Dexamethasone Therapy for Septic Arthritis in Children

Itay Fogel, MD, MHA[a], Jacob Amir, MD[a], Elhanan Bar-On, MD[b], Liora Harel, MD[c]

abstract

BACKGROUND AND OBJECTIVE: Prospective studies of children with septic arthritis report that adding dexamethasone to antibiotic therapy contributes significantly to clinical and laboratory improvement. This study sought to evaluate the effect of this regimen outside of a randomized controlled trial.

METHODS: The sample consisted of children with septic arthritis hospitalized at a tertiary pediatric medical center in 2008 to 2013. Disease course and outcome were compared between children treated with antibiotics alone or with adjuvant dexamethasone, according to the admitting department policy.

RESULTS: The cohort included 116 patients, 90 treated with antibiotics alone and 26 treated with antibiotics+dexamethasone. The groups were similar for age, symptom duration before hospitalization, body temperature, acute-phase reactant levels, and rate of positive fluid cultures (21.6% total). Compared with monotherapy, antibiotics+dexamethasone treatment was associated with a shorter duration of fever (mean 2.3 vs 3.9 days, $P = .002$), more rapid clinical improvement (mean 6.3 vs 10.0 days to no pain/limitation, $P < .001$), more rapid decrease in C-reactive protein level to <1 mg/dL (mean 5.3 vs 8.4 days, $P = .002$), shorter duration of parenteral antibiotic treatment (mean 7.1 vs 11.4 days, $P < .001$), and shorter hospital stay (mean 8.0 vs 10.7 days, $P = .004$). Recurrent symptoms of fever and joint pain occurred in 4 patients in the antibiotics+dexamethasone group after completion of the steroid course.

CONCLUSIONS: Children with septic arthritis treated early with a short course of adjuvant dexamethasone show earlier improvement in clinical and laboratory parameters than children treated with antibiotics alone.

WHAT'S KNOWN ON THIS SUBJECT: Two prospective studies of children with septic arthritis have shown that the addition of dexamethasone to antibiotic therapy contributes to clinical and laboratory improvement. Nevertheless, the mainstay of treatment remains antibiotics alone.

WHAT THIS STUDY ADDS: This study, which was conducted outside a randomized controlled trial, demonstrates that children with septic arthritis treated early with a short course of adjuvant dexamethasone show earlier improvement in clinical and laboratory parameters than children treated with antibiotics alone.

[a]*Department of Pediatrics C,* [b]*Orthopedic Clinic, and* [c]*Rheumatology Unit, Schneider Children's Medical Center of Israel, Petach Tikva, and Sackler Faculty of Medicine, Tel Aviv University, Tel Aviv, Israel*

Dr Fogel contributed to the acquisition of the data and design of the work, and drafted the initial manuscript; Dr Amir contributed to the conception of the work and interpretation of the data, drafted the initial manuscript, and critically revised the manuscript for important intellectual content; Dr Bar-On contributed to the acquisition and interpretation of the data, and revised the manuscript critically for important intellectual content; Dr Harel contributed to the conception of the work and analysis and interpretation of the data, and revised the manuscript critically for important intellectual content; and all authors approved the final manuscript as submitted.

www.pediatrics.org/cgi/doi/10.1542/peds.2014-4025

DOI: 10.1542/peds.2014-4025

Accepted for publication Jul 30, 2015

Address correspondence to Itay Fogel, MD, Department of Pediatrics C, Schneider Children's Medical Center of Israel, Petach Tikva 49202, Israel. E-mail: fogelitay@gmail.com

PEDIATRICS (ISSN Numbers: Print, 0031-4005; Online, 1098-4275).

Septic arthritis is a severe, rapidly progressive erosive disease.[1] Despite the use of antimicrobial treatment, the inflammatory process may be prolonged, leading to delayed recovery and residual joint damage.[2,3] Studies have shown that the host immune response is responsible for the ongoing inflammation, particularly activation of CD4 T lymphocytes induced by *Staphylococcus* exotoxins.[4,5] Sáez-Llorens et al[6] demonstrated that the synovial fluid of children with septic arthritis has high concentrations of tumor necrosis factor-α and interleukin (IL)-1β, which correlate with the severity of the inflammatory process.

Prompted by these findings and the good results obtained with the use of corticosteroids in meningitis,[7,8] researchers have suggested that the administration of systemic corticosteroids along with antibiotic therapy may be beneficial in septic arthritis. Studies in animal models reported a reduction in mortality rates and disease severity with the combined regimen.[5,9] These results were supported by 2 clinical studies in children. The first, by Odio et al,[10] showed that a short course of dexamethasone significantly shortened the duration of symptoms and reduced residual joint dysfunction. The second study was conducted by our group in 49 patients using a randomized double-blind placebo-controlled design. We found that the administration of dexamethasone as adjuvant therapy led to significant clinical and laboratory improvement, shortened the duration of hospitalization, and accelerated recovery.[11]

The aim of the current study was to further evaluate the effect of this regimen in children with septic arthritis outside a randomized controlled trial. The primary outcome measure was time to full recovery in children with septic arthritis who received dexamethasone as an adjunctive therapy relative to those who received antibiotics alone.

METHODS

Patients and Setting

A retrospective cohort study design was used. The sample consisted of children aged 2 months to 18 years hospitalized at our tertiary pediatric medical center from January 2008 (the end of our previous prospective study) to December 2013 who were discharged with a diagnosis of septic arthritis. Exclusion criteria were history of chronic arthritis, autoimmune disease, or immune deficiencies and arthritis secondary to a puncture wound. In addition, the medical records from discharge to last clinic follow-up visit were reviewed, and patients in whom another diagnosis was suspected on the basis of the follow-up data were excluded, as were patients with <6 months' follow-up.

The study was approved by the Institutional Review Board of Rabin Medical Center.

Departmental Diagnostic and Treatment Procedures

The diagnosis of septic arthritis at our center is based on the following criteria: acute onset of pain and limitation of motion in the hip or shoulder or acute onset of swelling, pain, local warmth, and limitation of motion in other joints, combined with an elevated level of C-reactive protein (CRP; normal upper limit, 1 mg/dL), with or without elevations in other acute-phase reactants, namely erythrocyte sedimentation rate (ESR; normal upper limit, 30 mm/h) and white blood cell (WBC) count (normal upper limit 14.0/mm^3). In addition, aspiration is routinely performed except in small or difficult-to-access joints (sacroiliac, intraphalangeal) in which small volumes are expected, and the presence of joint fluid with a turbid purulent appearance is a mandatory diagnostic criterion.

MRI was not used at our institution for routine diagnosis of septic arthritis or osteomyelitis during the study period.

Treatment of septic arthritis at our institution is primarily medical. Irrigation is routinely performed at the time of aspiration only when the hip joint is involved, and in these cases, repeated aspirations are done on a daily basis. If fluid has reaccumulated after 2 aspirations, patients undergo formal irrigation and debridement in the operating room.

In the present cohort, some of the patients were treated with antibiotics alone, whereas others were treated with intravenous dexamethasone 0.15 mg/kg per dose every 6 hours for 16 consecutive doses along with antibiotics, as previously reported. The administration of corticosteroids depended on the policy of the specific admitting department and was determined at the discretion of the attending physician. The switch from intravenous to oral treatment was based on a decrease in CRP to <1 mg/dL.

Data Collection and Analysis

For the current study, the following information was obtained from the medical records of each patient: gender, age, affected joint, body temperature; WBC, ESR, and CRP level at admission; duration of symptoms before hospitalization; type and duration of intravenous antibiotics; days of hospitalization; need for surgery; WBC count in joint fluid aspirate; microbiology findings in blood and joint cultures; findings on bone scan if performed; and use of corticosteroids or nonsteroidal antiinflammatory drugs (NSAIDs) during hospitalization.

Clinical and laboratory improvement after onset of treatment was compared between patients treated with antibiotics alone or with antibiotics+dexamethasone, according to the following

parameters: first day of hospitalization without fever (<38°C); number of days to full recovery, defined as no limitation of joint movement on physical examination and no complaints of joint pain until discharge (according to the daily medical records); number of days until CRP level dropped to <1 mg/dL; duration of intravenous antibiotic treatment; and length of hospital stay.

Symptom recurrence was defined as findings of fever >38°C and renewal of pain in the same affected joint during hospitalization after remission was achieved. Discharge was determined by the attending physician.

Statistical Analysis

No a priori analysis was performed to determine sample size. Data were analyzed using BMDP Statistical Software (Statistical Solutions Ltd, Boston, MA). Between-group differences in discrete variables were analyzed with Pearson χ^2 test or Fisher's exact test, as applicable. Continuous variables were compared by using analysis of variance with the Levene test. When the Levene test for variances was significant, we applied the Brown-Forsythe test for equality of means (variances not assumed to be equal). A $P \leq .05$ was considered significant.

RESULTS

Of the 155 children diagnosed with septic arthritis during the study period, 12 were excluded because of insufficient duration of posthospitalization follow-up and another 27 failed to meet the inclusion criteria. The remaining 116 patients included 90 (77.6%) treated with antibiotics alone and 26 (22.4%) treated with antibiotics and dexamethasone (Fig 1). The 2 groups were similar in gender distribution, age, body temperature on admission, level of acute-phase reactants, and duration of symptoms before hospitalization (Table 1). The median follow-up times reported for the

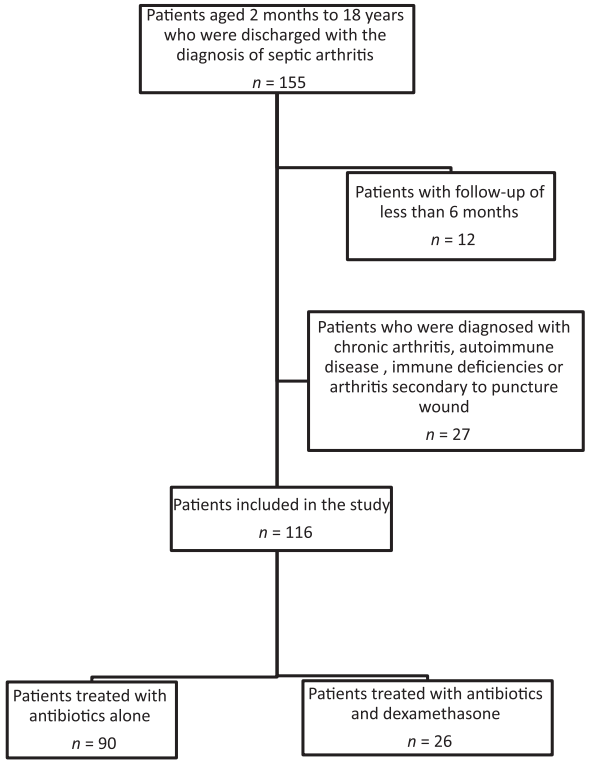

FIGURE 1
Flowchart of patient selection for the study.

patients included in the study were 53 months (range 9–75 months) in the antibiotics-only group and 30 months (range 6–58 months) in the antibiotics+dexamethasone group.

The joints affected included the knee (n = 54), hip (n = 23), ankle (n = 14), shoulder (n = 10), elbow (n = 8), wrist (n = 6), proximal interphalangeal joint (n = 2), and sacroiliac joint (n = 1). The knees and hips were the joints most often involved in the antibiotics +dexamethasone group (92.3%) as opposed to the antibiotics-only group (58.9%) (Table 2). There was a significant difference between the groups in the rate of involvement of the knee (P = .003) but not any of the other joints (Table 2). In 2 patients in the antibiotics-only group, 2 joints were involved: knee and hip or knee and shoulder; in the remaining 114 patients, only 1 joint was involved (Table 2).

Bone scan was performed in 47 patients, of whom 30 were diagnosed with arthritis without osteomyelitis and 10 were diagnosed with arthritis and osteomyelitis. The remainder had inconclusive results. All cases of osteomyelitis were found in the antibiotics-only group.

Microbiology studies were positive in 21.6% of the cohort. Bacteria were isolated from the synovial fluid in 24 patients and from the blood in 1 patient (Table 3). There was no significant difference between the groups in the rate of positive fluid cultures (P = .86). Broad-range 16S rRNA gene-based polymerase chain reaction (PCR) study of the joint fluid aspirate was positive for *Kingella kingae* in 1 patient for whom the culture results were negative. PCR testing was not performed in any other patient in the cohort. Although culture-negative patients were not tested routinely for other kinds of arthritis, the patient with sacroiliac joint involvement was evaluated for levels of antinuclear antibody, rheumatoid factor, and HLA-B27; all

TABLE 1 Characteristics of Children With Septic Joint Arthritis Treated With Antibiotics Alone or With Dexamethasone

Characteristics	Antibiotics Alone, Mean (95% CI)	Dexamethasone and Antibiotics, Mean (95% CI)	*P*
Age, mo	27.4 (20.7–34.2)	20.6 (15.6–25.6)	.88[a]
Fever on admission, °C	38.8 (38.6–39.0)	38.9 (38.5–39.2)	.68[b]
WBC on admission, /mm^3	14.4 (13.5–15.4)	15.4 (14.0–16.8)	.33[b]
CRP on admission, mg/dL	6.3 (4.9–7.7)	5.6 (3.8–7.4)	.96[a]
ESR on admission, mm/h	52.2 (45.9–58.6)	55.9 (44.2–67.6)	.46[a]
Duration of symptoms before hospitalization, d	3.7 (3.0–4.5)	3.5 (2.3–4.6)	.88[a]

CI, confidence interval.

[a] Nonparametric Mann-Whitney test.

[b] Student's *t* test.

results were negative. Mean cell count in the joint fluid was 109 855 cells/mm^3, with >90% polymorphonuclears in all aspirates, consistent with septic arthritis.

NSAIDs were administered during hospitalization to 19 patients in the antibiotics-only group (21.1%) and 1 patient (3.8%) in the antibiotics+dexamethasone group (P = .04). Among the 23 patients with an infected hip joint, 6 underwent irrigation and debridement: 5 (28%) of 18 in the antibiotics-only group and 1 (20%) of 5 in the antibiotics+dexamethasone group. No other joints were treated with irrigation and debridement, as per our hospital policy.

Findings for the clinical and laboratory follow-up parameters are shown in Table 4. Compared with the group treated with antibiotics alone, the antibiotics+dexamethasone group had a significantly shorter duration of fever (mean 2.3 vs 3.9 days, P = .002), shorter time to full recovery (mean 6.3 vs 10.0 days, $P < .001$), shorter time to a decrease in CRP level to <1 mg/dL (mean 5.3 vs 8.4 days, P = .002), shorter duration of intravenous antibiotic treatment (mean 7.1 vs 11.4 days, $P < .001$), and shorter hospital stay (mean 8.0 vs 10.0 days, P = .004). The total duration of antibiotic treatment (oral and parenteral) was 3 to 4 weeks for both groups, regardless of the clinical or laboratory parameters.

Four patients (15.4%) aged 12 to 22 months had a brief recurrence of symptoms during hospitalization, within <1 week after completing the 4-day corticosteroid course and while receiving parenteral antibiotic therapy. Three of the 4 patients were culture-negative, and 1 had *Streptococcus pneumoniae* in the joint fluid. All recurrences were mild, with no elevation in CRP levels, and resolved within 1 to 2 days. None of the patients required additional aspirations or prolonged antibiotic administration or additional corticosteroid therapy.

TABLE 2 Affected Joints in Children With Septic Arthritis Treated With Antibiotics Alone or With Dexamethasone

Affected Joint	Antibiotics Alone, n = 90, n (%)	Antibiotics and Dexamethasone, n = 26, n (%)	*P*
Knee	35 (38.9)[a]	19 (73.1)	.003
Hip	18 (20)	5 (19.2)	.999
Ankle	13 (14.4)	1 (3.8)	.187
Wrist	5 (5.6)	1 (3.8)	.999
Shoulder	10 (11.1)	0 (0)	
Elbow	8 (8.9)	0 (0)	
PIP	2 (2.2)	0 (0)	
Sacroiliac	1 (1.1)	0 (0)	

PIP, proximal interphalangeal joint.

[a] One patient had involvement of knee and hip simultaneously and another patient had involvement of knee and shoulder simultaneously.

DISCUSSION

The current study confirms earlier reports that the administration of adjunctive corticosteroids in children with septic arthritis enhances the rate of clinical and laboratory recovery.

The advantages of adding corticosteroids to antibiotics in the treatment of children with septic arthritis have been demonstrated in 2 randomized prospective double-blind controlled studies.[10–12] The results showed that a 4-day course of adjuvant dexamethasone shortened the duration of symptoms and hospital stay and reduced residual dysfunction at the end of therapy. The rationale for the dosing schedule was derived from the *Haemophilus influenzae B* meningitis protocol[13]; the use of corticosteroids was prompted by findings of a decrease in synovial T-cell and macrophage levels in animals with septic arthritis treated with dexamethasone and antibiotics.[5,9] The experimental studies also noted an association of lower synovial fluid concentrations of IL-1β, IL-1, tumor necrosis factor-α, and metalloproteinases, in addition to a decrease in cartilage degradation, which is mediated by these cytokines.[5,9] The authors speculated that the corticosteroids exerted an inhibitory effect on T- and B-cell proliferation and differentiation, leading to a decrease in cytokine production.

In the present observational study, which was started at the end of our previous prospective study, we sought to further evaluate the effect of adding dexamethasone to antibiotics on the clinical course of septic arthritis in children outside of a randomized controlled trial. We found a greater improvement in clinical and laboratory parameters in

TABLE 3 Microbiology Findings in Joint Fluid and Blood in 116 Children With Septic Arthritis

Isolated Pathogen	No. of Isolated Pathogens
Kingella kingae	8
Staphylococcus aureus (MSSA)[a]	6
Streptococcus group A	4
Streptococcus pneumoniae	2
Gram-negative bacilli	2
Streptococcus viridians[b]	1
Coagulase-negative *Staphylococcus*	1
Streptococcus group B	1
Corynbacterium	1

[a] Five of the MSSA bacteria were isolated from the synovial fluid and 1 from the blood.

[b] *Streptococcus viridians* and MSSA were isolated from the same synovial fluid aspiration.

the children treated with antibiotics +dexamethasone than in the children given antibiotics alone.

Regarding the treatment of septic arthritis of the hip, our institutional policy was changed in 2005 to include repeated ultrasound-guided aspirations and irrigations as the initial procedure, before surgical debridement. Reaccumulation of joint fluid after 2 aspirations coupled with a lack of clinical improvement after 48 hours are considered indications for surgical drainage. We do not typically treat joints other than the hip with repeated aspirations or irrigations. These practices are not the gold standard in many institutions, but they are acceptable in others.[14–16] As these differences might affect the clinical and laboratory parameters, we suggest that the administration of corticosteroids for septic arthritis be further evaluated in institutions in which repeated aspirations and irrigation or debridement are performed routinely.

The bacterium most often isolated in our study was *Kingella kingae*, followed by methicillin-sensitive *Staphylococcus aureus* (MSSA). None of the cultures grew methicillin-resistant *S aureus* (MRSA). *K kingae* infection was also one of the most common causes of childhood septic arthritis in several previous studies[17,18] and the earlier study from our center.[11] By contrast, Odio et al[10] found *S aureus* to be the most common pathogen. Because penetrance of antibiotics into the joint fluid was not directly evaluated in our study, we could not determine if it was affected by the corticosteroids. This treatment protocol needs to be further evaluated in patients positive for MRSA infection. One patient with negative culture results was found to be positive for *K kingae* on PCR study. We believe the growing use of PCR in this setting will increase the likelihood of isolating pathogens that cannot be identified by routine cultures. It is noteworthy that *K kingae*, which causes less virulent septic arthritis, predominates in our country and was the pathogen most often isolated in our study and other studies from our region.[17] Therefore, we cannot generalize the present findings for adjunctive corticosteroids to countries and regions harboring more virulent pathogens of septic arthritis.

TABLE 4 Clinical and Laboratory Parameters of Improvement in Children With Septic Arthritis Treated With Antibiotics Alone or With Dexamethasone

Parameter	Antibiotics, Mean (95% CI)	Antibiotics and Dexamethasone, Mean (95% CI)	P[a]
First day fever <38°C	3.9 (2.9–4.9)	2.3 (2.1–2.5)	.002
First day CRP <1 mg/dL	8.4 (6.9–9.9)	5.3 (4.0–6.6)	.002
Hospital stay, d	10.7 (9.4–12.1)	8.0 (6.8–9.2)	.004
Duration intravenous treatment, d	11.4 (9.7–13.1)	7.1 (5.9–8.3)	<.001
Time to full recovery, d	10.0 (8.5–11.6)	6.3 (4.9–7.7)	<.001

CI, confidence interval.

[a] Brown-Forsythe test (variances not assumed to be equal, following Levene test for variances).

The proportion of patients with large joint involvement (hip and particularly knee) was significantly higher in the antibiotics +dexamethasone group (92.3%) than in the antibiotics-only group (58.2%). Furthermore, infections of the shoulder, elbow, interphalangeal proximal joint, ankle, and sacroiliac joint were almost exclusively found in the antibiotics-only group. This unbalanced distribution suggests an important selection bias. We assume septic arthritis has a less indolent and more easily diagnosed presentation when it occurs in the larger joints, especially the knee. In patients with suspected septic arthritis in other joints, physicians may hesitate to treat with corticosteroids so as not to mask the diagnosis.

A second possible selection bias is suggested by the finding that the antibiotics-only group included all 10 patients in our cohort with osteomyelitis and both patients with 2 affected joints. It also contained a higher (albeit nonsignificant) proportion of patients with infected hip joints treated by irrigation and debridement (28% vs 20% in the antibiotics+dexamethasone group). Therefore, the more severe illness or greater number of surgeries may have accounted for the longer hospital stay of the antibiotics-only group, rather than the lack of corticosteroid treatment per se. Nevertheless, given the significantly greater improvement in clinical and laboratory parameters in the combined treatment group ($P < .001$ for some), we believe it is possible that the corticosteroids played a major beneficial role in their outcome. NSAIDs can potentially alleviate pain, although there is no scientific evidence of their usefulness in cases of septic arthritis. In the present cohort, NSAIDs were administered on an as-needed basis to 19 (21.1%) of 90 patients in the antibiotics-only group compared with only 1 (3.8%) of 26 patients in the antibiotics+dexamethasone group.

None of the patients in either group received opiates to alleviate pain. Therefore, it is possible that the antiinflammatory properties of corticosteroids were responsible for the lesser need for analgesics in the antibiotics+dexamethasone group. Despite their use of NSAIDs, patients in the antibiotics-only group improved at a slower rate than patients in the combined treatment group.

There were no side effects of corticosteroids during hospitalization. However, 4 patients treated with antibiotics+dexamethasone experienced a recurrence of symptoms less than a week after completing the steroid course, while still on antibiotics. Although the abrupt discontinuation of corticosteroids is known to be associated with a return of symptoms, short courses of corticosteroids (up to 7 days) are considered safe, with no or minimal effects of withdrawal.[19] Accordingly, all recurrent symptoms in the current study were mild and resolved spontaneously, and none of the patients required an additional course of corticosteroids or additional antibiotics.

Complications of septic arthritis include osteomyelitis, chronic infection, avascular necrosis, abnormal bone growth, limb-length discrepancy, pathologic fractures, deep vein thrombosis, and pulmonary emboli.[12,20] Neonatal age, immunosuppressive diseases, hip joint involvement, delay in antibiotic treatment, and MRSA infection are known predictors of complications.[20] In the current study, no complications of septic arthritis other than osteomyelitis were documented from discharge to the last clinic visit (minimum 6 months) in the patients selected for the study. Accordingly, in our previous prospective study, no sequelae were observed in either the corticosteroid or placebo group at the 1-year follow-up.[11] However, because children are in a dynamic state of growth, some of the known complications of corticosteroids might not become apparent for months or years.[1] Furthermore, most patients with risk factors for complications were excluded from our study. Hence, we cannot draw conclusions regarding the long-term adverse effects of corticosteroids from this study.

The main limitations of our study are the retrospective design and low rate of positive bacterial cultures from joint fluid aspirates. Although there is a possibility that up to 78.4% of the culture-negative patients did not have septic arthritis, it is likely that most of the patients who were culture-negative were infected with *K kingae*, which is the most prevalent pathogen in our area and the one most frequently responsible for negative cultures. Furthermore, we did not test for other rheumatologic diseases, but we assume they can be excluded in most of the patients with negative cultures, given the lack of development of any other joint problems after recovery, lack of any other extra-articular manifestations, and the much higher reported incidence of septic arthritis than chronic rheumatologic diseases in children.[21,22]

CONCLUSIONS

A short course of dexamethasone given early in addition to antibiotics to children with septic arthritis leads to significant clinical and laboratory improvement, shortens the duration of treatment, and accelerates recovery. Further studies are needed to examine possible long-term sequelae in children treated with antibiotics with or without adjunctive dexamethasone.

ABBREVIATIONS

CRP: C-reactive protein
ESR: erythrocyte sedimentation rate
IL: interleukin
MRSA: methicillin-resistant *Staphylococcus aureus*
MSSA: methicillin-sensitive *Staphylococcus aureus*
NSAIDs: nonsteroidal antiinflammatory drugs
PCR: polymerase chain reaction
WBC: white blood cell

FINANCIAL DISCLOSURE: The authors have indicated they have no financial relationships relevant to this article to disclose.

FUNDING: No external funding.

POTENTIAL CONFLICT OF INTEREST: The authors have indicated they have no potential conflicts of interest to disclose.

REFERENCES

1. Kaplan SL. Septic arthritis. In: Kliegman RM, Stanton BF, St. Geme JW, et al, eds. *Nelson Textbook of Pediatrics*. 19th international ed. Philadelphia, PA: Saunders Elsevier; 2011:2398
2. Welkon CJ, Long SS, Fisher MC, Alburger PD. Pyogenic arthritis in infants and children: a review of 95 cases. *Pediatr Infect Dis*. 1986;5(6):669–676
3. Howard JB, Highgenboten CL, Nelson JD. Residual effects of septic arthritis in infancy and childhood. *JAMA*. 1976;236(8):932–935
4. Abdelnour A, Bremell T, Holmdahl R, Tarkowski A. Role of T lymphocytes in experimental *Staphylococcus aureus* arthritis. *Scand J Immunol*. 1994;39(4):403–408
5. Sakiniene E, Bremell T, Tarkowski A. Addition of corticosteroids to antibiotic treatment ameliorates the course of experimental *Staphylococcus aureus* arthritis. *Arthritis Rheum*. 1996;39(9):1596–1605
6. Sáez-Llorens X, Mustafa MM, Ramilo O, Fink C, Beutler B, Nelson JD. Tumor

necrosis factor alpha and interleukin 1 beta in synovial fluid of infants and children with suppurative arthritis. *Am J Dis Child*. 1990;144(3):353–356

7. Brouwer MC, Heckenberg SG, de Gans J, Spanjaard L, Reitsma JB, van de Beek D. Nationwide implementation of adjunctive dexamethasone therapy for pneumococcal meningitis. *Neurology*. 2010;75(17):1533–1539
8. DE Gaudio M, Chiappini E, Galli L, DE Martino M. Therapeutic management of bacterial meningitis in children: a systematic review and comparison of published guidelines from a European perspective. *J Chemother*. 2010;22(4):226–237
9. Jafari HS, Sáez-Llorens X, Paris M, et al. Dexamethasone attenuation of cytokine-mediated articular cartilage degradation in experimental lapine *Haemophilus* arthritis. *J Infect Dis*. 1993;168(5):1186–1193
10. Odio CM, Ramirez T, Arias G, et al. Double blind, randomized, placebo-controlled study of dexamethasone therapy for hematogenous septic arthritis in children. *Pediatr Infect Dis J*. 2003; 22(10):883–888
11. Harel L, Prais D, Bar-On E, et al. Dexamethasone therapy for septic arthritis in children: results of a randomized double-blind placebo-controlled study. *J Pediatr Orthop*. 2011; 31(2):211–215
12. Dodwell ER. Osteomyelitis and septic arthritis in children: current concepts. *Curr Opin Pediatr*. 2013;25(1):58–63
13. Sáez-Llorens X, Ramilo O, Mustafa MM, Mertsola J, McCracken GH Jr. Molecular pathophysiology of bacterial meningitis: current concepts and therapeutic implications. *J Pediatr*. 1990;116(5): 671–684
14. Givon U, Liberman B, Schindler A, Blankstein A, Ganel A. Treatment of septic arthritis of the hip joint by repeated ultrasound-guided aspirations. *J Pediatr Orthop*. 2004;24(3):266–270
15. Tanwar YS, Jaiswal A, Singh S, Arya RK, Lal H. Acute pediatric septic arthritis: a systematic review of literature and current controversies. *Pol Orthop Traumatol*. 2014;79:23–29
16. John J, Chandran L. Arthritis in children and adolescents. *Pediatr Rev*. 2011; 32(11):470–479, quiz 480
17. Yagupsky P. *Kingella kingae*: from medical rarity to an emerging paediatric pathogen. *Lancet Infect Dis*. 2004;4(6): 358–367
18. 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 Infect Dis J*. 2007;26(5):377–381
19. Annane D, Sébille V, Charpentier C, et al. Effect of treatment with low doses of hydrocortisone and fludrocortisone on mortality in patients with septic shock [published correction appears in *JAMA*. 2008;300(14):1652]. *JAMA*. 2002;288(7): 862–871
20. Wang CL, Wang SM, Yang YJ, Tsai CH, Liu CC. Septic arthritis in children: relationship of causative pathogens, complications, and outcome. *J Microbiol Immunol Infect*. 2003;36(1):41–46
21. Yagupsky P, Bar-Ziv Y, Howard CB, Dagan R. Epidemiology, etiology, and clinical features of septic arthritis in children younger than 24 months. *Arch Pediatr Adolescent Med*. 1995;149(5): 537–540
22. Malleson PN, Fung MY, Rosenberg AM. The incidence of pediatric rheumatic diseases: results from the Canadian Pediatric Rheumatology Association Disease Registry. *J Rheumatol*. 1996; 23(11):1981–1987

PEDIATRICS®
OFFICIAL JOURNAL OF THE AMERICAN ACADEMY OF PEDIATRICS

Dexamethasone Therapy for Septic Arthritis in Children

Itay Fogel, Jacob Amir, Elhanan Bar-On and Liora Harel

Pediatrics 2015;136;e776; originally published online September 7, 2015;
DOI: 10.1542/peds.2014-4025