

***Staphylococcus aureus* type 83A as a cause of hospital cross-infection**

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Numerous studies of cross-infection by *Staphylococcus aureus*, in which typing by bacteriophages has been used, have made it clear that the majority of outbreaks have been due to a relatively small number of phage types. Of these, type 80 appears to have been the most frequent; but other group I types, and certain types of group III have constantly recurred (Williams, 1959; Williams & Jevons, 1961).

Although another type, namely 83 A, has been referred to as causing a number of epidemics in surgical units (Williams, Blowers, Garrod & Shooter, 1960) and incidental references to infections caused by it have been made in other communications (e.g. Barber & Waterworth, 1962; Dickinson & Pride, 1962), no extended study of it as a cause of cross-infection appears to have been published.

It may be of value, therefore, to describe the part which it has played in staphylococcal cross-infection in a hospital group, over a period of 2½ years. In this group, type 83A has shown a significant capacity to survive and spread in a hospital environment, and strains of it resistant to certain antibiotics have been isolated with a frequency not equalled by strains of other phage types.

MATERIALS AND METHODS

Period of study

A retrospective study has been made of the general incidence of this particular phage-type, over a period extending from October 1959 to March 1962.

Source of strains

The strains of *Staph. aureus* studied were isolated from clinical specimens during the routine work of a hospital laboratory. All were from in-patients of four main hospitals of a group. These were: a general hospital, acute medical and surgical; a fever hospital, also containing wards for acute medical cases from which most, if not all, of the staphylococci from this hospital were derived; a chest hospital; and an ex-poor-law hospital which now houses orthopaedic, geriatric and maternity units.

Only those strains which could reasonably be supposed to be playing a pathogenic role are included in the survey; this criterion has been difficult to apply in some cases, notably in the case of strains isolated from sputum.

Repeated isolations from a single patient have been excluded, except where the

later isolation has come from a different lesion from the earlier one, or has been of a different phage type.

All strains were, by definition, coagulase-positive. The terms 'staphylococcus' and 'staphylococci', when used without qualification in this paper, should be taken to mean coagulase-positive *Staph. aureus*.

Drug sensitivity tests

These were done routinely by a disk-plate method, tube dilution tests being done in a few cases where indicated.

Phage typing

During the relevant period, all coagulase-positive staphylococci that were isolated, and which were found to be resistant to one or more of the antibiotics used in the routine sensitivity test, were subcultured to agar slopes and stored for phage-typing. Typing was done in batches, the usual interval being 7-14 days.

The methods of typing used were those described by Williams (Anderson & Williams, 1956), and Blair & Williams (1961). The standard, internationally agreed set of 21 phages was used, plus phage 83A which throughout the period of the survey did not form part of that set.

RESULTS

Type 83A: powers of survival and spread

The total number of strains of *Staph. aureus* isolated during the period, which were likely to be acting as pathogens and which were resistant to more than one antibiotic, was 1131. Of these, 776 were resistant to tetracycline.

Since it has been found here, as elsewhere, that tetracycline-resistance in hospital staphylococci is a reasonably accurate index of their capacity to produce cross-infection, such strains only have been considered in Table 1, which has been designed to show how type 83A has, throughout the 2½-year period, continued to produce cases of cross-infection in the four hospitals.

So far as 83A itself is concerned, strains isolated during the period were almost invariably resistant to tetracycline (sensitive, 17; resistant, 263 strains). In addition, tetracycline-resistance, both in 83A strains and those of other phage-types was almost uniformly associated with resistance to penicillin and streptomycin.

In Table 1 the numbers of strains of tetracycline-resistant staphylococci isolated every quarter have been divided into those of type 83A, and those belonging to other phage-types; although, for convenience, the latter heading has been made to include also any untypable strains.

Among 'other types' those of group I greatly predominated, 52/52A/80 or 52/52A/80/81 being the commonest, followed by type 80 or 80/81. Group III strains, excluding 83A, followed in order of frequency, with a smaller number of strains lysed by phages of both groups I and III. Untypable strains numbered 89, or 11·3% of the total.

It will be seen that over the whole period some 34% of tetracycline-resistant strains were type 83A. It will also be seen that there was a rise in the number of

such strains in the first half of 1960, and a fall in the middle of 1961, but that, apart from these fluctuations, type 83A has pretty consistently constituted about one-third of the tetracycline-resistant strains isolated. It may, therefore, be reasonably supposed to have been responsible for something like one-third of the staphylococcal cross-infection occurring during this time.

Table 1. *Numbers of tetracycline-resistant Staph. aureus, isolated every quarter, October 1959 to March 1962, in four hospitals: showing the incidence of type 83A as compared with other types*

Hospital...	A		B		C		D		Totals		83A (%)
	83A	Other types	83A	Other types	83A	Other types	83A	Other types	83A	Other types	
Period											
1959											
Oct.-Dec.	7	17	4	10	14	14	1	12	26	53	32.9
1960											
Jan.-Mar.	10	21	7	5	9	10	4	6	30	42	41.7
Apr.-June	14	19	4	4	12	15	6	12	36	50	41.9
July-Sept.	1	10	1	4	7	7	7	10	16	31	34.0
Oct.-Dec.	3	10	1	9	11	8	6	7	21	34	38.2
1961											
Jan.-Mar.	4	26	1	14	10	6	15	10	30	56	34.9
Apr.-June	5	22	2	8	4	10	10	15	21	55	27.6
July-Sept.	4	23	3	11	3	7	5	16	15	57	20.8
Oct.-Dec.	7	24	7	9	8	12	7	15	29	60	32.6
1962											
Jan.-Mar.	11	23	6	3	17	20	5	29	39	75	34.2
Totals	66	195	36	77	95	109	66	132	263	513	33.9
83A (%)	25.3	—	31.9	—	46.6	—	33.6	—	33.9	—	—

Hospital A = general; B = fever and acute medical; C = chest; D = Orthopaedic, geriatric and maternity.

In the chest hospital about half the tetracycline-resistant strains belonged to type 83A, in the general hospital about one-quarter and in the other two hospitals about one-third. The high incidence of one particular type in four hospitals, the nearest of which are some miles apart, and which deal with a wide variety of clinical material, is a striking feature.

Type 83A: resistance to chloramphenicol, erythromycin and novobiocin

Staphylococci were not phage-typed unless resistant to one or more of the antibiotics routinely tested. These were: penicillin, streptomycin, chloramphenicol, tetracycline, erythromycin and novobiocin.

Where there was resistance to more than one antibiotic the commonest pattern was: resistant to penicillin, streptomycin, tetracycline; sensitive to chloramphenicol erythromycin, novobiocin. Resistance to any of the last three antibiotics was rare, but, during the period of study, it became apparent that if a strain did show

resistance to any of these it was likely to be of phage type 83A. Table 2 expresses this quantitatively.

It will be seen that the percentage of all strains resistant to chloramphenicol was 7.0, whereas the percentage of 83A strains thus resistant was 11.8. This is significantly more than occurs with strains of other groups, except group II, and here the number of strains involved is so small that their significance is doubtful. Of untypable strains, however, 8.8% were resistant.

The resistance rate to erythromycin is more striking, 29.6% of 83A strains being resistant, while the group with the next largest percentage—group III, excluding 83A—provides only 4.9% of resistant strains.

Table 2. *Phage types of strains of Staph. aureus resistant to chloramphenicol, erythromycin and novobiocin*

Type or group	Total no. of strains	No. of strains resistant to					
		Chloramphenicol		Erythromycin		Novobiocin	
		Total	%	Total	%	Total	%
83A	280	33	11.8	83	29.6	25	8.9
Group I	405	17	4.2	9	2.2	12	3.0
Group II	26	3	11.5	1	3.8	0	—
Group III other than 83A	203	9	4.4	10	4.9	0	—
Other types	46	2	4.3	2	4.3	0	—
Untypable	171	15	8.8	7	4.1	1	0.6
Totals	1131	79	7.0	112	9.9	38	3.4

So far as novobiocin-resistance is concerned, the small number of strains makes their significance more doubtful. However, of the 38 resistant strains, 25 belonged to phage-type 83A.

Type 83A: pathogenicity

To gauge the significance of 83A strains it is necessary to know not only the total number of isolations, but also something of the lesions which they caused and the severity of these.

The latter, in a retrospective survey, can be assessed only in the most general terms; but some idea of the nature of the infections can be gained from the clinical sources of the strains, and these are shown in Table 3.

This table deals with the 776 tetracycline-resistant strains already considered in Table 1: its value as evidence of infection varies with the clinical source from which such a strain was derived.

Strains from operation wounds may be taken to show true secondary infection in practically all cases, and provide an index of the capacity of type 83A to produce such infection. The second category of the table—'abscesses, boils, etc.'—covers a wide variety of infections of the skin and subcutaneous tissue, but here again the staphylococci isolated may almost invariably be taken to be causative.

The case is otherwise with strains isolated from sputum; and although a number were not included in the series as not significant, because of scanty growth or other

reasons, an unknown number of 'carrier strains' must still remain. On the other hand, among ample evidence to show that type 83A strains are capable of causing severe chest infection, is the fact that such strains were isolated post mortem from the lung on nine occasions. In five of these cases it appeared likely that the staphylococcus was the cause, or major contributory cause, of death.

There is no doubt about the pathogenic role of the urinary strains; and strains from faeces were all from cases which appeared to be true staphylococcal enterocolitis. Of the eighteen cases of enterocolitis, fourteen were caused by type 83A with one death.

Table 3. *Nature of infections caused by tetracycline-resistant strains of type 83A and those of other types*

Phage-type	83A	Other types	83A (%)
Clinical source of strains			
Operation wounds	35	68	33.9
Abscess, boils, etc.	31	94	24.8
Sputum	109	224	32.7
Eye	16	27	37.2
Ear, nose, throat	13	14	48.1
Urine	17	35	32.7
Faeces	14	4	77.8
Other sources	28	47	37.3
Totals	263	513	33.9

'Other sources' comprises a wide variety of infections, but a case of meningitis caused by type 83A is worth mentioning, as the only case of staphylococcal meningitis during the period. This was a fatal infection in a woman aged 74.

DISCUSSION

This survey is concerned only with the incidence of type 83A in the four hospitals during the period studied. No attempt has been made to describe individual outbreaks, or the investigation of these and the measures which were taken to combat them.

In spite of such measures it will be seen that staphylococcal cross-infection continued throughout the period, and that type 83A was responsible for about one-third of it.

The objects of this communication are, first, to draw attention to these powers of survival and spread of this type, and to suggest that its appearance in an environment where it has not previously been found should be taken seriously; and, secondly to indicate the frequency with which strains resistant to chloramphenicol, erythromycin and novobiocin may be encountered.

Since this work started, however, erythromycin and novobiocin have lost their pride of place in the treatment of multiple-resistant staphylococcal infections, to be supplanted by methicillin and cloxacillin. It has been of interest, therefore, particularly in view of their resistance to other antibiotics, to test strains of 83A against methicillin; and 214 such strains were thus tested, between September

1960 and May 1962, using a disk-plate method with 10 μ g. of methicillin in the disk. All strains were isolated from clinical specimens, but 32 were considered not to be acting as pathogens. Repeat isolations from the same patient were excluded. None of the strains tested by this method showed resistance.

This is encouraging, but it should be recorded that Barber & Waterworth (1962) have reported that of 4017 strains of staphylococci, 1078 being from infected patients, tested against methicillin, 88 strains showed some degree of resistance, and of these 88 strains, 12 belonged to phage-type 83A. Barber & Waterworth used a ditch-plate method of testing, and it seems possible that this might pick up minor degrees of resistance more frequently than the antibiotic disk.

It is, incidentally, of some interest, in view of our finding concerning erythromycin-resistance among 83A strains, that the 12 methicillin-resistant 83A strains isolated by Barber & Waterworth were all resistant also to erythromycin; whereas their remaining 76 methicillin-resistant strains of other phage types were all erythromycin-sensitive.

The prominence of 83A strains as a cause of cross infection in four widely-separated hospitals, over a period of more than 2½ years; the power of these strains, on occasion, to produce severe and sometimes fatal infection; the number of strains shown to be resistant to chloramphenicol, erythromycin or novobiocin, in addition to other antibiotics; and the demonstration, elsewhere, that 83A is one of the phage types of which there are very few at present, which may show resistance to methicillin, form a combination of characters which suggests that, even in comparison with other well-known epidemic types, 83A may be a particularly noteworthy cause of hospital cross-infection.

SUMMARY

1. A retrospective survey has been made to determine the amount of cross-infection caused by *Staphylococcus aureus* of one particular phage-type, 83A, in four main hospitals of a provincial hospitals group, over a period of 2½ years.

2. The total number of strains considered was 1131. Of these, 776 were resistant to tetracycline and therefore the most likely to be of significance in cross-infection. Of these 776 strains, about one-third belonged to phage-type 83A. In the hospital where 83A strains were most prevalent, they formed about one-half of the tetracycline-resistant strains; in that where they were least prevalent, about one-quarter.

The clinical sources of the tetracycline-resistant strains are described.

3. It was found that type 83A strains were the most likely to show resistance to erythromycin, chloramphenicol or novobiocin.

Of a series of 214 type 83A strains sensitivity tested against methicillin, using a disk-plate method, none was found to be resistant.

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