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# Short parenteral antibiotic treatment for adult septic arthritis after successful drainage☆

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SUMMARY

*Objectives:* To assess the risk factors for recurrence of septic arthritis with an emphasis on the duration of antibiotic treatment, to gather data for a prospective study on an optimized antibiotic treatment in adults with septic arthritis.
*Methods:* This was a retrospective single-center study conducted for the period 1996–2008.
*Results:* A total of 169 episodes of septic arthritis in 157 adult patients (median age 63 years; 65 females) were included. In 21 episodes (21/169, 12%), arthritis recurred after the end of antibiotic treatment. Multivariate analysis showed that Gram-negative infection (odds ratio (OR) 5.9, 95% confidence interval (CI) 1.4–25.3), immune suppression (OR 5.3, 95% CI 1.3–22.0), and lack of surgical intervention were associated with recurrence. The size of the infected joint, the number of surgical drainages (OR 1.3, 95% CI 1.0–1.7), arthrotomy vs. arthroscopic drainage (OR 0.5, 95% CI 0.2–1.8), duration of antibiotic therapy (OR 1.0, 95% CI 0.95–1.05), and duration of intravenous antibiotic therapy (OR 1.0, 95% CI 1.0–1.0) were not. Seven days of intravenous therapy had the same success rate as 8–21 days (OR 0.4, 95% CI 0.1–1.7) and >21 days (OR 1.1, 95% CI 0.4–3.1). Fourteen days or less of total antibiotic treatment had the same outcome as 15–28 days (OR 0.4, 95% CI 0.1–2.3) or >28 days (OR 0.4, 95% CI 0.1–1.6).
*Conclusions:* In this retrospective study of adults with septic arthritis, the duration of antibiotic therapy, or an early switch from intravenous to oral administration, did not statistically influence the risk of recurrence. Due to study limitations, the data cannot be used directly for antibiotic therapy recommendations for septic arthritis. Prospective randomized trials are warranted to optimize the antibiotic treatment of septic arthritis.


## 1. Introduction

Septic arthritis is a surgical as well as a medical emergency.[1–4] Although no studies have been published comparing drainage to non-drainage procedures, experts would probably recommend joint drainage, as this condition represents a closed abscess.[1–5] The optimal antibiotic treatment remains controversial since randomized controlled studies, at least in adults, are lacking.[6] We also have yet to determine whether interdigital arthritis and large size joint arthritis should be treated differently. Different antibiotic regimens have been recommended, such as 2 weeks intravenous (IV) therapy for streptococci, 3–4 weeks IV for staphylococci and Gram-negative bacteria,[7,8] and more than 4 weeks for immune suppressed patients or abnormal joints, e.g., severe osteoarthritis.[7] Others recommend parenteral treatment for 2 weeks, followed by another 2 weeks of oral treatment;[5,9] or for 4 weeks without indicating the means of administration.[6] Outpatient antibiotic therapy (OPAT) services have been developed in the USA and Europe to maintain parenteral treatment. In addition, many surgeons prescribe antimicrobials for longer periods without further justification.[1,4]

Parenteral medication should be limited as far as possible.[10] We hypothesize that if surgical drainage is adequately performed, septic arthritis could theoretically be treated with oral antibiotics and for shorter periods of time than reported in the literature.

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In this retrospective study of adults with septic arthritis, we determined the risk factors for recurrence and sequelae. This retrospective study was not designed to draw direct conclusions regarding antibiotic use in septic arthritis. Therefore our data should not be considered as any form of recommendation regarding the duration or administration route of antibiotic therapy in this neglected field of research.

## 2. Methods

### 2.1. Setting

The Orthopedic Service of Geneva University Hospitals has 135 acute care beds and a dedicated infectious diseases (ID) specialist.[11] Lavage for any septic arthritis is usually performed on admission as a surgical emergency. In severe infection or an unfavorable course (clinical and biological),[12] a surgical re-intervention is performed according to the decision of the responsible surgeon. The choice of antibiotic agents and the duration of their administration depend on the surgeon and the ID physician in charge of the individual patient.

### 2.2. Data collection

The Laboratory of Bacteriology and the hospital's Administrative Coding Office databases were retrospectively searched for adult native joint arthritis during the period January 1996 to December 2008. Forty-two variables for each episode were assessed pertaining to demographic characteristics, immune suppression, microbiology, surgical and antibiotic treatment, and outcomes. A surgeon (LT) and a physician (IU) independently recorded each variable on an Excel spreadsheet. In the case of discordance, a consensus was negotiated.

Patients were followed-up until December 31, 2010, i.e., 3 years after the inclusion of the last patient. The study was approved by the Hospital's ethics committee (No. 08-017R). No informed consent was requested.

### 2.3. Microbiology procedures

Aspirate material from suspected infected joints was cultured using microbiology procedures that were unchanged during the study period; these procedures were based on the Clinical and Laboratory Standards Institute (CLSI) guidelines.[13] To enhance specificity, only cultures positive on agar plates with significant growth were considered. Growth in enrichment broth was ignored.

### 2.4. Inclusion criteria and definitions

The definition of an infectious arthritis required the presence of intra-articular pus and a surgical and antibiotic treatment targeted to joint infection. Culture-negative septic arthritis cases were included because their omission would introduce a substantial selection bias. Bacteremia was defined as a documented positive blood culture with the same pathogen as that of the arthritis in cases where blood cultures had been sampled before the antibiotic treatment. Patients with an abscess in the surrounding soft tissue were included if the abscess could be excised or drained in toto during the first surgical intervention.

### 2.5. Exclusion criteria

Patients with the following conditions were excluded: arthritis due to other reasons, e.g., rheumatoid arthritis, crystal-induced arthropathy (even in the presence of concomitant infection), patients known or diagnosed during follow-up for rheumatic polyarthritis or other autoimmune diseases, patients with an episode of respiratory or gastrointestinal infection in the past 2 months (possibility of reactive arthritis) or gout, viral arthritis, preexisting implant material in the infected joint, and amputation as the primary therapeutic approach. Finally, infections with pathogens for which the literature suggests long-lasting antibiotic treatments or does not indicate surgical drainage were excluded: tuberculosis, other mycobacteria, fungi,[14] brucellosis,[15] borreliosis,[16] gonococcal arthritis,[17] nocardiosis,[18] and *Mycoplasma spp*. Also excluded were cases of secondary arthritis due to an underlying infection for which a total antibiotic treatment of more than 2 weeks is recommended: endocarditis, Lemierre's syndrome,[19] spondylodiscitis,[20] or suspected osteomyelitis[21] outside the joint wall.

### 2.6. Subgroup analyses

Two separate subgroup analyses for large joint arthritis and arthritis due to *Staphylococcus aureus* were added to the general analyses. Large joints were defined as: hip, knee, shoulder, sternoclavicular, sacroiliac, and the ankle joints.

### 2.7. Clinical outcomes

Cure was defined as complete clinical, laboratory, and microbiological resolution of arthritis after a minimum active follow-up time of 6 weeks following the end of antibiotic treatment.

Recurrence was defined as new clinical signs of infection with the same microorganism 2 weeks or more after the end of treatment for the first episode. Sequelae were persisting non-infectious handicaps (debilitating pain, limitation of joint movements) that were not resolved despite adequate physiotherapy and analgesia. The sequelae were not pre-existing and had to be attributed to the infection.

### 2.8. Statistical analyses

Group comparisons were performed using the Pearson Chi-square test or the Wilcoxon rank sum test. Logistic regression with cluster control (random effect) was used to determine associations with the outcomes recurrence and sequelae. Each of these analyses was separately repeated for the subgroups of large joint arthritis and arthritis due to *S. aureus*. Independent variables with a $p$-value of $\leq 0.05$ in the univariate analysis were introduced stepwise into a multivariate analysis. Exceptions were variables for surgical interventions and antibiotic treatment, which were automatically included in the final model. We included 6–10 predictor variables per outcome event.[22] Key variables were checked for collinearity and interaction, the latter by interaction terms and Mantel–Haenszel estimates. According to these criteria, included variables were: joint type, immune suppression, pathogens, number of surgical interventions, duration of IV antibiotic treatment, and duration of total antibiotic therapy. All remained in the final model.

We intended to analyze duration of antibiotic treatment variables within three strata (instead of dichotomous variables) in order to reveal more details. The strata of the categorical variables were around the median value, with inferior and superior limits relying on the 33% and 66% percentiles, rounded up to clinically practical duration times. According to this approach, the total duration of antibiotic therapy was divided into the following three strata: 0–14 days, 15–28 days, and more than 28 days. This approach was similar for parenteral antibiotic therapy with the strata 0–7 days, 8–21 days, and more than 21 days.

We assessed a possible linearity of the duration of antibiotic administration and recurrence of infection by linear and logistic