Differentiating Between Septic Arthritis and Transient Synovitis of the Hip in Children: An Evidence-Based Clinical Prediction Algorithm*{{dagger}}

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Differentiating Between Septic Arthritis and Transient Synovitis of the Hip in Children: An Evidence-Based Clinical Prediction Algorithm*†

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Abstract

Background: **A child who has an acutely irritable hip can pose a diagnostic challenge. The purposes of this study were to determine the diagnostic value of presenting variables for differentiating between septic arthritis and transient synovitis of the hip in children and to develop an evidence-based clinical prediction algorithm for this differentiation.**

Methods: **We retrospectively reviewed the cases of children who were evaluated at a major tertiary-care children's hospital between 1979 and 1996 because of an acutely irritable hip. Diagnoses of true septic arthritis, presumed septic arthritis, and transient synovitis were explicitly defined on the basis of the white blood-cell count in the joint fluid, the results of cultures of joint fluid and blood, and the clinical course. Univariate analysis and multiple logistic regression analysis were used to compare groups. A probability algorithm for differentiation between septic arthritis and transient synovitis on the basis of independent multivariate predictors was constructed and tested.**

Results: **Patients who had septic arthritis differed significantly ($p < 0.05$) from those who had transient synovitis with regard to the erythrocyte sedimentation rate, serum white blood-cell count and differential, weight-bearing status, history of fever, temperature, evidence of effusion on radiographs, history of chills, history of recent antibiotic use, hematocrit, and gender. Patients who had true septic arthritis differed significantly ($p < 0.05$) from those who had presumed septic arthritis with regard to history of recent antibiotic use, history of chills, temperature, erythrocyte sedimentation rate, history of fever, gender, and serum white blood-cell differential. Four independent multivariate clinical predictors were identified to differentiate between septic arthritis and transient synovitis: history of fever, non-weight-bearing, erythrocyte sedimentation rate of at least forty millimeters per hour, and serum white blood-cell count of more than 12,000 cells per cubic millimeter (12.0×10^9 cells per liter). The predicted probability of septic arthritis was determined for all sixteen combinations of these four predictors and is summarized as less than 0.2 percent for zero predictors, 3.0 percent for one predictor, 40.0 percent for two predictors, 93.1 percent for three predictors, and 99.6 percent for four predictors. The chi-square test for trend and the area under the receiver operating characteristic curve indicated excellent diagnostic performance of this group of multivariate predictors in identifying septic arthritis.**

Conclusions: **Although several variables differed significantly between the group that had septic arthritis and the group that had transient synovitis, substantial overlap in the intermediate ranges made differentiation difficult on the basis of individual variables alone. However, by combining variables, we were able to construct a set of independent multivariate predictors that, together, had excellent diagnostic performance in differentiating between septic arthritis and transient synovitis of the hip in children.**

The initial presentation of an acutely irritable hip in a child can pose a diagnostic challenge to the orthopaedic surgeon, pediatrician, emergency-room physician, or primary-care physician. After the more apparent radiographic abnormalities of Legg-Perthes disease, slipped capital femoral epiphysis, and fracture have been ruled out, the differential diagnosis commonly involves septic arthritis and transient synovitis.

The differentiation between septic arthritis and transient synovitis of the hip in children is essential, since the two clinical entities have different treatments and different potential for negative sequelae. Septic arthritis is treated with operative drainage and antibiotics, whereas transient synovitis is usually self-limited and is treated symptomatically[1,5,8,12,25,26,30]. Complications of septic arthritis include osteonecrosis, growth arrest, and sepsis, whereas transient synovitis usually has a benign

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clinical course[3,7,13,16,18,24,27,31]. In addition, early, accurate diagnosis of septic arthritis of the hip is essential, as poor outcomes have been associated with a delay in the diagnosis of this condition in children[9,10,17,21,23].

The differentiation between septic arthritis and transient synovitis of the hip in children can be difficult, since they often have a similar presentation: an atraumatic, acutely irritable hip in a child who has progressive symptoms and signs of fever, has a limp or refuses to bear weight, and has limited motion, joint effusion, and abnormal laboratory findings. Empirically, clinicians have used various clinical, laboratory, and radiographic variables to distinguish between septic arthritis and transient synovitis.

The purpose of this study was to determine the diagnostic value of presenting variables for differentiating between septic arthritis and transient synovitis of the hip in children and to develop an evidence-based clinical prediction algorithm for this differentiation.

Materials and Methods

The cases of all 282 patients who were evaluated at a major tertiary-care children's hospital between 1979 and 1996 because of an acutely irritable hip for which the differential diagnosis involved transient synovitis and septic arthritis were reviewed. The patients were identified with use of the hospital admissions database for inpatients and the hospital emergency-room database for outpatients. The records of identified patients were cross-tabulated with the clinical laboratory database for joint-fluid analysis and the radiology database for fluoroscopic or ultrasonographic aspiration of the hip.

The diagnosis of true septic arthritis (thirty-eight patients) was explicitly assigned when a patient had a positive finding on culture of joint fluid or a white blood-cell count in the joint fluid of at least 50,000 cells per cubic millimeter (50.0×10^9 cells per liter) with positive findings on blood culture. The diagnosis of presumed septic arthritis (forty-four patients) was explicitly assigned when a patient had a white blood-cell count in the joint fluid of at least 50,000 cells per cubic millimeter with negative findings on culture of joint aspirate and blood. The group with septic arthritis (eighty-two patients) included both the group with true and the group with presumed septic arthritis. The diagnosis of transient synovitis (eighty-six patients) was explicitly assigned when the patient had a white blood-cell count in the joint fluid of less than 50,000 cells per cubic millimeter with negative findings on culture, resolution of symptoms without antimicrobial therapy, and no further development of a disease process as documented in the medical record.

Excluded patients (114) included those in atypical groups, such as those with immunocompromise (fourteen patients), renal failure (six patients), neonatal sepsis (six patients), postoperative infection of the hip (four patients), later development of rheumatological disease (four patients), later development of Legg-Perthes disease (one patient), or associated proximal femoral osteomyelitis (six patients) confirmed with bone aspiration in patients who had either radiographic changes in the proximal aspect of the femur or failure to appropriately respond to arthrotomy and antibiotics given intravenously. To avoid information bias associated with incomplete data analysis and to avoid selection bias associated with inclusion of patients who had presumptive and inconsistent diagnoses, a patient was excluded if joint-fluid aspirate had not been obtained for a cell count, gram stain, or culture (fifty-seven patients); if peripheral blood had not been obtained for culture or a cell count (eight); if the white blood-cell count in the joint fluid was less than 50,000 cells per cubic millimeter with negative cultures but the patient was managed with an arthrotomy and intravenous administration of antibiotics (six); or if the white blood-cell count in the joint fluid was less than 50,000 cells per cubic millimeter with negative cultures but the patient was managed with intravenous administration of antibiotics alone on the medical service (two).

Data obtained for all of the patients included age, gender, date of presentation, duration of symptoms, history of fever, history of chills, weight-bearing status, history of trauma, history of concurrent or recent infection, history of recent antibiotic use, temperature, erythrocyte sedimentation rate, serum white blood-cell count and differential, platelet count, hematocrit, results of blood culture, evidence of effusion on radiographs, and results of gram-staining, cell count, differential, and culture of joint fluid. A history of fever was operationally defined as an oral temperature of more than 38.5 degrees Celsius during the week before the initial evaluation. A history of chills was operationally defined as positive documentation of chills; a negative history of chills was coded either for documentation of no chills or for no documentation of chills. Weight-bearing status was determined on the basis of the clinical history.

Univariate analysis was performed with use of the two-sample Student t test for continuous variables and Fisher's exact test for categorical variables. Comparison was made between the group with septic arthritis and the group with transient synovitis and between the group with true septic arthritis and the group with presumed septic arthritis. Stepwise multiple logistic regression with backward selection was performed to identify independent clinical predictors, with the same group comparisons as were performed for the univariate analysis. Variables with a p value of less than 0.20 in the univariate analysis were chosen as candidates for the multivariate model, with significance determined with use of the likelihood ratio chi-square test[14]. Regression model fit was estimated with the Hosmer-Lemeshow goodness-of-fit test[15]. Adjusted odds ratios and 95 percent confidence intervals were derived with the method of maximum likelihood, and the probability of septic arthritis of the hip was estimated for each combina-

TABLE I
UNIVARIATE ANALYSIS: SEPTIC ARTHRITIS COMPARED WITH TRANSIENT SYNOVITIS

Variable	Septic Arthritis (N = 82)*	Transient Synovitis (N = 86)*	P Value
Age *(yrs.)*	6.0 ± 4.2	5.3 ± 2.3	0.17
Male gender *(no.)*	41 (50%)	57 (66%)	0.03†
Duration of symptoms *(days)*	2.3 ± 1.7	2.1 ± 2.7	0.77
History of fever *(no.)*	67 (82%)	7 (8%)	<0.001†
History of chills *(no.)*	9 (11%)	0 (0%)	<0.001†
History of antibiotic use *(no.)*	20 (24%)	9 (10%)	0.02†
Radiographic effusion *(no.)*	63 (77%)	33 (38%)	<0.001†
Non-weight-bearing *(no.)*	78 (95%)	30 (35%)	<0.001†
Temperature *(degrees Celsius)*	38.7 ± 1.0	37.4 ± 0.6	<0.001†
Erythrocyte sedimentation rate *(mm per hr.)*	51.6 ± 23.5	21.3 ± 12.5	<0.001†
Hematocrit *(percent)*	34.5 ± 3.5	36.0 ± 2.6	0.003†
Platelet count *(× 10^9 cells per L)*	330.0 ± 114.3	307.8 ± 88.3	0.21
Serum white blood-cell count *(× 10^9 cells per L)*	15.0 ± 5.7	9.9 ± 3.1	<0.001†
Neutrophils *(percent differential)*	66.8 ± 12.7	60.1 ± 13.8	0.002†
Lymphocytes *(percent differential)*	19.9 ± 10.4	29.4 ± 12.6	<0.001†
Monocytes *(percent differential)*	6.7 ± 3.7	5.7 ± 2.6	0.06
Band forms *(percent differential)*	6.5 ± 9.5	4.0 ± 4.2	0.12
Atypical lymph *(percent differential)*	2.4 ± 2.2	2.5 ± 1.6	0.90
Eosinophils *(percent differential)*	1.8 ± 1.0	2.3 ± 1.8	0.13
Basophils *(percent differential)*	3.4 ± 2.8	1.2 ± 0.6	0.03†

*The values are given as the mean and the standard deviation for continuous variables and as the number of patients, with the p ercentage in parentheses, for categorical variables.
†A significant difference between groups.

tion of predictors. The Pearson chi-square test for trend was used to evaluate the relationship between the increasing number of predictors and the proportion of patients who had septic arthritis. In addition, a receiver operating characteristic curve was constructed to assess the diagnostic performance of the group of multivariate predictors in identifying septic arthritis[11]. Sensitivity and specificity were calculated with standard formulae[29]. Statistical analysis was performed with SPSS (version 8.0; SPSS, Chicago, Illinois) and SAS (version 6.12; SAS Institute, Cary, North Carolina) software packages.

Results

Descriptive Data

Arthrocentesis was performed in the operating room or the fluoroscopy suite in fifty-two (31 percent) of the 168 patients and in the ultrasound suite in the other 116 (69 percent). Of the eighty-two patients with septic arthritis, thirty-eight (46 percent) had positive results on culture and the remaining forty-four (54 percent) had negative results on culture. Of the thirty-eight patients who had positive results (true septic arthritis), twenty-six (68 percent) had positive joint-fluid and blood cultures, nine (24 percent) had a positive joint-fluid culture and a negative blood culture, and three (8 percent) had a negative joint-fluid culture and a positive blood culture. Organisms isolated on culture included *Staphylococcus aureus* (twenty-two patients; 58 percent), *Streptococcus pneumoniae* (six patients; 16 percent), *Hemophilus influenzae* (five patients; 13 percent), *Neisseria meningitidis* (three patients; 8 percent), and group-A Streptococcus (two patients; 5 percent). All infections with *Hemophilus influenzae* developed before 1988. Of the thirty-five patients who had a positive culture of joint fluid, twenty-seven (77 percent) had a positive gram stain of joint fluid. There were no positive gram stains of joint fluid from the patients who had negative cultures.

Univariate Analysis

Septic Arthritis Compared with Transient Synovitis

The eighty-two patients who had septic arthritis differed significantly ($p < 0.05$) from the eighty-six who had transient synovitis with regard to erythrocyte sedimentation rate (51.6 ± 23.5 compared with 21.3 ± 12.5 millimeters per hour), serum white blood-cell count (15,000 ± 5700 compared with 9900 ± 3100 cells per cubic millimeter [15.0 ± 5.7 compared with 9.9 ± 3.1 × 10^9 cells per liter]) and differential (neutrophils [66.8 ± 12.7 compared with 60.1 ± 13.8 percent], lymphocytes [19.9 ± 10.4 compared with 29.4 ± 12.6 percent], and basophils [3.4 ± 2.8 compared with 1.2 ± 0.6 percent]), temperature (38.7 ± 1.0 compared with 37.4 ± 0.6 degrees Celsius), non-weight-bearing status (seventy-eight patients [95 percent] compared with thirty pa-

TABLE II

UNIVARIATE ANALYSIS: TRUE SEPTIC ARTHRITIS COMPARED WITH PRESUMED SEPTIC ARTHRITIS

Variable	True Septic Arthritis* (N = 38)	Presumed Septic Arthritis* (N = 44)	P Value
Age *(yrs.)*	5.9 ± 5.1	6.1 ± 3.3	0.85
Male gender *(no.)*	24 (63%)	17 (39%)	0.03†
Duration of symptoms *(days)*	2.3 ± 1.5	2.3 ± 1.9	0.83
History of fever *(no.)*	36 (95%)	31 (70%)	0.005†
History of chills *(no.)*	9 (24%)	0 (0%)	<0.001†
History of antibiotic use *(no.)*	3 (8%)	17 (39%)	<0.001†
Radiographic effusion *(no.)*	33 (87%)	30 (68%)	0.06
Non-weight-bearing *(no.)*	29 (76%)	41 (93%)	0.06
Temperature *(degrees Celsius)*	39.4 ± 0.9	38.1 ± 0.7	<0.001†
Erythrocyte sedimentation rate *(mm per hr.)*	57.5 ± 25.8	46.4 ± 20.1	0.04†
Hematocrit *(percent)*	33.9 ± 3.7	35.0 ± 3.3	0.17
Platelet count *(× 10^9 cells per L)*	351.9 ± 154.1	316.5 ± 80.5	0.31
Serum white blood-cell count *(× 10^9 cells per L)*	16.2 ± 7.3	14.1 ± 3.5	0.11
Neutrophils *(percent differential)*	65.2 ± 13.7	68.1 ± 11.8	0.31
Lymphocytes *(percent differential)*	18.9 ± 10.7	20.9 ± 10.1	0.38
Monocytes *(percent differential)*	6.9 ± 3.7	6.6 ± 3.7	0.74
Band forms *(percent differential)*	9.0 ± 12.4	3.8 ± 2.5	0.05†
Atypical lymph *(percent differential)*	2.9 ± 2.8	2.2 ± 1.7	0.43
Eosinophils *(percent differential)*	1.7 ± 0.9	1.9 ± 1.2	0.66
Basophils *(percent differential)*	5.0 ± 2.8	1.4 ± 0.9	0.03†

*The values are given as the mean and the standard deviation for continuous variables and as the number of patients, with the percentage in parentheses, for categorical variables.

†A significant difference between groups.

tients [35 percent]), history of fever (sixty-seven patients [82 percent] compared with seven patients [8 percent]), evidence of effusion on radiographs (sixty-three patients [77 percent] compared with thirty-three patients [38 percent]), history of chills (nine patients [11 percent] compared with zero patients [0 percent]), history of recent antibiotic use (twenty patients [24 percent] compared with nine patients [10 percent]), hematocrit (34.5 ± 3.5 compared with 36.0 ± 2.6 percent), and male gender (forty-one patients [50 percent] compared with fifty-seven patients [66 percent]) (Table I).

Although the mean erythrocyte sedimentation rate and white blood-cell count differed significantly ($p < 0.001$) between the patients who had septic arthritis and those who had transient synovitis, there was considerable overlap in the intermediate range of values, which limited the utility of a single variable as a predictor of septic arthritis (Figs. 1 and 2).

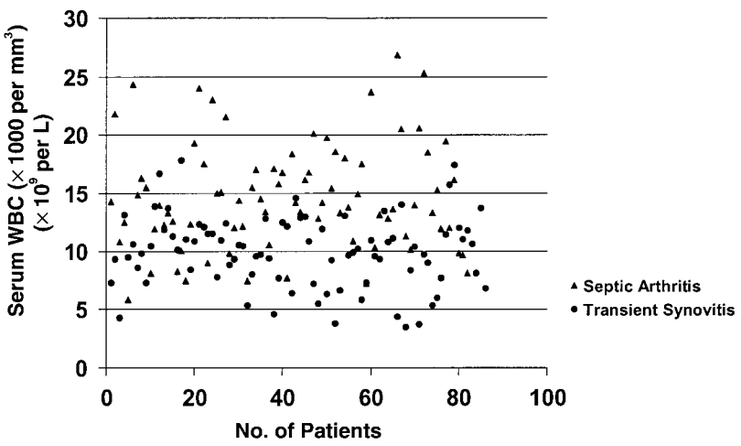

FIG. 1

Scatter diagram showing the serum white blood-cell count (WBC) for the patients who had septic arthritis and those who had transient synovitis.

TABLE III
MULTIVARIATE ANALYSIS: SEPTIC ARTHRITIS COMPARED WITH TRANSIENT SYNOVITIS

Multivariate Predictor	Regression Coefficient	Likelihood Ratio	P Value	Adjusted Odds Ratio	Ninety-five Percent Confidence Interval
History of fever	3.7	29.51	<0.0001	38.6	10.8-137.0
Non-weight-bearing	3.2	10.77	0.0009	24.3	5.6-85.2
Erythrocyte sedimentation rate ≥ 40 mm per hr.	3.3	19.09	<0.0001	25.9	6.5-112.6
Serum white blood-cell count > 12,000 cells per mm^3 (12.0×10^9 cells per L)	2.7	14.61	0.0001	14.4	4.0-51.5

True Septic Arthritis Compared with Presumed Septic Arthritis

The thirty-eight patients who had true septic arthritis differed significantly ($p < 0.05$) from the forty-four who had presumed septic arthritis with regard to history of recent antibiotic use (three patients [8 percent] compared with seventeen patients [39 percent]), history of chills (nine patients [24 percent] compared with zero patients [0 percent]), temperature (39.4 ± 0.9 compared with 38.1 ± 0.7 degrees Celsius), erythrocyte sedimentation rate (57.5 ± 25.8 compared with 46.4 ± 20.1 millimeters per hour), history of fever (thirty-six patients [95 percent] compared with thirty-one patients [70 percent]), male gender (twenty-four patients [63 percent] compared with seventeen patients [39 percent]), and serum white blood-cell differential (band forms [9.0 ± 12.4 compared with 3.8 ± 2.5 percent] and basophils [5.0 ± 2.8 compared with 1.4 ± 0.9 percent]) (Table II).

Multivariate Analysis

Septic Arthritis Compared with Transient Synovitis

We identified four independent multivariate predictors (Table III) for differentiation between septic arthritis and transient synovitis: history of fever, non-weight-bearing, an erythrocyte sedimentation rate of at least forty millimeters per hour, and a serum white blood-cell count of more than 12,000 cells per cubic millimeter (12.0×10^9 cells per liter). The Hosmer-Lemeshow goodness-of-fit test revealed no significant departure from good model fit ($p = 0.57$). Regression coefficients, likelihood ratios, p values, adjusted odds ratios, and 95 percent confidence intervals were determined (Table III). For example, the odds of a patient having septic arthritis of the hip were approximately twenty-six times greater when the erythrocyte sedimentation rate was at least forty millimeters per hour compared with when the erythrocyte sedimentation rate was less than forty millimeters per hour, with the lower and upper confidence limits of that estimation at 6.5 and 112.6 times greater odds, respectively.

Algorithm for Probability of Septic Arthritis

An algorithm was constructed to determine the predicted probability of septic arthritis on the basis of sixteen possible combinations ($2 \times 2 \times 2 \times 2$) of the four binary independent multivariate predictors (Table IV). For example, a child who has an acutely irritable hip and has a history of fever, is non-weight-bearing, has an erythrocyte sedimentation rate of fifty-one millimeters per hour, and has a serum white blood-cell count of 9500

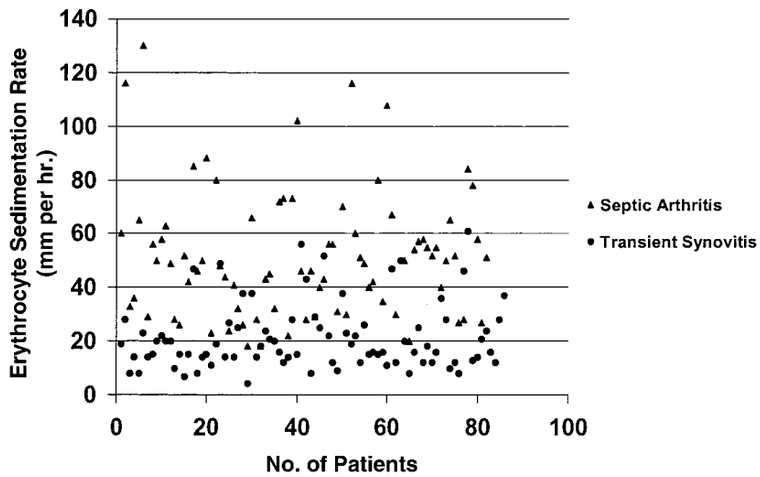

FIG. 2

Scatter diagram showing the erythrocyte sedimentation rate for the patients who had septic arthritis and those who had transient synovitis.

TABLE IV
ALGORITHM FOR PROBABILITY OF SEPTIC ARTHRITIS

Multivariate Predictor				
History of Fever	Non-Weight-Bearing	Erythrocyte Sedimentation Rate ≥ 40 mm per hr.	Serum White Blood-Cell Count > 12,000 cells per mm^3 (12.0×10^9 cells per L)	Predicted Probability of Septic Arthritis *(percent)*
Yes	Yes	Yes	Yes	99.8
Yes	Yes	Yes	No	97.3
Yes	Yes	No	Yes	95.2
Yes	Yes	No	No	57.8
Yes	No	Yes	Yes	95.5
Yes	No	Yes	No	62.2
Yes	No	No	Yes	44.8
Yes	No	No	No	5.3
No	Yes	Yes	Yes	93.0
No	Yes	Yes	No	48.0
No	Yes	No	Yes	33.8
No	Yes	No	No	3.4
No	No	Yes	Yes	35.3
No	No	Yes	No	3.7
No	No	No	Yes	2.1
No	No	No	No	0.1

cells per cubic millimeter (9.5×10^9 cells per liter) has a 97.3 percent predicted probability of having septic arthritis of the hip. Similarly, a child who has an acutely irritable hip and has no history of fever, limps but is able to bear weight, has an erythrocyte sedimentation rate of fifty-one millimeters per hour, and has a serum white blood-cell count of 9500 cells per cubic millimeter has a 3.7 percent predicted probability of having septic arthritis of the hip.

A simplified algorithm based on the number of multivariate predictors (zero to four) was constructed (Table V) and is summarized as less than 0.2 percent for zero predictors, 3.0 percent for one predictor, 40.0 percent for two predictors, 93.1 percent for three predictors, and 99.6 percent for four predictors. For example, a child who has an acutely irritable hip but only one multivariate predictor has a 3.0 percent predicted probability of having septic arthritis of the hip. Similarly, a child who has an acutely irritable hip and three multivariate predictors has a 93.1 percent predicted

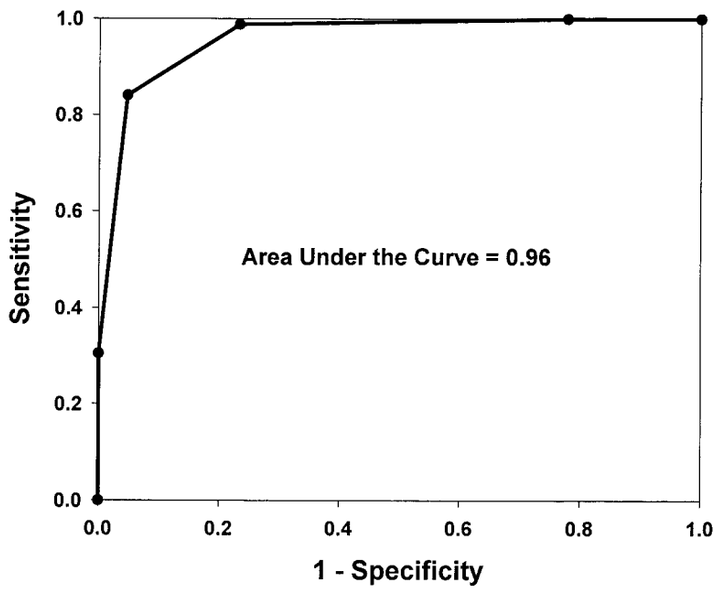

FIG. 3
Receiver operating characteristic curve of the simplified clinical prediction algorithm for septic arthritis.

probability of having septic arthritis of the hip. The Pearson chi-square test for trend indicated a very strong relationship between an increasing number of predictors and the proportion of patients who had septic arthritis (chi square = 121.96 on 4 degrees of freedom) ($p < 0.0001$). This relationship was also examined with receiver operating characteristic analysis (Fig. 3). The area under the receiver operating characteristic curve was 0.96, indicating excellent diagnostic performance of this group of four multivariate predictors in identifying septic arthritis.

True Septic Arthritis Compared with Presumed Septic Arthritis

Two independent multivariate predictors were identified to differentiate between true septic arthritis and presumed septic arthritis: history of chills (regression coefficient = 3.1, likelihood ratio = 12.21, $p < 0.001$, adjusted odds ratio = 22.7, and 95 percent confidence interval = 4.0 to 132.5) and male gender (regression coefficient = 1.5, likelihood ratio = 7.46, $p = 0.006$, adjusted odds ratio = 4.3, and 95 percent confidence interval = 1.7 to 11.5). For example, the odds that the accurate diagnosis is true septic arthritis as opposed to presumed septic arthritis are approximately twenty-three times greater for a patient who has a history of chills than for a patient who does not have a history of chills, with the lower and upper confidence limits of that estimation at 4.0 and 132.5 times greater odds, respectively.

TABLE V

DISTRIBUTION OF NUMBER OF MULTIVARIATE PREDICTORS AND SIMPLIFIED ALGORITHM FOR THE PREDICTED PROBABILITY OF SEPTIC ARTHRITIS

No. of Predictors*	Transient Synovitis (N = 86) *(no. of patients)*	Septic Arthritis (N = 82) *(no. of patients)*	Predicted Probability of Septic Arthritis *(percent)*
0	19 (22.1%)	0 (0%)	<0.2
1	47 (54.7%)	1 (1.2%)	3.0
2	16 (18.6%)	12 (14.6%)	40.0
3	4 (4.7%)	44 (53.7%)	93.1
4	0 (0%)	25 (30.5%)	99.6

*The four predictors are a history of fever, non-weight-bearing, an erythrocyte sedimentation rate of at least forty millimeters per hour, and a serum white blood-cell count of more than 12,000 cells per cubic millimeter (12.0×10^9 cells per liter).

Discussion

When a child has an acutely irritable hip, potential etiologies include Legg-Perthes disease, juvenile rheumatoid arthritis, osteomyelitis, psoas abscess, pyogenic sacroiliitis, and Lyme arthritis. However, the differential diagnosis commonly involves septic arthritis and transient synovitis. Differentiating between septic arthritis and transient synovitis in an accurate and timely manner is cardinal, as the two diagnoses have vastly different implications in terms of treatment and morbidity. Furthermore, a delay in the diagnosis of septic arthritis of the hip is associated with a poor outcome[9,10,17,21,23]. Nonetheless, the differentiation can often be challenging, since patients have similar demographic characteristics, symptoms, signs, and findings.

Clinicians have empirically used different variables to help distinguish between septic arthritis and transient synovitis. Bennett and Namnyak emphasized the white blood-cell count in children who are more than three years old[2]. Morrey et al.[23] and Klein et al.[19] focused on an elevated erythrocyte sedimentation rate. Chen et al. found both leukocytosis and an elevated erythrocyte sedimentation rate to be common[4]. However, because these case series of children with septic arthritis did not include a comparison group of children with transient synovitis, the authors were unable to establish differences between the two groups or to determine the diagnostic performance of assorted variables.

Various presenting clinical, laboratory, and radiographic data for distinguishing between children who have septic arthritis and those who have transient synovitis have been found to have poor diagnostic utility because of the substantial overlap between the two groups. Molteni retrospectively reviewed the cases of ninety-seven patients who had so-called nonspecific arthritis and thirty-seven patients who had septic arthritis of various joints, including the hip, knee, ankle, elbow, and wrist[22]. Diagnoses were established presumptively, with blood-cell analysis of specimens from twelve of the ninety-seven patients who had nonspecific arthritis and from thirty-two of the thirty-seven patients who had septic arthritis. Approximately 50 percent (nineteen) of the thirty-seven patients with septic arthritis had negative cultures, and the white blood-cell count ranged from 5000 to 385,000 cells per cubic millimeter (5.0 to 385.0 $\times$ 10^9 cells per liter). Without subjecting his findings to statistical analysis, Molteni compared the group with septic arthritis and the group with nonspecific arthritis with regard to age (5.8 compared with 6.0 years), male gender (twenty-two [59 percent] of thirty-seven patients compared with forty-nine [51 percent] of ninety-seven patients), temperature of more than 38.3 degrees Celsius (thirty-one [84 percent] of thirty-seven patients compared with thirty-seven [38 percent] of ninety-seven patients), serum white blood-cell count (7230 compared with 6300 cells per cubic millimeter [7.23 compared with 6.3×10^9 cells per liter]), and erythrocyte sedimentation rate (fifty compared with thirty-five millimeters per hour). Because of the similarities in values and the extent of overlap, he concluded that there were no reliable data with which to distinguish the two different joint processes. Del Beccaro et al. also found that overlap between presenting variables impeded the differentiation of septic arthritis from transient synovitis of the hip in children[6]. They compared ninety-four children who had transient synovitis (defined retrospectively on the basis of the clinical course) with thirty-eight patient who had septic arthritis (defined as pyarthrosis). Twenty-one of the ninety-four pa-

tients with transient synovitis had joint-fluid analysis, and twenty-eight of the thirty-eight patients with septic arthritis had joint-fluid cell counts. On univariate analysis, the authors found significant ($p < 0.05$) differences between the two groups with respect to temperature (38.1 compared with 37.2 degrees Celsius), erythrocyte sedimentation rate (forty-four compared with nineteen millimeters per hour), polymorphonuclear leukocytes (7800 compared with 6300 per cubic millimeter [7.8 compared with 6.3×10^9 per liter]), and band forms (903 compared with 295 per cubic millimeter [0.903 compared with 0.295×10^9 per liter]). Of note, with the numbers available for study, the serum white blood-cell count could not be shown to differ significantly ($p > 0.05$) (13,200 compared with 11,200 cells per cubic millimeter [13.2 compared with 11.2×10^9 cells per liter]). Although the erythrocyte sedimentation rate was significantly ($p < 0.05$) different between the two groups, a substantial amount of overlap made it a poor discriminator. The range of erythrocyte sedimentation rates for the group with septic arthritis of the hip was six to ninety millimeters per hour (24 percent of the patients had an erythrocyte sedimentation rate of less than twenty millimeters per hour), and the range for the group with transient synovitis was one to 125 millimeters per hour (28 percent of the patients had an erythrocyte sedimentation rate of more than twenty millimeters per hour). By combining an erythrocyte sedimentation rate of more than twenty millimeters per hour with a temperature of more than 37.5 degrees Celsius, Del Beccaro et al. were able to identify 97 percent of the cases of septic arthritis. However, those parameters were also found in 47 percent of the patients who had transient synovitis. Finally, Kunnamo et al. reviewed the cases of 278 children who were younger than sixteen years of age and had various arthritides, including transient synovitis, juvenile arthritis, septic arthritis, serum sickness, enteroarthritis, and Schönlein-Henoch purpura[20]. They found that the eighteen patients who had septic arthritis differed significantly ($p < 0.05$) from the other patients with respect to C-reactive protein level, a temperature of more than 38.5 degrees Celsius, and a serum white blood-cell count of more than 12,000 cells per cubic millimeter (12.0×10^9 cells per liter).

In the present study, we found several significant ($p < 0.05$) differences, on univariate analysis, between the group with septic arthritis and the group with transient synovitis. In general, the patients who had septic arthritis appeared to be more sick with fever, chills, an inability to bear weight, an elevated erythrocyte sedimentation rate, leukocytosis, a reduced hematocrit, and an altered peripheral blood differential. However, as in previous studies, there was substantial overlap between the two groups in the intermediate ranges of these variables (Figs. 1 and 2); thus, differentiation was difficult on the basis of individual variables alone. With logistic regression analysis, we were able to construct a set of powerful independent multivariate predictors (adjusted odds ratios = 14.4 to 38.6) that, together, had excellent diagnostic performance in differentiating between septic arthritis and transient synovitis of the hip in children. From the number or combination of predictors, we constructed clinical prediction algorithms to determine the predicted probability of septic arthritis (Tables IV and V).

In comparing the group that had true septic arthritis and the group that had presumed septic arthritis, we also found significant ($p < 0.05$) differences on univariate analysis. Again, the patients who had true septic arthritis appeared to be more sick with fever, chills, an elevated erythrocyte sedimentation rate, and an altered blood differential. In addition, the group with presumed septic arthritis had unique characteristics — namely, a history of recent antibiotic use and female gender. Multiple series of children with septic arthritis, ranging from thirty-one to 101 children, have had rates of negative cultures ranging from 9 percent (four of forty-five) to 61 percent (twenty-three of thirty-eight)[2,4-6,10,17,23]. These patients with presumed septic arthritis (that is, those with negative cultures) have symptoms similar to those of true septic arthritis, negative cultures, and high white blood-cell count counts (at least 50,000 cells per cubic millimeter of joint fluid). It is unclear what this presumed septic arthritis actually represents — partially treated septic arthritis, bacterial arthritis with organisms that are difficult to grow on culture, viral arthritis, arthritis from atypical organisms, inflammatory or rheumatoid arthritis, trauma, periarticular osteomyelitis, or an autoimmune process. Although, at present, true and presumed septic arthritis are managed identically from a therapeutic standpoint, it is interesting to note characteristics that differ between them. Our data might implicate the etiology of partially treated septic arthritis, since a history of recent antibiotic use was significantly ($p < 0.001$) more common in the group with presumed septic arthritis and this group appeared to be less sick, with a lower percentage of patients having a history of fever and chills and the patients having, on the average, a lower temperature, a lower erythrocyte sedimentation rate, and less alteration of the peripheral blood differential. Similarly, the higher proportion of female patients in the group with presumed septic arthritis might suggest an inflammatory or rheumatoid process, both of which are more frequent in female patients.

There have been attempts to make the art of diagnosis more objective with the use of clinical prediction rules to estimate the probability of a diagnostic outcome and to allow the clinician to classify patients according to the risk of disease[28]. Prediction rules originally took the form of clinical aphorisms based on the empirical experience of senior clinicians; however, more recently, they have been derived from evidence-based mathematical analyses[28]. For the clinician faced with the important but often difficult task of differentiating between septic ar-

thritis and transient synovitis, our predicted probability algorithm for septic arthritis based on independent multivariate predictors may be useful for guiding the diagnostic workup and for establishing a timely and accurate diagnosis. The management of patients based on the predicted risk of septic arthritis depends on the consequences of false-positive and false-negative diagnoses. The consequences associated with overlooking septic arthritis of the hip most likely outweigh the morbidity of considering a synovitic hip as infected and thus subjecting it to aspiration and even arthrotomy. Thus, we recommend judicious management based on the predicted risk of septic arthritis. Patients who have a very high probability of septic arthritis of the hip (three or four predictors) may be good candidates for aspiration in the operating room, given the likelihood that subsequent arthrotomy and drainage will be needed. Patients who have an intermediate probability of septic arthritis of the hip (two predictors) may be good candidates for aspiration in the fluoroscopy or ultrasound suite. Patients who have an extremely low probability of septic arthritis of the hip (zero predictors) may be appropriate candidates for careful observation without aspiration. There have been instances in which a clinical prediction rule was not as accurate for classifying patients as had been expected from the original report when it was applied prospectively in a new group of patients[28]. Like any new technology, a prediction rule should be evaluated carefully before it is used[28]. Future directions include prospective evaluation of the diagnostic performance of this clinical prediction algorithm in the same location and prospective validation in new clinical settings.

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