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Antimicrobial sensitivity patterns of hospital and non-hospital strains of *Staphylococcus aureus* isolated from nasal carriers

By M. O. PAUL, D. A. ADERIBIGBE, C. Z. SULE

Unit of Medical Microbiology, Faculty of Health Sciences, University of Ife, Ile-Ife, Nigeria

AND A. LAMIKANRA

Department of Pharmaceutics, Faculty of Pharmacy, University of Ife, Ile-Ife, Nigeria

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SUMMARY

The nasal carriage rate of *Staphylococcus aureus* was significantly higher in hospitalized persons (children, adult females and staff) – 53·8%, – than in similar persons at a local clinic – 29·8% ($P < 0{\cdot}001$) – in Ile-Ife, Nigeria. However, unlike studies carried out elsewhere, a higher proportion of *S. aureus* strains obtained from persons at the clinic were resistant to commonly used antimicrobial agents than were strains isolated in the hospital. This has been attributed to the ease at which these drugs can be obtained by the general population and used unsupervised and indiscriminately. Methicillin was the most effective antimicrobial agent against pathogenic staphylococci (2·2% resistance), followed by erythromycin (16·5% resistance), co-trimaxozole (28·0% resistance), chloramphenicol (76·9% resistance), tetracycline (78·6% resistance) and penicillin and ampicillin (97·8% resistance). The widespread resistance of *S. aureus* to penicillin and ampicillin (and other antimicrobial agents) is of clinical significance in the treatment of post-operative infections, since carriers are reportedly more prone to such infections than are non-carriers.

INTRODUCTION

The results of earlier work by Paul, Lamikanra & Aderibigbe (1982) show that, like some other places, namely Britain, the United States and Australia (Williams, 1963), approximately 50% of the population of a Nigerian hospital harbour pathogenic staphylococci in their anterior nares, i.e. are nasal carriers. Such carriers have been shown by Cruickshank (1953), Weinstein (1959) and Williams *et al.* (1959) to be more susceptible to endogenous infection and are more prone to post-operative infection with pathogenic staphylococci than non-carriers. Furthermore, such carriers act as a reservoir for *Staphylococcus aureus* which can

give rise to infection in non-carriers (Hare & Ridley, 1958; Ravenholt & Ravenholt, 1958).

Antimicrobial agents are usually prescribed to treat infections caused by pathogenic staphylococci; and the efficacy of these drugs on hospital strains of *S. aureus* has been the subject of many studies (Clarke, 1957; Bersten & Mc Dermott, 1960; Burr, Howells & Rees, 1978). The effect of antimicrobial agents on non-hospital strains of pathogenic staphylococci has, on the other hand, been investigated by only a few workers, perhaps because non-hospital strains of microorganisms are not usually exposed to antimicrobial agents (Goldie, Alder & Gillespie, 1971). The increasing use of anitmicrobial agents outside the hospital environment demands that more studies be done in this area; especially since Goldie *et al.* (1971) have also shown that non-hospital strains of pathogenic staphylococci are becoming resistant to commonly used antimicrobial agents.

In Nigeria, as in many other developing countries, control of antimicrobial agents outside the hospital is non-existent and so the problem of resistance of pathogenic staphylococci (and other pathogens) is very pressing. The extent of this problem has, however, not been quantified. This study compares the isolation rate of *S. aureus* among persons in a hospital setting with similar persons in the general population and reports the pattern of resistance of these pathogenic staphylococci to several of those antimicrobial agents which are prescribed most frequently in this locality.

MATERIALS AND METHODS

Subjects

Persons investigated included babies and young children and their accompanying mothers who visited the 'well' baby clinic at Mọrẹ, and babies, young children and adult females hospitalized at the State Hospital. Staff members of the two institutions were also investigated. Both institutions are located in Ile-Ife, a semi-urban town in Southwestern Nigeria (7° N latitude, 4° E longitude). Adult females at both localities were predominantly from the lower socio-economic groups: more than half the total were petty traders.

Specimen collection and isolation procedures

Nasal swabs were collected from each person by the method described by Cameron (1970). These swabs were inoculated by standard bacteriological techniques onto blood agar (BA base: Oxoid, CM 271, with 5% expired human blood) and mannitol salt agar plates (MSA: Oxoid, CM 85). After overnight incubation, colonies on BA plates which resembled staphylococci were tested for coagulase production by the slide technique (Cadness-Graves *et al.* 1943) and, if negative, by the tube technique (Williams & Harper, 1946). Colonies were checked by Gram-stained smears. Staphylococcal colonies were inoculated onto DNAse agar (Oxoid, CM 321) as a safeguard against missing atypical colonies of *S. aureus* (Blair, Emerson and Tull, 1967).

Table 1. *Frequency of coagulase-positive staphylococci isolated from the nares of babies and children, adult females and staff at the clinic and hospital*

	Persons at clinic			Persons at Hospital			*P* value judged by
Category	No.	No. pos.	% pos.	No.	No. pos.	% pos	(χ^2 test)
Babies and children	123	29	23·6	74	38	51·4	< 0·001 (14·67)
Adult females	105	36	34·3	84	45	53·6	< 0·05 (6·32)
Staff	14	7	50·0	52	30	57·7	> 0·5 (0·04)
Total	242	72	29·8	210	113	53·8	< 0·001 (25·93)

Sensitivity testing

Coagulase-positive staphylococci were tested for their resistance to antimicrobial agents, using DST agar (Oxoid, CM 261) and Oxoid multodiscs (code no. 1789 E). Potencies of each antimicrobial agent on the multodisc were as follows: penicillin G, 1·5 units; streptomycin, 10 μg; tetracycline, 10 μg; co-trimoxazole 25 μg; ampicillin, 2 μg; chloramphenicol, 10 μg; methicillin 5 μg; and erythromycin, 10 μg. *S. aureus* was classified as resistant or sensitive to each antimicrobial agent, using as a guide recommendations of Bailey & Scott (1970) and Stokes (1975).

RESULTS

Isolations

A total of 452 nasal swabs was examined. Of these, 185 (40·9%) yielded coagulase-positive staphylococci. Significantly higher numbers of coagulase-positive staphylococci were isolated from hospitalized babies and children and from adult females than from persons at the clinic. Differences in the isolation rate for staff in both institutions are not significant (see Table 1).

Age characteristics of babies and children

Among children, those less than 2 months old and between 3 and 12 years of age, differences in isolation rate between persons at the clinic and those at the hospital are significant. Numbers of hospitalized patients were small in the other age groups, but between 6 months and 2 years the isolation rate was approximately equal for hospitalized (31·3%) and clinic (29·3%) babies and young children (Table 2).

Resistance patterns to antimicrobial agents

Almost all isolates of coagulase-positive staphylococci were resistant to penicillin G and ampicillin simultaneously (97·8%). Resistance to antimicrobial agents was

Table 2. *Frequency of coagulase-positive staphylococci in the different age groups of babies and young children at the clinic and hospital*

Age group (years)	Clinic			Hospital			*P* value judged by (χ^2 test)
	No.	No. pos.	% pos.	No.	No. pos.	% pos.	
⩽ 2/12	16	2	12·5	41	21	51·2	< 0·05 (5·65)
3/12–5/12	34	7	20·6	2	1	50·0	> 0·9 (0·01)
6/12–11/12	30	7	23·3	9	2	22·2	> 0·5 (0·15)
1–2	28	10	35·7	7	3	42·9	> 0·9 (0·01)
3–12	15	3	20·0	14	10	71·4	< 0·05 (5·80)
Unrecorded	—	0	0	1	1	100·0	
Total	123	29	23·6	74	38	51·4	< 0·001 (14·67)

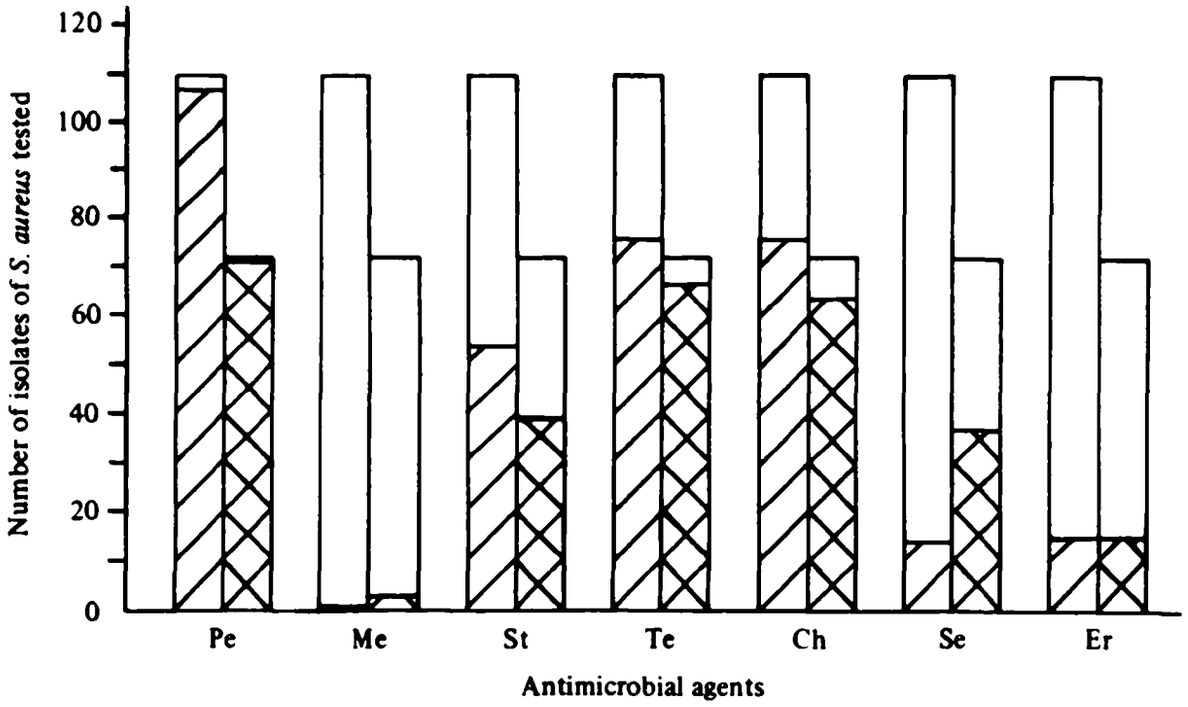

Fig. 1. Comparison of the resistance patterns of *Staphylococcus aureus*, isolated from the nares of persons at the hospital and clinic, to various antimicrobial agents. Pe, penicillin G (and ampicillin); Me, methicillin; St, streptomycin; Te, tetracycline; Ch, chloramphenicol; Se, co-trimoxazole; Er, erythromycin. □, total number; ▨, hospital (resistant strains); ▩, clinic (resistant strains).

generally higher in staphylococci isolated from persons at the clinic from those at the hospital and was significantly higher among persons at the clinic than at the hospital for tetracycline and co-trimoxazole and chloramphenicol. Differences in resistance to erythromycin are not significant in the two groups (see Figure 1 and Table 3).

Coagulase-positive staphylococci isolated from babies and children, adult females

Table 3. *Resistance patterns to antimicrobial agents of coagulase-positive staphylococci isolated from babies and children, adult females and staff at the clinic and hospital*

Antimicrobial agent	Babies and children		Adult females		Staff		N_{Cl} *v.* N_{Hl}, *P* value judged by (χ^2 test)
	Clinic, $n = 29$	Hospital, $n = 37$	Clinic, $n = 36$	Hospital, $n = 43$	Clinic, $n = 7$	Hospital, $n = 30$	
	Number positive (per cent)						
Penicillin G and Ampicillin	28 (96·6)	36 (97·3)	36 (100)	41 (95·3)	7 (100)	30 (100)	> 0·9 (0·01)
Methicillin	1 (3·4)	1 (2·7)	2 (5·6)	0 (0)	0 (0)	0 (0)	> 0·1 (0·9)
Streptomycin	17 (58·6)	23 (62·2)	20 (55·6)	21 (48·8)	2 (28·6)	10 (33·3)	> 0·5 (0·27)
Tetracycline	27 (93·1)	25 (67·6)	33 (91·7)	36 (83·7)	7 (100)	15 (50·0)	< 0·001 (13·45)
Chloramphenicol	25 (86·2)	26 (70·3)	32 (88·9)	29 (67·4)	7 (100)	21 (70·0)	< 0·01 (8·53)
Co-trimoxazole	15 (51·7)	7 (18·9)	18 (50·0)	4 (9·3)	4 (57·1)	3 (10·0)	< 0·001 (30·36)
Erythromycin	8 (27·6)	6 (16·2)	4 (11·1)	8 (18·6)	3 42·9)	1 (3·3	> 0·1 (1·16)

n = number of coagulase-positive staphylococci tested.
N = total number of coagulase-positive staphylococci tested.
Cl = Clinic; Hl = Hospital.

and staff were significantly more often resistant to co-trimoxazole among persons at the clinic than at the hospital. Resistance to tetracycline was significantly more frequent among *S. aureus* isolates from babies and children and staff at the clinic than in comparative babies and children and staff at the hospital. For erythromycin, differences in resistance among coagulase-positive staphylococci isolated from staff members at the clinic and hospital are significant. Chloramphenicol-resistant staphylococci were found significantly more often in isolates from adult females at the clinic than at the hospital (see Table 3).

DISCUSSION

As noted in other studies (Williams, 1963), carrier rates were significantly higher in hospitalized subjects than their counterparts at the clinic ($\chi^2 = 25{\cdot}93$, $P < 0{\cdot}001$). Because of the nature of the clinic (a 'well-baby clinic') persons attending this facility can be regarded as representing the general population. There was no significant difference in the carrier rates of staff members at the clinic and hospital; but staff members at the clinic are essentially in a hospital environment as far as constant and intimate contact with carriers are concerned. The general decline in carrier status, reported in other studies (Rycroft & Williams,

1960; Burr *et al.* 1978) during the first year of life was observed for both clinic and hospitalized babies and children (20·0% and 46·2% between 0 and 11 months and 30·2% and 61·9% for babies and children between 1 and 12 years for clinic and hospitalized persons respectively).

In contrast with other studies (Miller, Galbraith & Green, 1962; Noble *et al.* 1964), resistance to antimicrobial agents was generally higher in persons at the clinic than in hospitalized subjects. Work by Montefiore, Coker & Adedeji (1973) and Adekeye (1979) shows that some of the antibiotics used in this study (penicillin, tetracycline, chloramphenicol and streptomycin) are the most commonly used antibiotics in this region. These antibiotics are not only the most frequently used in hospitals but are also most easily obtainable from sources as diverse as pharmacies and roadside stalls. The ready availability of these drugs makes it impossible for any control to be imposed on their use. As the work of Bulger & Sherris (1968) has shown, the effectiveness of any antibiotic is rapidly diminished in the absence of a rational utilization policy as is the case with Nigeria. It can be assumed that because so many people have easy access to antimicrobial agents, the use of these drugs is largely unsupervised, hence the development of resistant strains of pathogenic staphylococci outside the hospital environment.

Several different antimicrobial agents were used in this study and, as the results indicate, the effectiveness of these drugs as measured by their activity against the isolated organisms varied from one antibiotic to the other. Both penicillin and ampicillin were found to be almost completely ineffective, possibly because of their popularity and consequent widespread use. The fact that resistance to methicillin was observed in only a few cases (2·2%) suggests that resistance to penicillin and ampicillin is due mainly to the production of β-lactamase enzymes (Kirby, 1944; Gots, 1945), methicillin being resistant to these enzymes retained its effectiveness (Barber & Waterworth, 1964).

In the case of the broad-spectrum antibiotics used in this study, widespread resistance to both chloramphenicol and tetracycline was encountered. The resistance of non-hospital strains to tetracycline is of considerable epidemiological significance. As reported by Lowbury & Ayliffe (1974), tetracycline-resistant strains of *S. aureus* are confined to hospitals. This is, however, only true of places where the use of tetracycline is restricted to the hospital. In Nigeria, both hospital and non-hospital strains of bacteria are liable to be exposed to tetracycline because of the widespread and unsupervised use of this drug in the general population; the high incidence of tetracycline-resistant strains of *S. aureus* both inside and outside the hospital is hardly unexpected.

Co-trimoxazole was found to be active against 72·0% of the isolates, a figure which is considerably higher than figures obtained with all of the antibiotics except methicillin and erythromycin. This difference is important because co-trimoxazole is formulated as tablets, a dosage form that has considerably less appeal to Nigerians than capsules, a dosage form that is associated with extraordinary efficacy. The result of this preference for capsules is that the unsupervised use of co-trimoxazole is not as widespread as that of the antibiotics. On the other hand, the observed effectiveness of co-trimoxazole against many of the isolates tested

may be because this drug consists of a combination of antimicrobial substances. The development of resistance to such a combination is expected to be delayed for a considerable period of time (Pollock, 1960).

The widespread resistance of nasal isolates of *S. aureus* to the most frequently used antibiotics in Nigeria is of clinical significance. Carriers of coagulase-positive staphylococci have been shown by Cruickshank (1953), Weinstein (1959) and Williams *et al.* (1959) to be more prone to post-operative infection than non-carriers. In the event of post-operative infection, preliminary observations show that ampicillin is one of the agents most frequently prescribed to control the infection. The results of this study demonstrate that in most cases this antibiotic is ineffective against infections caused by *S. aureus* and consequently such infections would be difficult to control.

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REFERENCES

Adekeye, D. (1979). Resistance of *Staphylococcus aureus* isolates of man and other animals to five antibiotics commonly used in Nigeria. *Nigerian Medical Journal* **9**, 195–197.

Bailey, W. R. & Scott, E. G. (1970). Determination of susceptibility of bacteria to antimicrobial agents. In *Diagnostic Microbiology* pp. 289–304. Saint Louis: C. B. Mosby.

Barber, M. & Waterworth, P. M. (1964). Penicillinase-resistant penicillins and cephalosporins. *British Medical Journal* ii, 344–349.

Bernsten, C. A. & McDermott, W. (1960). Increased transmissibility of staphylococci to patients receiving an antimicrobial drug. *New England Journal of Medicine* **262**, 637–647.

Blair, E. B., Emerson, J. S. & Tull, A. H. (1967). A new medium, salt mannitol plasma agar, for the isolation of *Staphylococcus aureus American Journal of Clinical Pathology* **47**, 30–39.

Bulger, R. J. & Sherris, J. C. (1968). Decreased incidence of antibiotic resistance among *Staphylococcus aureus Annals of Internal Medicine* **69**, 1099–1108.

Burr, M. L., Howells, C. H. L. & Rees, P. W. J. (1978). Antibiotic resistant staphylococci acquired during the first year of life. *Journal of Hygiene* **81**, 125–130.

Cadness-Graves, B., Williams, R., Harper, G. J. & Miles, A. A. (1943). Slide test for coagulase-positive staphylococci. *Lancet* i, 736–738.

Cameron, A. S. (1970). Staphylococcal epidemiology in Antarctica. *Journal of Hygiene* **68**, 43–52.

Clarke, S. K. R. (1957). Nasal carriage of *Staphylococcus aureus*. *Journal of Pathology and Bacteriology* **73**, 253–259.

Cruickshank, R. (1953). The epidemiology of some skin infections. *British Medical Journal* i, 55–59.

Goldie, D. J., Alder, V. G. & Gillespie, W. A. (1971). Changes in the drug resistance of *Staphylococcus aureus* in a non-hospital population during a 20-year period. *Journal of Clinical Pathology* **24**, 44–47.

Gots, J. S. (1945). Production of extracellular penicillin-inactivating substances associated with penicillin resistance in *Staphylococcus aureus*. *Proceedings of the Society for Experimental Biology and Medicine* **60**, 165–168.

Hare, R. & Ridley, M. (1958). Further studies on the transmission of *Staph. aureus*. *British Medical Journal* i, 69–73.

Kirby, W. M. M. (1944). Extraction of a highly potent penicillin inactivator from penicillin-resistant staphylococci. *Science* **99**, 452 453.

Lowbury, E. J. L. & Ayliffe, G. A. J. (1974). Staphylococcal infections. In *Drug Resistance in Antimicrobial Therapy*, pp. 51–90. Springfield: Charles Thomas.

MILLER, D. L., GALBRAITH, N. S. & GREEN, S. (1962). Nasal carriers of penicillin-resistant staphylococci in the general population. *British Journal of Preventive and Social Medicine* **16**, 203–206.

MONTEFIORE, D., COKER, G. O. & ADEDEJI, S. O. (1973). Methicillin-resistant *Staphylococcus pyogenes*. *Nigerian Medical Journal* **3**, 44–46.

NOBLE, W. C., WILLIAMS, R. E. O., JEVONS, M. P. & SHOOTER, R. A. (1964). Some aspects of nasal carriage of staphylococci. *Journal of Clinical Pathology* **17**, 79–83.

PAUL, M. O., LAMIKANRA, A. & ADERIBIGBE, D. A. (1982). Nasal carriers of coagulase-positive staphylococci in a Nigerian hospital community. *Transactions of the Royal Society for Tropical Medicine and Hygiene* (in the Press).

POLLOCK, M. R. (1960). Drug resistance and mechanisms for its development. *British Medical Bulletin* **16**, 16–22.

RAVENHOLT, R. T. & RAVENHOLT, O. H. (1958). Staphylococcal infections in the hospital and community. Hospital environment and staphylococcal disease. *American Journal of Public Health and the Nation's Health* **48**, 277–287.

RYCROFT, J. A. & WILLIAMS, R. E. O. (1960). Penicillin-resistant staphylococci in normal young children. *Proceedings of the Royal Society of Medicine* **53**, 258–260.

STOKES, J. (1975). Antibiotic sensitivity tests. In *Clinical Bacteriology*, pp. 208–238. London: Edward Arnold.

WEINSTEIN, H. J. (1959). The relation between the nasal-staphylococcal-carrier state and the incidence of post-operative complications. *New England Journal of Medicine* **260**, 1303–1308.

WILLIAMS, R. E. O. (1963). Healthy carriage of *Staphylococcus aureus:* its prevalence and importance. *Bacteriological Reviews* **27**, 56–71.

WILLIAMS, R. E. O. & HARPER, G. J. (1946). Determination of coagulase and alpha-haemolysin production by staphylo-cocci. *British Journal of Experimental Pathology* **27**, 72–81.

WILLIAMS R. E. O., JEVONS, M. P., SHOOTER, R. A., HUNTER, C. J. W., GIRLING, J. A., GRIFFITHS, J. D. & TAYLOR, G. W. (1959). Nasal staphylococci and sepsis in hospital patients. *British Medical Journal* ii, 658–662.