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# Distribution of mercury resistance among *Staphylococcus aureus* isolated from a hospital community

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## SUMMARY

Results from clinical isolations confirmed that mercury resistance is common among antibiotic-resistant strains of *Staphylococcus aureus* present in a large general hospital although the correlation is not as high as that found by Moore (1960).

The distribution of mercury-resistant strains among infections and carriers in surgical, medical, obstetric and geriatric patients and staff was studied. Attention was directed to the distribution among carriers since there are fewer extraneous factors operating among them, and a statistical analysis was made on the total number of mercury-resistant strains and the number of non-endemic strains; this latter figure was obtained by subtracting the dominant type 80/81, which is nearly always mercury-resistant and antibiotic-resistant, from the total. Analysis showed the geriatric patients to have a significantly higher proportion of mercury-resistant strains in both cases, and obstetric patients to have a significantly lower proportion when the total number of mercury-resistant strains was considered. Among the surgical, medical and staff categories, no significant difference in proportions could be found although a trend, in that order, of decreasing proportions of mercury-resistant strains present was noted.

In those cases infected on admission with tetracycline-resistant strains, although mercury-resistant strains still predominate, mercury-sensitive strains make a sizeable contribution. This is a reflexion of their dominance in the non-hospital environment.

## INTRODUCTION

It was observed (Moore, 1960) that *Staphylococcus aureus* were either resistant or sensitive to a discriminatory concentration of mercury salts. Furthermore, staphylococci of phage-types associated with hospital epidemics were more often mercury-resistant than non-epidemic strains. Moore found a close correlation between resistance to mercury salts and to antibiotics in general but to no antibiotic in particular. Within the different phage-types there were strains of the same phage-type and same mercury reaction that had different antibiotic sensitivity spectra, indicating that mercury resistance and specific antibiotic resistance are probably independent properties. Surveys carried out in West Africa (Akinlade,

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1962), England (Turner & Willis, 1962) and Denmark (Jessen *et al.* 1963) show a variation in this association.

The aim of this paper is to investigate the distribution of mercury resistance among strains of hospital staphylococci isolated from different departments of a hospital community. It is important to delineate the epidemiological pattern of infection with mercury-resistant staphylococci in order to assess the possible significance of mercury resistance as an epidemiological marker. A major effort to control antibiotic-resistant staphylococcal infection in the hospital was being planned and as this entailed a major sampling programme involving the taking of many swabs over a period of time from the general hospital population, it was decided to take advantage of this in order to obtain the necessary epidemiological information regarding mercury-resistant strains (Stokes, Hall, Richards & Riley, 1965).

*Description of hospital*

This has been described in full elsewhere (Hall, 1966). Briefly, the main hospital houses medical and surgical wards while adjacent buildings with communicating tunnels house the Obstetric Hospital, Ear, Nose and Throat Hospital and Private Patients' Wing. The geriatric wards are part of a completely separate hospital block one mile distant. In all about 1000 beds are served and there is an active outpatient department.

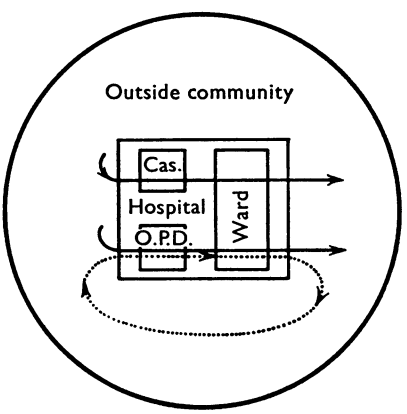


Fig. 1. Pathway of patients to and from the hospital community.

The hospital may be regarded as a community set aside from the outside world into which patients are admitted and from which they are discharged. The total number of inpatients is fairly constant, this being a function of the total number of beds. Patients may attend Casualty or an outpatient department. If the former they are unlikely to have had previous hospital contact and any staphylococci isolated from their lesions are likely to be representative of those present in the community at large. Patients attending outpatient departments will in many cases have been inpatients previously and may be carrying antibiotic-resistant strains. From both these departments they may be transferred to the wards and the

duration of hospital stay will be one factor in determining the chances of acquiring hospital staphylococci. If readmission is necessary, the time interval after previous discharge is important; if relatively short the patients may still carry hospital staphylococci, but if a longer period has elapsed the strain may have exchanged with one commonly present in the patient's normal home environment. The probable general pattern of the epidemiological situation may be summarized diagrammatically (Fig. 1). In addition there is the turnover among the staff although this does not approach that of the patients. Changes in their nasal flora are also less likely as they are not receiving therapeutic doses of antibiotics.

## MATERIALS AND METHODS

### *Plan of investigation*

To obtain a complete picture of the distribution of staphylococci in the hospital and outside population, ideally nasal swabs and wound swabs should be taken of the population surrounding the hospital, all patients attending Casualty and outpatient departments, all staff and all patients in wards; also nose swabs of the latter should be taken immediately before discharge. This is clearly impracticable and for the practical purposes of the control programme a more feasible plan of campaign was devised.

A sampling procedure for the detection of antibiotic-resistant strains was initiated by the nasal swabbing of the following categories: (*a*) patients already in hospital; (*b*) hospital staff in contact with inpatients; (*c*) new patients admitted and those transferred within hospital; (*d*) new staff in contact with inpatients; (*e*) nursing staff about to work in theatres; (*f*) nurses and students about to work in the obstetric hospital. In addition, all infected lesions were also swabbed (Stokes *et al.* 1965). Reference to Fig. 1 will show that these categories are related to the principal pathways and sources of infection.

For 2 years all tetracycline-resistant strains and some sensitive strains from infected patients and staff and from carriers were phage-typed and all tetracycline-resistant strains were tested for sensitivity to mercury salts. Tetracycline-sensitive strains were also tested for a period of 12 months (Stokes *et al.* 1965).

### *Mercury sensitivity test*

The agar plates containing mercuric chloride as described by Moore were found too laborious for the large number of strains to be tested. Paper strips impregnated with mercuric chloride solution were used and provided that mercury-resistant and -sensitive control organisms were included, thin plates were poured and the concentration of mercuric chloride (usually 1/5000 w/v) was adjusted to the nutrient agar employed, this modification was satisfactory. Large batches of strips were made at a time and dried in the incubator; they were stable when stored at 4° C. for several months. Plates were streaked from colonies or coagulase-broth cultures, in a parallel manner, six test strains and two controls per plate.

The resistant control (a type 80 strain resistant to penicillin and tetracycline) gave no zone in contrast to the sensitive Oxford staphylococcus, which gave a

small sharply defined zone of about 2 mm. Size of inoculum made a slight difference to zone size but the test was adjusted to give optimal results with heavily seeded streaks.

## RESULTS

Analysis of all *Staph. aureus* isolated from noses and wounds of different categories of persons in five different hospital departments during 12 months is shown in Fig. 2; it was only for this period that the majority of tetracycline-sensitive strains were tested for their mercury reaction. The *Staph. aureus* are divided into tetracycline-sensitive and tetracycline-resistant strains and further subdivided into those which are mercury-sensitive and mercury-resistant.

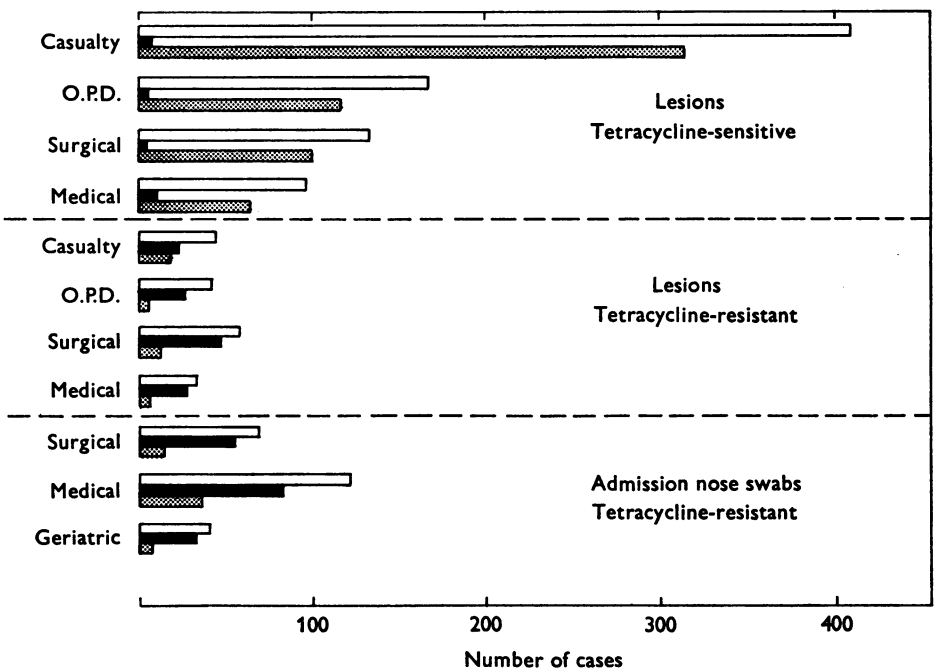


Fig. 2. Analysis of all strains isolated from different departments during a 12-month period. □, Total; ■, mercury-resistant; ▦, mercury-sensitive.

Mercury resistance is seen to follow a closely similar distribution pattern to tetracycline resistance. Less than 5% of tetracycline-sensitive strains were also mercury-resistant except in medical wards, where the figure is 13% (no tetracycline-sensitive strains from the geriatric wards were mercury tested). Amongst tetracycline-resistant strains, the mercury-resistant strains predominate in all departments, the proportion being least in Casualty and highest in medical and surgical wards. Analysis of the admission nose swabs shows that the proportion of mercury-resistant strains is highest in geriatric wards.

The percentage of mercury-resistant strains among the total *Staph. aureus* isolated over the same period is: Casualty 9%, outpatient departments 20%,

Table 1. *Mercury sensitivity of antibiotic-resistant strains isolated from different departments* 1961–64

| | Infections (hospital and admitted) | | | | | Carriers | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | | | | Other than 80/81 | | | | | Other than 80/81 | |
| Department | Total tested | Total Mercury-resistant | 80/81 and allied types | Mercury-resistant | Mercury-sensitive | Total tested | Total mercury-resistant | 80/81 and allied types | Mercury-resistant | Mercury-sensitive |
| Surgical | 137 | 111 | 77 | 34 | 26 | 151 | 119 | 83 | 37 | 31 |
| Medical | 86 | 61 | 50 | 15 | 21 | 229 | 162 | 113 | 51 | 65 |
| Geriatric | 47 | 36 | 24 | 12 | 11 | 87 | 77 | 38 | 39 | 10 |
| Obstetric | 12 | 5 | 3 | 2 | 7 | 14 | 7 | 4 | 3 | 7 |
| Staff | 23 | 12 | 13 | 3 | 7 | 112 | 77 | 51 | 25 | 36 |

surgical 31 % and medical 33 %. Thus as one goes from Casualty to outpatient departments to hospital wards the incidence rises.

Analysis of the phage-types showed that type 80/81 and allied types (including types 52/52A/80, 52/52A/80/81) were predominant among strains isolated in this hospital. This corroborates the findings of Stokes & Milne (1962) (Stokes *et al.* 1965).

The proportion of mercury-resistant strains isolated from infections and carriers in surgical, medical, obstetric and geriatric departments and the staff is shown in Table 1. Since the predominant strain is type 80/81, which is nearly always mercury-resistant, the contribution of this to the total is given. Mercury resistance may appear to be important simply because it is a property of the dominant strain. If, however, mercury resistance is itself an advantage for survival in hospital it should still be dominant even when the number of prevalent strain isolations is subtracted from the total figures. In fact mercury-sensitive strains of other types predominate in infections and in carriers among medical and obstetric patients and staff but in the surgical and geriatric patients the proportions are reversed.

The figures from the Obstetric Hospital, although small, show that the proportion of strains of the 80/81 complex is low both in infections and admitted carriers despite the connexion via the nursing staff with the main hospital.

Among the geriatric patients the proportion of mercury-resistant strains in both infections (77 %) and carriers (89 %) is high. Considering infections first, when the dominant type 80/81 is subtracted from the total, the number of mercury-resistant and mercury-sensitive strains other than type 80/81 are not very different from the other categories of patient. When these figures for nasal carriers are compared however, there were 39 mercury-resistant as compared with 10 mercury-sensitive strains. More emphasis should perhaps be placed on the distribution of mercury resistance among carriers than infections since in this location there are not so many extraneous factors operating. When $\chi^2$ test is applied to nasal carriers of types other than 80/81, it is revealed that: (1) it is not reasonable to assume that all departments have the same proportion of resistant strains ($\chi^2 = 22{\cdot}86$, $P < 0{\cdot}001$ on 4 degrees of freedom); (2) geriatric patients have a significantly higher proportion of resistant strains than the remainder; (3) there are no significant differences between the proportions of resistant strains in the surgical, medical and obstetric carriers and staff ($\chi^2 = 3{\cdot}76$, $P > 0{\cdot}1$ on 3 degrees of freedom); (4) the differences between the proportions are too small to be detected on the amount of data available. When $\chi^2$ test is applied to the total carriers of mercury-resistant strains it again follows that (1) it is not reasonable to assume that all departments have the same proportions of resistant strains ($\chi^2 = 18{\cdot}85$, $P < 0{\cdot}001$ on 4 degrees of freedom); (2) the geriatric patients have a significantly higher proportion of resistant strains than the remainder; (3) there is no significant difference between the proportions of resistant strains in the surgical, medical and staff categories ($\chi^2 = 4{\cdot}16$, $P > 0{\cdot}1$ on 2 degrees of freedom). However the proportion of mercury-resistant strains in the obstetric patients is significantly lower than in the other 3 categories ($\chi^2 = 7{\cdot}62$, $P = 0{\cdot}05$ on 3 degrees of freedom).

*Mercury sensitivity of tetracycline-resistant strains*

The mercury reaction of tetracycline-resistant strains isolated during 1960–64 from clinical infections is shown in Table 2. The infections are divided into those acquired in hospital and those admitted infected, and are contrasted with the nasal carriers. The proportions are seen to be significantly different in each category. If, as before, the incidence of the dominant epidemic type is subtracted from the total, the figures show more clearly the distribution of mercury resistance among the remaining strains, (Table 3). Among medical patients the proportions of mercury-resistant strains isolated from hospital-acquired infections differ significantly from those infected on admission ($\chi^2 = 7{\cdot}15$, $P < 0{\cdot}01$ on 1 degree of freedom). The distribution pattern for the surgical patients is similar ($\chi^2 = 4{\cdot}45$, $P < 0{\cdot}05$).

Table 2. *Mercury sensitivity of tetracycline-resistant strains*, 1960–64

| | Mercury-resistant strains | Mercury-sensitive strains | Proportion of mercury-resistant strains | 95% confidence limits |
|---|---|---|---|---|
| Hospital infections | 231 | 34 | 0·872 | 0·831–0·913 |
| Admitted infections | 62 | 40 | 0·608 | 0·511–0·704 |
| Nasal carriers | 446 | 142 | 0·758 | 0·723–0·793 |

Table 3. *Mercury sensitivity of tetracycline-resistant strains other than those of the* 80/81 *complex* (1961–63)

| | Infections | | | |
|---|---|---|---|---|
| | Hospital | | Admitted | |
| | Mercury-resistant | Mercury-sensitive | Mercury-resistant | Mercury-sensitive |
| Medical | 11 | 6 | 4 | 15 |
| Surgical | 28 | 15 | 6 | 11 |

*Overall pattern of nasal carriage*

The results are given in detail elsewhere (Stokes *et al.* 1965; Hall, 1966).

*Patients*

*Annual swabbing.* The carrier rate of tetracycline-resistant staphylococci in all inpatients swabbed in October of each year varied between 4·3 and 8·2% during 5 years of testing.

*Admission nose swabs.* Between 11,509 and 13,395 patients admitted or transferred were swabbed annually. The carrier rate of tetracycline-resistant strains remained more or less constant at 1·4–1·6%. The mercury-resistant strains were between 2·4 and 3·4 times more numerous than the sensitive in the 4 years of

testing. There was a high preponderance of 80/81 and allied types among these strains.

When the admitted carriers among the medical, surgical and geriatric patients are compared it is seen that the carrier rate for tetracycline-resistant staphylococci is highest in the geriatric wards (10 %) and higher in the medical (3·6 %) than surgical wards (1·8 %) (Stokes *et al.* 1965). In terms of absolute numbers, there are many more carriers admitted to medical wards than to surgical or geriatric wards. In addition, the percentage for obstetric patients was consistently less than 0·4 % and for ear, nose and throat patients less than 0·9 %.

*Staff*

The carrier rate of tetracycline-resistant staphylococci among the nursing staff when swabbed in October of three consecutive years was 4·9 % of 749, 3·9 % of 793 and 3·0 % of 703. The mercury-resistant strains outnumber the mercury-sensitive by a factor of 5 in the first, 2 in the second and 2·5 in the third year.

## DISCUSSION

These data have shown that:

(*a*) Mercury resistance is common in carriers who have been exposed to the hospital environment for long periods and is rare in carriers newly admitted or who stay in hospital for short periods.

(*b*) Although in strains isolated from both nasal carriers and infections mercury resistance and antibiotic resistance are commonly found together, the proportion of mercury-resistant strains is higher than would be expected in geriatric patients if this were only a chance association.

The number of mercury-resistant strains in the admitted infections category is probably artificially high since many of these patients may have had previous hospital experience and the actual difference between the two groups may be more pronounced than the figures in Table 2 would suggest.

Statistical analysis has shown that the higher proportion of mercury-resistant strains among surgical (79 %) than medical patients (71 %) is not significant both for the non-endemic strains ($\chi^2 = 1{\cdot}84$, $P > 0{\cdot}01$ on 1 degree of freedom) and the total mercury-resistant strains ($\chi^2 = 2{\cdot}35$, $P > 0{\cdot}1$ on 1 degree of freedom). Indeed, distinguishing between these two categories is difficult because of their previous histories. Many medical patients who are admitted carrying tetracycline-resistant mercury-sensitive strains have been receiving maintenance doses of tetracycline at home and their strains may have developed resistance to tetracycline as a result, or they may have acquired a tetracycline-resistant strain outside hospital where mercury-sensitive strains are common. Inpatients receiving tetracycline are likely to acquire mercury-resistant staphylococci which are more prevalent in hospital. The situation is further complicated because many surgical patients may previously have received treatment in medical wards. The proportions in the staff are not significantly different although there is a trend for the proportion to be less here than in the surgical and medical departments.

The incidence of strains of the 80/81 complex amongst infections and admitted carriers in the Obstetric Hospital is lower than in the other categories. This is in keeping with the expected low carrier rates; these patients have had little previous hospital history. The figures from the geriatric department suggest that mercury resistance itself is a factor in survival of staphylococci in this environment.

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