

# Antibiotic Use in Patients with Erysipelas: A Retrospective Study

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## Abstract

**Background:** Erysipelas is a skin infection generally caused by group A streptococci. Although penicillin is the drug of choice, some physicians tend to treat erysipelas with antibiotics other than penicillin.

**Objectives:** To define the pattern of antibiotic use, factors affecting antibiotic selection, and outcome of patients treated with penicillin versus those treated with other antimicrobial agents.

**Methods:** A retrospective review of charts of adult patients with discharge diagnosis of erysipelas was conducted for the years 1993–1996.

**Results:** The study group comprised 365 patients (median age 67 years). In 76% of the cases infection involved the leg/s. Predisposing condition/s were present in 82% of cases. Microorganisms were isolated from blood cultures in only 6 of 176 cases (3%), and *Streptococcus* spp. was recovered in four of these six patients. Cultures from skin specimens were positive in 3 of 23 cases. Penicillin alone was given to 164 patients (45%). Other antibiotics were more commonly used in the second half of the study period ( $P < 0.0001$ ) in patients with underlying conditions ( $P = 0.06$ ) and in those hospitalized in the dermatology ward ( $P < 0.0001$ ). Hospitalization was significantly shorter in the penicillin group ( $P = 0.004$ ). There were no in-hospital deaths.

**Conclusions:** We found no advantage in using antibiotics other than penicillin for treating erysipelas. The low yield of skin and blood cultures and their marginal impact on management, as well as the excellent outcome suggest that this infection can probably be treated empirically on an outpatient basis.

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Erysipelas is a skin infection characterized by the acute onset of sharply demarcated erythema, tenderness and swelling, and is most often accompanied by generalized symptoms such as fever and chills and sometimes by nausea and vomiting [1]. The great majority of cases are due to group A streptococci, but group B, C and G streptococci, and rarely staphylococci, may be involved [2].

Penicillin is the drug of choice for the treatment of erysipelas. Macrolides are usually recommended when there is a documented allergy to penicillin.

Many studies have demonstrated the clinical efficacy of penicillin in treating most group A streptococcal infections, including erysipelas [2]. Despite the widespread use of penicillin and other  $\beta$ -lactam antibiotics, *Streptococcus pyogenes* continues to be universally susceptible to penicillin but not to macrolides.

Antibiotics other than penicillin are frequently prescribed for patients with erysipelas. We describe a retrospective study that we conducted on patients with erysipelas to determine the rate of penicillin use, factors affecting the selection of antibiotics, and outcome of patients treated with penicillin versus those treated with other antimicrobial agents.

## Patients and Methods

The study took place at the Rabin Medical Center (Beilinson Campus), a 900 bed university hospital that serves an urban population of approximately 300,000 as a first-line facility. It is also a referral center for several hospitals in the vicinity.

## Study group

Adult patients who were discharged with the diagnosis of erysipelas during the period October 1993 to December 1996 were detected through the computerized registry of the hospital and their hospital records were reviewed retrospectively. For each patient, the following parameters were recorded: age, gender, department of hospitalization, duration of hospitalization, drug allergies, predisposing factors for erysipelas [3], previous episodes of erysipelas, site of current infection, previous prophylactic antibiotic therapy, blood and skin cultures, current antibiotic treatment including route and duration of administration, and outcome. Excluded from the study were 25 patients with either streptococcal toxic shock syndrome or bullous erysipelas.

Erysipelas was defined as a febrile condition (38.0°C) with acute onset of well-demarcated, warm and tender areas of skin erythema.

## Statistical analysis

Comparisons were made between patients who were treated only with penicillin and those who were given other antibiotic drugs. Statistical significance was tested by the chi-square test for contingency tables and the Wilcoxon rank-sum test for continuous variables.

## Results

The study group comprised 365 patients: 219 females (60%) and 146 males (40%). Half of the patients were older than 67 years. Table 1 summarizes the demographic data, site of infection, predisposing factors, and outcome. Of the patients, 203 (56%) were hospitalized in the dermatology department, 43% in the medical wards and 1% in other wards.

Overall, 298 patients (82%) had one or more predisposing factors for erysipelas. The most frequent predisposing factor was skin fungal infection (mostly tinea pedis) (23.6%). The lower extremities were the most common site of infection in 277 patients (75.8%), followed by face in 52 patients (14.2%), arms in 31 (8.4%), and trunk in 5 (1.3%).

The antimicrobial agents used in all patients are shown in Table 2. Only 164 patients (45%) were treated with penicillin alone. Penicillin was given intravenously in 130 patients (79%), intramuscularly in 28 (17%) and orally in 6 (4%). Antibiotics other than penicillin were given to 201 patients (55%) of whom 42 were allergic to penicillin. Amoxicillin-clavulanic acid was the most commonly used antibiotic in the non-penicillin group (24%), followed by clindamycin (7%), oxacillin (6%) and cefuroxime (4%). Clindamycin was given to 14 patients in 1993–1994 and to 40 patients in subsequent years. On univariate analysis [Table 3] two factors were associated significantly with administration of antimicrobial therapy other than penicillin: hospitalization in the dermatology ward

**Table 1.** Characteristics of 365 patients with erysipelas\*

| Age (yr)                                      |            |
|---|------------|
| Median (range)                                | 67 (21–96) |
| Gender  |            |
| M:F ratio                                     | 0.6        |
| <b>Residents of long-term care facilities</b> | 12         |
| <b>Site of infection</b>                      |            |
| Leg   | 76         |
| Face  | 14         |
| Arm   | 8          |
| Trunk   | 1          |
| <b>Predisposing factors</b>                   |            |
| Skin fungal infection                         | 24         |
| Diabetes mellitus                             | 19         |
| Edema   | 17         |
| Scar  | 16         |
| Mastectomy                                    | 10         |
| Paralysis                                     | 7          |
| Trauma  | 6          |
| Irradiation                                   | 3          |
| Previous episode/s of erysipelas              | 38         |
| Any   | 82         |
| Antibiotic prophylaxis                        | 16         |
| <b>Microbiological diagnosis</b>              | 3          |
| <b>Duration of hospitalization (days)</b>     |            |
| Median (range)                                | 5 (2–28)   |
| <b>Mortality</b>                              | 0          |

\* Numbers indicate percentages unless otherwise stated.

**Table 2.** Antimicrobial agents used in 365 patients with erysipelas

| Agent                       | No. of patients (%) |
|-----------------------------|---------------------|
| <b>Penicillin alone*</b>    | 164 (45)            |
| <b>Other drugs**</b>        | 201 (55)            |
| Amoxicillin-clavulanic acid | 87 (24)             |
| Clindamycin                 | 27 (7)              |
| Oxacillin                   | 21 (6)              |
| Cefuroxime                  | 15 (4)              |
| Erythromycin                | 12 (3)              |
| Cefazolin                   | 12 (3)              |
| Fucidic acid                | 7 (2)               |
| Ciprofloxacin               | 5 (1)               |
| Ampicillin                  | 4 (1)               |
| Others***                   | 11 (3)              |

\* Penicillin and no other antibiotic drug was administered during hospital stay.

\*\* The antibiotic drug that was administered for the longest duration during hospital stay.

\*\*\* Ceftriaxone (0.8%), cefotaxime (0.5%), ofloxacin (0.5%), gentamicin (0.5%), vancomycin (0.3%).

**Table 3.** Univariate analysis of penicillin vs. other antimicrobial therapy\*

|                                | Penicillin | Other    | P     |
|--------------------------------|------------|----------|-------|
| <b>Hospital ward</b>           |            |          |       |
| Dermatology                    | 69 (34)    | 134 (66) | 0.000 |
| Medicine                       | 95 (60)    | 63 (40)  |       |
| <b>Year of hospitalization</b> |            |          |       |
| 1993                           | 8 (62)     | 5 (38)   | 0.000 |
| 1994                           | 65 (61)    | 42 (39)  |       |
| 1995                           | 40 (34)    | 78 (66)  |       |
| 1996                           | 50 (39)    | 77 (61)  |       |
| <b>Hospital stay</b>           |            |          |       |
| Median (range)                 | 5 (2–20)   | 5 (2–28) | 0.004 |

\* Numbers indicate number of patients (%) if not stated otherwise

( $P < 0.0001$ ) and hospitalization in the second half of the study period ( $P < 0.0001$ ).

Patients with underlying predisposing factors were also treated more frequently with antibiotics other than penicillin ( $P = 0.06$ ). Hospital stay was significantly shorter in the penicillin-treated group ( $P < 0.004$ ) [Table 3]. The first and third quartile of hospital stay in the penicillin and the non-penicillin group were 3 vs. 4 days and 7 vs. 9 days, respectively.

Blood cultures were obtained in 176 (48%) patients and were positive in 6 cases (3.4%) only. Streptococci were recovered in four patients (*Streptococcus viridans* in two, groups A in 1; G-1), and *Staphylococcus aureus* and *Citrobacter diversus* in one case each. Culture from a skin biopsy was performed in 23 cases and was positive in 6 cases only. The cultures yielded coagulase-negative *Staphylococcus* in three cases, which were considered as contaminants, and group A Streptococcus, group B Streptococcus and *Citrobacter diversus* in one case each. The last three microorganisms grew also from blood cultures. All four patients with streptococcal bacteremia had been receiving amoxicillin-clavulanic acid before the results of the blood cultures became

available and were subsequently switched to penicillin. The patient with *Citrobacter diversus* bacteremia had received inappropriate initial empiric antibiotic therapy, which was subsequently changed according to *in vitro* susceptibility. The patient with *Staphylococcus aureus* bacteremia was empirically treated with clindamycin, which cured the infection.

## Discussion

Most of the patients with erysipelas in our report were treated with antibiotics other than penicillin. On univariate analysis, we identified two factors significantly associated with administration of antimicrobial agents other than penicillin: hospitalization in the dermatology ward and being hospitalized during the second half of the study period. Hospitalization of more severe cases in the dermatology department and the physician's "fear" of the possibility of group A streptococcal toxic shock syndrome could explain these findings. Indeed, during the second half of the study period we found an increased rate of clindamycin administration compared to the first half of the study period. Our results demonstrated no fatal cases in either group, and furthermore, the hospital stay was significantly shorter in the penicillin group.

In classic reports from the beginning of the twentieth century, erysipelas was commonly located on the face; and erysipelas of the trunk, leg or umbilicus was associated with a higher case fatality rate. Most cases were seen in the winter and spring months, in parallel with scarlet fever and streptococcal throat carriage [4–6]. In our study, erysipelas of the legs was the most frequent site of infection, followed by facial localization, and most patients had one or more underlying predisposing factors. Similar findings have been reported in other recent studies [7–10]. In accordance with previous studies, toe-web intertrigo [3] and previous episodes of erysipelas [11] were the most common predisposing factors.

Blood cultures were positive in only 3% of 176 cases and the majority yielded *Streptococcus* spp. Such cultures therefore seem to be of questionable value since in most cases they did not result in a modification of initial empiric therapy. Eriksson et al. [11] recently reported similar findings, and Perl and colleagues [12] also concluded that blood cultures in patients with cellulitis had a marginal impact on clinical management and were not cost-effective. Only in one of our patients who had multiple myeloma and was treated with cytotoxic drugs and corticosteroids did the finding of *Citrobacter diversus* bacteremia influence antibiotic management. Fine-needle aspiration of the skin to determine the etiology of erysipelas was performed in a very small proportion of our patients. The low yield of skin biopsy culture that we found was confirmed also by other studies [11,13].

The mortality rate in our study group was nil. In Eriksson's series [11] there were no deaths as a direct result of erysipelas, and Madsen [14] reported decreasing mortality in patients with erysipelas in Norway during the first half of the twentieth century and virtually no deaths after the advent of antibiotic treatment.

Our study has certain limitations: firstly, our patients were identified according to the data from the computerized hospital registry. Although these data are updated, we cannot be sure whether all patients with erysipelas were identified. Secondly, due to the retrospective design of the study, correlation between severity of disease, antibiotic therapy and outcome was not assessed and further study of this issue is clearly warranted.

In conclusion, penicillin probably remains the drug of choice for treating erysipelas in the vast majority of cases. In the present era of increasing antibiotic resistance this conservative approach may attenuate the widespread overuse of broad-spectrum antibiotics. Most patients with erysipelas can probably be safely treated in an outpatient setting. Prospective studies are needed to identify those patients who may benefit from hospitalization or antibiotic therapy other than penicillin.

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