**Staphylococcus aureus** Throat Colonization Is More Frequent than Colonization in the Anterior Nares

Peter Nilsson* and Torvald Ripa

Department of Clinical Microbiology and Infection Control, The County Hospital of Halmstad, Halmstad, Sweden

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The aim of this study was to determine the frequency and persistence of *Staphylococcus aureus* carriage in the throat in relation to anterior naris carriage. By use of a sensitive enrichment broth, *S. aureus* was cultured from the two sites from 259 patients upon admission to an orthopedic ward and from 87 staff members of the same ward. The throat was the most common carriage site in both groups. Forty percent of the patients and 54% of the staff were positive for *S. aureus* in the throat, compared to 31% and 36%, respectively, in the anterior nares.

To determine the persistence of carriage, 67 individuals were repeatedly sampled from the anterior nares and the throat over 2 years (5 to 10 sampling occasions; mean, 7.8). The majority, 58% (39/67), were defined as persistent carriers of *S. aureus*, considering culture results from both sites. Of the 39 persistent carriers, 15 individuals were culture positive from only the throat on more than half of the sampling occasions (these are called preferential throat carriers) while only 5% (two individuals) were preferential anterior naris carriers by use of the same definition. Typing of the collected *S. aureus* isolates by pulsed-field gel electrophoresis revealed that the same strain of *S. aureus* was present, over time, in the throat of an individual at least to the same extent as in the anterior nares. Throat carriage was at least as persistent as carriage in the anterior nares.

Besides being a major human pathogen (14), *Staphylococcus aureus* colonizes large proportions of human populations (27). The anterior nares are considered to be the primary colonization site (11, 14), and approximately 30% of healthy people carry the bacteria in their anterior nares. Carrier rates close to 60% have been described previously for certain populations (11). The human throat is less well studied as a carriage site, and various isolation rates have been reported previously. Boe et al. reported an isolation rate of 31% in patients admitted to a medical ward (4), and Uemura et al. reported an isolation rate of 29% in a group of healthy adult volunteers (22). Berkovitch et al. found the bacteria in the throats of 10% of healthy children under the age of 2 years (3). There have also been observations of higher-than-expected rates of methicillin-resistant *S. aureus* (MRSA) in infants’ throats (9). The perineal region seems to be a common carriage site but is rarely the only site to be colonized (4). Also, carriage in various skin areas has been described previously. However, this seems to be secondary to carriage or infection at other sites since removal of nasal colonization with topical treatment in most cases eliminates skin carriage (16, 20).

Three main carriage patterns have been described when individuals are repeatedly sampled in the anterior nares for *S. aureus* over longer periods. Between 6 and 60% have been reported never to carry the organism (noncarriers), and 14 to 33% have been repeatedly culture positive (persistent carriers). The remaining individuals yield positive cultures from time to time and are characterized as occasional or intermittent carriers (6, 10, 27). The variation between studies might be due to different sampling techniques and/or variations in the definitions of the different carrier states. Persistent carriers tend to carry the same phage type or genotype over time more often than the intermittent and occasional carriers (6, 27). To our knowledge, the carriage pattern over time has not been investigated for any sampling site other than the anterior nares.

The aim of this study was to determine the frequency and persistence of throat carriage in relation to that of anterior naris carriage of *S. aureus*. We used a sensitive culture technique to minimize errors arising from low recovery rates. All isolates were genotyped by Smal pulsed-field gel electrophoresis (PFGE).

**MATERIALS AND METHODS**

**Patients and ** *S. aureus* ** sampling.** All samples were collected as a routine infection control surveillance scheme at the County Hospital of Halmstad, Sweden. Specimens were collected using a rayon-tipped swab with Amies charcoal transport medium (14C.US) (Copan, Italy). The anterior nares were sampled by rotating the swab tip in both nostrils, and the throat was sampled by rotating the swab tip on both tonsils.

Patients admitted to the orthopedic ward at the County Hospital of Halmstad, Sweden, from March to September 2003 were sampled in both the anterior nares and the throat by staff upon arrival and investigated for the presence of *S. aureus*. Among the 259 patients sampled, 62% were females, with a mean age of 74.4 years, and 38% were males, with a mean age of 64.3 years. Twenty patients were sampled in March, 72 in April, 57 in May, 20 in June, 17 in July, 38 in August, and 35 in September.

Hospital staff in the orthopedic ward were instructed to sample themselves by rotating a swab in both anterior nares and a separate swab on both tonsils. Samples were taken from all staff members on duty during 1 week each month between March and September 2003 (except for June and July, when the ward was closed most of the time) and then during 1 week in November 2003, March 2004, and April 2005, nine occasions in total. Not all staff members were available at all times, and new staff members were included during the study period. In total, 87 individual staff members were sampled at the orthopedic ward (70 females, with a mean age of 40 years, and 17 males, with a mean age of 34 years). A group of 67 individuals were repeatedly sampled from the anterior nares and throat for up to 24 months. The group consisted of 34 staff members from the orthopedic ward and 33 staff members from the Department of Clinical Microbiology and Infection Control at the County Hospital of Halmstad, Sweden. Of
these 67 individuals, 63 were females and 4 were males, with a mean age of 44 years at the time of the first sampling occasion. They were sampled at least five times during the period between March 2003 and March 2005 (mean, 7.8 times; range, 5 to 10). In total, 384 isolates of S. aureus were collected and their clonal relationships were determined by PFGE analysis.

S. aureus isolation. All swab samples were incubated for 16 to 18 h at 37°C in a shaker (100 rpm) under aerobic conditions in 3 ml enrichment broth with the following composition: 15.0 g proteose peptone (Oxoid, Basingstoke, England), 2.5 g liver digest (Oxoid), 5.0 g yeast extract (Oxoid), 25.0 g NaCl, 10.0 g mannitol, 16 mg/liter phenyl red, and 8 mg aztreonam in a final volume of 1 liter (final pH, 7.0 ± 0.1). A portion (10 µl) of the broth was then plated on a blood agar plate and incubated at 37°C overnight. Suspected colonies were isolated on a blood agar plate and identified as S. aureus by use of DNase testing and a Staphaurex latex test (Remel Europe Ltd., Dartford, England). When these methods disagreed, the presence of the thermostable nuclease gene was assayed by PCR as described by Nilsson et al. (15). One single isolate of S. aureus was isolated from each sample. The possible presence of more than one strain in each sample was not taken into account. All isolated strains of S. aureus were collected and stored at −70°C for further analysis.

PFGE. The strains collected in the study were analyzed by PFGE as described by Bannerman et al. (2). The banding patterns from the isolates were analyzed using Molecular Analyst software, version 1.6 (Bio-Rad Laboratories, Hercules, Calif.), with the unweighted-pair group clustering method using average linkages and Dice coefficient. Strains with more than 80% similarity were grouped into clonal groups and named with a capital letter from A to X. Isolates from the same individual but collected on different occasions were also compared to each other. In all cases, when they belonged to the same clonal group, they were within three band differences (21). This means that isolates from different individuals but named with the same letter had at least 80% similarity by the computerized clustering analysis, while isolates from one individual and with the same name had <4 band differences.

Calculations and definitions. Carrier index (CI) was defined as the number of positive swabs divided by the total number of swabs for each individual, as described by Eriksen et al. (6). However, the definitions of carrier states differ from those used by Eriksen et al. In our work, a persistent carrier is defined as an individual with a CI of >0.5; for an occasional carrier, 0 < CI ≤ 0.5; and for a noncarrier, CI = 0. The study period was defined as the number of months between the first and last samples, and the carrier time was the number of months between the first and last positive samples during the study period for an individual. The time an individual carried the same strain was defined as the number of months an S. aureus strain within three band differences by PFGE was sampled from the individual. Intervening negative samples were tolerated, but intervening findings of strains with more than three band differences by PFGE were not.

RESULTS

S. aureus carriage in patients and staff. During the study period from March 2003 to September 2003, 259 patients admitted to an orthopedic ward were sampled at admittance, both in the anterior nares and in the throat. The rates of S. aureus isolation from the different sites are presented in Table 1. In total, S. aureus was isolated from 125 of the 259 patients (48%) from either of the sites. The most common site of isolation was the throat (40% of the patients), followed by the anterior nares (31% of the patients). The difference in isolation frequency between the anterior nares and the throat was statistically significant (P = 0.037). If anterior nares had been the only screening site, 64% (80/125) of S. aureus carriers would have been identified, while sampling from only the throat would have identified 83% (104/125). No significant differences between men and women concerning isolation rates from the different sites were found (data not shown).

During the study period, all members of the staff on the ward were prompted to sample anterior nares and throat each month. In Table 1, we have summarized the rates of S. aureus isolation from the first sampling occasion of the 87 staff members. Sixty-two percent (54/87) were positive in either of the sites. As with the patient group, the most common site of isolation was the throat (54% positive, compared to 36% in the anterior nares; P = 0.023).

In total, 346 patients and staff members were screened; 32%
were positive in the anterior nares (95% confidence interval, 27 to 37%) and 44% were positive in the throat (95% confidence interval, 38 to 49%). The difference in isolation frequency between the anterior nares and the throat was statistically significant, with a P value of 0.003.

Figure 1 shows the isolation rates in staff and patients for each month. The total numbers of individuals sampled were 67 in March, 114 in April, 99 in May, 82 in August, and 76 in September. No data are presented for June and July because the ward was closed during most of that time. The overall carriage rate was highest in March (66%) and lowest in August (48%). Also, throat carriage tended to drop, from 58% to 38% over the same period. On every sampling occasion, throat carriage was more frequent than nasal carriage.

**Carriage over time.** To study *S. aureus* carriage patterns over time, a group of 67 individuals was repeatedly sampled from the anterior nares and the throat for up to 24 months. In total, 521 swabs were taken from anterior nares and throat; 152 (29%) turned out positive for *S. aureus* in the anterior nares and 232 (45%) in the throat.

The 67 individuals were grouped into persistent carriers, occasional carriers, and noncarriers based on CIs calculated from culture results from the anterior nares alone, results from the throat alone, and the combined results from both sites (Table 2). Based on the results from the anterior nares alone, 25% (17/67) of the individuals were classified as persistent carriers, compared to 58% (39/67) when the results from the throat swabs were added. The culture results on each sampling occasion for the 39 individuals classified as persistent carriers are presented in Fig. 2.

Based on the most frequent carriage site over time, the 39 persistent carriers could be grouped into the following groups: preferential anterior naris carriers, i.e., individuals positive in only anterior nares on more than half of the sampling occasions; preferential throat carriers, i.e., individuals positive in only throat on more than half of the occasions; preferential anterior naris/throat carriers, i.e., individuals positive in anterior nares and throat on more than half of the occasions; and indeterminable carriers, persistent carriers with a mixed pattern of carriage based on the sampling site. With these definitions, 5% of the persistent carriers were preferential anterior naris carriers (individuals 1 and 2 [Fig. 2]), 38% were preferential throat carriers (individuals 3 to 17 [Fig. 2]), 28% were preferential anterior naris/throat carriers (individuals 18 to 28 [Fig. 2]), and another 28% had a mixed pattern of carriage based on sampling location (individuals 29 to 39 [Fig. 2]) (Table 3).

PFGE analysis of the collected *S. aureus* isolates showed that carriage in the throat was stable over time. The 39 persistent carriers spent, on average, 20 months as *S. aureus* carriers during the 25-month study period. The average time spent with the same strain in the anterior nares was 8 months, compared to 12 months in the throat (Table 3). The 11 preferential anterior naris/throat carriers spent, on average, 21 months with the same strain in the anterior nares, compared to 19 months in the throat. Four of the individuals classified as preferential throat carriers carried the same strain of *S. aureus* throughout the study period of 25 months (Fig. 3) (individuals 5, 9, 12, and 13 [Fig. 2]). The majority of the preferential anterior naris/throat carriers carried the same strain of *S. aureus* at both

<table>
<thead>
<tr>
<th>Group</th>
<th>No. (%) of individuals in group, classified by culture from:</th>
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<tbody>
<tr>
<td></td>
<td>Nares</td>
</tr>
<tr>
<td>Persistent carriers</td>
<td>17 (25)</td>
</tr>
<tr>
<td>Occasional carriers</td>
<td>21 (31)</td>
</tr>
<tr>
<td>Noncarriers</td>
<td>29 (43)</td>
</tr>
</tbody>
</table>

*Persistent carriers (CI > 0.5), occasional carriers (0 < CI ≤ 0.5), and noncarriers (CI = 0) were grouped according to the results of anterior naris cultures only, the results of throat cultures only, or carriage of *S. aureus* in either of the sites.*

**DISCUSSION**

*S. aureus* was isolated more frequently from the throat than from the anterior nares in two unrelated populations. Since the 259 patients were sampled upon admission to an orthopedic ward, their colonization status is probably unrelated within the group or to the 87 members of the staff in the same ward who were also sampled. The mean age of the patient group was much higher than the mean age of the staff group. Females were overrepresented in both groups, but no significant difference in isolation rates was observed between males and females in the patient group (data not shown). We therefore do not think our findings are related to sex or age, and we do not think the findings present a phenomenon in one single population.

Our results demonstrate that *S. aureus* rarely was carried only in the anterior nares. If the anterior nares were colonized, the bacteria were, with few exceptions, also present in the throat. This could have some important implications. Since anterior naris carriage of *S. aureus* is a well-documented risk factor for *S. aureus* infections (11), prophylactic decolonization of carriers has been tried with different patient groups (12). The spread of MRSA among patients and staff in health care institutions also calls for effective regimens for decolonization. A commonly used protocol includes topical treatment of the anterior nares with mupirocin, sometimes combined with application of disinfecting agents for the skin. For most patient groups, studies have not been able to show significant reduction of infection (12, 26). Some exceptions are hemodialysis patients (5), peritoneal dialysis patients (1), and general surgery patients (18). Recolonization with the same strain of *S. aureus* after the treatment period has been observed to occur (17, 27). The source of bacteria in these cases could be other carriage sites on the patient (for example, the throat) or people or items in the patient’s environment. Repeated treatment has been shown to result in development of resistance to mupirocin (13, 23). During treatment of the anterior nares, low concentrations of mupirocin in the throat have been observed (24). Furthermore, the effect of nasal mupirocin treatment on
throat colonization has been questioned (8, 25). Taken together, this might mean that the standard protocol for decolonization of S. aureus might create a situation favoring development of mupirocin resistance in the throats of treated individuals. Residual bacteria in the throat could also be one reason (of several) for recolonization after treatment. Kluytmans and Wertheim proposed that one way to increase efficacy of future treatment regimens could be to eliminate S. aureus also from extranasal sites (12). Considering our results, a treatment also targeting the throat might reduce problems with mupirocin resistance and recolonization and possibly lead to better efficacy in terms of infection reduction.

A large group was preferentially colonized only in the throat, in most cases with the same strain over several months and even years. Obviously, these individuals would not have been detected as carriers if only the anterior nares had been sampled. Nasal carriage seems to have a central role in S. aureus epidemiology and pathogenesis of infection (11, 12), and the risks associated with throat carriage are largely unknown. Half of the preferential throat carriers were culture positive in the

![FIG. 2. S. aureus carriage in the anterior nares and the throat among 39 persistent carriers. A red box represents positive results only from the anterior nares on that sampling occasion, an orange box positive from the anterior nares and the throat, a yellow box positive only from the throat, a blue box negative in both locations, and a gray box means no sample was taken. The letter(s) in each box designates the clonal type(s) of the isolated S. aureus strains as determined by PFGE. In orange boxes (positive in anterior nares and throat), the first letter gives the clonal type in the anterior nares and the second in the throat. "$" represents a clonal type unique for that individual. Sampling times are indicated at the top with the following abbreviations: M3, March 2003; A, April 2003; Mj, May to June 2003; Jn, June 2003; J, July 2003; Au, August 2003; S, September 2003; O, October 2003; N, November 2003; D, December 2003; J, January 2004; F, February 2004; M4, March 2004; A5, April 2005.]}
anterior nares at least once during the study period. Further studies are needed to determine what risk this group of *S. aureus* carriers constitutes in terms of spread of the organism and infection. Meanwhile, it seems reasonable to use an enrichment broth (15) and to include the throat when trying to identify MRSA and *S. aureus* carriers in different situations. If only one site is to be sampled, the throat is probably a better choice than the anterior nares.

In this study, 39 of 67 individuals, or close to 60%, were characterized as persistent carriers. This is roughly twice or even three times as many as the number described earlier (27). This discrepancy is probably due to the combination of a sensitive screening technique, the inclusion of the throat as a carriage site, and a different definition of persistent carriage (CI > 0.5). The change of definition is mainly due to the group of preferential throat carriers. Intervening negative samples reducing the CI for this group were probably due to false-negative results and not the fact that the individual had become a noncarrier. This conclusion seems reasonable since in most cases the same strain was recovered before and after negative sampling occasions. The observed lower CI for preferential throat carriers means that sampling of the throat yields fewer organisms than sampling of the anterior nares either because the sampling technique is suboptimal or, more probably, because there are small numbers of organisms present at the sampling site. A probable reason for the higher-than-expected rate of *S. aureus* in the throat (compared to the rate in the anterior nares) is that we increased the sensitivity by using an enrichment broth. Usage of the same broth with methicillin increased the rate of MRSA isolation by 35% in a previous study (15).

We observed almost 20% higher carrier rates of *S. aureus* during the spring months of March and April than in the summer month of August. The higher rate was more pronounced for the throat. Since colonization and adherence of *S. aureus* (and other bacteria) to the pharynx increase during viral infection (7, 19), an explanation might be that the peak of upper respiratory tract infections during spring in Sweden results in a greater number of individuals colonized. Alternatively, viral infections cause an increase in the number of bacteria in the throat, thereby increasing the chance of a positive culture. This seasonal variation is probably also the explanation for the observation of a more than 10% higher carriage rate among staff than among patients. The first samples from most of the staff were taken in March, but patients were sampled from March through September. To our knowledge, a seasonal variation of *S. aureus* carriage has not been described before but deserves further attention.

### FIG. 3

SmaI PFGE band patterns for *S. aureus* strains isolated from four individuals defined as preferential throat carriers (individuals 5, 9, 12, and 13 [Fig. 2]). Sampling times are indicated above the samples with the following abbreviations: m3, March 2003; A, April 2003; M, May 2003; J, June 2003; Au, August 2003; S, September 2003; N, November 2003; m4, March 2004; a5, April 2005. Individual 5 was positive in the anterior nares and the throat on two occasions. The samples from the anterior nares are underlined.

### TABLE 3. Results from 39 *S. aureus* persistent carriers grouped by most frequent carriage site(s)

<table>
<thead>
<tr>
<th>Groupa</th>
<th>No. (%) of individuals in group</th>
<th>Avg no. of samplings</th>
<th>Avg CI</th>
<th>Avg study period (mo)</th>
<th>Avg carrier time (mo)</th>
<th>Avg no. of mo same strain carried in:</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pref. naris carriers</td>
<td>2 (5)</td>
<td>7.0</td>
<td>0.8</td>
<td>25</td>
<td>25</td>
<td>15</td>
</tr>
<tr>
<td>Pref. throat carriers</td>
<td>15 (38)</td>
<td>7.8</td>
<td>0.8</td>
<td>21</td>
<td>17</td>
<td>0</td>
</tr>
<tr>
<td>Pref. naris/throat carriers</td>
<td>11 (28)</td>
<td>7.8</td>
<td>1.0</td>
<td>25</td>
<td>25</td>
<td>21</td>
</tr>
<tr>
<td>Indeterminable carriers</td>
<td>11 (28)</td>
<td>7.1</td>
<td>0.8</td>
<td>22</td>
<td>18</td>
<td>6</td>
</tr>
<tr>
<td>All</td>
<td>39</td>
<td>7.6</td>
<td>0.8</td>
<td>23</td>
<td>20</td>
<td>8</td>
</tr>
</tbody>
</table>

a Pref, preferential.
In conclusion, the throat has to be considered as an important carriage site for *S. aureus* and should be included when screening for *S. aureus*, including MRSA. Our results also show that *S. aureus* carriage in the anterior nares in most cases indicates presence of the organism in the throat, although in lower numbers. This has to be taken into account when designing decolonization protocols.

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REFERENCES