

# ANTIBIOTIC SUSCEPTIBILITY OF COMMUNITY-ACQUIRED *STAPHYLOCOCCUS AUREUS*

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## SUMMARY

55% of a sample of patients in a rural community, and 76% of a sample of patients and staff in the local district hospital were found to be nasal carriers for *Staphylococcus aureus*. The in vitro antibiotic susceptibility patterns of 46 strains of *S. aureus* isolated in nasal carriers as well as of 43 strains in community-acquired skin infections were characterised. High levels of resistance were expressed to penicillin (73%), cephalexin (64%) and tetracycline (46%). Resistance to erythromycin (18%) was moderate. A few strains showed resistance to methicillin (5 isolates), vancomycin (4), fusidic acid (3), cotrimoxazole (1), and none to gentamicin. Penicillin can no longer be recommended for treating community-acquired *S. aureus* infections.

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## INTRODUCTION

*Staphylococcus aureus* remains an important pathogen in the community and the hospital.

In 1980-82, nosocomial infection surveillance was conducted by the Centers for Disease Control in the United States; 5% of hospitalized patients developed nosocomial infections which contributed directly or indirectly to 5% of deaths.<sup>1</sup> *S. aureus*, after *E. coli*, was the second most common nosocomial pathogen, accounting for 11% of such infections. It was the leading cause in the following categories: 35% of cutaneous infections, 17% of surgical wound infections and 13% of primary bacteremia. It is not only the incidence of *S. aureus* infections that is worrisome, but the emergence of multiple-resistant strains.<sup>2</sup>

The introduction of penicillin in the 40's was rapidly followed by the appearance of beta-lactamase producing *S. aureus*. Beta-lactamase resistant semi-synthetic penicillins, as typified by methicillin, were introduced in 1959 to overcome this problem. Within a decade however, in the United Kingdom and Europe, methicillin-resistant *S. aureus* (MRSA) multiplied to epidemic proportions (in places up to 30% of strains were MRSA) before levelling off.<sup>3</sup> Two decades later, the initially low incidence of MRSA in the United States is now rising.<sup>2</sup> In the period 1980-82 under surveillance, the incidence of MRSA rose from 2% to 9%, chiefly in the large teaching hospitals

which individually reported up to 18% MRSA strains among their isolates.<sup>1</sup>

Methicillin-resistant *S. aureus* is particularly alarming because it is usually associated with multiple resistance to other antibiotics like aminoglycoside, chloramphenicol, erythromycin and tetracycline.<sup>4</sup> These multiple-resistant *S. aureus* are mainly associated with nosocomial infections. Staphylococcal infections acquired in the community are usually considered to be still sensitive to penicillin. However, reports from the United States show that this is no longer true.<sup>5</sup> Furthermore, in some areas, MRSA has become prevalent in the community; for instance, among drug addicts.<sup>6,7</sup>

We undertook this survey of nasal carriage and a study of community-acquired *S. aureus* skin infection to determine the antibiotic susceptibility and prevalence of multiple-resistant *S. aureus* in the community.

## METHODS

### Nasal carriage

This study was carried out in the rural district hospital of Banting, Selangor. Swabs were taken from the anterior nares of 36 unselected outpatients and 34 unselected inpatients and hospital staff who had not taken any antibiotics in the preceding two weeks.

### Impetigo infection

This part of the study was carried out on 60

patients in an urban clinic in Sentul, Kuala Lumpur and 33 patients in the rural outpatient clinic of Banting Hospital. Swabs were taken from active impetiginous skin lesions and transported to the laboratory in Stuart's transport media.

## Microbiology

Identification of *S. aureus* was made on the basis of morphologic characteristics of the colony on 10% sodium chloride agar plates, Gram stain and a positive tube coagulase test. Antibiotic sensitivity was tested by the comparative disc method<sup>8</sup> using Oxford *Staphylococcus* NCTC 6571 as control. Methicillin resistance was tested by incubating inoculated nutrient agar plates at 30°C for 18–24 hours.<sup>9</sup>

## Statistical analysis

Variance between cases was analysed using chi-square and Fisher's exact test.

## RESULTS

55% of outpatients and 76% of hospital staff and patients carried *S. aureus* in their anterior nares (Table II). Transient and chronic nasal carriers were not differentiated.

76% of all *S. aureus* isolates in nasal carriage were penicillin-resistant (Table II). *S. aureus* from outpatients was just as likely as those from hospital staff and patients to be penicillin-resistant. In all the carriers, multiple resistances to cephalixin (70%) and tetracycline (33%) were present. An occasional isolate was resistant to erythro-

TABLE I  
NASAL CARRIAGE OF *S. AUREUS* AT A RURAL DISTRICT HOSPITAL

	Clinic n = 36		Hospital n = 34		Total n = 70		p value
	No.	%	No.	%	No.	%	
<i>Staphylococcus</i> sp.	26	—	34	—	60	—	
<i>S. aureus</i>	20	55	26	76	46	68	NS

NS = not significant; p value > 0.10; Beta value > 0.10.

mycin (15%), fusidic acid (two isolates) and vancomycin (one isolate). No resistance to gentamicin and cotrimoxazole was recorded. Four isolates of *S. aureus* from outpatients and only one hospital isolate were methicillin-resistant. Overall, the antibiotic susceptibility of *S. aureus* in nasal carriage was similar in the community and within the district hospital.

A similar pattern was found in *S. aureus* isolated from skin impetigo acquired in the community (Table III). 70% of the *S. aureus* were penicillin-resistant. Associated antibiotic resistances were again expressed to cephalixin (52%), and tetracycline (60%). Some isolates were resistant to erythromycin (21%), and occasional ones to fusidic acid (one isolate), vancomycin (three), and cotrimoxazole (one). In this group, no resistance to gentamicin or methicillin was recorded. Interestingly, no differences were detected in the antibiotic susceptibility pattern between the isolates from an urban (Sentul) and a rural (Banting) community.

## DISCUSSION

*S. aureus* is a facultative aerobic, gram-positive coccus; it is pathogenic to man by virtue of its

production of enzymes like lipase, hyaluronidase, DNAse, coagulase, as well as cell wall Protein A and extracellular capsule which accounts for its invasiveness, resilient survival within polymorphonuclear leucocytes and tendency to abscess formation.<sup>10</sup>

*S. aureus* found in nasal carriage is a useful and valid source for studying and monitoring the prevalence of antibiotic susceptibility patterns because the nose is the main reservoir of pyogenic *Staphylococcus*. Wound infections often originate directly or indirectly from nasal strains. The phage type of *S. aureus* found in infected lesions have been found to correspond in general with those found in the patients' nares.<sup>11</sup> Furthermore, they share the same virulence.<sup>12,13</sup>

The nasal carriage of *S. aureus* in this study was 55–76%, with no significant difference ( $p$  value  $> 0.10$ ) between community and hospital-related carriers. This is comparable to most studies which report 40–60% nasal carriage in the community, although hospital rates are usually slightly higher around 60–80%.<sup>13–15</sup>

Almost all *S. aureus* are lysogenic, and many

TABLE II

ANTIBIOTIC RESISTANCE PATTERN OF *S. AUREUS* IN NASAL CARRIERS AT A RURAL DISTRICT HOSPITAL

Antibiotics	Clinic n = 36		Hospital n = 26		Total n = 46		p value
	No.	%	No.	%	No.	%	
Penicillin	14	70	21	81	35	76	NS
Methicillin	4	20	1	4	5	11	NS
Cephalexin	12	60	20	77	32	70	NS
Tetracycline	3	15	12	46	15	33	NS
Erythromycin	4	20	3	12	7	15	NS
Gentamicin	0	0	0	0	0	0	—
Vancomycin	0	0	1	4	1	2	—
Fusidic acid	2	10	0	0	2	4	—
Cotrimoxazole	0	0	0	0	0	0	—

NS = not significant;  $p$  value  $> 0.05$ .

**TABLE III**  
**ANTIBIOTIC RESISTANCE PATTERN OF *S. AUREUS* ISOLATED FROM IMPETIGINOUS SKIN LESIONS ACQUIRED IN AN URBAN (SENTUL) AND RURAL (BANTING) COMMUNITY**

Antibiotics	Sentul n = 20		Banting n = 23		Total n = 43		p value
	No.	%	No.	%	No.	%	
Penicillin	16	80	14	61	30	70	NS
Methicillin	0	0	0	0	0	0	NS
Cephalexin	NA	—	12	52	NA	—	—
Tetracycline	11	55	15	65	26	60	NS
Erythromycin	2	10	7	30	9	21	NS
Gentamicin	NA	—	0	0	NA	—	—
Vancomycin	NA	—	3	13	NA	—	—
Fusidic acid	0	0	1	4	1	2	—
Cotrimoxazole	0	0	1	4	1	2	—

NA = not available; NS = not significant; p value > 0.05.

contain inducible beta-lactamase coded on non-conjugative r plasmids which are transducible.<sup>16,17</sup> In the first decade following the introduction of penicillin, penicillin-resistant *S. aureus* was isolated only in hospital-related infections.<sup>18</sup> However, by the 70's, up to 80% of *S. aureus* in the community were reported to be penicillin-resistant.<sup>5</sup> In the present study, 70–76% of the *S. aureus* isolated in the community were penicillin-resistant regardless of whether they were involved in active infections or by nasal carriage. Such high rates of beta-lactamase production in *S. aureus* may reflect the selection pressure from the general and indiscriminate use of beta-lactam antibiotics in both rural and urban communities.

Given such high rates of penicillin-resistant *S. aureus*, it is no longer tenable to treat any acute community-acquired infection of *S. aureus* requiring antibiotics with penicillin (including ampicillin). Neither is cephalexin nor tetracycline recommended for that matter (Tables II and III). Erythromycin or cotrimoxazole may be more appropriate for such infections.

The phenomenon of methicillin resistance, on the other hand, is neither related to plasmid trans-

mission nor to enzyme inactivation. It may represent a chromosomal mutation affecting cell wall permeability or receptor binding to the drug.<sup>19</sup>

Recently isolated MRSA strains are just as virulent as penicillin-sensitive *S. aureus*.<sup>4,20-22</sup> The dangers of transmission of MRSA is further compounded by the additional association with resistance to multiple antibiotics.<sup>4</sup> The MRSA isolates found in this study were indeed consistently associated with antibiotic resistance to cephalosporin, and additionally to tetracycline or erythromycin or fusidic acid.

Methicillin-resistant *S. aureus* has already made inroads in this country. A survey of nosocomial infections in the General Hospital, Kuala Lumpur in 1982 revealed that 25% of the *S. aureus* isolated were methicillin-resistant.<sup>23</sup> Fortunately, in the present study, none of the community-acquired infections was caused by MRSA.

Interestingly, four nasal carriers in the rural community carried MRSA. Methicillin resistance in *S. aureus* can be naturally occurring, but is rare.<sup>2</sup> However with the widespread use of beta-

lactam antibiotics in general, MRSA is selected out because these strains always produce beta-lactamase in large amounts. A carrier state could then occur through exposure to previous infection treated with beta-lactam antibiotics.

While nasal carriage of *S. aureus* forms one of the reservoir habitats for the continued maintenance of recurrent *S. aureus* infections, carrier rates of MRSA are generally low because MRSA strains exhibit lower adherence to the nasal mucosa.<sup>2,4</sup>

In the treatment of serious infections caused by MRSA, vancomycin is the drug of choice.<sup>2,5,26</sup> From this perspective, the presence of even a few isolates of *S. aureus* in this study exhibiting resistance to vancomycin (Tables II and III) should be viewed with concern. Periodic surveillance to determine the prevalence of this pattern should be maintained.

Even after treatment with vancomycin for MRSA infections, patients may remain as nasal carriers. Nasal carriers need not be treated unless they are a source of recurrent infections to themselves or to other patients.<sup>2,5,27</sup> Intranasal application of bacitracin ointment is ineffective.<sup>2,8</sup> When treatment is necessary, oral rifampicin may be given together with vancomycin or cotrimoxazole.<sup>2,5,29,30</sup>

## CONCLUSION

In this study, the nasal carriage rate for *S. aureus* in a rural community was found to be almost as high as in the local district hospital. Penicillin resistance was widespread in *S. aureus* isolated in both the urban and rural community and in the rural district hospital. This was associated with multiple antibiotic resistances to cephalosporin, tetracycline, and to a smaller extent, to erythromycin as well.

Although only a few isolates of *S. aureus* from the community expressed resistance to methicillin, and to vancomycin, surveillance needs to be continued to monitor their prevalence.

Based on the *in vitro* antibiogram of *S. aureus*, the treatment of acute, non-life-threatening, community-acquired staphylococcal infections which require antibiotics should include erythromycin, cotrimoxazole or dicloxacillin (in order of rising cost).

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