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Diagnosis of acute haematogenous osteomyelitis and septic arthritis: 20 years experience at the University Children's Hospital Basel

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Summary

Objective: To review the diagnostic experience with acute haematogenous osteomyelitis (AHOM) and/ or septic arthritis at our institution.

Methods: Retrospective review of the medical records of those patients with a bacteriologically and/or radiologically confirmed diagnosis, hospitalised in the University Children's Hospital Basel, Switzerland between January 1980 and July 2000.

Results: 90 patients (61% males), 4 weeks to 14 years of age, met the inclusion criteria. Median duration of disease prior to hospitalisation was 3 days (range 0–14); 88% were admitted during the first week after onset of complaints. 81 patients received no antimicrobial therapy prior to hospitalisation and are the subject of this presentation. ESR (1st hour in mm; median 36; range 11–124), CRP (mg/l; median 64; range 0–221) and WBC ($\times 10^9$/l; median 13; range 5–34) were elevated in 100%, 82% and 58% of patients, respectively. Blood cultures (BC) and/or tissue cultures (TC) were performed in 79 (98%) patients. Overall, bacteria were isolated from 53 patients (65%) with *Staph. aureus* as the most frequent organism (n = 31; 50%). BC were performed in 67 patients and yielded 35 (52%) positive cultures; TC (n = 47) yielded 27 (57%) isolates. In 34 patients with both BC and TC performed, only 12 (35%) were positive in both tests. Diagnostic findings were observed in 23 (59%) of 39 plain radiographs, 31 (56%) of 55 sonograms, 39 (89%) of 44 ^{99m}Tc-labeled bone scans and 4 (100%) of 4 MRI. 41 patients with diagnostic radiological findings had consecutive TC yielding 30 (73%) bacteriological isolates. Median duration of hospitalisation was 15 days (range 2–66).

Conclusion: Our data indicate that the diagnostic procedures of choice should be 1) early bone scan or MRI, 2) BC and 3) TC. Of supportive laboratory parameters, ESR and CRP were most valuable in our hands.

Key words: acute osteomyelitis; septic arthritis; children; organism; diagnosis

Introduction

Osteomyelitis is a serious disease characterised by an infection of the bone marrow, compacta and periosteum. Various classifications have been proposed [1]. For clinical decision making differentiation of acute from chronic, haematogenous from contiguous and unifocal from multifocal osteomyelitis is helpful.

The spectrum of causative organisms varies by age group [2–6]. The most commonly identified pathogen in children above 5 years of age is *Staphylococcus aureus*. It is implicated in 50–90 percent of cases in otherwise healthy children [2, 7–9]. A broader spectrum of causative organisms is found particularly in infants, where Streptococci, gram-negative bacteria such as *H. influenzae* and *E. coli* are responsible for up to 60 percent of cases [3, 10–12]. In about one third of cases no causative organism can be isolated [11, 13–15]. It was proposed that fastidious organisms like *Kingella kingae* might be responsible for a considerable proportion of osteomyelitis cases with negative routine cultures [16].

The present study focuses on acute haematogenous osteomyelitis (AHOM) and septic arthritis, the most common presentation of osteomyelitis in childhood. Due to slow blood flow in the capillary bed of ossifying tissue, bacteraemia can lead to migration of bacteria through the capillary endothelium and cause secondary local infection. Commonly a single focus in a metaphyseal area of long bones is affected. Due to the vascular anatomy

infants are particularly prone to develop concomitant septic arthritis.

Since the introduction of antibiotics and modern diagnostic techniques, AHOM can be treated conservatively with good prognosis – provided diagnosis is made early [4, 17]. Unless the hip joint is involved and/or diagnosis is delayed, septic arthritis can be treated without surgery as well [17]. Various diagnostic approaches have been discussed in the recent literature [3, 12, 15, 18, 19]. Here we present the diagnostic experience made during 20 years in our institution.

Methods

Patients were identified in our medical record register by ICD code of discharge diagnosis between January 1980 and July 2000.

Based on the diagnostic criteria for osteomyelitis proposed by Waldvogel et al. [18] we included all patients fulfilling the following criteria:

1. suspicious and/or characteristic clinical signs and symptoms of bone and/or joint infection of <2 weeks duration

and/or

2. positive blood or tissue culture

and/or

3. typical radiological findings (deep soft-tissue swelling, and/or periosteal reaction, and/or bony destruction) at some stage during hospitalisation

and/or

4. surgical finding of pus in bone and/or joint

The following data were collected from medical records of each patient who met the inclusion criteria: date of birth, gender, date of admission, history of presenting complaint, other symptoms present, risk factors, clinical signs, current medication, laboratory, radiological, bacteriological and histopathological findings, type and duration of antimicrobial therapy, any interventions and complications, discharge diagnosis and outcome.

ESR ≥10 mm in the first hour, CRP ≥20 mg/l and WBC ≥12 × 10^9/l were considered abnormal. Blood cultures (BC) typically consisted of one sample pair on admission. Specimens for tissue cultures (TC) were obtained by aspiration or open surgical procedure. Radiological findings were considered "characteristic" according to the radiology report. Osteomyelitis was considered "acute" if the history of complaint was shorter than 2 weeks and considered "haematogenous" in origin in the absence of penetrating wounds adjacent to the site of disease. Arthritis was considered "septic" if blood and/or or tissue cultures were positive. According to our inclusion criteria and definitions, patients were classified into three diagnostic groups, irrespective of the discharge diagnosis: AHOM, septic arthritis and AHOM with septic arthritis.

Results

Study population

A summary of the study population is shown in figure 1. Data of 81 patients (50 males = 61%) were available. Median age was 4 years in the septic arthritis group and 9 years in both the AHOM and the AHOM with septic arthritis group. Overall 50% of cases occurred until the age of 6 years (range 0–14 years); 6 cases occurred in the neonatal period. Age distribution is demonstrated in figure 2. 46 (57%) of patients were diagnosed as acute haematogenous osteomyelitis (AHOM) with or without concomitant effusion in the adjacent joint. 23 (28%) were diagnosed as septic arthritis and 12 (15%) as AHOM with septic arthritis. Median duration of complaints

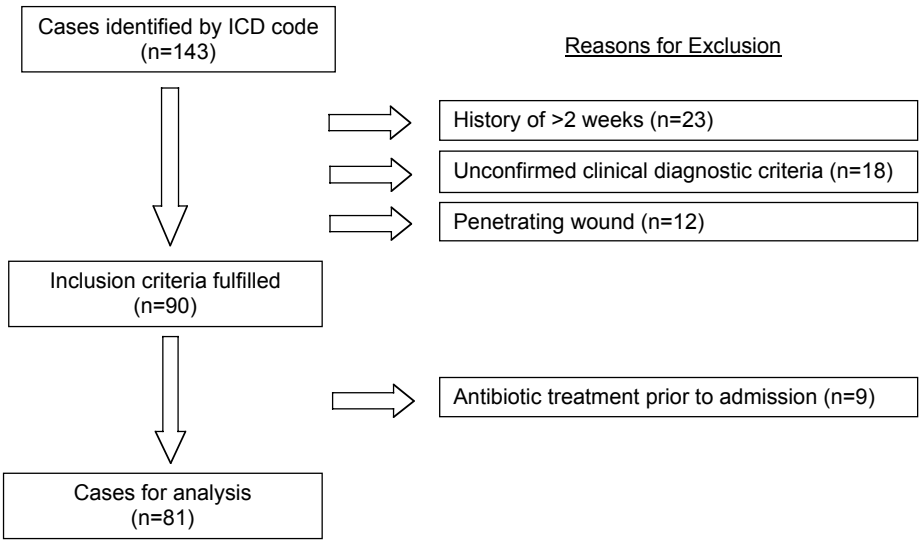


Figure 1
Study population.

Figure 2

Age distribution of 81 patients with acute hematogenous osteomyelitis and/or septic arthritis.

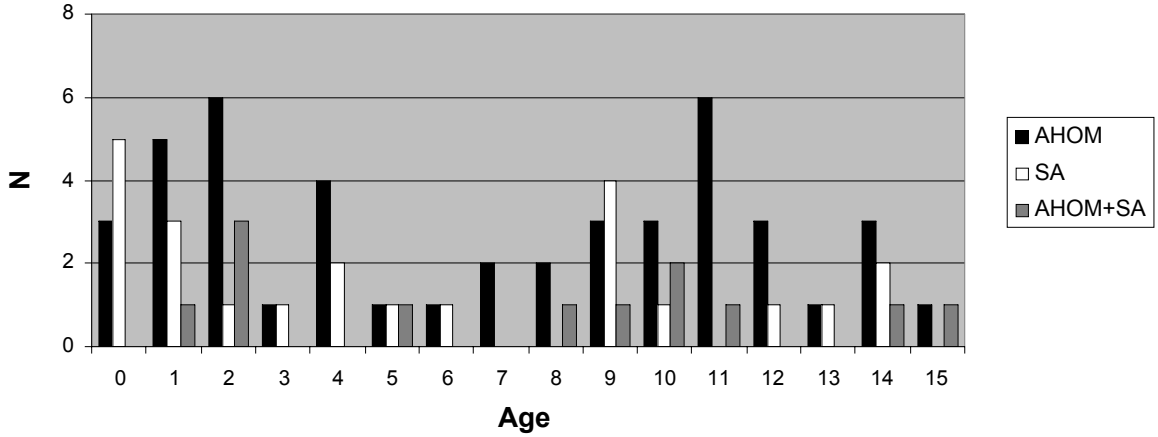


Table 1

Results of bacterial culture in 81 patients with acute haematogenous osteomyelitis and/or septic arthritis.

Investigation	performance	positive cultures
Blood cultures (BC) or tissue cultures (TC)	79 (98%)	53 (65%)
BC	67 (83%)	35 (52%)
TC	47 (58%)	27 (57%)

prior to hospitalisation was 3 days (range 0–14 days). 88% were admitted during the first week of complaints. Median duration of hospitalisation was 15 days (range 2–66 days). It varied between patients with AHOM (14 days), septic arthritis (16 days) and AHOM with septic arthritis (26 days). The time to admission as well as the duration of hospitalisation were independent of the causative organism and patient age (data not shown).

Clinical presentation

On admission 77 (95%) of 81 patients presented with pain, 65 (80%) with fever, 61 (75%) with local signs and 49 (60%) with restricted joint motility. All four symptoms were present in 32 (39%) patients. In two infants poor feeding was the main presenting symptom. In the majority of patients (77%) the location of the process was in the lower extremity. In patients with AHOM the following bones were involved: femur 24%, tibia18%, foot 10%, pelvis 13%, humerus 5%, clavicle and hand 3%, radius, patella and fibula and spine 2% each. Multifocal involvement was found in 13% of patients (6 months to 14 years of age).

In patients with septic arthritis the following joints were involved: hip 38%, knee 30%, ankle 18%, elbow 10% and shoulder 4%.

The following results are presented summarising patients with AHOM and/or septic arthritis. When analysed separately, no significant differences were found between groups (data not shown).

Imaging

In 79 patients (97%) radiological imaging techniques were used. Overall diagnostic radiological findings on admission were observed in 69 (85%) of these patients. 23 (59%) of 39 plain radiographs, 31 (56%) of 55 sonograms, 39 (89%) of 44 (^{99m}Tc)-labeled bone scans and 4 (100%) of 4 MRI were consistent with the suspected diagnosis. During the first week after onset of symptoms, however, only 42% of radiographs were diagnostic as compared to 87% of bone scans.

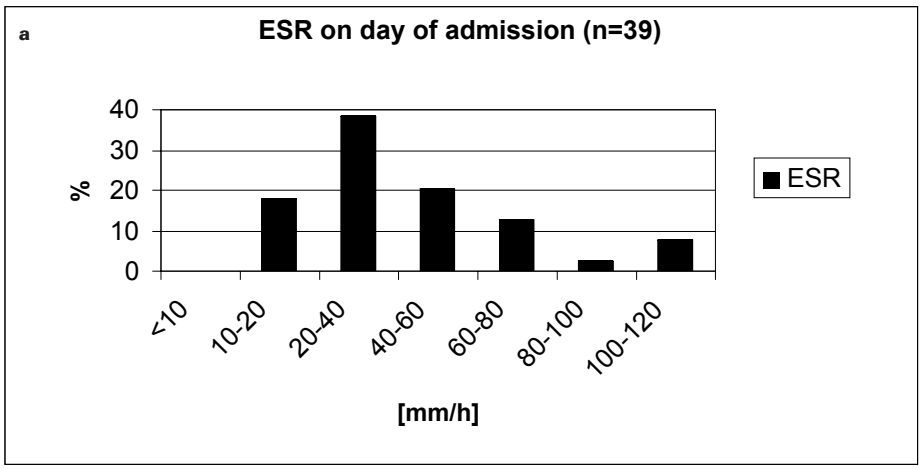
Laboratory findings

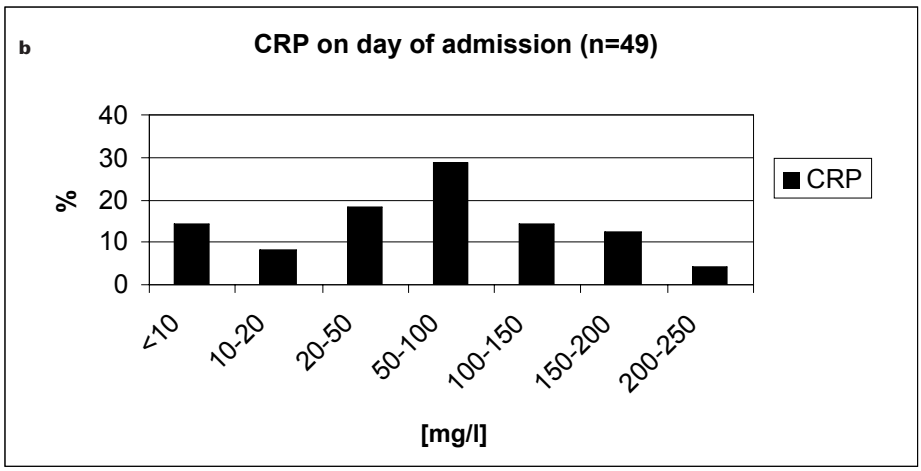
At the time of admission ESR was performed in 39 (48%), CRP in 49 (60%) and WBC in 77 (95%) of patients. ESR (1st hour in mm; median 36; range 11–124), CRP (mg/l; median 64; range 0–221) and WBC ($\times 10^9$/l; median 13; range 5–34) were above normal limits in 100%, 82% and 58% of patients, respectively. The level of laboratory parameters did not correlate with duration of history before hospitalisation (data not shown). A detailed distribution of laboratory results is depicted in figure 3a–c.

Table 2

Prevalence of isolated organisms by age of patients with acute haematogenous osteomyelitis and/or septic arthritis.

Organism	0–4 years (n = 28)	5–9 years (n = 18)	10–14 years (n = 16)	total (n = 62)
Staphylococcus sp.	14 (50%)	11 (61%)	14 (88%)	39 (63%)
Staph. aureus	8 (28%)	9 (50%)	14 (88%)	31 (50%)
coagulase-negative	6 (21%)	2 (11%)	0	8 (13%)
Streptococcus sp.	8 (29%)	4 (22%)	2 (12%)	14 (23%)
S. pyogenes	3 (11%)	4 (22%)	2 (12%)	9 (15%)
S. pneumoniae	3 (11%)	0	0	3 (5%)
S. agalacticae	2 (7%)	0	0	2 (3%)
H. influenzae	4 (14%)	0	0	4 (6%)
Others	2 (7%)	3 (16%)	0	5 (8%)





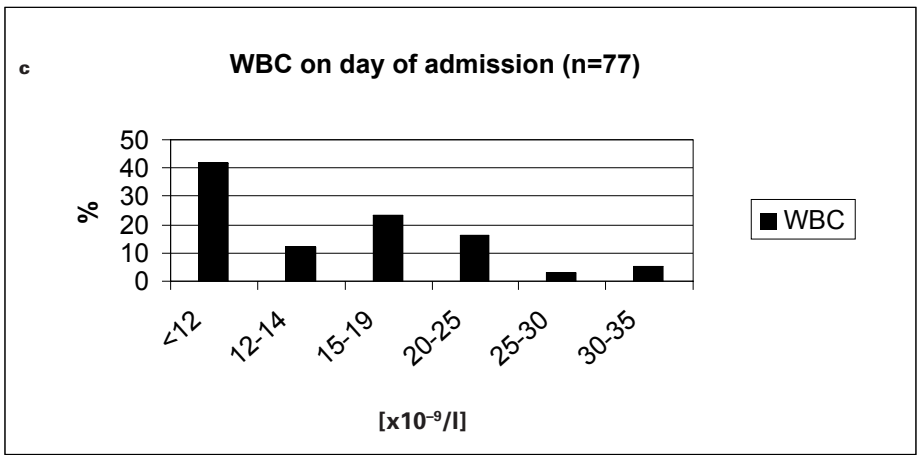


Figure 3a–c
Distribution of laboratory results in patients with acute hematogenous osteomyelitis and/or septic arthritis.
3a: ESR levels
3b: CRP levels
3c: white blood count

Bacteriology

Blood cultures (BC) and/or tissue cultures (TC) were performed in 79 (98%) of 81 patients. Overall, bacteria were isolated from 53 patients (65%). BC were performed in 67 patients (83%) and yielded 35 (52%) positive cultures. A fine needle aspirate was performed in 40 (49%), biopsies in 8 (10%) of patients. One aspirate was a *punctio sicca*. 47 samples yielded pus, infected tissue or joint fluid. Bacteriological cultures yielded 27 (57%) isolates.

In 34 patients with both BC and TC performed, 12 (35%) were positive in both tests. In 7 (20%) instances only BC and in 7 (20%) only TC were positive. Bacterial cultures were negative in 8 (23%) patients. The spectrum of organisms identified was similar in blood and tissue cultures (data not shown). A total of 62 organisms was detected. In 8 patients more than one organism could be identified. There were 39 (63%) Staphylococci (31 *S. aureus*, 8 coagulase-negative *S.*), 14 (23%) Streptococci (9 *S. pyogenes*, 2 *S. agalacticae*, 3 *S. pneumoniae*), 4 (6%) *Haemophilus influenzae*, and 5 other bacteria (2 *Enterococcus faecalis*, 1 *Corynebacterium sp.*, 1 *Actinomyces sp.*, 1 *Propionibacterium sp.*). The prevalence of isolated organisms by patient age is shown in table 2. Of the 8 cultures (from 8 patients) yielding coagulase negative Staphylococci, 4 derived from BC and 4 from TC. In the corre-

sponding other bacterial cultures of 4 of these patients, Enterococci, *Haemophilus influenzae*, Streptococci or *Proteus sp*. were found. In the remaining 4 patients, corresponding cultures were negative.

The four patients with cultures positive for *Haemophilus influenzae* (not typed) were 6 months and 1, 2 and 4 years of age. All cases occurred before 1992 (the year of introduction of Hib [Haemophilus influenzae] immunisation in Switzerland).

Therapy and outcome

Initially all patients received parenteral antibiotic therapy for 1–3 weeks, followed by oral administration to be continued after discharge. Amoxicillin/clavulanic acid was the most common initial choice (48%). An aminoglycoside was used in combination in 18% of patients.

40 patients (50%) underwent therapeutic surgery. Lavage and drainage, curettage and drainage and bone resection and drainage of the site was performed in 27, 11 and 3 patients respectively.

On discharge, 38 patients were free of signs and symptoms, 12 had minor symptoms (such as residual pain and fatigue) and in 31 patients restricted motility was still noted. 21 of these 31 patients had undergone surgery during admission.

Discussion

Our diagnostic criteria used for AHOM and septic arthritis are similar to those previously suggested [18–21]. In the majority of our patients (77%) the location of the process was in the lower extremity. The most frequent sites of AHOM were femur 24% and tibia18%. Septic arthritis was most commonly observed in the hip in 38% and the knee 30%. Multifocal involvement was found in 13%. The distribution of involved sites reported in the literature are 14–50% for the femur, 19–31% for the tibia, 14–30% for the hip, 35–45% for the knee and 7–12% for multiple lesions [2, 3, 5, 7, 10, 22–25].

On admission most frequent signs and symptoms were pain, fever, local signs of infection and restricted joint motility, which is in accordance with previously published case series [2, 3, 20–22]. Although pain and fever are the most frequent symptoms in most case series, our data demonstrate the variability of clinical presentation and emphasise the need for early investigation looking for objective parameters to confirm the diagnosis.

Prompt diagnosis of acute haematogenous osteomyelitis in children is essential as complications and long term sequelae rise dramatically if the diagnosis is not made within 3 days of onset of symptoms with a subsequent delay in implementing appropriate treatment [7, 16]. Median duration of symptoms of three days before admission in our study is in accordance with previous reports [2, 17, 20, 21]. Radiographic imaging constitutes the basis of diagnostic procedures. Sensitivity of early bone scans was 88% in our hands and this is in the upper range of previous results and render them suitable for early diagnosis. MRI, which has only recently been introduced as a valuable tool for diagnosing AHOM and also appears to be very sensitive (positive in all 4 patients tested). Numbers are, however, too small yet to make definitive statements as to the role of MRI. This is consistent with data by Elgazzar et al. reviewing 13 studies comparing imaging modalities for the assessment of osteomyelitis. A mean sensitivity of 88% for ^{99}Tc-bone scans and 92% for MRI was calculated in this review [27]. Jaramillo et al. reviewed 26 children with osteomyelitis and reported a positive predictive value of 85% for MRI and 83% for bone scans [28]. Although deep tissue swelling can be appreciated on conventional radiographs as early as 48 hours after onset of disease, earliest signs of bone destruction can usually only be demonstrated after 7–21 days. This renders conventional radiographs not helpful for early diagnosis. Ultrasound is a useful method to suspect the diagnosis relatively early since subperiostal exudates can be seen as early as 24 h after onset of disease [29]. However, interpretation of ultrasound findings is highly user and device dependent and relies on the presence of significant exudates or joint effusion. Hence, its sensitivity is considerably variable. Therefore, MRI or bone scan should be performed if unifocal involvement is suspected. If multifocal bone or joint involvement is considered, a bone scan should be the modality of choice.

Our data confirm initial values of ESR and CRP to be normal only in a small percentage of patients whereas WBC is a poor indicator of AHOM and septic arthritis. In a prospective study of 44 children with osteomyelitis, Unkila-Kallio et al. demonstrated initial ESR, CRP and WBC values to be elevated in 92%, 98% and 34% of patients, respectively [19]. Similar data were shown for septic arthritis by the same group [30]. In a review of 86 children Dahl et al. reported that ESR was elevated in 96%, CRP in 89% and WBC in 12% [20]. Klein and coworkers reviewed 26 paediatric cases of septic hip infections. They observed ESR to be elevated in 95% and emphasised that the WBC was increasing with age and turned out to be positive in 73% of their cases [31]. The age dependence of WBC levels could not be confirmed in our analysis (data not shown). Initial values of CRP in our series were less helpful for a diagnosis of AHOM and/or septic arthritis compared to ESR values. We have no ready explanation for this observation.

The diagnosis of AHOM depends on a high index of suspicion and is strongly supported by imaging techniques but is only secured if bacterial culture is positive [24, 32]. In our study 52% of BC and 57% of TC were positive. Reviewing ten case series providing data on positive BC, a mean of

46% (range 24–74%) can be found [2, 3, 9, 12, 15, 19–21, 26, 30].The mean value for positive TC in ten previous studies was 67% (range 45–83%) [2, 3, 12, 15, 19–23, 30]. Performing both, BC and TC, increased the sensitivity by 20% in comparison to BC alone in our hands. Still, in one third of patients no causative agent could be identified. This is in line with many other previously reported case series [5, 11, 13–15]. Thus, there is a need to further improve microbiological diagnostic procedures. Although Jalava et al. could not demonstrate an increase of organisms found by the use of PCR in septic arthritis [33], other reports indicate that PCR may be promising in this respect [34, 35].

Gram positive organisms are the most common pathogens causing AHOM and SA. A 50% occurrence of *Staph. aureus* as the infective agent in our series is in accordance with previous results. Cole et al. found *Staph. aureus* in 48% in a prospective study of 76 patients with AHOM in Australia, Dich et al. reported a *Staph. aureus* rate 59% in a review of 163 cases of AHOM during 15 years (1959–73) in the US, Karwowska el al. found 69% of isolated organisms to be *Staph. aureus* in their review of 128 patients with AHOM between 1984 and 96 in the US [2, 7, 21]. Unkila-Kallio et al. identified *Staph. aureus* even in 89% of bacteria in a prospective study of AHOM in Finland [19]. A recent study by Caksen et al. reviewing 40 patients with septic arthritis demonstrates the overall frequency of 50% *Staph. aureus* in children between 6 months and 14 years of age in Turkey [22]. The observation of a decrease over time of *Staph. aureus* as the causative agent of AHOM from 55% to 31% as described by Craigen et al. in a retrospective study of 275 patients in Scotland between 1979 and 1990 is not confirmed by our data [26].

The reason for the variability of *Staph. aureus* isolation rates in previous studies is probably due to the wide range of age distribution in these case series. The predominance of *Staph. aureus* as the causative organism was strikingly age-dependent in our investigation. *Staph. aureus* represented only 50% of isolates in children younger than 5 years of age compared to 60% in those 5–9 years of age and 90% in those 10–14 years of age. Although Dich et al. and Nelson et al. report highest relative *Staph. aureus* incidences between 2 and 10 years of age [2, 15] our findings correlate with those of several other reports providing age related data on causative organisms [3, 6, 10–12, 23, 36]. For children with AHOM Highland et al. reported a 50% occurrence of *Staph. aureus* in infants and an 80% occurrence above 5 years of age [36]. Green et al. [10] emphasised the high frequency (63%) of Streptococci in infants with AHOM whereas Welkon et al. found 82% *H. influenzae* in infants with septic arthritis [11]. Nelson et al, in a review of 117 patients with septic arthritis in the US between 1955 and 1965, and thus long before introduction of immunisation against Haemophilus, demonstrated that the major pathogen in the younger age group was *H. influenzae* (17% of positive cultures). In contrast *S. aureus* (37% of positive cultures) was the predominant organism in the older age group [5]. Thus, the diversity of other organisms found particularly in the younger age groups emphasises the importance to aim for identification of the causative pathogen. A needle biopsy or surgical sampling of infected tissue provides indispensable information. A direct gram stain of aspirates sometimes helps to determine the nature of the organism at the earliest possible occasion. In some instances only the histo-pathological examination of a bone-biopsy specimen will reveal the accurate diagnosis [24]. Bone and joint aspirate should be obtained from every patient with suspected AHOM or septic arthritis particularly if blood cultures are negative. For septic arthritis this is mandatory for a favorable outcome. For both, AHOM and septic arthritis, it not only promotes the effectiveness of antimicrobial therapy but also increases the probability to identify the causative organism [5, 12, 15, 21]. This will guide the change to the safest, specific, narrow-range antibiotic therapy after the required initial, broad empiric treatment.

In conclusion our data suggest that the diagnostic procedures of choice should be early MRI or bone scan, accompanied by blood culture *and* tissue culture. Of supportive laboratory parameters, ESR and CRP were most valuable in our hands.

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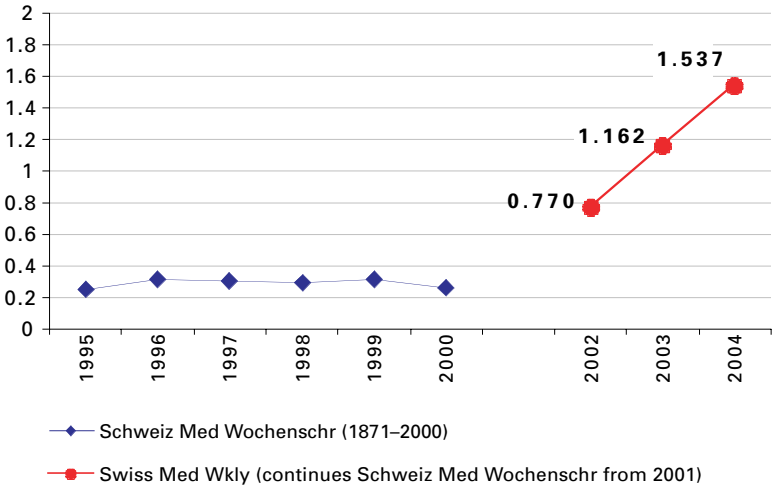

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