■ INSTRUCTIONAL REVIEW: CHILDREN'S ORTHOPAEDICS

Haematogenous acute and subacute paediatric osteomyelitis

A SYSTEMATIC REVIEW OF THE LITERATURE

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A delay in the diagnosis of paediatric acute and subacute haematogenous osteomyelitis can lead to potentially devastating morbidity. There are no definitive guidelines for diagnosis, and recommendations in the literature are generally based on expert opinions, case series and cohort studies.

All articles in the English literature on paediatric osteomyelitis were searched using MEDLINE, CINAHL, EMBASE, Google Scholar, the Cochrane Library and reference lists. A total of 1854 papers were identified, 132 of which were examined in detail. All aspects of osteomyelitis were investigated in order to formulate recommendations.

On admission 40% of children are afebrile. The tibia and femur are the most commonly affected long bones. Clinical examination, blood and radiological tests are only reliable for diagnosis in combination. *Staphylococcus aureus* is the most common organism detected, but isolation of *Kingella kingae* is increasing. Antibiotic treatment is usually sufficient to eradicate the infection, with a short course intravenously and early conversion to oral treatment. Surgery is indicated only in specific situations.

Most studies were retrospective and there is a need for large, multicentre, randomised, controlled trials to define protocols for diagnosis and treatment. Meanwhile, evidence-based algorithms are suggested for accurate and early diagnosis and effective treatment.

Acute and subacute haematogenous osteomyelitis in children is potentially devastating, with a high morbidity.[1,2] Delay in diagnosis and inappropriate treatment can result in sepsis, chronic infection, disruption of longitudinal bone growth and angular deformity.[2,3] Correct and timely treatment improves outcome; however, with evolving microbiology, including the emergence of methicillin-resistant *Staphylococcus aureus* (MRSA), early selection of the correct antibiotic is vital.

There are no definitive guidelines for the diagnosis and treatment of paediatric osteomyelitis, and recommendations are based on expert opinions, case series and cohort studies. We performed a systematic review of the literature in order to identify trends in causative organisms and formulate evidence-based recommendations for diagnosis and treatment.

Materials and Methods

The databases examined were MEDLINE (Medical Literature Analysis and Retrieval System Online), CINAHL (Cumulative Index to Nursing and Allied Health Literature, Ipswich, Massachusetts), EMBASE (Exerpta Medica Database, Amsterdam, The Netherlands), the Cochrane Library without date restriction up to 31 December 2010, and the search engine Google Scholar. The keywords used were 'p(a)ediatric', 'osteomyelitis', 'infection', 'bone infection', 'antibiotics', 'drainage' and 'surgery'. The articles were selected in two stages. First, the title and abstract of all citations identified by the above searches were downloaded and the list was narrowed using the inclusion/exclusion criteria in Table I. Secondly, the full texts of this short list were retrieved and similarly evaluated for eligibility. The most common reason for exclusion at the second stage was because the results for osteomyelitis were indistinguishable from those for septic arthritis in articles on osteoarticular infections. The reference lists of reviewed studies were searched for any additional relevant articles, and these were subjected to the same two levels of screening. Two independent reviewers (JD, MK) examined the citations with regard to their eligibility, and any doubts were resolved by discussion. Figure 1 indicates how the final papers were selected.

Information from the articles was stored in a spreadsheet and the methodology of each was discussed. The total number of patients involved in these studies was > 12 000. This is an approximate number as several of the

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doi:10.1302/0301-620X.94B5.28523 $2.00

J Bone Joint Surg Br 2012;94-B:584–95.

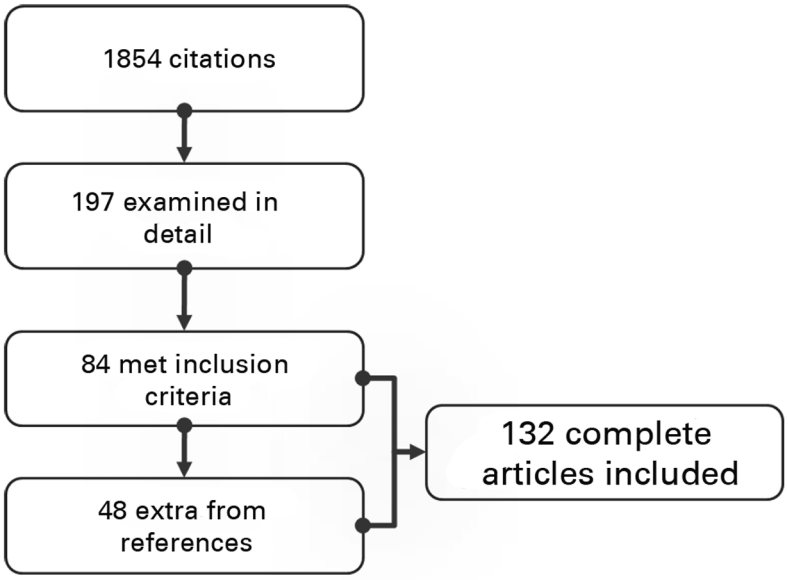

Fig. 1

Flow diagram showing the identification of relevant articles.

Table I. Inclusion and exclusion criteria

Inclusion	Exclusion
Randomised studies	Patients > 18 years old
Observational, retrospective studies	Case series < 20 patients
Controlled clinical trials	Studies not on osteomyelitis e.g. septic arthritis
Meta-analyses	Review articles
English language articles	Chronic osteomyelitis

Table II. Epidemiology of paediatric osteomyelitis

		Notes
Incidence		Uncommon but nearly twice that of septic arthritis[71]
Developed countries	1.94[71] to 13[77]/100 000	
Developing countries	43/100 000 (Polynesia[78])	
	200/100 000 (Aborigines[5])	
Children < 3 years	28/100 000[77]	
Mean age (yrs)	6.6	40% of cases occur in pre-school age children[4,53,58,81]
Pelvic	10.2[18,68,79]	
Calcaneal osteomyelitis	2.9[80]	
Male:female	1.82:1	
Risk factors (%)		
Unknown	47.0	
Blunt trauma	29.4	
Recent systemic infection	37.4	

research groups published repeatedly on similar cohorts. A large part of the data interpretation is purely descriptive, and statistical analysis comparing studies was only possible where there was full documentation of results.

Results

Epidemiology. This is summarised in Table II. Whereas several studies report a > 50% fall in incidence over 20 to 30 years,[3-5] others report either little change or an increase.[4,6,7]

Table III. Presenting features

Symptom	Incidence* (%)
Pain	81.1
Localised signs/symptoms	70.0
Fever	61.7
Reduced range of movement	50.3
Reduced weight-bearing	49.3

* values were calculated using studies that provided adequate information to produce overall figure

Table IV. Skeletal distribution of osteomyelitis

Site	Incidence* (%)	Site	Incidence (%)
Femur	*26.9*	Vertebra	*3.8*
Tibia	*26.0*	Fibula	*3.7*
Pelvis	*9.2*	Hand	*2.0*
Humerus	*8.1*	Clavicle	*0.8*
Foot	*7.7*	Rib	*0.6*
Forearm	*4.8*	Patella	*0.2*
Calcaneum	*4.6*	Other	*1.6*

* values were calculated using studies that provided adequate information to produce overall figure

Table V. Summary of inflammatory markers (WCC, white cell count; ESR, erythrocyte sedimentation rate; CRP, C-reactive protein)

Marker	Abnormal on presentation (%)	Normalisation time (wks) (presuming effective treatment)	Significantly influenced by*	Peak day(s)	Sensitivity/Specificity
WCC	*35.9*	2[13,43]	MRSA[14] Streptococcus pneumonia Group A strep[15,16] Concurrent septic arthritis[13,17]		Low – especially in young children[84]
ESR	91 *100* (with concomitant septic arthritis)	3 to 4[11,25,38,57]	MRSA[14,38] Concurrent septic arthritis[13]	3 to 5[57]	0.96/0.6[84]
CRP	*80.5* *100* (with concomitant septic arthritis)	1[11,25,38,57]	MRSA[14,38,45] Concurrent septic arthritis[13,20]	2[25,38,57]	

* influenced by: higher values and longer to normalise. MRSA, methicillin-resistant *Staphylococcus aureus*

Sickle cell disease (SCD). This is a known risk factor owing to its effect on the microvasculature causing bone infarction. The skeletal distribution is similar to that in non-SCD patients, with long bones predominating,[8] but multifocal osteomyelitis is more common.[8,9] Only two articles were specific for osteomyelitis related to SCD,[8,9] although there were several in excluded reviews. The principal causative organism is either *Staph. aureus* or *Salmonella*, with no definitive evidence favouring either. If an organism is not isolated on culture, the antibiotic chosen should cover both.[8]

Symptoms and signs. The clinical features are shown in Table III and vary significantly depending on the site of infection. Pelvic osteomyelitis is especially difficult to diagnose, with an mean delay of 12 days reported.[10] A fever of > 37.5°C for more than seven days and localised signs or symptoms beyond ten days suggest that a complicated course is more likely.[11]

Skeletal distribution. The distribution of osteomyelitis is shown in Table IV. The majority of osteomyelitis occurs in the metaphysis owing to the blood flow characteristics of its sinusoids.[12] No additional information was available to allow further analysis of the specific location of osteomyelitis within a bone.

Inflammatory markers. The characteristic changes in white cell count (WCC), erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP) in paediatric osteomyelitis are summarised in Table V. It was not possible to determine the mean values for each, as studies varied in their definitions of normal values and used different techniques for analysis. Therefore, using the definition of an individual study, the proportion of patients presenting with raised markers was used.

No studies looked specifically at the WCC response in different age groups. This varies greatly depending on the organism and whether there is concurrent septic arthritis, thereby making it the most useful marker in alerting the clinician to the possibility of an unusual or particularly virulent organism or concurrent septic arthritis.[13-17]

Although the ESR and CRP levels are not affected by gender, the involved bone, previous courses of antibiotics[11,15] and a raised ESR may indicate abscess formation. A retrospective study of 38 cases of pelvic osteomyelitis found a significant correlation between the presence of an abscess and an ESR > 55 mm/h.[18] Similarly, a larger study of 199 children with generalised osteomyelitis found no periosteal abscesses or pyomyositis with an ESR < 22 mm/h, and recommended further imaging if the ESR was higher.[19]

The CRP is the most useful marker in the blood for helping to distinguish between osteomyelitis alone or osteomyelitis complicated by septic arthritis.[11,13,20] A study of

Table VI. Summary of imaging for osteomyelitis

	Sensitivity	Specificity	Positive predictive value	Advantages	Notes
Radiography[19,24,84]	16% to 20%	80% to 100%	96%	Cheap, easily obtainable and safe way of monitoring disease progression[24,25]; do not use to prompt treatment changes[21]	Abnormal admission X-rays (not soft-tissue swelling) seen less often in acute osteomyelitis but in 67% to 100% of subacute osteomyelitis (bone destruction, lytic lesions and periosteal reaction/elevation)[67,85-87]
Tc99 bone scan[12,24,77]	53% to 100%	50% to 100%	39% to 82%	No anaesthetic, widely available. Good for localising lesion(s)	5% to 18% positive scans are cold and patients need aggressive treatment[28,29]
MRI[12,24,31,77]	80% to 100%	70% to 100%	84% to 93%	No radiation Identifies local complications: abscess or joint/physeal involvement	
CT[12,24]	67%	50%	65%	Best at demonstrating cortical destruction, bone gas and sequestrum but these are often absent until later stages	Reserved for when other investigations are not possible or inconclusive
Ultrasound scan[24]	55%	47%	82%	Reliable, cheap, quick, non-ionising and easily obtainable. Good aid in deciding if surgery is required and in differentiating between osteomyelitis and soft-tissue abscesses, cellulitis and pyomyositis[48,88]	If treated non-surgically, repeat ultrasound scans are useful to monitor abscess resolution or progression.[33] Improvement on ultrasound and falling C-reactive protein (CRP) correlates well with clinical findings.[48] Sensitivity and specificity are high for detecting complications (74% and 95%, respectively)[24]

44 patients comparing the CRP and ESR levels between patients with osteomyelitis alone and those with concurrent septic arthritis found that 40% of patients with both on admission had a CRP > 100, which increased to 70% the following day, compared to 19% and 14%, respectively, in those with osteomyelitis alone.[20] The same trend was seen with the ESR but at a slower rate, making it a less useful indicator. A prospective study of 33 patients showed that a CRP > 100 mg/l on admission was the best predictor of the need for more than six days of intravenous antibiotics.[21] Also, it has been shown that a CRP > 10 mg/l was significantly associated with a subperiosteal abscess or pyomyositis, and neither was present with a CRP < 36 mg/l.[19] From Costa Rica, a scoring system based on clinical evaluation and regular CRP monitoring predicted those likely to develop complications early (within two months) or late (> six months) with a sensitivity and specificity of 0.86 and 0.81, and 0.92 and 0.69, respectively.[22] These authors also reported on a cohort of 63 patients, of whom those with a CRP > 100 on day four of treatment were significantly more likely to have a complicated course both clinically and radiologically.[11] Similar findings were shown recently whereby an increasing CRP on or after day four should alert the clinician to the possibility of a complication.[23]

Imaging. Plain radiographs are essential to exclude other pathologies, and those taken two weeks after the onset of disease are more likely to be abnormal, as changes can take two to three weeks to develop in long bones and even longer (four to six weeks) in flat bones.[24-27] The advantages and disadvantages of imaging options in osteomyelitis are shown in Table VI.

Tc99 bone scintigraphy. Direct comparison of individual studies is not possible because of the use of different scanning techniques, and particular care must be taken in neonatal osteomyelitis and patients with SCD, where sensitivity is reduced.[28]

In contrast with other series, a recent study reported that nearly half of bone scans showed a false negative result.[19] Such scans are thought to be due to a transitional phase in the disease process from decreased to increased cellular activity, and repeat scans of previously negative patients with osteomyelitis are nearly always positive.[12] Therefore, where other imaging modalities are not available, a repeat scan may be considered. False positive scans are usually due to soft-tissue infection overlying normal hyperaemic bone.[28]

Patients with positive cold scans have higher fevers and blood markers, positive cultures (86% compared with 57% with hot scans[29]), and need surgery more frequently, and therefore should be treated aggressively.[28,29] This may be due to abscess formation causing raised intra-osseous pressure, which then increases further if a subperiosteal abscess exerts extramedullary pressure. This leads to medullary thrombosis as the microcirculation is compressed and compromised. Also, thrombophlebitis of local blood vessels causes ischaemia, which makes it more difficult for systemic antibiotics to reach affected areas.[29]

Bone scans are useful for localising the problem, which can often be a challenge in younger children, and confirming whether the lesion is solitary or multifocal, as in 7% of children and 22% of neonates.[12]

Magnetic resonance imaging (MRI). A retrospective study of 156 patients comparing all the imaging modalities showed that bone scintigraphy and MRI are the most useful techniques at the onset of disease.[24] The benefit of contrast enhancement is controversial in children, as the metaphysis is highly vascularised and gives a greater signal, which makes any pathological changes more difficult to differentiate from normal. Although the addition of contrast does not improve the sensitivity or specificity of the scan[30,31] it increases observer confidence in the diagnosis when oedema is visible on unenhanced scans, and its use should be reserved for these patients.[31]

A retrospective study of 213 patients comparing bone scintigraphy with MRI suggested that sufficient diagnostic information was obtained in 84% of patients from the bone scan alone, and whereas 92% did not require an MRI to make the diagnosis, 47% needed it to guide treatment.[32] Correlation with CRP and ESR gives an indication as to whether MRI will give any further information. For example, pelvic osteomyelitis is difficult to diagnose and treat, and MRI illustrates abscesses well and defines anatomy pre-operatively.

Ultrasound. In developed countries the increasing availability of MRI, CT and bone scanning has meant that ultrasound is rarely used for the diagnosis of osteomyelitis. Its sensitivity and specificity are low as it relies on detecting cortical destruction and is unable to distinguish bone marrow changes. Its interpretation is also very user-dependent.[19,24] In developing countries and areas where investigations are limited, however, ultrasound is useful and when used in conjunction with radiographs, the sensitivity is greatly increased.[24] Deep soft tissue swelling is an early sign of osteomyelitis and a reliable diagnostic indicator.[33] A hypoechoic area away from the bone was confirmed as a periosteal abscess in 81% of patients in one prospective study[34] but in only 42% in another.[35] In this, however, periosteal elevation > 2 mm was a good indicator of an abscess needing drainage.[35] In a review of 38 scans, periosteal abscesses > 3 mm resolved successfully without surgery, implying that the decision to drain an abscess should be made on clinical grounds, specifically the response of localised symptoms to antibiotics.[33] Finally, ultrasound has high sensitivity and specificity for detecting complications of osteomyelitis such as periosteal thickening, soft tissue/periosteal abscess and joint effusions.[24]

Microbiology. Although the predominant causative organism is *Staph. aureus*, *Streptococcus* and Gram-negative organisms cause up to 60% of cases of osteomyelitis in children under four years, with the remainder being *Staph. aureus*.[36-39] The most common organisms, including how they have changed in the post-vaccination era, are shown in Figure 2.

Many studies comment on the higher yield of positive cultures from samples of tissue or pus compared with blood, and reports over the past three decades show an overall slight deterioration in the ability to obtain positive cultures even as technology develops and the causative bacteria change (Fig. 3).[7,40-43]

In one study of culture-negative osteomyelitis, 85 patients had a longer duration of symptoms but were less likely to have fever, localised symptoms, signs, preceding trauma and need for surgical drainage.[44] They were treated successfully in the same way as those with confirmed staphylococcal disease.

Methicillin-resistant *Staph. aureus* (MRSA) is increasingly isolated in patients with osteomyelitis and of great concern. An early study of the treatment of paediatric osteomyelitis with penicillin reported resistance rates of only 2.4%.[2] Over the next 50 years these rose rapidly to 60% to 80%, and since 1999 the rates for MRSA are addressed specifically. They vary enormously, depending largely on geographical location, from 0% in Saudi Arabia[40] to 71.4% in the USA.[45] It is widely accepted that over the past 20 years the rates of MRSA have increased overall,[45,46] but there is no firm correlation with paediatric osteomyelitis.

Panton–Valentine leukocidin (PVL) is a gene whereby bacteriophages infect *Staph. aureus*. It encodes a necrotising cytotoxin which, when released, degrades white blood cells, resulting in an extremely virulent strain of the bacterium. It is usually seen in major respiratory, skin and soft tissue infections but can also cause a severe form of osteomyelitis. The gene is mainly associated with MRSA,[47] which to some extent explains its high virulence. Only about 10% of methicillin-sensitive *Staph. aureus* (MSSA) is PVL+, which confers a similar clinical course to PVL+ MRSA. The identification of PVL+ strains could allow gene modification to reduce its virulence.[47]

A conjugate vaccine for *Haemophilus influenzae* type B (Hib) was introduced in the early 1990s, resulting in a dramatic decline in infections caused by this organism in young children. Whereas it was hitherto the commonest Gram-negative organism in paediatric osteomyelitis, it is now usually seen only in areas of low vaccine uptake or limited vaccination programmes.[48] A retrospective Canadian study of 560 patients reported a 5% rate for Hib before the vaccination era and 0% afterwards.[49]

Kingella kingae (KK), formerly *Moraxella kingae,* has occasionally been reported to cause skeletal infections.[50] It is a slow-growing, aerobic, fastidious Gram-negative coccobacillus, which is usually found in the respiratory tract of children and is notoriously difficult to isolate on culture. There is recent interest in the development of more sophisticated molecular detection mechanisms, such as polymerase chain reaction with specific ribosomal DNA primers.[37,51,52] These allow microbiological diagnosis where earlier cultures were negative. The rates of KK-confirmed osteomyelitis are increasing and KK has overtaken

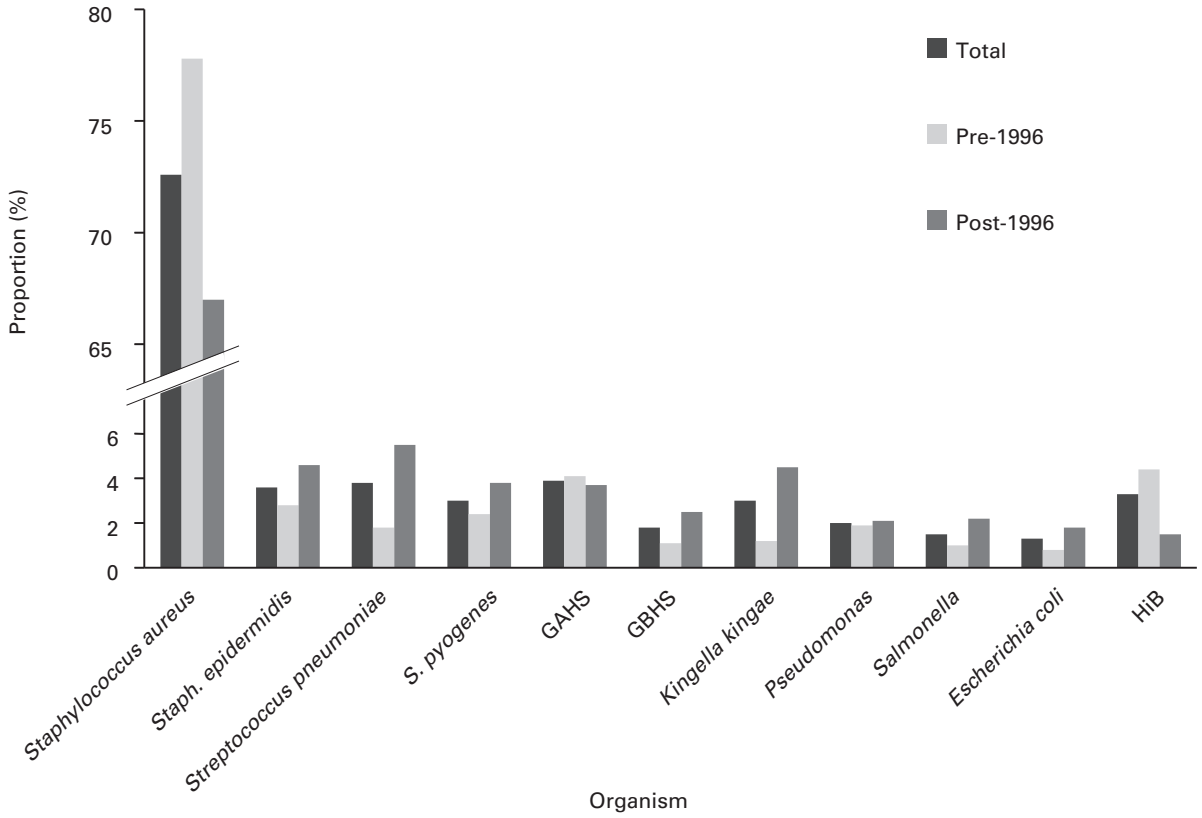

Fig. 2

Bar chart showing the causative organisms in paediatric osteomyelitis (GAHS, Group A beta-haemolytic streptococcus; GBHS, group B beta-haemolytic streptococcus; HiB, *Haemophilus influenza* type B).

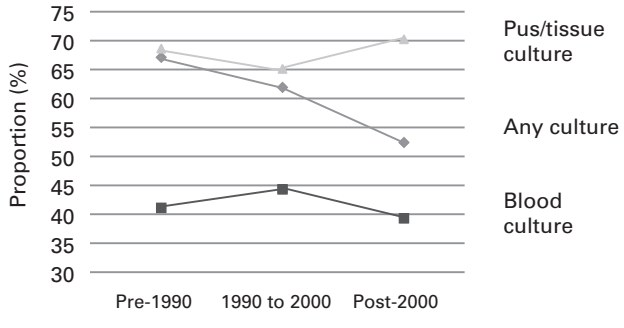

Fig. 3

Graph showing the percentage of positive cultures and trends by decade.

Hib as the most common Gram-negative organism causing osteomyelitis in young children (Fig. 2). Some studies from France[37,41,51] and the USA[50] have indicated rates that encroach on the previously unrivalled *Staph. aureus*.

Antibiotics. Liaison with the microbiologist and use of the correct antibiotic are important. Little good prospective evidence exists to suggest the best choice of initial antibiotic, although flucloxacillin is generally favoured owing to the dominance of *Staph. aureus*. Benzylpenicillin or a cephalosporin should be added in unvaccinated children.[21,53,54] Antibiotics should preferably be started after all necessary culture specimens have been sent, as this gives the highest chance of a positive culture.[17] An urgent Gram stain should also be performed. The definitive antibiotics depend on culture and sensitivity results and the initial antibiotics should be changed or continued accordingly (Table VII).

Because of the increase in cases of MRSA some authors have suggested that patients should receive empirical cover until the results of culture are available.[55] This is not widely accepted, mainly due to the fear of inducing selective antimicrobial resistance.[14] The excellent bone penetration and oral bioavailability of clindamycin make it extremely useful in MRSA osteomyelitis.[23,25]

The duration and route of antibiotic treatment are debatable. Much of the evidence advocating longer parenteral treatment stems from a study that reported a complication rate of 19% for patients treated with less than three weeks of intravenous antibiotics, compared with 1% for those treated for longer.[56] Clinical improvement, specifically lack

Table VII. Important facts for different causative organisms

Organism*	Important facts	Antibiotics
MSSA	Isolated in 67% culture positive isolates Prevalence increases in children > 4 yrs[36-39]	β-Lactamase-resistant antibiotic e.g. flucloxacillin Cephalosporin (if allergic)[21,23,54]
Streptococcus	More common in younger children (< 4 yrs) Causes significantly higher fever on admission (38.9°C) than *Pneumococcus* (38.2°C) and *Staphylococcus* (38.1°C)[15]	Add in benzylpenicillin/cephalosporin[21,53,54]
MRSA	Highly virulent and must be treated aggressively Patients have significantly longer and higher fevers (39°C), worse inflammatory markers, require hospitalisation and antibiotics for longer, have worse complications and are more likely to need surgery[14,15,29,38,45,61,89]	Clindamycin: 97% to 98% sensitive[25,45,89] If no response add vancomycin[45,89]
PVL+	Very severe localised reaction and systemic inflammatory response Inflammatory markers are higher, radiology often abnormal, need for longer antibiotic therapy, admission to intensive care and repeated surgeries[14,29,47,61,89]	As per *MRSA* Linezolid also useful[47,61]
HiB	If isolated in blood cultures, perform a lumbar puncture to exclude meningitis – present in 16%[7]	No need to cover routinely as incidence now so low[49]
KK	Produces a milder, probably subacute form of osteomyelitis with fewer complications[37,52] Usually in younger children (6 months to 4 years)[51] Often found in more unusual, smaller bones (sternum, metatarsal, vertebrae, calcaneum)[37,50] Radiographs often show bony destruction – possibly due to a more subacute process[50]	Good sensitivity to penicillin and cephalosporin, but resistant to nalidixic acid and tobramycin[50,51]
Pneumococcus	A child with pneumococcal bacteraemia, usually from pneumonia, is much more likely to develop osteomyelitis – as high as one in 100[16]	Add benzylpenicillin/cephalosporin

* MSSA, methicillin-sensitive *Staphylococcus aureus*; MRSA, methicillin-resistant *Staph. aureus*; PVL+, Panton–Valentine leukocidin-positive *Staph. aureus*; HiB, *Haemophilus influenzae* type B; KK, *Kingella kingae*

of tenderness and a normal temperature, is a good indicator for conversion to oral antibiotics.[7,14,21,53,54] Haematological markers, especially CRP, can also monitor improvement or prompt a change of treatment.[11,13,21,23,25,57]

There is only one prospective randomised study on the subject. In this, 131 patients received a short course (two to four days) of i.v. clindamycin or a cephalosporin followed by high-dose oral treatment for either 20 or 30 days. Excellent outcomes were reported in both groups, with no significant clinical, radiological or haematological differences. The authors concluded that if the child is improving clinically and CRP returning to normal, 20 days of antibiotics are enough.[23]

A recent review of 37 patients with acute uncomplicated osteomyelitis found that, based on improving clinical and haematological parameters, 63% patients needed < four days of i.v. antibiotics, 89% < six days and 11% > six days, followed by three weeks of oral antibiotics. The most reliable parameters on admission to suggest the need for prolonging i.v. antibiotics were fever > 38.4°C and CRP > 100 for over three and five days, respectively.[21]

Another cohort of 50 patients was treated successfully with a mean of four days' i.v. and three weeks' oral antibiotics,[25] and short i.v. courses are recommended by several other retrospective studies, including one of nearly 2000 patients.[58,59] This evidence suggests that in acute uncomplicated osteomyelitis a short course of i.v. antibiotics, guided by clinical and haematological parameters and followed by an early switch to oral treatment, is acceptable. Closer and longer follow-up is recommended. This is an important consideration, especially where follow-up may be restricted for logistical or financial reasons. The indicators that a longer course of antibiotics will be needed are a requirement for surgical debridement, limited clinical response, MRSA, PVL+, radiological abnormalities, poor compliance, underlying additional medical conditions and failure of haematological markers to improve.[4,7,17,27,54,58,60,61]

The total duration of antibiotic treatment is also contentious. Some studies suggest that a total of three weeks may be sufficient in uncomplicated cases,[21,25] although slightly longer courses are used by others, with Bachur and Pagon[59] reporting a median of 32 days.

The complications of i.v. therapy need to be considered, the majority of which are line problems, such as sepsis and blockage. Over 40% of patients receiving more than two weeks of i.v. therapy had a complication, with young age and low socioeconomic status being risk factors.[63] In one study 31% of all i.v. antibiotic courses had a catheter-related complication (from both central venous lines and

Table VIII. Summary

Summary	Key points
Presentation	40% of children will be afebrile
	Pain and local signs/symptoms are the most common clinical features
	Nearly 50% will not have a known risk factor
	The tibia and femur most commonly affected
Inflammatory markers	A raised white cell count may indicate a severe form of osteomyelitis
	ESR and CRP together are the most sensitive diagnostic markers
Imaging	Radiographs are essential for exclusion of other diagnoses
	MRI is the gold standard imaging technique. If unavailable or a delay is likely, bone and ultrasound scans usually give adequate diagnostic information
Organisms	*Staphylococcus aureus* remains the most common organism
	Kingella kingae is becoming more detectable so rates are increasing
	Methicillin-resistant and Panton-Valentine leukocidin-positive *Staph. aureus* and *Pneumococcus* cause a severe form of osteomyelitis
Antibiotics	A short course of intravenous antibiotics followed by three weeks orally are likely to be sufficient for uncomplicated osteomyelitis
	Temperature > 38.4°C and C-reactive protein > 100 are the best indicators for need for continuing intravenous antibiotics
	The clinical condition is a good indicator for conversion to oral therapy
Surgery	Surgery is not routinely required and is reserved for concurrent septic arthritis, disseminated sepsis, failure to improve with antibiotics or pelvic abscesses > 2 cm
Follow-up	Close follow-up is needed after discharge

peripherally inserted central catheters (PICC)), which occurred on average by day 21.[63] General anaesthetic (GA) is needed for paediatric central lines and often for some peripheral lines. If not performed at the same time as surgery this requires an extra anaesthetic. An extra GA for insertion was needed in 53% of patients in one study,[42] a further one for reinsertion in 7% to 20% and for removal in 77%.[42,62] An increased risk of allergenic sensitisation to antibiotics is also reported with i.v. courses > 20 days.[42]

There is little firm evidence as to whether the measurement of serum concentrations of bactericides is an aid to treatment.[25] Some authors insist that its use is vital in monitoring oral therapy to ensure that adequate concentrations are maintained, and suggest that complication and readmission rates are thereby reduced.[26,64-66] Others report that provided that the oral antibiotic dose is the maximum possible for the weight of the child, no problem should arise and side effects are rare.[23,25,60]

There is no evidence to support the use of antibiotic-impregnated cement in paediatric osteomyelitis.

Surgery. Historically, despite little evidence, early biopsy and debridement were recommended. There is nowadays an increasing trend towards medical treatment, although no prospective studies support this. A review of 44 patients with subacute osteomyelitis showed no difference between medical and surgical treatment.[67] Many authors recommend that if the child is not improving with antibiotics alone, surgery is warranted to treat the osteomyelitis and allow for samples of tissue and pus, which have a higher chance of allowing a bacteriological diagnosis.[21,23,25,61,67-69]

One report of 38 cases of pelvic osteomyelitis noted that abscesses < 1 cm on MRI were treated successfully by medical management alone, whereas abscesses > 2 cm required surgical drainage, which the authors suggested should ideally should be undertaken within 24 hours of diagnosis.[18] Although pelvic osteomyelitis is very responsive to i.v. antibiotics owing to its rich local blood supply, thereby reducing the risks of complications,[68] approximately 20% of pelvic abscesses need draining, compared with 6% in long bones.[32]

The effect of operative intervention on blood markers is debatable and based on small case series.[13,57] It is generally accepted that their levels are higher in this group and proportional to the extent of surgery. It is important to be aware that markers will take significantly longer to normalise (CRP seven days and ESR 16 days) in surgically treated patients than in those treated medically. It is not known whether this is due to the operation itself or because these patients are more unwell.[13] Surgery is not thought to influence the efficacy of MRI in the diagnosis of osteomyelitis.[70]

Prognosis. The mortality rates for paediatric patients with osteomyelitis are now extremely low compared with the pre-antibiotic era, where femoral and tibial osteomyelitis had rates > 50% and > 30%, respectively.[2] Calculation of complication rates for all studies is not possible, as they have different follow-up times and definitions of complications including chronicity and recurrence. However, there are risk factors for a worse prognosis that should prompt a more cautious approach to treatment and follow-up. These include: 1) the infecting organism being MRSA, *S. pneumonia* or PVL+[15,16,38,47,61]; 2) concurrent septic arthritis,

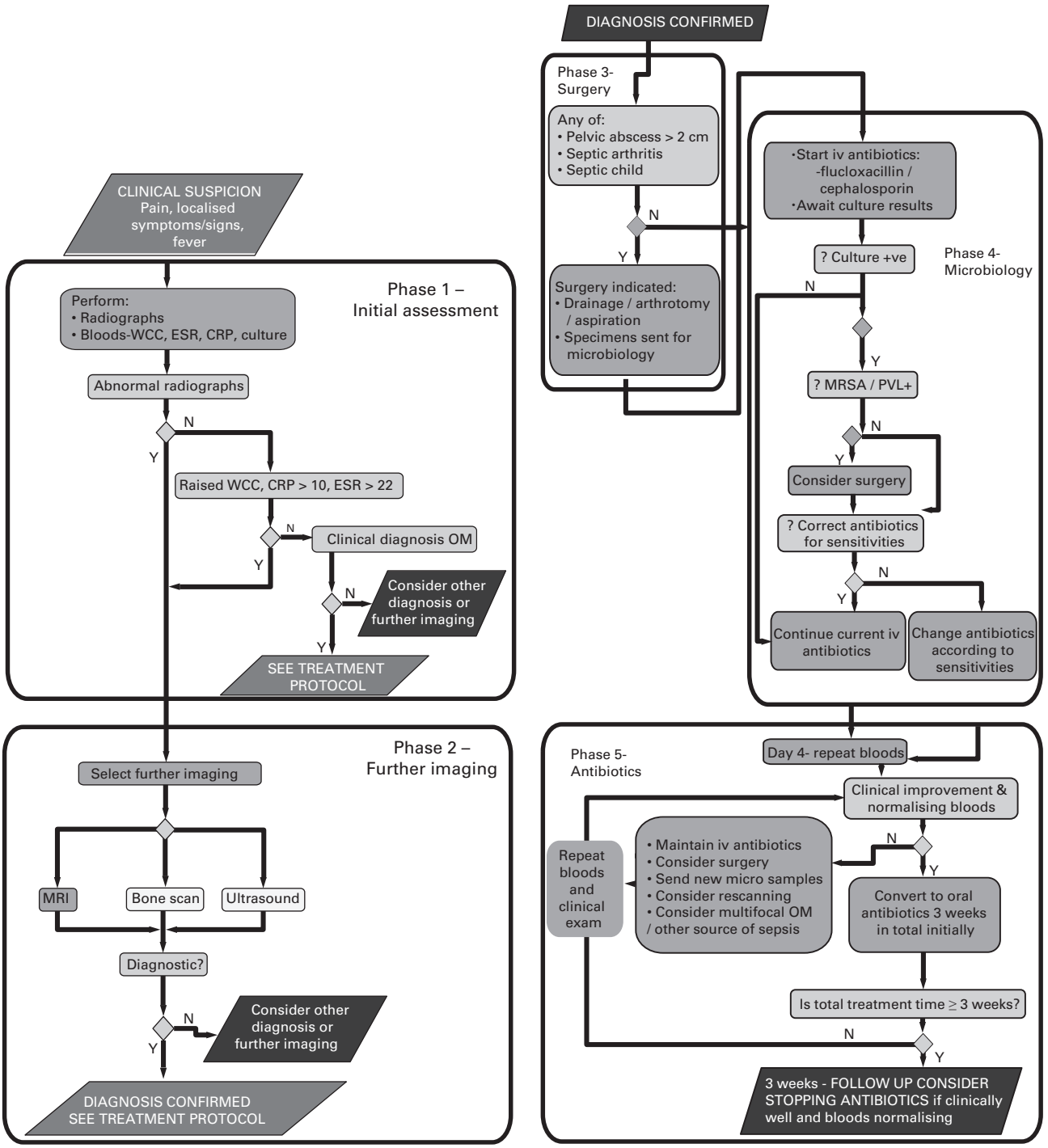

Fig. 4a

Fig. 4b

Algorithms for a) the diagnosis and b) the treatment of paediatric osteomyelitis (OM).

pyomyositis and/or abscess[71]; 3) location – involvement of the hip is at the highest risk of complications (40%) followed by the ankle (33%) and knee (10)[72]; 4) a positive culture – this is thought to be partly due to KK, a more benign pathogen and one difficult to isolate, being present in the majority of negative cultures[38]; 5) younger age – this is not fully understood, but may be due to delays in diagnosis, presentation and treatment, as well as differences in anatomy and immune system[16]; and 6) a delay in treatment. One study found that the 'cure rate' fell from 92% to 25%

when treatment was delayed by > 5 days,[54] and other authors have warned against similar delays.[55,69,72]

The duration of follow-up that is required has not been investigated. Some authors recommend an early review at three weeks before stopping antibiotics, then at six weeks and three, six and 12 months.[21] Others state that if a complication were to occur it is most likely to be within the first six months.[58]

Discussion

This paper presents an up-to-date, comprehensive systematic review of the English literature on paediatric osteomyelitis and involves over 12 000 cases. However, the inclusion of English language papers alone can lead to an overestimation of the effects of osteomyelitis, as negative studies from non-English-speaking countries are more likely to be published in local journals.[73-75] Also, although some included reports from developing countries provide useful information, care should be taken in extrapolating this to developed nations.

Twelve of the studies described themselves as prospective, but there was only one randomised controlled trial and therefore statistical analysis of the studies was rarely possible. Also, because paediatric osteomyelitis is relatively uncommon, the undertaking of a large randomised controlled trial would be difficult, needing a long-term multicentre approach.

The change in incidence of osteomyelitis may be due to improvements in health-care facilities, urbanisation of remote populations and changes in the predominant organisms. Lower socioeconomic status is unlikely to be significant, but access to medical resources may be relevant.[3,38] It is hoped that pneumococcal vaccination programmes, initiated at the beginning of this decade, should result in a decline in pneumococcal osteomyelitis similar to that in Hib.

Historically, the classic features of osteomyelitis were a sick child with high fever and a high white cell count. Currently, pain, localised signs and symptoms and fever are more common, and nearly 40% of children will be afebrile with minimal signs and symptoms (Table III). This could be due to earlier presentation and administration of antibiotics that prevent the systemic spread of infection. There appears to be no single symptom, sign or investigation that can easily diagnose paediatric osteomyelitis. A raised CRP and ESR together increase their sensitivity to nearly 98%[76] and are important in diagnosis. The half-life of CRP is considerably shorter than that of ESR, so changes can be detected sooner, making it more useful in management decisions.[11]

Emergency MRI is becoming more widely available and is the best imaging technique for diagnosing osteomyelitis. However, if this is unavailable or likely to be delayed, a bone scan or ultrasonography should be performed.

There is much interest in sophisticated methods of detection for identifying causative organisms, but it appears that the ability to do so has slightly deteriorated. This could be due to earlier diagnosis and initiation of antibiotic treatment. Six of the 12 prospective studies, including the randomised controlled trial, focus on the type and duration of antibiotics. The literature suggests an initial short i.v. course with anti-staphylococcal cover, then changing according to sensitivities. There is increasing evidence that longer courses do more harm than good. Provided the oral antibiotic is effective and the correct dose is given, the child should be converted as soon as there is clinical improvement and the haematological markers are normalising. A total of three weeks of antibiotic treatment is usually sufficient in uncomplicated cases, but the clinician must be guided by the individual patient. The role of surgery is diminishing and reserved for selected patients.

Table VIII summarises the important points raised in this paper and Figure 4 suggests an algorithm for the diagnosis and treatment of paediatric patients with osteomyelitis.

A multidisciplinary approach is essential in the management of these patients to ensure early diagnosis and effective treatment. Regular re-evaluation of the child throughout treatment and recovery is vital. An evidence-based approach to the disease is likely to ensure the best outcomes, and this review has demonstrated the need for a randomised controlled trial regarding treatment. In order to obtain sufficient numbers this would need to be multicentred and strictly regulated, but is theoretically possible.

No benefits in any form have been received or will be received from a commercial party related directly or indirectly to the subject of this article.

References

1. **Stott NS.** Review article: pediatric bone and joint infection. *J Orthop Surg (Hong Kong)* 2001;9:83–90.
2. **White M, Dennison W.** Acute haematogenous osteitis in childhood. *J Bone Joint Surg [Br]* 1952;34-B:608–623.
3. **Blyth MJ, Kincaid R, Craigen MA, Bennet GC.** The changing epidemiology of acute and subacute haematogenous osteomyelitis in children. *J Bone Joint Surg [Br]* 2001;83-B:99–102.
4. **Craigen MA, Watters J, Hackett JS.** The changing epidemiology of osteomyelitis in children. *J Bone Joint Surg [Br]* 1992;74-B:541–545.
5. **Gillespie W.** The epidemiology of acute haematogenous osteomyelitis of childhood. *Int J Epidemiol* 1985;14:600–606.
6. **Malcius D, Trumpulyte G, Barauskas V, Kilda A.** Two decades of acute hematogenous osteomyelitis in children: are there any changes? *Paediatr Surg Int* 2005;21:356–359.
7. **Christiansen P, Frederiksen B, Glazowski J, Scavenius M, Knudsen FU.** Epidemiologic, bacteriologic and long-term follow-up data of children with acute hematogenous osteomyelitis and septic arthritis: a ten year review. *J Pediatr Orthop B* 1999;8:302–305.
8. **Akakpo-Numado GK, Gnassingbé K, Abalo A, et al.** Locations of osteomyelitis in children with sickle-cell disease at Tokoin teaching hospital (Togo). *Pediatr Surg Int* 2009;25:723–726.
9. **Sadat-Ali M.** The status of acute osteoyelitis in sickle cell disease: a 15 year review. *Int Surg* 1998;83:84–87.
10. **Zvulunov A, Gal N, Segev Z.** Acute hematogenous osteomyelitis of the pelvis in childhood: diagnostic clues and pitfalls. *Pediatr Emerg Care* 2003;19:29–31.
11. **Roine I, Faingezicht I, Arguedas A, Herrera JF, Rodríguez F.** Serial serum C-reactive protein to monitor recovery from acute hematogenous osteomyelitis in children. *Pediatr Infect Dis J* 1995;14:40–44.
12. **Jaramillo D, Treves TT, Kasser JR, et al.** Osteomyelitis and septic arthritis in children: appropriate use of imaging to guide treatment. *AJR Am J Radiol* 1995;165:399–403.
13. **Khachatourians AG, Patzakis MJ, Roidis N, Holtom PD.** Laboratory monitoring in pediatric acute osteomyelitis and septic arthritis. *Clin Orthop Relat Res* 2003;409:186–194.

14. **Hawkshead J, Patel N, Steele R, Heinrich S.** Comparative severity of pediatric osteomyelitis attributable to methicillin-resistant versus methicillin-sensitive staphylococcus aureus. *J Pediatr Orthop* 2009;29:85–90.
15. **Ibia E, Imoisili M, Pikis A.** Group A Beta Hemolytic streptococcal osteomyelitis in children. *Pediatrics* 2003;112:22–26.
16. **Bradley JS, Kaplan SL, Tan TQ, et al.** Pediatric pneumococcal bone and joint infection. The Pediatric Multicenter Pneumococcal Surveillance Study Group (PMPSSG). *Pediatrics* 1998;102:1376–1382.
17. **Vinod MB, Matussek J, Curtis N, Graham HK, Carapetis JR.** Duration of antibiotics in children with osteomyelitis and septic arthritis. *J Paediatr Child Health* 2002;38:363–367.
18. **Connolly SA, Connolly LP, Drubach LA, Zurakowski D, Jaramillo D.** MRI for detection of abscess in acute osteomyelitis of the pelvis in children. *AJR Am J Roentgenol* 2007;189:967–972.
19. **Browne L, Mason E, Kaplan S, et al.** Optimal imaging strategy for community-acquired Staphylococcus aureus musculoskeletal infections in children. *Pediatr Radiol* 2008;38:841–847.
20. **Unkila-Kallio L, Kallio M, Peltola H.** The usefulness of C-reactive protein levels in the identification of concurrent septic arthritis in children who have acute hematogenous osteomyelitis: a comparison with the usefulness of the ESR and white blood count. *J Bone Joint Surg [Am]* 1994;76-A:848–853.
21. **Jagodzinski NA, Kanwar R, Graham K, Bache CE.** Prospective evaluation of a shortened regimen of treatment for acute osteomyelitis and septic arthritis in children. *J Pediatr Orthop* 2009;29:518–525.
22. **Roine I, Arguedas A, Famgezicht I, Rodriguez F.** Early detection of sequela-prone osteomyelitis in children with use of simple clinical and laboratory criteria. *Clin Infect Dis* 1997;24:849–853.
23. **Peltola H, Pääkkönen M, Kallio P, et al.** Short- versus long-term antimicrobial treatment for acute hematogenous osteomyelitis of childhood: prospective, randomized trial on 131 culture-positive cases. *Pediatr Infect Dis J* 2010;29:1123–1128.
24. **Malcius D, Jonkus M, Kuprionis G, et al.** The accuracy of different imaging techniques in diagnosis of acute hematogenous osteomyelitis. *Medicina (Kaunas)* 2009;45:624–631.
25. **Peltola H, Unkila-Kallio L, Kallio MJ.** Simplified treatment of acute staphylococcal osteomyelitis of childhood. *Pediatrics* 1997;99:846–850.
26. **Kao HC, Huang YC, Chiu CH, et al.** Acute hematogenous osteomyelitis and septic arthritis in children. *J Microbiol Immunol Infect* 2003;36:260–265.
27. **Karwowska A, Davies HD, Jadavji T.** Epidemiology and outcome of osteomyelitis in the era of sequential intravenous-oral therapy. *Pediatr Infect Dis J* 1998;17:1021–1026.
28. **Tuson CE, Hoffman EB, Mann MD.** Isotope bone scanning for acute osteomyelitis and septic arthritis in children. *J Bone Joint Surg [Br]* 1994;76-B:306–310.
29. **Pennington WT, Mott MP, Thometz JG, Sty JR, Metz D.** Photopenic bone scan osteomyelitis: a clinical perspective. *J Pediatr Orthop* 1999;19:695–698.
30. **Kan JH, Young RS, Yu C, Hernanz-Schulman M.** Clinical impact of gadolinium in the MRI diagnosis of musculoskeletal infection in children. *Pediatr Radiol* 2010;40:1197–1205.
31. **Averill LW, Hernandez A, Gonzalez L, Peña AH, Jaramillo D.** Diagnosis of osteomyelitis in children: utility of fat-suppressed contrast-enhanced MRI. *AJR Am J Radiol* 2009;192:1232–1238.
32. **Connolly LP, Connolly SA, Drubach LA, Jaramillo D, Treves ST.** Acute hematogenous osteomyelitis of children: assessment of skeletal scintigraphy-based diagnosis in the era of MRI. *J Nucl Med* 2002;43:1310–1316.
33. **Mah ET, LeQuesne GW, Gent RJ, Paterson DC.** Ultrasonic features of acute osteomyelitis in children. *J Bone Joint Surg [Br]* 1994;76-B:969–974.
34. **Taneja K, Mittal SK, Marya SK, et al.** Acute osteomyelitis: early diagnosis by ultrasonography. *Australas Radiol* 1992;36:77–79.
35. **Howard C, Einhorn M, Dagan R, Nyska M.** Ultrasound in diagnosis and management of acute haematogenous osteomyelitis in children. *J Bone Joint Surg [Br]* 1993;75-B:79–82.
36. **Bonhoeffer J, Haeberle B, Schaad U, Heininger U.** Diagnosis of acute haematogenous osteomyelitis and septic arthrits: 20 years experience at the University Children's Hospital Basel. *Swiss Med Wkly* 2001;131:575–581.
37. **Chometon S, Benito Y, Chaker M, et al.** Specific real-time polymerase chain reaction places Kingella kingae as the most common cause of osteoarticular infections in young children. *Pediatr Inf Dis J* 2007;26:377–381.
38. **Saavedra-Lozano J, Mejías A, Ahmad N, et al.** Changing trends in acute osteomyelitis in children: impact of methicillin-resistant Staphylococcus aureus infections. *J Pediatr Orthop* 2008;28:569–575.
39. **Faden H, Grossi M.** Acute osteomyelitis in children: reassessment of etiologic agents and their clinical characteristics. *Am J Dis Child* 1991;145:65–69.
40. **Al Zamil FA, Al Saadi MM, Bokhary NA, et al.** The clinical profile of childhood osteomyelitis: a Saudi experience. *J Pediatr Infect Dis* 2008;3:235–240.
41. **Moumile K, Merckx J, Glorion C, et al.** Bacterial aetiology of acute osteoarticular infections in children. *Acta Paediatrica* 2005;94:419–422.
42. **Ceroni D, Regusci M, Pazos JM, Saunders CT, Kaelin A.** Risks and complications of prolonged parenteral antibiotic treamtent in children with acute osteoarticular infections. *Acta Orthop Belg* 2003;69:400–404.
43. **Mollan R, Piggot J.** Acute osteomyelitis in children. *J Bone Joint Surg [Br]* 1977;59-B:1–7.
44. **Floyed RL, Steele RW.** Culture-negative osteomyelitis. *Pediatr Infect Dis J* 2003;22:731–735.
45. **Arnold SR, Elias D, Buckingham SC, et al.** Changing patterns of acute hematogenous osteomyelitis and septic arthritis. *J Pediatr Orthop* 2006;26:703–708.
46. **Chambers HF.** The changing epidemiology of Staphylococcus aureus? *Emerg Infect Dis* 2001;7:178–182.
47. **Bocchini C, Hulten KG, Mason EO Jr, et al.** Panton-Valentine Leukocidin genes are assocated with enhanced inflammatory response and local disease in acute hematogenous staphylococcus aureus osteomyelitis in children. *Pediatrics* 2006;117:433–440.
48. **Azam Q, Ahmad I, Abbas M, Syed A, Haque F.** Ultrasound and colour Doppler sonography in acute osteomyelitis. *Acta Orthop Belg* 2005;71:590–596.
49. **Howard AW, Viskontas D, Sabbagh C.** Reduction in osteomyelitis and septic arthritis related to Haemophilus influenzae Type B vaccination. *J Pediatr Orthop* 1999;19:705–709.
50. **Lundy D, Kehl D.** Increasing prevalence of Kingella kingae in osteoarticular infections in young children. *J Pediatr Orthop* 1998;18:262–267.
51. **Verdier I, Gayet-Green A, Ploton C, et al.** Contribution of a broad range polymerase chain reaction to the diagnosis of osteoarticular infections caused by Kingella kingae: description of twenty-four recent pediatric diagnoses. *Pediatr Infect Dis J* 2005;24:692–696.
52. **Ceroni D, Cherkaoui A, Ferey S, Kaelin A, Schrenzel J.** Kingella kingae osteoarticular infections in young children: clinical features and contribution of a new specific real-time PCR assay to the diagnosis. *J Pediatr Orthop* 2010;30:301–304.
53. **Groegrens ED, McEvoy A, Watson M, Barrett IR.** Acute osteomyelitis and septic arthritis in children. *Paediatr Child Health* 2005;41:59–62.
54. **Cole WG, Dalziel RE, Leitl S.** Treatment of acute osteomyelitis in childhood. *J Bone Joint Surg [Br]* 1982;64-B:218–223.
55. **Gwynne-Jones DP, Stott NS.** Community-acquired methicillin-resistant Staphylococcus aureus: a cause of musculoskeletal sepsis in children. *J Pediatr Orthop* 1999;19:413–416.
56. **Dich VQ, Nelson JD, Haltalin KC.** Osteomyelitis in infants and children: a review of 163 cases. *Am J Dis Child* 1975;129:1273–1278.
57. **Unkila-Kallio L, Kallio M, Peltola H, Eskola J.** Serum C-reactive protein, erythrocyte sedimentation rate and white blood cell count in acute hematogenous osteomyelitis of children. *Pediatrics* 1994;93:59–62.
58. **Zaoutis T, Localio AR, Leckerman K, et al.** Prolonged intravenous therapy versus early transition to oral antimicrobial therapy for acute osteomyelitis in children. *Pediatrics* 2009;123:636–642.
59. **Bachur R, Pagon Z.** Success of short-course parenteral antibiotic therapy for acute osteomyelitis of childhood. *Clin Pediatr (Phila)* 2007;46:30–35.
60. **Syrogiannopoulos G, Nelson JD.** Duration of antimicrobial therapy for acute suppurative osteoarticular infections. *Lancet* 1988;1:37–40.
61. **Dohin B, Gillet Y, Kohler R, et al.** Pediatric bone and joint infections caused by Panton-Valentine Leukocidin-positive staphylococcus aureus. *Pediatr Infect Dis J* 2007;26:1042–1048.
62. **Ruebner R, Keren R, Coffin S, et al.** Complications of central venous catheters used for the treatment of acute hematogenous osteomyelitis. *Pediatrics* 2006;117:1210–1215.
63. **Maraqa NF, Gomez MM, Rathore MH.** Outpatient parenteral antimicrobial therapy in osteoarticular infections in children. *J Pediatr Orthop* 2002;22:506–510.
64. **Prober CG, Yeager AS.** Use of the serum bactericidal titer to assess the adequacy of oral antibiotic therapy in the treatment of acute hematogenous osteomyelitis. *J Pediatr* 1979;95:131–135.
65. **Nelson J, Bucholz R, Kusmiesz H, Shelton S.** Benefits and risks of sequential parenteral-oral cephaolsporin therapy for suppurative bone and joint infections. *J Pediatr Orthop* 1982;2:255–262.
66. **Nelson JD.** Toward simple but safe management of osteomyelitis. *Pediatrics* 1997;99:883–884.
67. **Hamdy RC, Lawton L, Carey T, Wiley J, Marton D.** Subacute hematogenous osteomyelitis: are biopsy and surgery always indicated? *J Pediatr Orthop* 1996;16:220–223.
68. **Davidson D, Letts M, Khoshhal K.** Pelvic osteomyelitis in children: a comparison of decades from 1980-1989 with 1990-2001. *J Pediatr Orthop* 2003;23:514–521.
69. **Vaughan PA, Newman NM, Rosman MA.** Acute hematogenous osteomyelitis in children. *J Pediatr Orthop* 1987;7:652–655.

70. Kan JH, Hilmes MA, Martus JE, Yu C, Hernanz-Schulman M. Value of MRI after recent diagnostic or surgical intervention in children with suspected osteomyelitis. *AJR Am J Roentgenol* 2008;191:1595–1600.

71. Gafur OA, Copley LA, Hollmig ST, et al. The impact of the current epidemiology of pediatric musculoskeletal infection on evaluation and treatment guidelines. *J Pediatr Orthop* 2008;8:777–785.

72. Jackson MA, Nelson JD. Etiology and medical managment of acute suppurative bone and joint infections in pediatric patients. *J Pediatr Orthop* 1982;2:313–323.

73. Khan K, Kunz R, Kleijnen J, Antes G. *Systematic reviews to support evidence-based medicine: how to review and apply findings of healthcare research.* London: Royal Society of Medicine Press, 2003:33.

74. Gregoire G, Derderain F, Le Lorier J. Selecting the language of the publications included in a meta-analysis: is there a Tower of Babel bias? *J Clin Epidemiol* 1995;48:159–163.

75. Egger M, Zellweger-Zähner T, Schneider M, et al. Language bias in randomised controlled trials published in English and German. *Lancet* 1997;350:326–329.

76. Pääkkönen M, Kallio MJ, Kallio PE, Peltola H. Sensitivity of erythrocyte sedimentation rate and C-reactive protein in childhood bone and joint infections. *Clin Orthop Relat Res* 2010;468:861–866.

77. Riise Ø R, Kirkhus E, Handeland KS, et al. Childhood osteomyelitis-incidence and differentiation from other acute onset musculoskeletal features in a population based study. *BMC Pediatrics* 2008;8:45.

78. Rossaak M, Pitto R. Osteomyelitis in Polynesian children. *Int Orthop* 2005;29:55–58.

79. Klein J, Leach K. Pediatric pelvic osteomyelitis. *Clin Pediatr (Phila)* 2007;46:787–790.

80. Jaakkola J, Kehl D. Hematogenous calcaneal osteomyelitis in children. *J Pediatr Orthop* 1999;19:699–704.

81. Tröbs R, Möritz R, Bühligen U, et al. Changing pattern of osteomyelitis in infants and children. *Pediatr Surg Int* 1999;15:363–372.

82. Petersen S, Knudsen FU, Andersen EA, Egeblad M. Acute haematogenous osteomyelitis and septic arthritis in childhood: a 10-year review and follow-up. *Acta Orthop Scan* 1980;51:451–457.

83. Nixon G. Hematogenous osteomyelitis of metaphyseal-equivalent locations. *AJR Am J Roentgenol* 1978;130:123–129.

84. Aronson J, Garvin K, Seibert J, Glasier C, Tursky EA. Efficiency of the bone scan for occult limping toddlers. *J Pediatr Orthop* 1992;12:38–44.

85. González-López JL, Soleto-Martín FJ, Cubillo-Martín A, et al. Subacute osteomyelitis in children. *J Pediatr Orthop B* 2001;10:101–104.

86. Roberts JM, Drummond DS, Breed AL, Chesney J. Subacute hematogenous osteomyelitis in children: a retrospective study. *J Pediatr Orthop* 1982;2:249–254.

87. Auh JS, Binns HJ, Katz BZ. Retrospective assessment of subacute or chronic osteomyelitis in children and young adults. *Clin Pediatr (Phila)* 2004;43:549–555.

88. Kaiser S, Rosenborg M. Early detection of subperiosteal abscesses by ultrasonography. *Pediatr Radiol* 1994;24:336–339.

89. Martínez-Aguilar G, Avalos-Mishaan A, Hulten K, et al. Community-acquired methicillin-resistant and methicillin-susceptible Staphylococcus aureus musculoskeletal infections in children. *Pediatr Infect Dis J* 2004;23:701–706.