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Long-Term *Staphylococcus aureus* Carrier State in Hospital Patients

CHARLES H. ZIERDT

Microbiology Service, Clinical Pathology Department, Clinical Center, National Institutes of Health, Bethesda, Maryland 20205

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Staphylococcus aureus colonization of 326 predominantly chronic-care (long-term) patients was studied for 24 years. There were 5,827 upper respiratory cultures positive for *S. aureus*, ranging from 10 to 88 per patient, determined by the number of years (1 to 21; average, 4.6) that the patient was studied. Patients on the average carried 2.8 *S. aureus* strains. One patient carried eight strains. Each patient had a predominant strain. Predominant strains tended to be permanent, with 87% persistence over the studied years. Lytic group III strains were more than twice as frequent as group I strains and eight times as frequent as group II strains. Patient carriage of multiple *S. aureus* strains was usual. A collection of large numbers of cultures over an extended period was necessary for this statistical study, since cultures positive for predominant strains were interspersed with negative cultures and cultures positive for minor strains. Thus, persistence of carriage of a predominant *S. aureus* strain in a patient continues despite frequent negative cultures and cultures positive for minor strains.

Despite the use of phage typing in many epidemiological reports, there are very few studies, such as that of Ayliffe et al. (1), restricted to the carrier state of *Staphylococcus aureus*. There have been no previous studies of specific *S. aureus* strain carriage that followed the patients for more than a few months. A staphylococcal carrier was defined for this study as a person harboring *S. aureus* in the upper respiratory tract.

MATERIALS AND METHODS

Data on *S. aureus* isolations from the upper respiratory tract were taken from a computer file of 23,000 phage-patterned strains for the period from 1957 to 1980, inclusive (7). The present study is of 326 patients (Table 1) from whom cultures were taken for 1 to 21 years (average, 4.6 years) as inpatients or outpatients or both. No patient had fewer than 10 upper respiratory cultures (range, 10 to 88 cultures; average, 18 cultures) positive for *S. aureus*. A total of 5,827 *S. aureus* isolates were studied (Table 2). Upper respiratory cultures included swab cultures taken from the anterior nares, nasopharynx, throat, and sputum. Typically pigmented, hemolytic colonies of gram-positive cocci in clusters were coagulase tested and phage typed for confirmation as strains of *S. aureus*. Phage typing was performed as described previously (7).

Numbers of *S. aureus*-negative cultures were not available in this retrospective study, except a culture positive for lesser strains was at the same time negative for the predominant strain. Only one colony was selected for typing. Experience has shown that all colonies on a single culture plate are likely to have the same phage pattern. Cultures were taken at random intervals throughout the years, but the yearly distribution of cultures for individual patients was fairly uniform. For each patient the *S. aureus* strain that occurred most often was identified, and the number of years that it persisted in that patient was determined.

RESULTS AND DISCUSSION

Most patients had a predominant strain and a number of lesser strains. The number of *S. aureus* strains per patient ranged from 1 to 8 (Table 3), with an average of 2.8. It was interesting that the average number of strains per patient did not increase according to the number of study years, but remained at a level of two to four strains per patient. This suggests that the acquisition of additional strains was blocked by resident strains of *S. aureus*, an example of bacterial interference. This conforms to the guidelines set forth by Boris et al. (2).

The number of years from the appearance of a predominant strain to its evident disappearance from the patient was expressed as a percentage of the total number of years that the patient was studied. The persistence of predominant strains was 87% overall, 89% for the period from 10 to 19 years, and 86% for the period from 15 to 19 years.

A logical study would be whole-body mapping of selected patients and normal individuals for *S. aureus* carriage over extended periods, with even more cultures taken and more colonies

TABLE 1. *S. aureus* carriers[a]

No. of patients	No. of yr studied (avg, 4.6)	No. of strains per patient (avg, 2.8)
58	1	2.2
60	2	2.8
64	3	2.8
35	4	2.9
19	5	3.3
16	6	3.1
12	7	2.6
12	8	3.4
11	9	3.6
7	10	2.4
9	11	2.7
3	12	3.3
3	13	3.0
4	14	2.8
4	15	3.8
2	16	3.5
2	17	3.0
4	19	5.3
1	21	4.0

[a] Each patient had 10 or more isolates (average, 18).

phage typed to better delineate site distribution and population numbers of colonizing strains as well as changes in strain distribution and number. The effect of such a study on the present data might raise the figures of 2.8 strains per colonized patient and 86% persistence of predominant strains over the 24-year study period. To what extent these figures would be elevated is conjectural.

The most pathogenic *S. aureus* strains in our hospital have been certain strains of lytic groups I and III. These strains also were most frequently predominant in this study (Table 4). Group II strains have been very weakly pathogenic (manuscript in preparation). Group II strains have outnumbered group I strains by two to one in the patients in this hospital over the last 25 years. However, group I strains outnumbered group II strains by three to one in long-term carriers. Group III strains were more than twice as frequent as group I and eight times as frequent as group II in the 326 carriers.

TABLE 2. *S. aureus* carrier state patients studied for 1 to 21 years

No. of patients studied	326
Total no. of *S. aureus* isolates	5,827
No. of *S. aureus* isolates per patient	17.9
No. of *S. aureus* distinct phage-patterned strains per patient	2.8
Average no. of study years per patient	4.6
Total no. of years for carriage of predominant strains	1,148
Total no. of patient years	1,313
Persistence of predominant strains	87.4%

TABLE 3. Number of strains colonizing long-term *S. aureus*-carrying patients

No. of colonizing strains	No. of patients
1	47
2	103
3	77
4	73
5	17
6	7
7	1
8	1

Nontypable (NT) strains numbered only 50 (1%) of the 5,827 upper respiratory *S. aureus* strains from 326 long-term carriers. Only three long-term carriers (1%) had an NT strain as the predominant strain. However, NT strains comprised 16% (2,849 of 17,807 cultures) of all hospital strains. This disparity indicates that NT strains had far less ability to persist as predominant upper respiratory flora. NT strains have caused fewer infections in this hospital than have the groups I and III strains shown in Table 4. It appears that *S. aureus* strains having high rates of infection are also likely to be persistent and predominant colonizers in carriers.

It is evident from the study of Miles et al. (6) that there is a discontinuity of positive cultures from nasal swabs taken on a weekly basis in most *S. aureus*-colonized patients. Some negative nasal cultures may reflect a failure to take the sample correctly, but the majority must result from an ebb and flow of *S. aureus* population density in the anterior nares. According to Miles, persistent carriers, in the sense of 100% positive cultures over a period of, say, 20 weekly cultures, judging from various studies, would be about 20% of patient carriers. By this definition, 80% of patient carriers are intermittent carriers, providing a mix of positive and negative nasal cultures. As the present study demonstrates, the term intermittent carrier perhaps should not be construed to mean alternate states of freedom from *S. aureus* colonization. In the majority (about 90%) of patient carriers, a negative swab culture meant only that at the swabbed site on the day of culture, an insufficient number of organisms were present to provide a positive culture. The patient may still be colonized by the previously cultured strain of *S. aureus*. This condition is well exemplified in studies of the effects of nasal or systemic antibiotics or both on the carrier state. A negative nasal culture, or even consecutive weekly negative nasal cultures, is not proof that the carrier state has been cured. Whether this temporary or false cure is

TABLE 4. Lytic groups and phage patterns of predominant *S. aureus* strains in 326 long-term carriers

Group (% of carriers)	Phage pattern of *S. aureus* strain	No. of carriers
I[a] (25)	42B/52/52A/80/81	38
	80/81	20
	52/52A/80	9
	52/52A/80/83A	4
	52A/80	3
	52A/80/83A	2
	29/52A/80/81	2
	29/42B/80/81	2
	29/42B/52/80	1
	52A/80	1
II (8)	3B/3C/55/71	26
III[b] (63)	83A	20
	53/86	12
	53/83A/86	11
	77	10
	77/83A	9
	83A/86	7
	53/83A	3
	53/77/83A	1
	53/77	1
	6/7/42B/42E/47/53/54/75/77/83A[c]	132
Miscellaneous (3)	44A	3
	86	2
	94/292/96	4
NT (1)	NT	3

[a] Complex of group I strains consisting of phages 29, 52, 52A, and 80 plus some admixture with group III (phages 42B and 83A) and miscellaneous (phage 81).

[b] Group III phages plus some admixture with miscellaneous phage 86.

[c] A representative phage pattern. In retrospect these could not be subgrouped accurately because of diversity of pattern and admixture with groups I and II and miscellaneous phages.

worth achieving in the control of an epidemic is another question. Leedom et al. (5) stated that 15 consecutive negative monthly samples are required to segregate noncarriers from intermittent carriers.

It is interesting that patients who leave the hospital as *S. aureus* carriers may become noncarriers within a year after discharge (3). This creates a disparity between the rate of reduction of the carrier state in patients who leave the hospital and the rate in those who remain. A partial answer may lie in the requirement for a large number of cultures before the individual can definitely be considered a noncarrier. Most follow-up studies of the treated carrier state include insufficient nasal cultures to definitively state that the individual has become a noncarrier. The results of the present study indicated that the *S. aureus* carrier state in long-term patients was stable and generally unbroken by periods of absence of colonization. Also, antibiotic therapy usually made no permanent change in the carrier state of long-term patients or in the specific strains colonizing these patients. Many of these long-term patients had courses of systemic antibiotics during the study period for infections caused by predominant *S. aureus* strains. Although specific infections were cured by antibiotic therapy, the carrier state was not permanently affected.

Temporary conversion to negative nasal cultures after topical treatment with antibiotic cream has been reported by Gould (4), but 51% of 124 treated carriers returned to culture positive within a month, with only a single culture as evidence. Additional cultures would probably have raised that figure.

It is probable that the carrier state of specific *S. aureus* strains in the long-term patient is much more permanent than previously recognized and that this stability of the carrier state in the individual patient usually includes two to four strains of organism.

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