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REVIEW ARTICLE

The ecology of *Staphylococcus* species in the oral cavity

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Whilst the diversity of organisms present in the oral cavity is well accepted, there remains considerable controversy as to whether *Staphylococcus* spp. play a role in the ecology of the normal oral flora. Surprisingly little detailed work has been performed on the quantitative and qualitative aspects of colonisation or infection either by coagulase-negative staphylococci (CNS) or *S. aureus*. The latter is especially interesting in the light of present difficulties in eradicating carriage of methicillin-resistant *S. aureus* (MRSA) from the oropharynx in affected individuals. This paper reviews the current knowledge of staphylococcal colonisation and infection of the oral cavity in health and disease. *S. aureus* has been isolated from a wide range of infective oral conditions, such as angular cheilitis and parotitis. More recently, a clinical condition classified as staphylococcal mucositis has emerged as a clinical problem in many debilitated elderly patients and those with oral Crohn's disease. Higher carriage rates of both CNS or *S. aureus*, or both, in patients prone to joint infections raises the interesting possibility of the oral cavity serving as a potential source for bacteraemic spread to compromised joint spaces. In conclusion, there is a surprising paucity of knowledge regarding the role of oral staphylococci in both health and disease. Further work in this area may lead to benefits, such as improved decolonisation regimens for eradication of MRSA and acknowledgement of the mouth as a source of bacteraemic staphylococci.

Introduction

Despite the extensive literature on *Staphylococcus aureus* and coagulase-negative staphylococci (CNS), relatively little attention has been paid to the oral cavity as a reservoir for these organisms. The oral flora contains >300 known species of bacteria in addition to numerous non-cultivable organisms which are being discovered as a result of molecular biological techniques [1]. Whilst the importance of staphylococci as medical pathogens has been recognised for many years, the presence of *Staphylococcus* species as a component of the resident oral flora is controversial but, surprisingly, there have been relatively few detailed studies of the distribution of staphylococci in the mouth. Some infections in the circum-oral region are caused, at least in part, by *S. aureus.* These include angular cheilitis [2], some endodontic infections [3–5], osteomyelitis of the jaw [6], parotitis [7, 8] and, more recently recognised, a form of oral mucositis in elderly, highly dependent patients receiving parenteral nutrition [9]. Interestingly, there is now a growing body of evidence to suggest that staphylococci can be isolated frequently from the oral cavity of particular patient groups such as children [10], the elderly [9] and some groups with systemic disease such as the terminally ill [11], those with rheumatoid arthritis [12] and patients with haematological malignancies [13]. Of further concern is the observation that the oropharynx is frequently colonised with strains of methicillin-resistant *S. aureus* (MRSA) which may prove difficult to eradicate [14]. Therefore, it is apparent that the oral cavity may represent a hitherto poorly recognised reservoir of staphylococci, some of which may, under appropriate conditions, cause local or systemic infection. There is also the potential for dissemination of oral staphylococcal strains to re-colonise other body sites or as a source of cross-infection to other patients or staff. The aim of this review is to examine the current knowledge of the ecology of staphylococcal species in the oral cavity and their impact on systemic health.

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The normal oral flora

The normal oral flora comprises a diverse group of micro-organisms, including bacteria, fungi, protozoa

and possibly even viruses [15]. More than 300 species inhabit the oral cavity [1], of which about 30 are found routinely and account for the majority of the cultivable strains. These factors, together with the fact that the oral cavity has a wide range of sites with different environmental conditions, make the study of oral microbiology complex and difficult.

Staphylococci in the healthy oral cavity

There are several early qualitative reports of *S. aureus* isolated from the healthy oral cavity but detailed information on the intra-oral distribution of staphylococci is lacking. Most studies sample the oral cavity by use of swabs, rinses or plaque scrapings, although one group [16] found staphylococci in plaque from the fissures of teeth. Percival and colleagues [17] reported the isolation of staphylococci, albeit with low mean percentage counts, from *c*. 12% of supragingival plaque samples in 79 healthy individuals with ages ranging from 27 to 84 years. There were no clear age-related trends in the isolation frequency or proportions of staphylococci in this study. Another study [10] investigating oral staphylococcal carriage in 307 children aged $<1-5$ years attending a paedodontic department found that 84% carried staphylococcal species, 33% of which were *S. aureus* (5% of the *S. aureus* isolates were MRSA). Of interest was the fact that 19% of the *S. aureus* isolates produced exfoliative toxin and 40% produced enterotoxin [10]. A more recent study [13] found that 64% of healthy children carried *S. aureus* in the oral cavity.

In studies of student populations, oral carriage rates of *S. aureus* have ranged from 17% [18] to 48% [19]. More recently, workers have revealed that between 94% and 100% of healthy adults had oral colonisation with *Staphylococcus* spp. [17, 20, 21] and oral carriage of *S. aureus* ranged from 24% to 36% [20, 21]. The presence of prosthetic devices within the oral cavity, such as acrylic dentures, may encourage carriage of staphylococci [22]. In studies of denture-wearing patients, carriage rates of *S. aureus* varied from 23% to 48% [23, 24].

Staphylococci have been isolated from supragingival plaque (see Table 1 for details) [16, 25, 26] and from subgingival plaque [27–34]. Relatively few plaque samples have been collected from non-diseased sites and, therefore, no definitive interpretation of the available qualitative and quantitative data for staphylococci in health is possible. The species of staphylococci most frequently reported from oral samples are *S. epidermidis* and *S. aureus*, but *S. haemolyticus*, *S. hominis*, *S. warneri*, *S. capitis*, *S. saprophyticus*, *S. xylosus* and *S. simulans* have also been reported [32, 35].

Most investigators employ selective agar (mannitol salt agar, MSA) to identify the presence of *S. aureus* from oral specimens. Very few studies report actual numbers (cfu/ml) of staphylococci in healthy or compromised patients, which makes comparison between different studies difficult. Furthermore, few longitudinal studies have been performed, so that there is little definitive evidence to confirm or refute the general impression that *Staphylococcus* spp. may be transitory members of the oral microflora.

Staphylococci in oral disease

Despite its pathogenic potential, *S. aureus* is only infrequently associated with acute dento-alveolar infections [36, 37]. Other oral infections from which *S. aureus* has been cultured include infected jaw cysts [38], oral mucosal lesions [23, 39] and denture-induced

Table 1. Summary of studies in which *Staphylococcus* spp. have been isolated from dental plaque

Patient group	Mean age of patient (years)	Number of patients sampled	Number of sites sampled	*S. aureus* isolation rate n (% isolation frequency)	CNS n (% isolation frequency)	Ref. no.
Tooth fissures	NR	10	1	1 (10%)	8 (80%)	16
Healthy dentate adults	27	30	1	2 (7%)	3 (10%)	17
Healthy dentate adults	50	23	1	0	1 (4%)	17
Healthy dentate adults	73	16	1	1 (6%)	2 (12%)	17
Healthy dentate adults	84	10	1	0	1 (10%)	17
Gingivitis	39	18	1	9 (50%)	NR	32
Periodontal disease	32–66	21	1	11 (52%*)	11 (52%*)	27
Periodontal disease	40–49	72	1	0	16 (22%)	28
Advanced adult periodontal disease	50	506	3	253 (50%)	NR	32
Adult periodontal disease	45	535	2	43 (8%)	289 (54%)	33
Early onset periodontal disease	35	108	3	49 (45%)	NR	32
Localised juvenile periodontitis	18	13	3	4 (31%)	NR	32
Failing dental implants	58	13	3	9 (69%)	NR	32

NR, not recorded.
*Staphylococci isolated but *S. aureus* isolation rate not specified.

stomatitis [22, 40]. More usually, *S. aureus* infection is associated with angular cheilitis. Workers have found an isolation rate of 63% for *S. aureus* from this condition – usually in the presence of other micro-organisms such as *Candida albicans* or *Streptococcus pyogenes* [41]. Angular cheilitis is thought to be due to a combination of ill-fitting dentures, nutritional deficiencies and infection by *S. aureus* or *C. albicans*, or both. Whilst there are few studies on the presence of *Staphylococcus* spp. in the healthy oral cavity, more has been reported from patients demonstrating ill health. In a study of 110 patients attending a dental hospital with a range of oral diseases [42], there was an observed prevalence of *S. aureus* in saliva of 21% and from gingival swabs of 11%. Salivary carriage of *S. aureus* in a cohort of patients with reduced salivary flow rates attending an oral medicine clinic was found in 41% of patients with a range of concentrations from 3.7×10^1 to 5.2×10^3 cfu/ml [43].

Oral mucosal infection with *S. aureus* has recently been incriminated in a severe form of mucositis reported in some groups with systemic disease such as patients with oral Crohn's disease [44] and geriatric patients [9]. The case for *S. aureus* in the aetiology of oral mucositis is complicated by the complexity of the normal oral flora and by healthy carriage of *S. aureus* in some patient groups. However, both clinical and microbiological data lend support to this hypothesis. The clinical presentation of staphylococcal mucositis commonly takes the form of oral discomfort and pan-oral mucosal erythema which may progress to marked crusting and bleeding of the oral mucosa [9, 11, 44]. Treatment of this condition with appropriate anti-staphylococcal agents leads to marked clinical improvement [9, 44]. The reason for the breakdown in colonisation of the oral mucosa is unclear, although in some groups of patients, notably elderly patients receiving parenteral nutrition and patients with advanced malignant disease, reduced salivary flow rate is an important risk factor. Saliva, in addition to its mechanical cleaning effects, also contains many antimicrobial factors, such as lysozyme and secretory IgA. An alternative hypothesis for the clinical presentation of staphylococcal mucositis includes colonisation by toxin-producing strains of *S. aureus*. In one study, three of five patients with mucositis were colonised by toxic-shock syndrome toxin (TSST)-1-producing strains, suggesting that heavy colonisation of the oral cavity with toxin-producing strains may cause local mucosal damage [9].

In a study of children with haematological malignancies [13], only 6 (5%) of the 120 children with haematological malignancy carried oral *S. aureus* compared with 64% of 25 healthy children. It seems likely that the lower levels of *S. aureus* from children with malignancies are a result of frequent antibiotic treatment. In the same study, a significantly smaller proportion of the children with malignant disease (37%) carried CNS compared with the healthy control children (64%), but levels of carriage are higher than previously reported (Tables 2 and 3).

Rams and colleagues [32] discovered that *c*. 50% of periodontal lesions harboured staphylococci. Only low proportions (<1%) of staphylococci were present in the cultivable subgingival flora in 95% of the patients studied. No significant differences were detected in the occurrence of *S. aureus* between patients with gingi-

Table 2. Summary of studies in which *Staphylococcus* spp. have been isolated from saliva or oral swabs in patients with systemic or oral disease

Patient group	Mean age of patient (years)	Number of patients sampled	Number of sites sampled	Specimen(s) collected	*S. aureus* isolation rate n (% isolation frequency)	CNS n (% isolation frequency)	Ref. no.
Children with neoplasia	8	125	1	Oral swab	6 (5%)	46 (37%)	13
Adults with neoplasia	69	197	1	Saliva	50 (25%)	NR	11
Rheumatoid arthritis	59	111	4	Saliva and oral swab	16 (14%)	0	63
Rheumatoid arthritis	60	25	2	Saliva and oral swab	14 (56%)	10 (40%)	20
Geriatric unit	70	107	4	Oral swab	20 (19%) (20 MRSA)	NR	71
Chronically ill and elderly clinic	NR	40	4	Saliva and oral swabs	12 (30%)	NR	42
Xerostomia (out-patient clinic)	NR	75	1	Saliva	31 (41%)	NR	43
Mucositis	68–87	5	4	Oral swabs	5 (100%)	NR	9
Dentate patients with mucosal oral disease	0–90	155	1	Curettings and swabs	30 (19%)	NR	23
Orofacial granulomatosis and Crohn's disease	NR	450	1	Oral rinse	4 (0.8%)	NR	44
Denture stomatitis	0–90	116	1	Curettings and swabs	27 (23%)	NR	23
Patients with oral abscess/osteomyelitis	NR	10	1	Oral swab	3 (30%)	7 (70%)	21
Dental out-patients	NR	80	4	Saliva and oral swabs	40 (50%)	NR	42
Surgical in-patients	NR	40	4	Saliva and oral swabs	13 (33%)	NR	42

NR, not recorded.

Table 3. Summary of studies in which *Staphylococcus* spp. have been isolated from saliva or oral swabs in healthy patients

Patient group	Mean age of patient (years)	Number of patients sampled	Number of sites sampled	Specimen(s) collected	*S. aureus* isolation rate n (% isolation frequency)	CNS n (% isolation frequency)	Ref. no.
Healthy children	11	25	1	Oral rinse and oral swab	16 (64%)	20 (80%)	13
Healthy children	0–5	307	1	Tongue swab	100 (33%) (5 MRSA)	157 (51%)	10
Healthy children	7–8	539	1	Oral rinse	200 (37%) (4 MRSA)	NR	72
Students	NR	100	2	Oral swab	27 (27%)	69 (69%)	18
Dental students	NR	70	2	Saliva	32 (46%)	NR	19
Healthy dentate adults	27	30	1	Saliva	9 (30%)	9 (30%)	17
Healthy adults	32	50	2	Saliva and oral swab	12 (24%)	35 (70%)	20
Healthy dentate adults	50	23	1	Saliva	7 (30%)	7 (30%)	17
Healthy Adults	56	83	4	Saliva and oral swab	3 (4%)	0	63
Healthy adults	NR	22	1	Oral swab	8 (36%)	14 (64%)	21
Healthy denture-wearing adults	65	29	2	Oral swab	14 (48%) (3 MRSA)	3 (10%)	24
Healthy elderly	83	27	4	Oral swabs	11 (41%)	NR	9
Healthy elderly	82	25	2	Saliva and oral swab	9 (36%)	16 (64%)	20
Healthy dentate elderly	73	16	1	Saliva	7 (44%)	7 (44%)	17
Healthy dentate elderly	84	10	1	Saliva	3 (30%)	4 (40%)	17

NR, not recorded.

vitis or other more destructive forms of periodontal disease. Some workers [45] have reported elevated proportions of *S. xylosus* in actively destructive periodontal disease that was non-responsive to treatment. Other workers have isolated staphylococci from periodontitis in healthy persons [46–48], those with diabetes mellitus [47] and acute periodontal abscesses in immunocompromised patients [49]. In early studies [50, 51], cellular components of *S. aureus* were found in the subepithelial connective tissues of 47% of specimens of inflamed gingival tissue, but not in healthy gingival tissue. However, in cases of failing dental implants, a significant proportion (69%) of the affected sites had high proportions of *Staphylococcus* spp. (15–100% of total flora) in the associated dental plaque [52]. This association has not been confirmed in other studies [53].

Oral staphylococci as a source of systemic infection

Classically, the mouth is recognised as a source of bacteraemia in infective endocarditis, but in studies of organisms isolated from bacteraemia associated with dental procedures [54, 55] *S. aureus* is infrequently detected. Nevertheless, there is an increasing number of reports suggesting that staphylococci from an oral source may cause infection at distant sites [56, 57]. For example, *S. lugdenensis* endocarditis has been reported after a tooth extraction [56]. These bactaeraemic episodes may assume greater significance in medically compromised patients. Oral infections have been associated with septicaemias among those with haematological malignancy [35, 58]. CNS are frequently isolated from blood cultures in patients receiving treatment for malignant disease [35]. This is commonly a result of colonisation of venous access devices, but in some cases no such source of infection is present. The mouth has not been generally considered to play a role in such infections, but many patients receiving chemotherapeutic drug regimens develop severe oral ulceration (mucositis) as a result of the effect of these drugs on the oral mucosa [59]. Such ulceration provides a portal of entry for organisms in the oral flora, and has already been identified in relation to septicaemia caused by oral streptococci in children receiving treatment for leukaemia. This has been demonstrated more recently by a *S. epidermidis* and *Strep. oralis* bacteraemia in a bone marrow transplant patient [58]. Identical isolates, as analysed by pulsed-field gel electrophoresis (PFGE), of *S. epidermidis* were found in the mouth and bloodstream, but not at the site of venous access. In many patients with serious staphylococcal infections the original source of the organism is unknown, but the mouth has not usually been sought as a primary focus, as staphylococci are not considered part of the normal oral flora. There has been a long-standing debate over the role of oral micro-organisms in the aetiology of late prosthetic joint infections [60] and the possible need for antibiotic prophylaxis in such patients during dental treatment. Staphylococci are the most important cause of prosthetic joint infections. *S. aureus* is a significant pathogen in acute septic arthritis, affecting both native and prosthetic joints, whereas *S. epidermidis* is responsible for a large percentage of late or chronic infections [61]. Such joints are frequently placed in patients with rheumatoid arthritis and the possibility of a bacteraemia from an oral source resulting in a prosthetic joint infection should be of considerable interest. At present, the source of staphylococcal joint

sepsis cannot be identified in up to 30% of cases [62]. However, it has been reported [63] that individuals with rheumatoid arthritis had a higher prevalence of *S. aureus* in the oral cavity compared with gender-matched control subjects. A recent study [20] investigated oral carriage of staphylococci in patients with rheumatoid arthritis (Table 2) and showed that a significantly higher proportion (56%) of these patients carried oral *S. aureus* than controls (24%) ($p < 0.05$). This is unlikely to be an age-related effect, as there was no significant difference between colonisation rates for the two adult control groups ($p > 0.05$) and the rheumatoid arthritis patients were considerably younger than the healthy elderly individuals. It is well recognised that many patients with rheumatoid arthritis have a reduced salivary flow rate, and the dry mouth may result in significant changes to the oral flora [64]. The drug regimens used in the treatment of rheumatoid arthritis, many of which are immunosuppressive or cytotoxic, will also affect the mucosal immunity in the mouth and some (e.g., methotrexate) can cause oral ulceration, further enhancing the possibility of an oral source for staphylococcal joint sepsis. In a retrospective literature review of 23 cases of late prosthetic joint infection, in which it was suggested that the causal bacteria originated from the oral cavity as a result of treatment or infection, 10 cases (43%) were caused by *Staphylococcus* spp., the most common being *S. aureus* (eight cases) [65].

MRSA in the oral cavity

The prevention of horizontal transmission of MRSA has become increasingly important as the prevalence of this pathogen increases. Oral carriage of MRSA may serve as a reservoir for re-colonisation of other body sites or for cross-infection to other patients or health-care workers. At least two cases have been reported of cross-infection from a general dental practitioner to patients [66]. The practitioner had probably been colonised whilst a patient in hospital. Nursing homes are another important source of colonisation and infection and two cases of acute parotitis caused by MRSA in elderly patients have been described [67].

Attempts are frequently made to eradicate carriage of MRSA from either patients or medical staff colonised by this organism. However, clinical experience has shown that oropharyngeal carriage of MRSA can be difficult to eradicate [14]. Therefore, it is important that consideration be given to the oral cavity if eradication of colonisation by MRSA is clinically appropriate. Mupirocin is rarely effective alone in clearing oropharyngeal colonisation. Successful eradication of throat carriage of MRSA in a health-care worker has been achieved by the use of rifampicin and fusidic acid, in addition to topical mupirocin [68]. However, eradication of throat carriage of MRSA has been achieved with use of topical chlorhexidine (0.2%) in addition to normal control measures of patient isolation, nasal mupirocin and chlorhexidine body washes [69]. Within the oral cavity MRSA may preferentially colonise denture surfaces. One group of workers [24] found 10% of unselected denture-wearing patients carrying MRSA on their dentures which proved difficult to eradicate with conventional denture-cleaning agents. In a subsequent study, eradication of the long-term carriage of MRSA from denture-wearing patients was successful only after heat sterilising or remaking the dentures that had become persistently colonised by MRSA [70]. More recently, 19% of an elderly institutionalised veteran population were shown to be colonised by MRSA in the oral cavity, compared with a prevalence of 20% in the nares. Interestingly, 4% of subjects were culture positive for oral MRSA without evidence of nasal carriage [71].

Carriage of MRSA is not restricted to the chronically ill or institutionalised patients. One study [10] showed that a small proportion of children (5 from 307) carried MRSA, a larger proportion than a more recent study (4 from 539) [72]. Another group demonstrated that MRSA clones may colonise the oral cavity of healthy children for relatively long periods of time (5 years), challenging the hypothesis that staphylococci are transient members of the oral flora [73]. Surprisingly little work has been performed on factors affecting oropharyngeal colonisation by MRSA.

Conclusion

Our current knowledge of the role of staphylococci in the ecology of the oral flora in health and disease is incomplete. The majority of workers report the presence or absence of staphylococci using selective agar (MSA), which makes it difficult to compare isolation rates between different studies and different patient groups. Much of the data relates to mucosal swabs and salivary rinses with relatively little information linked specifically to plaque samples that have been both carefully collected and subsequently investigated by appropriate laboratory techniques. There is increasing interest in the oral ecology of opportunist micro-organisms, which may include MRSA. As micro-organisms growing in a biofilm such as plaque tend to be less susceptible to a range of antimicrobial agents, this could have important implications in diseases caused by these organisms, with regard to the creation of reservoirs of infection, re-infection and treatment failure due to antimicrobial resistance.

Future work in this area may provide clues for more successful eradication of carriage of MRSA strains. Advances in molecular microbiology may provide some interesting insights into the source of bacteraemic staphylococcal infection and these may challenge current concepts of antibiotic prophylaxis in groups of at-risk patients undergoing dental treatment.

The results of this review clearly demonstrate that staphylococcal species can be frequently isolated in the oral flora of children and adults in both health and disease. Further longitudinal studies are required to establish whether this is a transient presence. This also implies that the oral cavity should be considered a potential source of infection for distant sites when other more obvious foci have been eliminated.

References

1. Wilson MJ, Weightman AJ, Wade WG. Applications of molecular ecology in the characterization of uncultured microorganisms associated with human disease. *Rev Med Microbiol* 1997; **8**: 91–101.
2. MacFarlane TW, Helnarska SJ. The microbiology of angular cheilitis. *Br Dent J* 1976; **140**: 403–406.
3. Kaufman AY, Henig EF. The microbiologic approach in endodontics. *Oral Surg Oral Med Oral Pathol* 1976; **42**: 810–816.
4. Tronstad L, Barnett F, Riso K, Slots J. Extraradicular endodontic infections. *Endod Dent Traumatol* 1987; **3**: 86–90.
5. Wyman TP, Dowden WE, Langeland K. *Staphylococcus aureus* isolation from a clinically nonexposed root canal. *J Endodont* 1978; **4**: 122–128.
6. Koorbusch GF, Fotos P, Goll KT. Retrospective assessment of osteomyelitis. Etiology, demographics, and management in 35 cases. *Oral Surg Oral Med Oral Pathol* 1992; **74**: 149–154.
7. Goldberg MH. Infections of the salivary glands. In: Topazian RG, Goldberg MH (eds) Management of infections of the oral and maxillofacial regions. Philadelphia, WB Saunders. 1981: 293–311.
8. Lamey P-J, Boyle MA, MacFarlane TW, Samaranayake LP, Biol MI. Acute suppurative parotitis in outpatients: microbiological and posttreatment sialographic findings. *Oral Surg Oral Med Oral Pathol* 1987; **63**: 37–41.
9. Bagg J, Sweeney MP, Harvey-Wood K, Wiggins A. Possible role of *Staphylococcus aureus* in severe oral mucositis among elderly dehydrated patients. *Microb Ecol Health Dis* 1995; **8**: 51–56.
10. Miyake Y, Iwai M, Sugai M, Miura K, Suginaka H, Nagasaka N. Incidence and characterization of *Staphylococcus aureus* from the tongues of children. *J Dent Res* 1991; **70**: 1045–1047.
11. Jobbins J, Bagg J, Parsons K, Finlay I, Addy M, Newcombe RG. Oral carriage of yeasts, coliforms and staphylococci in patients with advanced malignant disease. *J Oral Pathol Med* 1992; **21**: 305–308.
12. Jacobson JJ, Patel B, Asher G, Wooliscroft JO, Schaberg D. Oral staphylococcus in older subjects with rheumatoid arthritis. *J Am Geriat Soc* 1997; **45**: 590–593.
13. Jackson MS, Bagg J, Kennedy H, Michie J. Staphylococci in the oral flora of healthy children and those receiving treatment for malignant disease. *Microb Ecol Health Dis* 2000; **12**: 60–64.
14. Working Party Report. Revised guidelines for the control of methicillin-resistant *Staphylococcus aureus* infection in hospital. *J Hosp Infect* 1998; **39**: 253–290.
15. Marsh P, Martin MV. Oral microbiology, 4th edn. Oxford, Wright. 1999.
16. Theilade E, Fejerskov O, Karring T, Theilade J. Predominant cultivable microflora of human dental fissure plaque. *Infect Immun* 1982; **36**: 977–982.
17. Percival RS, Challacombe SJ, Marsh PD. Age-related microbiological changes in the salivary and plaque microflora of healthy adults. *J Med Microbiol* 1991; **35**: 5–11.
18. Murphy RA. Elastase production by oral staphylococci. *J Dent Res* 1974; **53**: 832–834.
19. Knighton HT. Coagulase-positive staphylococci in oral and nasal areas of dental students: a four-year study. *J Dent Res* 1965; **44**: 467–470.
20. Jackson MS, Bagg J, Gupta MN, Sturrock RD. Oral carriage of staphylococci in patients with rheumatoid arthritis. *Rheumatology* 1999; **38**: 572–575.
21. Kim KJ, You YO, Kim ES *et al*. δ-Hemolysin like gene of *Staphylococcus lugdenensis* in acute oral infection have partial homology with δ-hemolysin gene of *Staphylococcus aureus*. *J Oral Biol* 1995; **19**: 61–65.
22. Theilade E, Budtz-Jorgensen E. Predominant cultivable microflora of plaque on removable dentures in patients with denture induced stomatitis. *Oral Microbiol Immunol* 1988; **3**: 8–13.
23. Dahlen G, Linde A, Moller AJR, Ohman A. A retrospective study of microbiologic samples from oral mucosal lesions. *Oral Surg Oral Med Oral Pathol* 1982; **53**: 250–255.
24. Tawara Y, Honma K, Naito Y. Methicillin-resistant *Staphylococcus aureus* and *Candida albicans* on denture surfaces. *Bull Tokyo Dent Coll* 1996; **37**: 119–128.
25. Gibbons RJ, Socransky SS, de Araujo WC, Van Houte J. Studies on the predominant cultivable microbiota of dental plaque. *Arch Oral Biol* 1964; **9**: 365–370.
26. Piochi BJA, Zelante F. Contribution to the study of staphylococcus isolated from the mouth. III Staphylococcus isolated from dental plaque. *Rev Fac Odont Sao Paulo* 1995; 91–98.
27. Rams TE, Babalola OO, Slots J. Subgingival occurrence of enteric rods, yeasts and staphylococci after systemic doxycycline therapy. *Oral Microbiol Immunol* 1990; **5**: 166–168.
28. Helovuo H, Hakkarainen K, Paunio K. Changes in the prevalence of subgingival enteric rods, staphylococci and yeasts after treatment with penicillin and erythromycin. *Oral Microbiol Immunol* 1993; **8**: 75–79.
29. Gibbons RJ, Socransky SS, Sawyer S, Kapsimalis B, Macdonald JB. The microbiology of the gingival crevice area of man. II The predominant cultivable organisms. *Arch Oral Biol* 1963; **8**: 281–289.
30. Sanchez-Cordero S, Hoffman H, Stahl SS. Occurrence of staphylococcus in periodontal pockets of diabetic and non-diabetic adults. *J Periodontol* 1979; **50**: 109–113.
31. Moore WEC, Holdeman LU, Cato EP *et al*. Comparative bacteriology of juvenile periodontitis. *Infect Immun* 1985; **48**: 507–519.
32. Rams TE, Feik D, Slots J. Staphylococci in human periodontal diseases. *Oral Microbiol Immunol* 1990; **5**: 29–32.
33. Dahlen G, Wikstrom M. Occurrence of enteric rods, staphylococci and candida in subgingival samples. *Oral Microbiol Immunol* 1995; **10**: 42–46.
34. Kamma JJ, Nakou M, Baehni PC. Clinical and microbiological characteristics of smokers with early onset periodontitis. *J Periodont Res* 1999; **34**: 25–33.
35. Jackson MS. Oral staphylococci in health and disease. FIBMS thesis, Institute of Biomedical Science. 1998.
36. Lewis MAO, MacFarlane TW, McGowan DA. A microbiology and clinical review of acute dentoalveolar abscess. *Br J Oral Maxillofac Surg* 1990; **28**: 359–366.
37. Labriola JD, Mascaro J, Albert B. The microbiologic flora of orofacial abscesses. *J Oral Maxillofac Surg* 1983; **41**: 711–714.
38. Iatrou IA, Legakis N, Ioannidou E, Patrikiou A. Anaerobic bacteria in jaw cysts. *Br J Oral Maxillofac Surg* 1988; **26**: 62–69.
39. Bergmann OJ. Oral infections and septicemia in immunocompromised patients with haematologic malignancies. *J Clin Microbiol* 1988; **26**: 2105–2109.
40. Theilade E, Budtz-Jorgensen E, Thelaide J. Predominant cultivable microflora of plaque on removable dentures in patients with healthy oral mucosa. *Arch Oral Biol* 1983; **28**: 675–680.
41. Öhman S-C, Dahlén G, Möller Å, Öhman A. Angular cheilitis: a clinical and microbial study. *J Oral Pathol* 1986; **15**: 213–217.
42. Kondell PA, Nord CE, Nordenram G. Characterization of *Staphylococcus aureus* isolates from oral surgical outpatients compared to isolates from hospitalized and non-hospitalized individuals. *Int J Oral Surg* 1984; **13**: 416–422.
43. Samaranayake LP, MacFarlane TW, Lamey P-J, Ferguson MM. A comparison of oral rinse and imprint sampling techniques for the detection of yeast, coliform and *Staphylococcus aureus* carriage in the oral cavity *J Oral Pathol* 1986; **15**: 386–388.
44. Gibson J, Wray D, Bagg J. Oral staphylococcal mucositis. A new clinical entity in orofacial granulomatosis and Crohn's disease. *Oral Surg Med Pathol Oral Radiol Endod* 2000; **89**: 171–176.
45. Socransky SS, Haffajee AD, Dzink JL. Relationship of subgingival microbial complexes to clinical features at the

sampled sites. *J Clin Periodontol* 1988; **15**: 440–444.
46. Moore WEC, Holdeman LV, Cato EP *et al*. Comparative bacteriology of juvenile periodontitis. *Infect Immun* 1985; **48**: 507–519.
47. Sànchez-Codero S, Hoffman H, Stahl SS. Occurrence of staphylococcus in periodontal pockets of diabetic and non-diabetic adults. *J Periodontol* 1979; **50**: 109–113.
48. Williams BL, Pantalone RM, Sherris JC. Subgingival flora and periodontitis. *J Periodont Res* 1976; **11**: 1–18.
49. Peterson DE, Minah GE, Overholser CD *et al*. Microbiology of acute periodontal infection in myelosuppressed cancer patients. *J Clin Oncol* 1987; **5**: 1461–1468.
50. Tsutsui M, Utsumi N, Tsubakimoto K. Cellular components of staphylococci and streptococci in inflamed human gingiva. *J Dent Res* 1968; **47**: 663.
51. Takeuchi H, Sumitani M, Tsubakimoto K, Tsutsui M. Oral microorganisms in the gingiva of individuals with periodontal disease. *J Dent Res* 1974; **53**: 132–136.
52. Slots J, Feik D, Rams TE. Age and sex relationships of superinfecting microorganisms in periodontitis patients. *Oral Microbiol Immunol* 1990; **5**: 305–308.
53. Listgarten M, Lai CH. Comparative microbiological characteristics of failing implants and periodontally diseased teeth. *J Periodontol* 1999; **70**: 431–437.
54. Roberts GJ, Holzel HS, Sury MR, Simmons WA, Gardner P, Longhurst P. Dental bacteremia in children. *Pediatr Cardiol* 1997; **18**: 24–27.
55. Lockhart PB. An analysis of bacteremias during dental extractions. A double-blind, placebo-controlled study of chlorhexidine. *Arch Intern Med* 1996; **156**: 513–520.
56. Kralovic SM, Melin-Aldana H, Smith KK, Linnemann CC. *Staphylococcus lugdenensis* endocarditis after tooth extraction. *Clin Infect Dis* 1995; **20**: 715–716.
57. Etienne J, Fleurette J, Ninet JF, Favet P, Gruer LD. Staphylococcal endocarditis after dental extraction. *Lancet* 1986; **2**: 511–512.
58. Kennedy HF, Morrison D, Kaufmann ME *et al*. Origins of *Staphylococcus epidermidis* and *Streptococcus oralis* causing bacteraemia in a bone marrow transplant patient. *J Med Microbiol* 2000; **49**: 367–370.
59. Rosenberg SW. Oral complications of cancer chemotherapy: a review of 398 patients. *J Oral Med* 1986; **41**: 93–97.
60. Bartzokas CA, Johnson R, Jane M, Martin MV, Pearce PK, Saw Y. Relation between mouth and haematogenous infection in total joint replacements. *BMJ* 1994; **309**: 506–508.
61. An YH, Friedman RJ. Prevention of sepsis in total joint arthroplasty. *J Hosp Infect* 1996; **33**: 93–108.
62. Kaandorp CJE, Dinant HJ, Van de Laar MAFJ, Moens HJB, Prins APA, Dijkmans BAC. Incidence and source of native and prosthetic joint infection: a community based prospective survey. *Ann Rheum Dis* 1997; **56**: 470–475.
63. Jacobson JJ, Patel B, Asher G, Woolliscroft JO, Schaberg D. Oral staphylococcus in older subjects with rheumatoid arthritis. *J Am Geriat Soc* 1997; **45**: 590–593.
64. MacFarlane TW. The oral ecology of patients with severe Sjögrens syndrome. *Microbios* 1984; **41**: 99–106.
65. Thyne GM, Ferguson JW. Antibiotic prophylaxis during dental treatment in patients with prosthetic joints. *J Bone Joint Surg B* 1991; **73**: 191–194.
66. Martin MV, Hardy P. Two cases of oral infection by methicillin-resistant *Staphylococcus aureus*. *Br Dent J* 1991; **170**: 63–64.
67. Rousseau P. Acute suppurative parotitis. *J Am Geriat Soc* 1991; **38**: 897–898.
68. Lessing MPA, Jordens JZ, Bowler ICJ. When should healthcare workers be screened for methicillin-resistant *Staphylococcus aureus*? *J Hosp Infect* 1996; **34**: 205–210.
69. Balfour A, Higgins J, Brown M, Gallacher G. Eradication of throat carriage of methicillin-resistant *Staphylococcus aureus*. *J Hosp Infect* 1997; **35**: 320–321.
70. Rossi T, Peltonen R, Laine J, Eerola E, Vuopio-Varkila J, Kotilainen P. Eradication of the long-term carriage of methicillin-resistant *Stapylococcus aureus* in patients wearing dentures: a follow-up of 10 patients. *J Hosp Infect* 1997; **34**: 311–320.
71. Owen MK. Prevalence of oral methicillin-resistant *Staphylococcus aureus* in an institutionalized veterans population. *Spec Care Dentist* 1994; **14**: 75–79.
72. Millar MR, Walsh TR, Linton CJ *et al*. Carriage of antibiotic-resistant bacteria by healthy children. *J Antimicrob Chemother* 2001; **47**: 605–610.
73. Suzuki J, Komatsuzawa H, Sugai M *et al.* A long-term survey of methicillin-resistant S*taphylococcus aureus* in the oral cavity of children. *Microbiol Immunol* 1997; **41**: 681–686.