ORIGINAL ARTICLE

Stomatococcus mucilaginosus septicemia in leukemic patients

Margareta Granlund[1,2], Mats Linderholm[3], Mari Norgren[1], Carin Olofsson[1], Anders Wahlin[3] and Stig E. Holm[1]

[1]Department of Clinical Bacteriology, [2]Department of Oral Microbiology, [3]Department of Internal Medicine, Umeå University Hospital, Sweden

Objective: To report an unexpectedly high number of cases of septicemia with *Stomatococcus mucilaginosus*, and try to identify predisposing factors.

Methods: All blood cultures obtained during 1991–93 from patients treated at the hematologic ward were bacteriologically identified. The medical records of patients with *S. mucilaginosus*-positive blood cultures were retrospectively reviewed and evaluated. The antibiotic susceptibility pattern and restriction fragment length polymorphism (RFLP) of *S. mucilaginosus* were tested.

Results: *S. mucilaginosus* blood isolates from patients with hematologic malignancies were found to be as common as isolates of *Staphylococcus aureus*. Eleven patients with myelogenous leukemia and isolation of *S. mucilaginosus* from the blood are reported on. One patient had concomitant meningitis. All patients were neutropenic and most had oral mucositis and had been given ciprofloxacin prophylaxis. *S. mucilaginosus* isolates from these patients were resistant to ciprofloxacin in contrast to isolates from patients who had received other prophylactic regimens and seven isolates found in healthy individuals not recently treated with antibiotics. The resistant *S. mucilaginosus* were found to be of diverse genetic origin as determined by RFLP.

Conclusions: The appearance of resistant strains during ciprofloxacin prophylaxis may be a predisposing factor for *S. mucilaginosus* septicemia. There was no evidence of a nosocomial spread of *S. mucilaginosus* strains.

Key words: *Stomatococcus mucilaginosus*, septicemia, ciprofloxacin resistance, neutropenia, restriction fragment length polymorphism, antibiotic prophylaxis

INTRODUCTION

Intensive chemotherapy for acute leukemia regularly causes neutropenia, making the patients susceptible to bacterial and fungal infections [1]. During the last two decades a change in the spectrum of organisms responsible for infections in neutropenic patients has been reported [2]. Gram-positive bacteria such as viridans streptococci and multiresistant coagulase-negative staphylococci are now the predominant cause of these infections, replacing Gram-negative bacteria, which were the most prevalent species during the 1970s [3,4]. The reason for this shift is not fully understood, but the wider use of indwelling catheters, as well as the use of certain cytotoxic agents, may be contributing factors. An increased incidence of alpha-hemolytic streptococcal septicemia has been reported after treatment with high doses of cytosine arabinoside [5,6]. Also, the introduction of prophylactic regimens often containing fluoroquinolones has been suggested as a cause of this shift [7,8].

Stomatococcus mucilaginosus is a Gram-positive coccus which is a normal inhabitant of the human oral flora. It was first described as causing infection in 1978, when Rubin et al. reported a patient with endocarditis [9]. Since 1982, when it was described as a new genus [10] there have been sporadic reports of cases with invasive disease, e.g. endocarditis and catheter-related septicemia

Corresponding and reprint requests:

Margareta Granlund, Department of Clinical Bacteriology, University of Umeå, S-90185 Umeå, Sweden

Tel: 46-90101121 Fax: 46-90102225

E-mail: Margareta.Granlund@climi.umu.se

Accepted 15 April 1996

[11]. In the last 4 to 5 years reports have begun to accumulate regarding *S. mucilaginosus* as a pathogen in neutropenic patients [12–15]. In an attempt to find predisposing factors common in patients affected by this pathogen and to see if the occurrence of *S. mucilaginosus* septicemia seen in the hematologic ward was caused by a nosocomial spread of a specific *S. mucilaginosus* strain, we retrospectively studied 11 leukemic patients with *S. mucilaginosus* septicemia, including one patient with concomitant meningitis.

MATERIAL AND METHODS

Patients

All blood cultures obtained during 1991–93 from patients treated at the hematologic ward at the Department of Internal Medicine, Umeå University hospital were bacteriologically identified. The medical records of the patients with *S. mucilaginosus*-positive blood cultures were retrospectively reviewed and evaluated. Neutropenia was defined as an absolute neutrophil count (ANC) of $<0.5\times10^9$/L. Temperature was measured by digital axillary thermometer at least twice daily. Fever was defined as a body temperature of ≥38.5 °C or two consecutive measurements of ≥38 °C within 12 h. Resolution of fever was defined as two consecutive measurements of ≤37.5 °C.

Healthy individuals

Samples from tonsils and gingiva were taken with a cotton swab from 10 healthy individuals without antibiotic treatment, attending the Department of Infectious Diseases for vaccination. The samples were cultivated on blood agar and hematin agar plates and incubated for 18 h at 37 °C in air, and in 5% CO_2, respectively. From the mixed flora obtained on the plates, transparent-to-white, mucoid, convex colonies were isolated. The colonies were identified as *S. mucilaginosus* and tested for antibiotic susceptibility as described in the bacterial strain section.

Blood cultures

Ten milliliters of blood was divided into one aerobic and one anaerobic diphasic bottle (Laboratory of Clinical Bacteriology, Sundsvall Hospital, Sweden). This was repeated once or twice within a few hours, giving a total yield of 20–30 ml of blood. The bottles were incubated for 10 days and read twice daily by ocular inspection. Bottles showing visible growth on the agar slant, hemolysis, or turbidity in the broth were subcultured on blood agar, hematin agar, and, if growth in the anaerobic bottle was seen, also on brain–heart infusion agar plates.

Bacterial strains

The first blood isolate of *S. mucilaginosus* found was sent to Prof. Tom Bergan, Rikshospitalet, Oslo, for confirmation. The rest of the stomatococcal strains were identified by microscopic and colonial characteristics together with *S. mucilaginosus* ATCC 25296. *S. mucilaginosus* had transparent-to-white, mucoid, convex colonies. All strains grew well on hematin agar incubated in 5% CO_2 and were negative in routine slide test for catalase. A test panel originally developed for viridans streptococci [16], testing glycosidase activities with 4-methylumbelliferyl-linked fluorogenic substrates and conventional fermentation tests, resulted in positivity only in alpha- and beta-glucosidase. In Api 20 STREP (bioMérieux, Marcy-l'Etoile, France) the code for *S. mucilaginosus* ATCC 25296 was 5140010. The isolated strains had the codes 5140010 (four strains), 5150010 (six strains) 5150000 (one strain) or 5170010 (nine strains). There was no biochemical diversity among the strains from healthy and septicemic individuals.

Antibiotic susceptibility testing

Overnight cultures in Todd-Hewitt broth, diluted 1/50 in physiologic saline, were used for susceptibility testing. Blood agar plates were swabbed with the saline suspension and then incubated with E-test strips (AB Biodisk, Stockholm, Sweden). The plates were incubated for 18 h in 5% CO_2.

Restriction fragment length polymorphism (RFLP)

Chromosomal DNA for pulsed-field gel electrophoresis (PFGE) was obtained by modifications of previously described methods [17,18]. Briefly, 750 µL of an overnight culture with stomatococci grown in 5 mL of Todd-Hewitt broth (Difco, Detroit, Michigan, USA) incubated in 5% CO_2 was centrifuged and resuspended in 100 µL of TBE buffer (45 mM Tris-HCl, 45 mM borat, 1.0 mM EDTA, pH 8.3). The samples were warmed to 50 °C and 4 µL of lysozyme (25 mg/mL, Sigma Chemical Co., St Louis, Mo., USA), 4 µL of mutanolysin (5000 U/mL, Sigma) and 100 µL of 50 °C 2% agarose (Bio-Rad Laboratories, Hercules, California, USA) were added. The mixtures were pipetted into plug molds and the agarose was allowed to solidify. The plugs were placed in 1 mL of EC (lysis) buffer (6 mM Tris-HCl [pH 7.6], 1 M NaCl, 100 mM EDTA [pH 7.5], 0.5% Brij-58, 0.2% deoxycholate, 0.5% sodium lauroyl sarcosine) [18] with 40 µL of lysozyme (25 mg/mL) and 40 µL of mutanolysin (5000 U/mL) and were incubated for 3.5 h at 37 °C. After washing in 2 mL of TE wash buffer (10 mM Tris-HCl, 1 mM EDTA [pH 7.6]), 40 µL of proteinase K (25 mg/mL, Boehringer

Mannheim, Indianapolis, Indiana, USA) and 1 mL of EDTA solution (0.5 M EDTA [pH 7.6] and 0.5% sodium lauroyl sarcosine) were added [17] and the plugs were incubated overnight at 50 °C. After washing in TE wash buffer, proteinase K was inactivated with 10 μL/mL of 100 mM phenylmethylsulfonyl fluoride for 1 h at room temperature. The washing was then repeated three times. For PFGE, DNA was restricted with *Vsp*I (MBI Fermentas, Vilnius, Lithuania) 25 U per plug, in restriction buffer (50 mM Tris-HCl [pH 7.5], 10 mM $MgCl_2$, 100 mM NaCl, 0.1 mg/mL bovine serum albumin) at 37 °C overnight. After incubation, slices of the plugs were loaded into wells of 1.25% agarose gels in 0.5×PFGE buffer. *Saccharomyces cerevisiae* chromosomal DNA (Bio-Rad) was used as standard. Electrophoresis was performed with a Contoured-Clamped Homogeneous Electric Field apparatus (Gene Path System, Bio-Rad) using the program for *Staphylococcus aureus* for 20 h. Gels were stained with ethidium bromide and photographed under UV illumination.

RESULTS

In the 3-year study period, 1991–93, a total of 5444 blood cultures was drawn from indoor patients at the hematologic ward, each comprising two bottles. In total, 229 blood culture-positive episodes from 149 patients were identified (Table 1). The growth of all bacteria or yeast recovered in blood cultures from a patient within the same week is referred to as an episode. Of the isolated microorganisms, 148 (57%) were Gram-positive aerobic/facultative anaerobic organisms. *S. mucilaginosus* was found in 11 (4%) episodes. The bacteria most commonly considered as contaminants in blood cultures are: coagulase-negative staphylococci, *Corynebacterium* species, and *Propionibacterium* [19,20]. If episodes with growth of any of these species, in only one out of four to six bottles from a patient, were excluded, the stomatococci accounted for 9% of the aerobic/facultative anaerobic Gram-positive species found.

Patients

During the observation period, *S. mucilaginosus* were isolated from the blood of 11 patients with myelogenous leukemias, including one patient with concomitant meningitis. There were seven males and four females with a median age of 45 years (range 26 to 77 years). Individual patient characteristics are summarized in Table 2.. At the time of *S. mucilaginosus* septicemia, all patients had profound neutropenia (ANC $<0.1\times10^9$/L) due to intensive combined chemotherapy, including cytosine arabinoside combined with amsacrine-etoposide (patients no. 2, 5, 8, 9 and 10), mitoxantrone (patients no. 1 and 11), or daunorubicin-idarubicin (patients no. 3, 4, 6 and 7). The duration of neutropenia preceding the septicemia ranged from 5 to 19 days (median 10 days).

All patients had indwelling intravenous catheters. Seven patients had clinical signs of oral mucositis, esophagitis, or gastritis (Table 2). All but one patient received oral prophylactic antibacterial treatment; nine patients received ciprofloxacin, one of them also trimethoprim-sulfamethoxazol, and one patient trimethoprim-sulfamethoxazol only (Table 2). Most patients also received oral antifungal and antiviral prophylaxis. None of the patients received H_2-antagonist therapy.

Treatment and outcome

The initial antibiotic treatment varied considerably as indicated in Table 2. Vancomycin was given within

Table 1 Distribution of 258 microorganisms causing 229 episodes of septicemia in patients with hematologic malignancies in Umeå, Sweden, during 1991–93

	No.	% of all strains
Aerobic/facultative anaerobic species		
Gram-negative strains		
E. coli	16	6
Klebsiella	16	6
Enterobacter	9	3.5
Pseudomonas aeruginosa	5	2
Citrobacter	4	1.5
Others	14	5
Subtotal	64	25(31[b])
Gram-positive strains		
Coagulase-negative staphylococci	72(51[a])	28
Viridans streptococci	22	8.5
Corynebacterium	13(8[a])	5
Staphylococcus aureus	12	5
Stomatococcus mucilaginosus	11	4
Pneumococci	8	3
Others	10	4
Subtotal	148	57(59[b])
Anaerobic species		
Propionibacteria	29(3[a])	11.2
Clostridium spp.	4	1.5
Others	3	1
Subtotal	36(10[a])	14(5[b])
Yeast		
Candida albicans	6	2
Candida glabrata	4	1.5
Subtotal	10	4(5[b])

The numbers in the perentheses represent the number[a] and the percentage[b] of all strains after exclusion of common contaminants.

Table 2 Characteristics of 11 patients with *S. mucilaginosus* septicemia

Patient no.	1	2	3	4	5	6	7	8	9	10	11
Sex/age (years)	F/35	M/31[a]	F/42	M/26	M/77	M/76	M/29	M/73	M/45	F/57	F/50
Diagnosis	AML	CML	AML	CML	AML	RAEBT	AML	AML	AML	AML	AML
Anitbacterial prophylaxis	Cipro-floxacin	Cipro-floxacin[b]	Cipro-floxacin	Cipro-floxacin	Cipro-floxacin	Cipro-floxacin	Cipro-floxacin	Cipro-floxacin	None	Cipro-floxacin	TMP/SMZ
Days of neutropenia prior to septicemia	>12	13	10	19	7	8	>12	>7	5	12	7
Mucocutaneous lesions	Gingivitis Gastro-esophagitis	Oral muscositis		Sore throat	Oral mucositis	Oral mucositis Esophagitis		Gastritis	Subcu-taneous catheter bleeding		Gingivitis
Initial treatment (within 48 h)	Imipenem Vanco-mycin	Vanco-mycin	Imi-penem Vanco-mycin	Imi-penem	Ceftazidime Vanco-mycin	Ceftazidime Vanco-mycin	Ceftazidime Vanco-mycin	Imi-penem Ampho-tericin B	Ceftazidime	Cef-pirome Vanco-mycin	Pipera-cillin Amikacin

Abbreviations: F = female; M = male; AML = acute myelogenous leukemia; CML = chronic myelogenous leukemia; RAEBT = refractory anemia in excess of blasts in transformation; TMP/SMZ = trimethoprim-sulfamethoxazole.
[a]Patient with concomitant meningitis. [b]Ciprofloxacin replaced by TMP/SMZ 2 weeks before the septicemia.

48 h after onset of fever in 7/11 patients, and was subsequently added (day 3 to 8) after the results of the blood culture in the remaining four patients were obtained. The overall response to proper antibiotic treatment was slow, and fever persisted for a median of 16 days (range 7 to 35 days). The duration of fever was similar in the groups given initial or delayed treatment with vancomycin. Due to the long duration of the fever, addition of antifungal therapy (amphotericin B) was made in seven of the patients. Only one patient had any sign of fungal infection (oral and esophagal candidiasis). No fungi were found in the blood culture. Repeated blood cultures were done in most patients, but were all sterile. In two patients, the indwelling intravenous catheter was removed; cultures from the tips were both negative. None of the remaining patients had recurrent *S. mucilaginosus* bacteremia after resolution of fever. The septicemic condition of patient no. 2 was complicated by meningitis with progressive headache and nuchal rigidity. *S. mucilaginosus* could be isolated in the cerebrospinal fluid on day 14 in spite of treatment with vancomycin and cefotaxime in a dose usually given for treatment of meningitis. The patient died, still febrile, 22 days after onset of fever. At follow-up in December 1994, 10/11 patients had died between 19 to 550 days (median 162.5 days) after the *S. mucilaginosus* septicemia; however, only one death (no. 2) directly related to the *S. mucilaginosus* septicemia episode. One patient (no. 4) is still alive 600 days after the infection.

S. mucilaginosus in healthy individuals

Stomatococci were isolated from gingival and tonsillar regions in 7/10 healthy individuals. In three cases the *S. mucilaginosus* organisms were only found in the gingival sample and in one case only in the throat culture.

Antibiotic susceptibility

The minimum inhibitory concentrations (MICs) of all tested antibiotics were lower for *S. mucilaginosus* isolated from the healthy individuals than for those from the blood isolates from the patients (Table 3). The difference was statistically significant for cefuroxime ($p<0.05$) and for ciprofloxacin ($p<0.001$, Mann-Whitney U-test). The MICs for ciprofloxacin for *S. mucilaginosus* ranged from 0.25 to 0.5 mg/L in isolates from healthy individuals. Only two patients had strains with MICs for ciprofloxacin of 0.5 mg/L. These two strains were from patients (nos 9 and 11) not given ciprofloxacin as prophylaxis. The patients who had received ciprofloxacin as prophylaxis had MICs ranging from 3 to >32 mg/L (Table 3). No common antibiotic resistance pattern could otherwise be revealed in the strains isolated from the bacteremic patients.

Table 3 MIC_{50} (mg/L) of twelve strains of *S. mucilaginosus* isolated from blood and cerebrospinal fluid (CSF) from hematologic patients compared to MIC_{50} of seven colonizing strains from throat and gingiva of healthy individuals

	Hematologic patients Blood/CSF isolates		Healthy individuals Throat/gingival isolates	
	MIC_{50}	MIC range	MIC_{50}	MIC range
Cefotaxime	0.12	<0.016–1.5	0.016	0.006–0.06
Vancomycin	1.5	0.5–1.5	0.75	0.5–1.0
Cefuroxime	0.12	<0.016–2.0	0.016	<0.016–0.06
Penicillin G	0.02	<0.016–1.5	0.016	0.006–0.016
Gentamicin	6	3–8	3	2–4
Trimethoprim-sulfamethoxazole	0.06	0.02–4	0.05	0.02–0.12
Ciprofloxacin	12	(0.5[a])3 to >32	0.38	0.25–0.5

[a]MIC of strains from patients no. 9 and no. 11, not receiving ciprofloxacin prophylaxis.

Restriction fragment length polymorphism

Digestion with restriction enzyme *Vsp*I demonstrated distinct cleavage patterns in all the *S. mucilaginosus* strains (Figure 1). No corresponding phenotypic diversity was found in the biochemical tests used. The two isolates from blood and cerebrospinal fluid of patient no. 2 had identical restriction patterns. Except for these two strains, a common pattern was found neither between the highly resistant strains with MIC >32 mg/L nor between the susceptible strains (Figure 1).

DISCUSSION

In a retrospective study of the etiology behind bacterial septicemia in the hematologic ward, we found *S. mucilaginosus* as a common cause of septicemia in a well-defined population of patients with hematologic malignancies. All patients were severely neutropenic, had indwelling intravenous catheters and had received intensive cytotoxic therapy including cytosine arabinoside. The majority of patients also had signs of oral mucosal lesions and had been treated prophylactically with ciprofloxacin.

Ciprofloxacin has been used in selected patients as a prophylactic agent in our hematologic ward during the last 5 years. Several reports of *S. mucilaginosus* infections have described a high proportion of fluoroquinolone resistance in *S. mucilaginosus* strains isolated from hospitalized patients [21,22]. This corroborates our findings. In contrast, we found that the isolates from healthy individuals and from those patients who had not received ciprofloxacin prophylaxis were sensitive to ciprofloxacin. This indicates that the reported fluoroquinolone resistance is not caused by inherent resistance of these strains. Fluoroquinolones act on

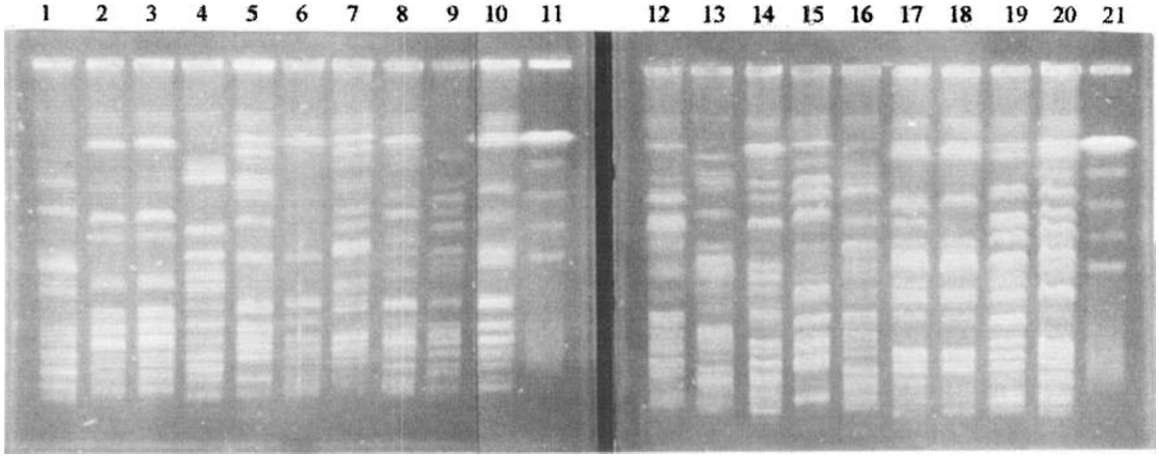

Figure 1 Fragment patterns of the *S. mucilaginosus* genome restricted with *Vsp*I analyzed by pulsed-field gel electrophoresis. Lane 1 represent the strain isolated from blood from patient no. 1. Lanes 2 and 3 contain the blood and the cerebrospinal fluid isolate from patient no. 2. Lanes 4 to 10 and 12 to 13 represent strains isolated from blood from patients no. 3 to no. 11. Lanes 11 and 21 are the *Saccharomyces cerevisiae* standard (Biorad). Lanes 14 to 20 represent the colonizing *S. mucilaginosus* strains from healthy individuals.

bacteria by altering the association of DNA gyrase (topoisomerase type II) with DNA, a process required for DNA supercoiling [22,23]. Resistance to quinolones in staphylococci, which form another genera of the family Micrococcaceae has primarily been attributed to chromosomal mutations in the DNA gyrase gene *gyr*A [24]. There are no reports of clinically isolated strains with plasmid-encoded quinolone resistance [22,25]. The diverse antibiotic sensitivity pattern, as well as the RFLP banding pattern, showed that the resistant *S. mucilaginosus* isolates were not derived from a single clone. All patient strains revealed restriction enzyme patterns which were as diverse as those found in *S. mucilaginosus* isolated from healthy individuals. Taken together, these observations indicate that the antibiotic treatment of the individual patients accounted for the development of resistant strains rather than a nosocomial spread.

The persistence of fever in spite of seemingly adequate antibiotic treatment is in accordance with other reports [12]. The indwelling intravenous catheter was removed in only a minority of the patients. Due to the prolonged fever this could have been an appropriate measure. However, after resolution of fever none of the surviving patients had recurrent *S. mucilaginosus* bacteremia, and cultures from extracted catheters were negative. Thus, a catheter-related infection as an explanation of the prolonged fever is less likely.

The *S. mucilaginosus* infections have subsequently resolved in most cases and the mortality associated with *S. mucilaginosus* septicemia is predominantly seen in patients with concomitant meningitis. McWhinney et al. [12] reviewed 19 cases of systemic infection with *S. mucilaginosus* from the literature in addition to data from eight neutropenic patients with *S. mucilaginosus* septicemia. Together with our cases, this comprises 38 patients. Five deaths assigned to the *S. mucilaginosus* infection (13% mortality) are reported among those patients. Three of the five cases were associated with meningitis.

Little is known about the virulence properties of *S. mucilaginosus*. The case reports of infections caused by *S. mucilaginosus* indicate it to be an opportunistic pathogen. The lesions of the mucous membranes often seen in the neutropenic patients could facilitate the stomatococcal entrance into the bloodstream.The emergence of resistant strains during ciprofloxacin prophylaxis may favor the growth of stomatococci in the oral cavity over bacterial species sensitive to ciprofloxacin. However, two of the patients displayed stomatococcal septicemia without prior ciprofloxacin treatment, indicating that other factors are also of importance for the pathogenicity of stomatococci.

The emergence of quinolone resistance among *S. aureus* and coagulase-negative staphylococci after quinolone treatment is a matter of great concern [26]. The data presented in this report, showing stomatococci as a relatively common cause of septicemia in neutropenic patients as well as the high tendency to acquire ciprofloxacin resistance, adds to this concern. A continued recognition of the problem, and evaluation of alternative regimens for prophylaxis which include Gram-positive bacteria, should be pursued, especially for such high-risk groups as neutropenic patients.

References

1. Bodey GP, Buckely M, Sathe YS, Freireich EJ. Quantitative relationships between circulating leukocytes and infection in patients with acute leukemia. Ann Intern Med 1966; 64: 328–40.
2. Pizzo PA, Ladisch SL, Gill F, Levine AS. Increasing incidence of gram-positive sepsis in cancer patients. Med Pediatr Oncol 1078; 5: 241–4.
3. Cohen J, Donnelly JP, Worsley AM, Catovsky D, Goldman JM, Galton DAG. Septicemia caused by viridans streptococci in neutropenic patients with leukemia. Lancet 1983; ii: 1452–4.
4. Brown AE. Neutropenia, fever, and infection. Am J Med 1984; 76: 421–8.
5. Sotiropoulos S, Jackson MA, Woods GM, Hicks RA, Cullen J, Freeman AI. Alpha-streptococcal septicemia in leukemic children treated with continuous or large dosage intermittent cytosine arabinoside. Pediatr Infect Dis J 1989; 8: 755–8.
6. Kern W, Kurrle E, Vanek E. High risk of streptococcal septicemia after high dose cytosine arabinoside treatment for acute myelogenous leukemia. Klin Wochensch 1987; 65: 773–80.
7. Kern W, Kurrle E, Vanek E. Ofloxacin for prevention of bacterial infections in granulocytopenic patients. Infection 1987; 15: 427–32.
8. De Pauw BE, Donnelly JP, DeWitte T, Nova-Kova IRO, Schattenberg A. Options and limitations of long-term oral ciprofloxacin as antibacterial prophylaxis in allogenic bone marrow transplant recipients. Bone Marrow Transplant 1990; 5: 179–82.
9. Rubin SJ, Lyons RW, Murcia AJ. Endocarditis associated with cardiac catheterization due to a gram-positive coccus designated *Micrococcus mucilaginosus*. J Clin Microbiol 1978; 7: 546–9.
10. Bergan T, Kocur M. *Stomatococcus mucilaginosus* gen. nov., sp. nov., ep. rev., a member of the family *Micrococcaceae* Int J Syst Bacteriol 1982; 32: 374–7.
11. Ascher DP, Zbick C, White C, Fischer G. Infections due to *Stomatococcus mucilaginosus*: 10 cases and review. Rev Infect Dis 1991; 13: 1048–52.
12. McWhinney PH, Kibbler CC, Gillespie SH, et al. *Stomatococcus mucilaginosus*: an emerging pathogen in neutropenic patients. Clin Infect Dis 1992; 14: 641–6.

13. Oppenheim BA, Weightman NC, Prendeville J. Fatal *Stomatococcus mucilaginosus* septicaemia in a neutropenic patient. Eur J Clin Microbiol Infect Dis 1989; 8: 1004–5.
14. Mustafa MM, Carlson L, Krisher K. *Stomatococcus mucilaginosus* fatal sepsis in a child with leukemia. Pediatr Infect Dis J 1993; 12: 784–5.
15. Henwick S, Koehler M, Patrick C. Complications of bacteremia due to *Stomatococcus mucilaginosus* in neutropenic children. Clin Infect Dis 1993; 17: 667–71.
16. Beighton JM, Hardie JM, Whiley RA. A scheme for the identification of viridans streptococci. J Med Microbiol 1991; 53: 367–72.
17. Fasola E, Livdahl C, Ferrieri P. Molecular analysis of multiple isolates of the major serotypes of group B streptococci. J Clin Microbiol 1993; 31: 2616–20.
18. Smith CL, Cantor CR. Purification, specific fragmentation, and separation of large DNA molecules. Methods Enzymol 1987; 155: 449–67.
19. Krumholz HM, Cummings S, York M. Blood culture phlebotomy: switching needles does not prevent contamination. Ann Intern Med 1990; 113: 290–2.
20. Roberts FJ. The value of the second blood culture. J Infect Dis 1993; 168: 795–6.
21. Mitchell PS, Huston BJ, Jones RN, Holcomb L, Koontz FP. *Stomatococcus mucilaginosus* bacteremias. Diagn Microbiol Infect Dis 1990; 13: 521–5.
22. Wolfson JS, Hooper DC. The fluoroquinolones: structures, mechanisms of action and resistance, and spectra of activity in vitro. Antimicrob Agents Chemother 1985; 28: 581–6.
23. Archer GL, Climo MW. Antimicrobial susceptibility of coagulase-negative staphylococci. Antimicrob Agents Chemother 1994; 38: 2231–7.
24. Sreedharan S, Peterson LR, Fisher LM. Ciprofloxacin resistance in coagulase-positive and -negative staphylococci: role of mutations at serine 84 in the DNA gyrase A protein of *Staphylococcus aureus* and *Staphylococcus epidermidis*. Antimicrob Agents Chemother 1991; 35: 2151–4.
25. Piddock LJV. New quinolones and gram-positive bacteria. Antimicrob Agents Chemother 1994; 38: 163–9.
26. Cruciani M, Bassetti D. The fluoroquinolones as treatment for infections caused by gram-positive bacteria. J Antimicrob Chemother 1994; 33: 403–17.