SMALL DOSES OF METHICILLIN IN THERAPY OF FURUNCULOSIS

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METHICILLIN† is a synthetic penicillin that has the same antibacterial spectrum as penicillin G. Its outstanding advantage is its high degree of resistance to staphylococcal penicillinase, thus suggesting its use in the therapy of infections from penicillin-resistant staphylococci.

Since methicillin is destroyed by gastric juice, it must be given intramuscularly or intravenously. The rapid renal excretion of methicillin has been thought to necessitate its frequent administration. The recommended dosage is 1 gm. every four to six hours, a difficult schedule for outpatients to follow. This problem has been repeatedly encountered in patients having furunculosis, for whom the antibiotic might be useful, yet hospitalization is undesirable. In an effort to determine whether or not less frequent administration would be effective, a consecutive series of patients with furunculosis were each treated by daily intramuscular injections of methicillin. This report presents the results of the study.

Method

Between April and October of 1961, 26 patients with furunculosis each received 1 gm. of methicillin intramuscularly daily for from 3 to 10 days. In addition, each patient was given concurrent local therapy consisting of compresses, germicidal soaps, topical antibiotics, and surgical drainage where indicated.

Of the 26 patients, 18 had boils for more than one month, and 13 had failed to respond to other systemic antibacterial therapy, including penicillin, novobiocin, erythromycin, sulfonamides, oxytetracycline, tetracycline, phenethicillin, furaltadone, and staphylococcal vaccines. Studies of bacterial cultures were done in 13 cases. All cultures grew *Staphylococcus aureus* (coagulase positive).

The nature of furunculosis is such that recurring lesions are common and it is difficult to determine when a patient is cured. For the purposes of this paper, freedom from furuncles for one month was considered an apparent cure. However, most patients were followed for from three to eight months.

Results

Table 1 shows the results of the first course of methicillin. In all patients definite relief of pain and inflammation occurred within 24 hours after the first injection of methicillin. This response appeared to be more prompt than that produced by other

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Table 1.—*Response to first course of methicillin—26 patients with furunculosis*

Patient no.	Associated disease	Culture	Duration of boils before study, months	Use of prior antibiotic therapy	Methicillin (1st course), total grams	Concurrent systemic therapy	Apparently cured
1	None	—	< 1	No	5	None	Yes
2	Pemphigus vulgaris	Staphylococcus	< 1	No	8	Corticosteroids, chloramphenicol	Yes
3	None	—	< 1	No	5	None	Yes
4	Diabetes mellitus	—	< 1	No	3	Insulin	Yes
5	None	Staphylococcus	< 1	Yes	7	None	Yes
6	Lichen planus	Staphylococcus	< 1	No	5	None	Yes
7	None	—	1	No	4	None	Yes
8	Psoriasis	—	1	Yes	3	None	Yes
9	S.L.E.*	Staphylococcus	3	No	7	None	Yes
10	None	Staphylococcus	3	No	7	None	Yes
11	None	Staphylococcus	16	Yes	7	None	Yes
12	None	—	17	Yes	7	Staphylococcal vaccine	Yes
13	Contact dermatitis	Staphylococcus	< 1	No	8	Corticosteroids, erythromycin	No
14	Ulcerative colitis	—	< 1	Yes	4	Corticosteroids, salicylazosulfapyridine	No
15	Generalized neurodermatitis	—	2	Yes	7	None	No
16	Contact dermatitis	—	3	No	10	None	No
17	None	—	3	No	3	None	No
18	Diabetes mellitus	—	5	No	7	None	No
19	Diabetes mellitus	Staphylococcus	6	Yes	5	Chlorpropamide	No
20	None	Staphylococcus	9	Yes	5	None	No
21	Generalized eczematoid dermatitis	Staphylococcus	11	Yes	4	None	No
22	None	Staphylococcus	11	Yes	5	Penicillin	No
23	Atopic dermatitis	—	12	No	7	None	No
24	Atopic dermatitis	Staphylococcus	12	Yes	7	None	No
25	None	—	12	Yes	7	None	No
26	None	Staphylococcus	26	Yes	5	Staphylococcal vaccine	No

**Systemic lupus erythematosus.*

antibiotics in the treatment of furunculosis. Most patients received injections for from five to seven days. However, in two patients favorable results were noted with only three days of therapy.

Twelve of the 26 patients have had no furunculosis for from one to eight months since their first course of methicillin. In the remaining 14 patients additional boils developed after the first course of methicillin, seven of whom were given one or two more courses of therapy. Of these seven patients, three had no more furuncles after the additional injections (*Table 2*); thus, 15 patients recovered. Eleven patients

Table 2.—*Response to further courses of methicillin for furunculosis—seven patients*

Patient no.	Methicillin, gm.			Apparently cured
	First course	Second course	Third course	
13	8	7	7	No
16	10	10	11	No
17	3	5	—	Yes
20	5	2	—	Yes
23	7	1	—	Yes
24	7	3	3	No
25	7	6	—	No

still have chronic furunculosis. It should be emphasized that 8 of these 11 patients with chronic furunculosis also have chronic generalized eczema, diabetes mellitus, or ulcerative colitis, each of which may decrease skin resistance to infection. Among the 15 patients who recovered, only two have such complicating diseases.

There were no clinical signs of toxicity to methicillin. In one patient a fibrositic reaction developed in the thigh at the site of injection. Blood counts and hepatic and renal function tests were not performed as part of this study. None of the patients gave a history of penicillin allergy, and all had negative skin tests to methicillin before starting therapy. We observed no reactions suggestive of penicillin allergy.

Discussion

Other authors[1,2] have reported prompt healing of furunculosis upon administration of methicillin in a dosage of 1 gm. intramuscularly every four to six hours for five days. In several of their patients treated with that schedule, relapses occurred after apparent cures, but the information given did not permit comparison with our data.

In vitro tests[3,4] indicated that from 2 to 4 μg. per milliliter of methicillin inhibited the growth of both penicillin-sensitive and penicillin-resistant staphylococci. Within two and one-half hours after the intramuscular injection of 1 gm. of methicillin, the concentration of it in the serum dropped below the inhibitory level.[2] The satisfactory clinical responses produced by one daily injection of methicillin with its brief inhibitory effect in the serum may be partially explained by the stationary phase[5] during which staphylococci temporarily stop multiplying after brief exposure to penicillin. The duration of this stationary phase has been found to be directly related to the initial lag period of growth, and to the penicillin sensitivity of the bacterial strain. In addition, serum levels and tissue levels of methicillin may not necessarily be the same.

The kidneys rapidly excrete approximately two thirds of the methicillin, unchanged. Probenecid has been found useful in prolonging the serum concentration of methicillin at an effective level for from six to eight hours,[2] a phenomenon that might be utilized when infrequent doses of methicillin are given.

Although methicillin is a synthetic agent, penicillin allergy is still a problem. Cross-sensitivity to penicillin G has been reported.[2,6]

The chief value of methicillin appears to be its resistance to staphylococcal penicillinase: it is effective against staphylococci that are resistant to other penicillins. We have found no reports of staphylococcal resistance developing in vivo secondary to the use of methicillin. However, in the laboratory it is possible to induce resistance in staphylococci by repeated subculture in the presence of methicillin.[7] At least one strain of staphylococcus has a naturally occurring resistance to methicillin, not because of penicillinase.[8] This finding suggests that indiscriminate use of methicillin may result in the familiar problem of antiobiotic-resistant infection.

Summary

Twenty-six patients with furunculosis received intramuscular injections of methicillin, 1 gm., daily for from 3 to 10 days. Conventional local therapy was also employed. In all but one patient, the administration of the antibiotic was followed by prompt and dramatic healing of all active furuncles present at that time. Fifteen of the 26 patients have remained free of furuncles after one or two courses of methicillin. Of the 11 patients with recurring furunculosis in spite of treatment, eight have other dermatologic or medical conditions that may be contributory to the continuation of the furunculosis.

We do not recommend the described course of methicillin for seriously ill or hospitalized patients. The 1-gm. daily regimen represents a compromise that makes outpatient treatment possible. In any event, methicillin should be reserved for staphylococcal infections that have proved resistant to other penicillins.

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