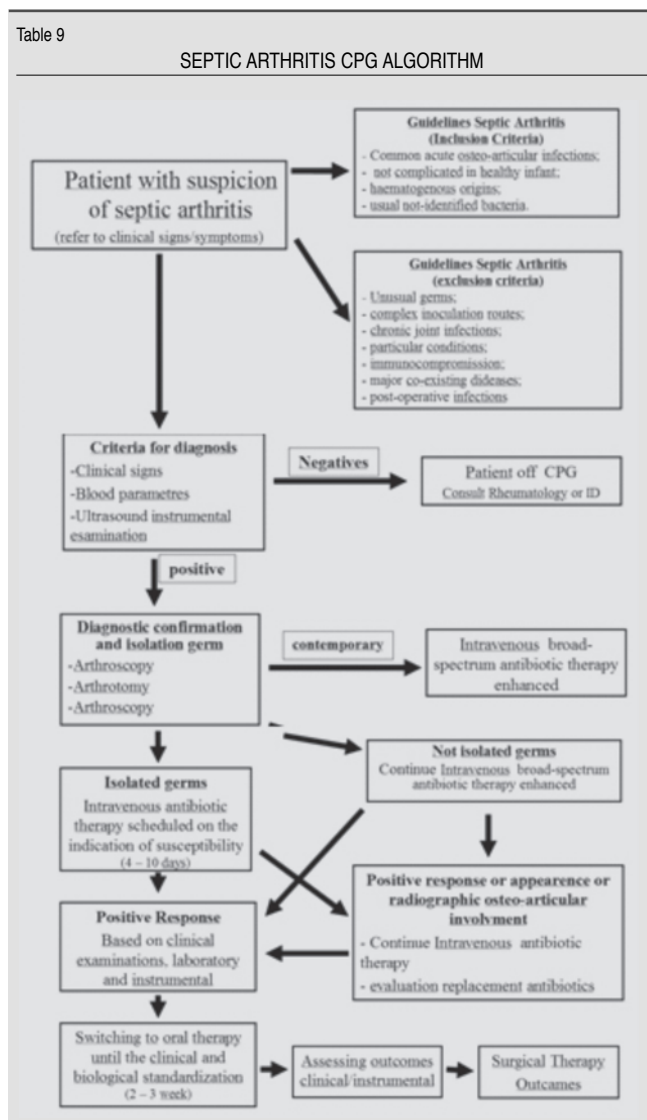
Staphylococcus aureus in 70% of cases there is now a consequence of a strain of multidrug-resistant nosocomial infection that is the source of the most important osteo-cartilaginous destruction.

Beta-hemolytic streptococcus group B in 10 -25% of cases seems to increase today, but the clinical and biological frame is good and with a benign functional prognosis.

the *Haemophilus influenzae* in 10-15% of cases, often associated with an infection of the airways from 3 months of age.

Pneumococcus more rarely than *haemophilus* but with the same characteristics

Table 8	
THE RISK FACTORS	
Age < 1 year	
Location: Hip, Knee and elbow	
The aggressiveness of the germ	
The beginning of treatment (>4 days of infection)	
Serology ++++	



Candida albicans, particularly in intensive care, in malnourished infants or in parenteral nutrition after a gastro-intestinal tract intervention.

Rarely *Proteus*, *Escherichia coli*, *Pseudomonas*, *Klebsiella*, *meningococci*, *enterococci*, etc. (Table 5) can be isolated.^{12, 21-23, 43}

If the responsible germ is identified, an intravenous antibiotic therapy will be scheduled on the indication of susceptibility and continued for 4-7 days (Table 6) if, as often happens, the germ is not isolated, we will continue an intravenous broad-spectrum antibiotic therapy enhanced or modified if we don't get a positive response (Table 7).^{13, 37}

Assessment of a therapeutic response: Even in this case the parameters to take into consideration are clinical, laboratorial and imaging. After 3 and 7 days a clinical and biological balance will be achieved. The improvement in symptoms, the value of CRP and ESR are good indexes of a response to therapy.

As regards the instrumental balance, according to some authors, the first radiographic signs may appear after only 24-48 hours, but most of the authors argued that they appear between 4 and 10 days. The early radiographic signs may have hard evidence. A first sign is the soft-tissue edema associated with a disappearance of muscular physiological interstices, later to a swelling of periarticular soft tissue and the presence of an eccentric head of the femur in hip due more to reflected muscle contracture of the adductors than to endoarticular effusion. After 8-10 days the signs appear such as geodes metaphyseal bone sign of local interests, more or less complete disappearance of the epiphyseal nuclei and periosteum detachment, sometimes significant in the infant. In older children the first radiographic signs stand out more late (10-15 days).

In relation to the possibility of multiple asymptomatic outbreaks we need for infants a complete radiographic systemic osteo-articular examination on day 15.

CT and MRI may have an important role in defining the involvement of both bone and cartilage epiphysis in the evolution of physical outcomes.^{15, 18}

Depending on the appearance or absence of radiographic signs, clinical and laboratorial response, intravenous antibiotics duration may vary according to different authors from 4 to 10 days. It will follow an oral antibioticotherapy duration of 2-3 weeks until the normalization of serological data.

Outcomes: After a treatment well conducted in emergency, outcomes are rare. Wang⁴¹ reported the risk factors related to age, location, serology if much altered, the aggressiveness of the germ and the beginning of treatment (Table 8). The outcomes can be represented by epiphyseal, physeal, and metaphyseal alterations.^{15, 26, 43}

In case of epiphyseal interest we can get even to an epiphyseal extended necrosis and a dislocation of the hip. If the growth of the cartilage is involved, it can develop some asymmetric epiphysiodesis which can lead to osteoarticular deformities or, if it is involved, all the physis can lead to remarkable shortenings of the interested bone.^{2, 25, 38}

There were many classifications of outcomes especially for the hip and the knee.

At the same time, many interventions have been proposed for their correction (Table 9).⁴

All these actions can admit some shared indications or not, but all the authors agree on the necessity to

- proscribe an equalization of limb lengthening on an unstable hip
- avoid attempts to delay surgical reduction of the hip
- not to carry out arthrodesis, for the advent of prosthesis.
- not to make a joint mobilization under general anesthesia.

Conclusions

The frequency and severity of outcomes, and the therapeutic difficulties that they show, once more underline the importance of urgency in the empirical antibiotic therapy and the evacuation of joints, which remain the key pillars of the treatment of septic arthritis.

The gold standard we should aim at is to obtain a mobile and indolent joint even if not perfectly stable in the case of the hip.

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