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Staphylococcal infection in an intensive-care unit, and its relation to infection in the remainder of the hospital

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SUMMARY

A survey of the staphylococcal infections occurring in a general hospital over a period of four and a half years showed that multiple-resistant strains of phage type 77 were endemic in the medical and surgical wards. Strains of this phage type were uncommon among patients attending the casualty department, and those found were usually either fully sensitive to antibiotics or resistant to benzylpenicillin only. Regular monitoring of patients admitted to the intensive-care unit showed that 58% of staphylococcal infections in such patients were present at the time of admission to the unit. Although the wards thus constituted a significant reservoir of infection for the intensive-care unit, there was no evidence to suggest that the return of patients from the unit to the wards was responsible for the transfer of infection in the opposite direction. The possibility of reducing the numbers of multiple-resistant staphylococci in the general wards, by the screening of all new admissions for the presence of tetracycline-resistant strains, appears to be impracticable in this area.

INTRODUCTION

The problems created by staphylococcal infections occuring in general surgical wards are well known, and have received considerable attention. Much less consideration has been given to the study of such infections occurring in intensive-care units, where the emphasis has largely been on the epidemiology of infections caused by Gram-negative bacilli. However Rountree & Beard (1968), studying a two-bedded unit, found that 20 out of 22 tracheostomies performed in the course of a year became colonized by *Staphylococcus aureus*. Jensen & Lassen (1969), recording 32 cases of staphylococcal tracheostomy colonization, found that in 11 of the patients the staphylococci responsible were resistant to methicillin. Both groups of workers emphasize the unique opportunities for dissemination inherent within an intensive-care unit, but less account is taken of the effect which such a unit may have on the incidence of staphylococcal infection elsewhere in the hospital.

In theory the temporary aggregation of susceptible patients in a unit where there may be numerous opportunities for spread of infection, and where there is extensive use of antibiotics leading to the selection of resistant strains of bacteria, could lead to the establishment of a reservoir of infection. Patients who acquired

multiple-resistant staphylococci in the intensive-care unit might carry these with them when they no longer required the special facilities and were returned to the general wards.

In this hospital, over the period 1968–71, there has been a high incidence of methicillin-resistance among strains of *Staph. aureus* isolated from infective lesions of in-patients, the majority of the resistant strains belonging to phage type 77. An intensive-care unit had been opened in the hospital in June 1967, and a preliminary survey (Harris, 1970) indicated virtually no difference in the incidence of methicillin-resistance between strains of *Staph. aureus* isolated within the unit and those isolated from the general wards of the hospital in the period ending July 1969. However, it was felt worth while to make a more detailed study of the interrelationship (in terms of both phage types and antibiotic sensitivities) of staphylococcal infections occurring in the intensive-care unit, in the general medical and surgical wards, and in the out-patient community. A limited amount of information was also obtained on the nasal carriage of staphylococci by nursing staff. This study, which extended over the period June 1967 to December 1971, forms the basis of the present report.

METHODS

Nature of the unit, and submission of specimens

The five-bedded intensive-care unit in question has already been described in detail, together with particulars of the methods routinely employed to limit cross-infection (Harris, Orwin, Colquhoun & Schroeder, 1969). It caters primarily for the treatment of respiratory insufficiency, but also undertakes the monitoring of cardiac arrhythmias following myocardial infarction. More detailed information on the type of cases treated has been published elsewhere (Colquhoun & Harris, 1971). Patients may be admitted either directly from the community via the casualty department or transferred from the general wards. Very few patients are admitted from the wards of other hospitals. Respiratory care is given by members of the anaesthetic staff, but in other respects patients remain under the supervision of general physicians and surgeons. Specimens for laboratory examination (sputum, urine, swabs from tracheostomies and other wounds) are submitted where appropriate, on the patient's admission to the unit and thereafter twice weekly for the duration of his stay.

Bacteriological methods

Specimens were examined by conventional cultural techniques. Sensitivity tests (for all antibiotics except methicillin) were carried out by a disk-diffusion method which has been described in full elsewhere (Harris, 1970). Sensitivity to methicillin was determined by inoculating a broth culture of the staphylococcus on plates containing 10 μg. methicillin per ml. which were incubated at 30° C. The Oxford staphylococcus was used as control organism. For the purposes of this study, a special record was kept of the sensitivity of *Staph. aureus* to the following antibiotics: benzylpenicillin, methicillin, streptomycin, tetracycline,

erythromycin and kanamycin. All strains of coagulase-positive staphylococci isolated in this laboratory are phage-typed, employing the standard phages, methods and criteria of the Central Public Health Laboratory, Colindale (Williams & Rippon, 1952; Blair & Williams, 1961). In this study, strains from any given patient which possessed the same phage-type and antibiotic-sensitivity pattern were considered to be identical. Strains differing in phage-type or in sensitivity to at least two antibiotics were regarded as representing distinct infections. During the period under review, 111 strains were isolated from 103 patients.

Accumulation of data on other patients and nursing staff

A record of the phage type and antibiotic sensitivity was available for all strains of *Staph. aureus* isolated in the general medical, surgical and orthopaedic wards, and for all strains derived from patients attending the casualty department. In view of the large numbers involved, a representative selection was made for this study by recording the phage types and sensitivity pattern of every third strain isolated from the wounds and sputa of in-patients, and every third strain isolated from wounds in the casualty department. This procedure provided information on 437 strains derived from in-patients and 582 strains isolated from patients attending the casualty department.

At this hospital there is no policy of systematic swabbing of nursing staff for the purpose of detecting nasal staphylococcal carriers. However, during the period under review several hundred nasal swabs from the staff had been examined, for various reasons. In all cases where the growth obtained had consisted predominantly of *Staph. aureus*, the strain had been phage-typed and tested for sensitivity to antibiotics. Such information was available on 57 strains, derived from 52 members of the nursing staff.

RESULTS

Relative incidence of various phage types in the different populations

The incidence of the various phage types in the different populations studied is shown in Table 1. A slight simplification has been introduced in the interests of clarity, namely the grouping together of closely related phage types. For example, the '3c/55/71' group includes strains lysed only by the individual phages 3c, 55 and 71, in addition to those strains which were lysed by all three phages.

Strains of phage type 77 were endemic in the hospital environment, and were apparently almost twice as common among strains isolated within the intensive care unit, when compared with those isolated from patients in general wards. In contrast, this phage type was rarely encountered in patients attending the Casualty department. Strains of phage type 84/85 also appeared to be commoner within the hospital. Unlike strains of type 77, the incidence of type 84/85 strains was lower among staphylococci from the intensive-care unit. The probable explanation lies in the fact that type 77 was distributed throughout the medical and surgical wards of the hospital, whereas type 84/85 was essentially endemic only in the orthopaedic wards (from which comparatively few patients are transferred to the intensive care unit).

Table 1. *The incidence of various phage types among strains of* Staphylococcus aureus *isolated from different groups of hospital patients, and from nursing staff*

	Source of strains			
Phage-type	I.C.U. patients	Other hospital in-patients	Casualty patients	Nursing staff
77	57 (51)*	119 (27)	15 (3)	4 (7)
84/85	6 (5)	39 (9)	4 (1)	1 (2)
'29/52/52A/80 group'	10 (9)	65 (15)	156 (27)	18 (32)
'3C/55/71 group'	5 (5)	19 (4)	121 (21)	9 (16)
42E	1 (1)	6 (1)	33 (6)	1 (2)
Other types	17 (16)	96 (21)	86 (15)	9 (16)
Untypable	15 (14)	93 (21)	167 (29)	15 (26)
Total	111	437	582	57

* Figures in parentheses indicate percentages.

Table 2. *The incidence of resistance to various antibiotics among strains of* Staphyloccus aureus *isolated from the various populations*

	Source of strains			
Resistance pattern	I.C.U. patients	Other hospital in-patients	Casualty patients	Nursing staff
Completely sensitive	5 (5)	63 (14)	219 (36)	16 (28)
Resistant to penicillin only	21 (19)	139 (32)	327 (56)	32 (56)
Resistant to penicillin and two or more others	30 (27)	72 (17)	10 (2)	1 (2)
Methicillin-resistant*	43 (39)	108 (25)	3 (1)	1 (2)
Others	12 (11)	55 (13)	23 (4)	7 (12)
Totals	111	437	582	57

* Methicillin-resistant strains were always resistant to four or five other antibiotics.

Strains belonging to phage type 42E, the '29/52/52A/80' group and the '3c/55/71' group, appeared to be essentially external strains which did not establish themselves permanently to any significant extent within the hospital. The phage types of strains isolated from the noses of the nursing staff corresponded in general with those of the staphylococci obtained from the casualty patients.

Relative incidence of resistance to antibiotics in staphylococci isolated from the different populations

As might be expected, the great majority of strains isolated from casualty patients were either completely sensitive to the antibiotics tested or resistant to penicillin only, while multiple resistance (and methicillin-resistance in particular) were prominent features of the staphylococci derived from in-patients. The

sensitivity-patterns of the staphylococci carried by the nursing staff tended to resemble those of the strains isolated from the lesions of out-patients (see Table 2). Only one of the 52 nurses carried a methicillin-resistant strain in her nose.

Certain correlations existed between phage types and antibiotic sensitivity patterns. For example, 56% of strains in the '29/52/52A/80' group (whether isolated from in- or out-patients) were either completely sensitive or were resistant to penicillin only; strains falling into this group therefore appeared to be endemic in the community and transferred from there into the hospital, where they were responsible for a small number of infections. However, they appeared to lack the ability to develop multiple resistance, and have thus never represented a major proportion of the strains isolated from hospital patients.

Conversely, 85·7% of the 176 strains belonging to phage type 77 which were isolated from hospital in-patients (including intensive-care cases) were found to be multiple-resistant; the majority also displayed methicillin resistance. However, 12 out of the 15 strains of this phage type isolated from casualty patients were either completely sensitive or resistant to penicillin only; the remaining three were multiple-resistant (two being methicillin-resistant), and had almost certainly been acquired through previous exposure to the hospital environment. The probable inference from these findings is that antibiotic-sensitive strains of phage type 77 normally exist as a small proportion of the staphylococci carried by the out-patient community, which, if introduced into the hospital, possess a great capacity for the acquisition of antibiotic-resistance and for spread between patients.

Relation of infection in the intensive care unit to infection in the hospital as a whole

The results presented above superficially suggest that the intensive-care unit has the highest incidence of multiple-resistant, endemic phage-type staphylococci of all the populations studied. To determine whether this was a fair reflexion of the actual position, a more detailed analysis was made of the situations in which the staphylococcal strains from the unit were isolated.

Seventy-six of the 111 strains were isolated from sputum or tracheostomy discharge, and the remainder from non-respiratory sources. Sixty-four of the infections were already present at the time of the patient's admission to the unit (Table 3). Virtually all the staphylococci isolated from patients who had been admitted directly from the community were either sensitive to all antibiotics or resistant to penicillin only. Conversely strains isolated from patients who had been transferred after a stay on another ward showed a high incidence of multiple resistance, and often belonged to phage type 77 or some other phage type essentially characteristic of the hospital environment.

The 47 strains of *Staph. aureus* acquired within the unit were isolated from 45 patients (25 admitted direct, and 20 transferred from other wards). Twenty-two of these strains were isolated from the respiratory tracts of patients in whom some form of artificial airway was operating (endotracheal tube or tracheostomy). Seventeen of these strains belonged to phage-type 77, and 16 showed multiple antibiotic-resistance. The time elapsing between the institution of assisted venti-

Table 3. *Antibiotic resistance in relation to the source from which the patient was admitted to the intensive care unit in* 111 *cases of* Staphylococcus aureus *infection*

	Infections in patients admitted from outside the hospital		Infections in patients transferred from another ward	
Resistance pattern	Infection present on admission	Acquired in I.C.U.	Infection present on admission	Acquired in I.C.U.
Fully sensitive or penicillin-resistant only	13	5	11	3
Multiple-resistant	1	14	39	25

lation and isolation of the staphylococcus from the respiratory tract varied between 1 and 22 days (median 5 days). In 5 of these 22 patients acquiring staphylococcal respiratory tract colonization within the unit there had been a preceding colonization with some other potentially pathogenic species (*Streptococcus pneumoniae* in 2, *Klebsiella* spp. in 3). Antistaphylococcal therapy was followed by colonization with *Pseudomonas aeruginosa* or resistant coliforms in 14 cases.

Of the total of 103 patients with staphylococcal colonizations, 45 were eventually returned to a general ward. On the basis of the specimens submitted to the laboratory, it appeared that the staphylococcal colonization had been eliminated before transfer in all but five of these patients. In three cases the persistent colonization was due to a strain of phage type 77, and it was impossible to assess the exact influence of this common type on the subsequent incidence of staphylococcal infection in the ward. For the remaining two patients the colonizing staphylococcus was of a distinctive phage type, and no further infections due to similar strains were recorded in the transfer wards during the patients' stay.

DISCUSSION

The findings reported here indicate that, in the absence of the selective influence exerted by the hospital environment, most staphylococcal wound and respiratory infections are caused by strains which are either sensitive to all antibiotics or resistant to benzylpenicillin only. However, this applies to less than a third of the staphylococcal colonizations seen in the intensive care unit of this hospital. The chief reason for this is clearly the very high incidence of multiple-resistant staphylococcal infections already present in patients admitted to the unit for respiratory care. Rountree & Beard (1968) found that staphylococci were widely dispersed from such patients, producing extensive contamination of the surroundings, making it difficult to avoid aerial cross-infection of the newly admitted case when patients were nursed in close proximity. The present intensive care unit is far from ideal in this respect, but is probably fairly typical of the accommodation which has been extemporized for this purpose in older hospitals. It is true that most of the isolations, especially those from the respiratory tract, represented colonizations, rather than invasive infection; however, patients nursed in intensive-care units commonly suffer from one or more of the conditions which are known to be

associated with impaired pulmonary bactericidal activity (Wright, 1961; Green & Kass, 1964; Goldstein & Green, 1966) and there is always a possibility of pneumonia if the numbers of colonizing bacteria reach a level sufficient to overwhelm the pulmonary clearance mechanism. Consequently, continual bacteriological monitoring of the respiratory tract is essential, so that clinicians can be apprized of colonization at the earliest possible moment. However, antibacterial therapy given at the stage of asymptomatic colonization is of doubtful value, since it may merely result in the supplanting of a relatively sensitive organism by a more resistant one. Price & Sleigh (1970) showed that it was advantageous to abandon antibiotic therapy in the management of *Klebsiella* colonizations, the sole methods of treatment being tracheal toilet and physiotherapy. More recently, Klastersky, Beuner & Daneau (1971) have shown that these principles can be applied with equal success in the field of methicillin-resistant staphylococcal infections, even when there is radiological evidence of pulmonary consolidation. It has been suggested that methicillin-resistant staphylococci have a special predilection for the respiratory tract (Jensen & Lassen, 1969); however, it is probably more likely that the frequency of their isolation from this site in the intensive care unit merely reflects the endemicity of the organisms in the unit. Certainly a previous study from this laboratory showed no difference in the incidence of respiratory and non-respiratory methicillin-resistant staphylococci in the hospital as a whole (Harris, 1970).

The amount of infection introduced into an intensive-care unit can best be reduced by closer attention to measures for the prevention of infection on the general wards from which the patients are derived. It has been suggested (Stokes *et al.* 1972) that routine screening for the presence of tetracycline-resistant staphylococci in the noses of hospital workers and newly admitted patients is a useful measure in identifying strains which may subsequently become endemic and develop multiple resistance. The findings in the present survey indicate that this policy may not be universally applicable. For example, the great majority of multiple-resistant strains within the hospital belonged to phage type 77, yet 12 out of 15 strains of this phage type isolated from casualty patients were either completely sensitive to antibiotics or resistant to penicillin only. Such strains would remain undetected by the screening method.

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