Oral carriage of staphylococci in patients with rheumatoid arthritis

M. S. Jackson, J. Bagg, M. N. Gupta1 and R. D. Sturrock1

Infection Research Group, University of Glasgow Dental School and 1Centre for Rheumatic Diseases, Department of Medicine, Glasgow Royal Infirmary, University of Glasgow, Glasgow, UK

Abstract

Objective. To determine the prevalence of oral staphylococcal carriage in patients with rheumatoid arthritis compared with healthy controls.

Methods. Fifty healthy adults, 25 healthy elderly volunteers and 25 patients with rheumatoid arthritis were studied. An oral rinse, tongue swab and nasal swab were collected for culture on blood agar and a range of selective agars. Isolates of staphylococci were identified and antibiotic sensitivity profiles determined by standard methods.

Results. Staphylococci were isolated from the mouths of 94% of the healthy adults, 24% of whom carried Staphylococcus aureus. All the healthy elderly carried oral staphylococci and 36% were colonized with S. aureus. Staphylococci were isolated from 96% of the rheumatoid arthritis patients and this group had the highest carriage rate of S. aureus (56%), significantly higher than the healthy adults (P < 0.05). In all three groups, Staphylococcus epidermidis was isolated from the mouths of >80%. No methicillin-resistant strains of S. aureus were isolated.

Conclusion. Oral carriage of S. aureus appears to be common in patients with rheumatoid arthritis and studies of the mouth as a source of infection in septic arthritis would be merited.

KEY WORDS: Staphylococci, Oral cavity, Oral flora, Rheumatoid arthritis, Septic arthritis.

The oral flora contains >300 known species of bacteria [1], but surprisingly there have been no formal studies of staphylococci in the mouth. Staphylococcus aureus is implicated in some oro-facial infections, e.g. angular cheilitis [2] and oral mucositis in elderly patients receiving parenteral nutrition [3].

Oral bacteria can translocate to cause systemic infection, e.g. streptococcal infective endocarditis [4] or septicaemia in the immunocompromised [5]. By analogy, the mouth may also be an unrecognized source of staphylococci in septic arthritis. The annual incidence of bacterial arthritis in the rheumatoid arthritis population is 30–70/100 000 compared with 2–10/100 000 in the general population [6, 7]. Fifty per cent of patients develop joint damage and 10–16% of patients die during the acute episode [7–9]. Staphylococci are the commonest cause of bacterial arthritis in adults [10]. Staphylococcus aureus is the primary cause of bacterial arthritis in 40% of cases from England and Wales [9], and causes 80% of joint infections in patients with concurrent rheumatoid arthritis [10]. Coagulase-negative staphylococci have also emerged in recent years as important medical pathogens, particularly in relation to implanted biomaterials, and Staphylococcus epidermidis is now responsible for 40% of all prosthetic joint infections [11].

In native joints, it is generally believed that bacterial arthritis is secondary to the haematogenous seeding of a joint during a bacteraemia [10], but at present the source of the bacteraemia cannot be identified in up to 30% of cases [12]. Many patients with rheumatoid arthritis have a reduced salivary flow rate, which may result in significant changes to the normal oral flora [13]. Furthermore, the drugs used in the treatment of rheumatoid arthritis, many of which are immuno-suppressive or cytotoxic, may cause oral ulceration, providing a portal of entry for oral bacteria.

The data reported in this paper demonstrate that the mouths of many patients with rheumatoid arthritis are colonized by both S. aureus and S. epidermidis, suggesting that the oral cavity should be given serious consideration as a source of infection in septic arthritis.

Materials and methods

Patients

Two control groups of healthy adults were studied. The first comprised 13 male and 37 female adults with ages ranging from 18 to 54 (mean 32) yr. The second control group of healthy elderly comprised 10 male and 15 female residents of a geriatric unit, all of whom were
well at the time of sampling. Their ages ranged from 65 to 92 (mean 82) yr.

The study group comprised three male and 22 female out-patients receiving treatment for rheumatoid arthritis. Their ages ranged from 21 to 82 (mean 60) yr.

**Sampling**

The mouths of all subjects were sampled by the concentrated oral rinse technique [14] and a tongue swab. A swab was also collected from the anterior nares.

For the patients with rheumatoid arthritis, a Salivette® (Sarstedt Ltd, Leicester, UK) specimen was collected to allow assessment of the degree of oral dryness [15].

**Culture and identification**

All specimens were inoculated onto Columbia blood agar with 5% defibrinated horse blood (Prolab Diagnostics, Merseyside, UK), mannitol salt agar (Prolab Diagnostics, Merseyside, UK), milk agar [16] with no added methicillin and P agar [17], and incubated at 37°C for 72 h. This extended incubation enhanced colony pigmentation and therefore visualization of different species. Blood agar purity plates of the different morphological colony types were established. Catalase-positive Gram-positive cocci were tested for coagulase production by slide agglutination (Staphaurex, Murex Diagnostics Ltd, Dartford, UK) and all positive isolates checked by a tube coagulase test using rabbit plasma (Medical Wire & Equipment Co. Ltd, Corsham, UK). Strains positive in both of these tests were identified as S. aureus.

**Antibiotic sensitivity testing**

*Staphylococcus epidermidis* was identified on the basis of a set of eight sugar fermentation tests and susceptibility to novobiocin and polymyxin B [18] on P agar [17]. Other coagulase-negative staphylococci were speciated by a two-step procedure [19] utilizing Rosco Diagnostica tablets (Biocoutines, Barnsley, UK).

**Statistical analysis**

Where appropriate, differences between groups were analysed by the χ² test. A value of *P* < 0.05 was accepted as indicative of a statistically significant difference.

**Results**

**Isolation rates of Staphylococcus species**

These are summarized in Table 1. The weight of growth varied widely, but in most cases was light to moderate. Staphylococci were isolated from the mouths of 47/50 (94%) healthy adults. *Staphylococcus aureus* was present in the mouths of 12 (24%), of whom 8 (67%) were also nasal carriers of *S. aureus*. Conversely, six adults were nasal carriers in the absence of oral carriage. Coagulase-negative staphylococci were isolated from the mouths of 46/50 (92%) of the adults, predominantly *S. epidermidis* and *S. warneri*.

Staphylococci were isolated from the mouths of all the healthy elderly. *Staphylococcus aureus* was present in the mouths of 9/25 (36%). This was not significantly greater than the rate of colonization among the younger adult controls. Forty per cent of those with oral *S. aureus* were nasal carriers. None were nasal carriers in the absence of oral carriage. Coagulase-negative staphylococci were isolated from the mouths of 23/25 (92%) of the healthy elderly adults, predominantly *S. epidermidis*, *S. warneri* and *S. haemolyticus*.

Overall, staphylococci were isolated from the mouths of 24/25 (96%) of the adults with rheumatoid arthritis. *Staphylococcus aureus* was present in the mouths of 14 (56%) of this group, a significantly greater rate of colonization than the healthy adults (*P* < 0.01). Eleven (78%) of those with oral carriage of *S. aureus* were also nasal carriers of the organism. Three patients in this group were nasal carriers in the absence of oral carriage. Coagulase-negative staphylococci were isolated from the mouths of 22/25 (88%) of those with rheumatoid arthritis, predominantly *S. epidermidis*, *S. haemolyticus* and *S. warneri*.

**Salivary flow rates**

The mean volume of saliva collected in the Salivette® specimens from the rheumatoid arthritis patients was 117 µl (range 0–570 µl). This compares with a mean value of 250 µl quoted for healthy controls [15].

**Antibiotic sensitivity profiles**

All of the isolates from the three groups were sensitive to methicillin, vancomycin and cephradine. With the exception of one isolate from the healthy adults, they were also sensitive to erythromycin and fusidic acid. Very few of the strains were sensitive to penicillin, ampicillin or co-amoxiclav.

**Discussion**

This study demonstrates clearly that staphylococci are part of the normal oral flora in most humans. Staphylococci were isolated from the mouths of >90% of the healthy adults and we have recently shown that 92% of a group of healthy children carried staphylococci in their mouths, 64% of which were *S. aureus* (submitted).

The mouths of most of the healthy adults were colonized with coagulase-negative staphylococci, predominantly *S. epidermidis* and *S. warneri*. However, *S. haemolyticus*, *S. schleiferi* and *S. lugdunensis* were also identified. Twenty-four per cent of the healthy adults were colonized with *S. aureus*, an unexpectedly high oral carriage rate. Among the healthy elderly patients, the distribution of coagulase-negative staphylococci was similar to that of the healthy adult group, with *S. epidermidis* by far the commonest isolate, followed by *S. warneri* and *S. haemolyticus*. Whilst more
Table 1. Carriage of *Staphylococcus* spp. in the oral cavity of healthy adults, healthy elderly and patients with rheumatoid arthritis

<table>
<thead>
<tr>
<th>Study group</th>
<th><em>S. aureus</em></th>
<th><em>S. epidermidis</em></th>
<th><em>S. warneri</em></th>
<th><em>S. haemolyticus</em></th>
<th>Other species</th>
</tr>
</thead>
<tbody>
<tr>
<td>Healthy adults</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>(n = 50)</td>
<td>12 (24%)</td>
<td>44 (88%)</td>
<td>14 (28%)</td>
<td>7 (14%)</td>
<td><em>S. schleiferi</em> (4%)</td>
</tr>
<tr>
<td>Healthy elderly</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td><em>S. lugdunensis</em> (2%)</td>
</tr>
<tr>
<td>(n = 25)</td>
<td>9 (36%)</td>
<td>23 (92%)</td>
<td>9 (36%)</td>
<td>10 (40%)</td>
<td><em>S. schleiferi</em> (8%)</td>
</tr>
<tr>
<td>Rheumatoid arthritis</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td><em>S. capitis</em> (4%)</td>
</tr>
<tr>
<td>(n = 25)</td>
<td>14 (56%)</td>
<td>21 (84%)</td>
<td>4 (16%)</td>
<td>7 (28%)</td>
<td><em>S. lugdunensis</em> (8%)</td>
</tr>
</tbody>
</table>

of the elderly patients (36%) were found to have oral colonization with *S. aureus*, the difference between the two control groups was not statistically significant.

A wide range of coagulase-negative staphylococci was isolated from the mouths of the patients with rheumatoid arthritis. Staphylococci are the most important cause of prosthetic joint infections and *S. epidermidis* is responsible for a large percentage of late or chronic infections [21]. Such joints are frequently placed in patients with rheumatoid arthritis and the possibility of a bacteremia from an oral source resulting in a late prosthetic joint infection merits consideration. The potential pathogenic importance of the less common species that were isolated should not be underestimated. For example, a recent case study [22] showed that a previously healthy 26-yr-old male developed endocarditis caused by *S. lugdunensis* after a tooth extraction.

A significantly higher proportion (56%) of the patients with rheumatoid arthritis carried oral *S. aureus* than the adult controls (24%) (P < 0.01). This is not a purely age-related effect, since there was no significant difference between colonization rates for the two control groups and the rheumatoid arthritis patients were significantly younger than the healthy elderly individuals. It is more likely to reflect other disease-associated factors such as the oral dryness indicated by the Salivette® readings. Since *S. aureus* is a significant pathogen in septic arthritis [9, 10], this finding is potentially important. At present, the source cannot be identified in up to 30% of cases [12] and all possible sites, including the mouth, should be given consideration.

The antimicrobial susceptibility patterns of the strains of *S. aureus* isolated from the patients with rheumatoid arthritis and the controls were very similar and mirrored the typical sensitivity profile of *S. aureus* strains currently isolated in the community.

In summary, these results have demonstrated that staphylococci are frequently isolated from the oral cavity and that *S. aureus* is present in the mouths of significantly more patients with rheumatoid arthritis than healthy controls. There is a very real possibility that these organisms could translocate to cause disease at distant sites and may, therefore, be of relevance to the pathogenesis of septic arthritis.

Acknowledgement

We acknowledge the support of the Arthritis Research Campaign. MG is the Mary Miller Clinical Research Fellow.

References