Eur. J. Clin. Microbiol. Infect. Dis., June 1992, p. 491–498
0934-9723/92/06 0491-08 $3.00/0

Streptococcus milleri Group: Renewed Interest in an Elusive Pathogen

S.C. Piscitelli[1], J. Shwed[2], P. Schreckenberger[3], L.H. Danziger[1]*

The following review examines the bacteriological characteristics, epidemiology, pathogenicity and antimicrobial susceptibility of the *"Streptococcus milleri* group". *"Streptococcus milleri* group" is a term for a large group of streptococci which includes *Streptococcus intermedius, Streptococcus constellatus* and *Streptococcus anginosus*. Usually considered commensals, these organisms are often associated with various pyogenic infections including cardiac, abdominal, skin and central nervous system infections. Organisms of the *"Streptococcus milleri* group" are often unrecognized pathogens due to the lack of uniformity in classifications and difficulties in microbiological identification. Penicillin G, cephalosporins, clindamycin and vancomycin all possess activity against these streptococci. Use of agents with poor activity may promote infections with *"Streptococcus milleri* group" and allow it to exhibit its pathogenicity. An understanding of these organisms may aid in their recognition and proper treatment.

"*Streptococcus milleri* group" is the name sometimes used for a large group of medically important streptococci associated with serious pyogenic infections. Guthof (1) was the first to use the name *"Streptococcus milleri"* in 1956 in reference to oral non-haemolytic streptococcal species. Subsequently, Colman and Williams (2) proposed that the minute beta-haemolytic streptococci along with other nonhaemolytic streptococci referred to as the *"Streptococcus milleri* group" all be included in the species *"Streptococcus milleri"*. Facklam (3, 4), from the Centers for Disease Control, Atlanta, USA, favored the separation of *"Streptococcus milleri"* into a number of distinct species, thus giving rise to two systems of nomenclature for these streptococci. Coykendall et al. (5) proposed the unification of these streptococci into a single species *Streptococcus anginosus* which is the oldest approved name for these bacteria and therefore has precedence over the name *"Streptococcus milleri"*. Recently, Whiley et al. (6) have performed DNA relatedness studies on strains classified as *Streptococcus anginosus* and observed that three DNA homology groups could be identified that correspond to the type strains of *Streptococcus constellatus, Streptococcus intermedius* and *Streptococcus anginosus*. On the basis of the DNA-DNA hybridization and different phenotypic properties exhibited by these three species, they proposed the reinstatement of the nomenclature *Streptococcus constellatus, Streptococcus intermedius* and *Streptococcus anginosus* for three distinct species (7). A comparison of the different classifications used for the *"Streptococcus milleri* group" is given in Table 1.

Although the term *"Streptococcus milleri"* is not included on the approved list of bacterial names (8), it is often used by UK authors and continues to be used in both the European and American literature to describe streptococci that are found in suppurative infections. As such, the term *"Streptococcus milleri"* carries a message to clinicians managing patients. This review will not address the complexities of identification of the *"Streptococcus milleri* group"organisms, but will describe their characteristics, their antimicrobial susceptibility and the infections they cause, and examine the reasons for renewed interest in these streptococci.

[1] Department of Pharmacy Practice, University of Illinois at Chicago, 833 South Wood Street, Chicago, Illinois, 60612, USA.
[2] Department of Hospital Pharmacy Practice and Administration, Medical University of South Carolina, 171 Ashley Avenue, Charleston, South Carolina, 29425-0810, USA.
[3] Department of Pathology, University of Illinois at Chicago, 840 South Wood Street, Chicago, Illinois, 60612, USA.

Table 1: Various classifications of the *"Streptococcus milleri* group".

Hemolysis	Group antigen	UK Colman and Williams (2)	USA Facklam 1977 (3)	USA Facklam 1984 (4)	Coykendall et al. 1987 (5)	Whiley et al. 1990, 1991 (7, 14)
Alpha or none	none	*S. milleri*	*S. milleri* group-*intermedius*	*S. intermedius*	*S. anginosus*	*S. intermedius*
Alpha or none	none	*S. milleri*	*S. anginosus-constallatus*	*S. constellatus*	*S. anginosus*	*S. constellatus*
Alpha or none	F	*S. milleri*	not recognized	not recognized	*S. anginosus*	*S. anginosus*
Beta	F	*S. milleri*	*S. anginosus*	*S. anginosus* group F	*S. anginosus*	*S. constellatus*
Beta	A	*S. milleri*	minute colony group A	*S. anginosus* group A	*S. anginosus*	*S. anginosus*
Beta	C	*S. milleri*	minute colony group C	*S. anginosus* group C	*S. anginosus*	*S. anginosus*
Beta	G	*S. milleri*	minute colony group G	*S. anginosus* group G	*S. anginosus*	*S. anginosus*
Beta	not group A, B, C, D, F or G	*S. milleri*	minute colony no group	*S. anginosus* no group	*S. anginosus*	*S. constellatus* or *S. intermedius*

Bacteriological Characteristics

In general, the streptococci are a heterogenous group of organisms whose classification is based on haemolysis patterns observed on blood agar plates, Lancefield serological reactions, growth characteristics and biochemical reactions.

The species comprising the *"Streptococcus milleri* group" are commensals commonly isolated from the mouth, oropharynx, gastrointestinal tract and vagina, and are responsible for a variety of human and animal infections (9, 10). Sometimes mistaken for anaerobic streptococci, they form minute colonies (less than 0.5 mm in diameter), may require carbon dioxide for isolation, and have a characteristic caramel odor when cultured on agar plates (10, 11). On Gram stain they characteristically appear as spherical or ovoid cells which form chains or pairs in broth culture.

Misidentification of *"Streptococcus milleri* group" organisms commonly occurs due to the variety of physiologic and serologic characteristics exhibited. Most of the *"Streptococcus milleri* group" display beta-haemolytic or non-haemolytic reactions on blood agar plates. Of the 259 isolates described by Ball and Parker (12), 56 % were non-haemolytic, 25 % were beta-haemolytic and 19 % were alpha-haemolytic. Poole and Wilson (13) reported 75 % of their strains of the *"Streptococcus milleri* group" as non-haemolytic. Kambal (11) reported on 80 strains of the *"Streptococcus milleri* group" of which 54 % were non-haemolytic, 29 % beta-haemolytic and 17 % alpha-haemolytic. Whiley et al. (14) examined 157 strains of the *"Streptococcus milleri* group" and found that virtually all *Streptococcus intermedius* (93 %) were non-haemolytic (alpha- or gamma-haemolysis), whereas 38 % of the *Streptococcus constellatus* and 12 % of *Streptococcus anginosus* were beta-haemolytic. They further showed that of those strains of *Streptococcus constellatus* and *Streptococcus anginosus* that belonged to Lancefield serological group F, nearly all of the *Streptococcus constellatus* were beta-haemolytic and all of the *Streptococcus anginosus* were non-haemolytic.

Lancefield antigenic serologic reactions are of little value in identifying *"Streptococcus milleri* group" organisms because a variety of antigens may be exhibited. Some 30–55 % of isolates are group F, 25–30 % of the *"Streptococcus milleri* group" are non-typable, while a representative portion of the remaining typable isolates are of group A, C and G (12, 13, 15, 16). Strains carrying the group F antigen may also cross-react with the other grouping sera.

The diversity of serologic haemolytic reactions, and disagreement regarding the speciation and taxonomy of the *"Streptococcus milleri* group" may contribute to a lack of recognition of these pathogens. Many laboratories will identify beta-haemolytic *"Streptococcus milleri* group" organisms as beta-haemolytic streptococci with a given Lancefield classification while non-haemolytic *"Streptococcus milleri* group" organisms are identified as viridans streptococci without further identification to species level. Some laboratories may report these organisms as microaerophilic streptococci since they tend to grow better in anaerobic conditions or when incubated with increased CO_2. Routine identification to species level of viridans streptococci (non-group D) is not considered necessary by some because they are usually susceptible to penicillin (17). However, differences in antimicrobial susceptibility between organisms may be unrecognized due to the lack of exact speciation.

Conventional biochemical testing (Table 2) remains the method of choice for identification of viridans streptococci including the *"Streptococcus milleri* group". Hinnebusch et al. (18) have evaluated five commercial systems (API Rapid Pos ID, Analytab Products, Plainview, NY; Baxter MicroScan Rapid Pos ID Panel, Baxter MicroScan, West Sacramento, CA; BBL Minitek Differential System, Becton Dickinson Microbiology Systems, Cockeysville, MD; IDS RapID STR system, Innovative Diagnostic Systems, Atlanta, GA; and Vitek GPI, bioMérieux Vitek, Hazelwood, MO) for identification of viridans streptococci. They reported that none of the systems showed more than 74 % agreement with conventional biochemical tests. Of the pathogenic species, those most frequently identified incorrectly or not identified were *Streptococcus constellatus, Streptococcus intermedius* and *Streptococcus sanguis* I (18).

Epidemiology

"Streptococcus milleri group" organisms have been isolated from the developing lesions of dental caries and periodontal disease; however, their pathogenicity has not been determined (11). They are responsible for the development of deep-seated, necrotic odontogenic abscesses (19–21). When isolated from blood, they are associated with a pyogenic focus (10, 11, 17). The *"Streptococcus milleri* group" comprises 3–15 % of all viridans streptococci isolated from endocarditis and is associated with preceding dental trauma, gastrointestinal carcinoma or gastrointestinal perforation (22–24). *"Streptococcus milleri* group" endocarditis is commonly as-

Table 2: Phenotypic differentiation of *Streptococcus constellatus, Streptococcus intermedius,* and *Streptococcus anginosus* within the "Streptococcus milleri group" (data from Reference 14).

Test	*S. constellatus*	*S. intermedius*	*S. anginosus*
Esculin hydrolysis	positive	positive	positive
Voges-Proskauer Test	positive	positive	positive
Arginine dihydrolase	positive	positive	positive
Production of:			
Beta-D-fucosidase	negative	positive	negative
Beta-N-acetylglucosaminidase	negative	positive	negative
Beta-N-acetylgalactosaminidase	negative	positive	negative
Sialidase	negative	positive	negative
Beta-galactosidase	negative	positive	negative
Beta-glucosidase	negative	variable	positive
Alpha-glucosidase	positive	positive	variable
Hyaluronidase	variable	positive	negative
Hydrogen peroxide	negative	negative	variable
Acid from:			
Amygdalin	variable	variable	positive
Lactose	variable	positive	positive
Mannitol	negative	negative	variable
Raffinose	negative	negative	variable

Positive = 90 % or more of strains positive; negative = 90 % or more of strains negative; variable = 11 %–89 % of strains positive.

sociated with the development of pyogenic complications and myocardial abscess formation (22, 24–26). Pericarditis has also been reported to occur following dental trauma (27). *"Streptococcus milleri* group" organisms have been isolated from 56–81 % of bacterial brain abscesses either in pure or mixed culture (10). Factors associated with *"Streptococcus milleri* group" brain abscess include congenital heart defects, sinusitis, otitis media, liver disease and trauma (10).

"Streptococcus milleri group" organisms rarely cause meningitis; however when they do, it is often preceded by trauma or purulent infection at another site (28, 29). In addition to these central nervous system (CNS) infections, these organisms have also been isolated from acute spinal epidural abscesses and a subdural empyema (30, 31).

Approximately, 7–40 % of all infections caused by these organisms occur within the abdominal cavity. They are often infecting pathogens following gastrointestinal surgery, appendectomy or colonic perforation (10). Hepatic abscesses have occurred following gastrointestinal perforation in Crohn's disease, perirectal abscess, colon carcinoma and abdominal surgery (32–36). In a review of 15 cases involving organisms of the *"Streptococcus milleri* group" in liver abscesses, overall mortality was reported to be 13 %. The organism was isolated from the abscess in pure culture in 13 of 15 patients, while blood cultures were positive in 65 % of the cases (37). Hepatic abscess with *"Streptococcus milleri* group" organisms has also been reported in association with use of an intrauterine device (38). *"Streptococcus milleri* group" organisms have been isolated in pure and mixed culture from abdominal wound infections, peritonitis, subphrenic and pelvic abscesses, and cholangitis (10).

"Streptococcus milleri group" organisms are occasionally isolated in obstetrical infections and neonatal sepsis (39, 40). Additionally, subcutaneous abscesses in intravenous drug abusers and hidradenitis caused by these organisms have been reported (41, 42). Septic arthritis and osteomyelitis have also occurred in isolated cases (13, 43, 44).

"Streptococcus milleri group" organisms have also been implicated in the development of purulent empyema or lung abscess following aspiration pneumonia (39). Brook et al. (45) described two cases of *"Streptococcus milleri* group" lung infections: one a large abscess, the other a complication of previously scarred lung. In both reports the organism could not be isolated in expectorated sputum but required needle aspiration and blood cultures for isolation.

A case of community-acquired *"Streptococcus milleri* group" bacteremia secondary to probable tricuspid endocarditis was reported in a patient with AIDS (46). The patient, an i.v. drug abuser, developed a secondary meningitis but responded to a six-week course of therapy with vancomycin.

Despite the increasing awareness of the clinical significance of the *"Streptococcus milleri* group", the association between particular species and specific sites of isolation and disease conditions has not been clear. Whiley et al. (47) have recently reported on the association of *Streptococcus intermedius, Streptococcus constellatus* and *Streptococcus anginosus* with clinical infections, and sites of isolation. In their study there was a marked association of *Streptococcus intermedius* with infections involving the central nervous system.

Streptococcus anginosus was the species most frequently identified in the gastrointestinal tract and genitourinary specimens, while *Streptococcus constellatus* was the species most frequently identified in specimens from the respiratory tract (47).

One common denominator in infections associated with the *"Streptococcus milleri* group" is the tendency of the organisms to cause abscess formation, either alone or in combination with anaerobic organisms and gram-negative pathogens. The means by which these organisms survive within an abscess have not been determined.

Antimicrobial Susceptibility

Minimum inhibitory concentrations (MICs) of various antibiotics for the *"Streptococcus milleri* group" are listed in Table 3. Penicillin G is usually very active against the *"Streptococcus milleri* group". Most strains have MICs ≤ 0.25 µg/ml (17, 48–50). Occasionally, strains of the *"Streptococcus milleri* group" may require penicillin G concentrations of 4–8 µg/ml for inhibition (50). Therefore, uniform susceptibility to penicillin cannot be assumed. *"Streptococcus milleri* group" organisms are also susceptible to methicillin and ampicillin; however, MICs for ampicillin are occasionally ≥ 0.5 µg/ml. Cephalosporins such as cephalothin and cefotaxime possess excellent activity against the *"Streptococcus milleri* group" as

Table 3: In vitro activity of various antibiotics against the *"Streptococcus milleri* group" (adapted from References 15, 17, 46–48, 59).

Antimicrobial agent	MIC range (μg/ml)	No. of strains tested
Penicillin G	<0.125–1.0	133
Methicillin	0.5–2.0	68
Nafcillin	1.0–2.0	18
Ampicillin	0.25–1.0	68
Cephalothin	1.0–4.0	68
Chloramphenicol	<0.5–8.0	68
Clindamycin	≤0.25	133
Vancomycin	≤2.0	20
Teicoplanin	≤0.015–1.0	33
Trimethoprim	0.03–2.0	68
Gentamicin	0.24–4.0	68
Amikacin	16.0–128	30
Rifampin	0.06–0.12	18
Tetracycline	<0.25–0.5	68
Erythromycin	<0.25–2.0	77
Nitrofurantoin	4.0–64.0	68
Sulfamethoxazole	16.0–512	68
Imipenem	0.007–0.25	33

do clindamycin and vancomycin. Chloramphenicol, erythromycin and tetracycline are suitable alternative antimicrobial agents in penicillin-allergic patients. Other agents such as gentamicin, nitrofurantoin and sulfamethoxazole have activity against the *"Streptococcus milleri* group" as well, however resistance may be exhibited (48, 49).

Pathogenicity

The mechanisms by which the *"Streptococcus milleri* group" becomes pathogenic are unclear. There are several factors involved which can be offered as explanation. It is thought that extracellular enzymes produced by the *"Streptococcus milleri* group" may contribute to its pathogenicity and facilitate the liquification of pus (19). Hyaluronidase, which degrades connective tissue and facilitates the spread of the organism through tissue planes, has been isolated from beta-haemolytic group F *"Streptococcus milleri* group" organisms (51). Whiley et al. (7, 14) have noted that hyaluronidase is produced by most strains of *Streptococcus constellatus,* virtually all strains of *Streptococcus intermedius,* but very few strains of *Streptococcus anginosus.* Production of deoxyribonuclease, ribonuclease, gelatinase and collagenase have also been observed (51–53). The *"Streptococcus milleri* group" also releases an immunosuppressive substance that has not yet been identified (54). This substance may promote pathogenicity and allow the organisms to survive within an abscess. The ability of the *"Streptococcus milleri* group" to adhere to buccal epithelial cells and bind fibronectin may be another factor contributing to its pathogenicity (55). Additionally, Brook and Walker (56) have suggested that the presence of a polysaccharide capsule, which prevents phagocytosis, may be a virulence factor in suppurative infection.

The *"Streptococcus milleri* group" may also become pathogenic when antibiotics with minimal or no activity against the organisms are used in surgical prophylaxis. Specifically, metronidazole and gentamicin combinations used to suppress fecal flora prior to abdominal surgery and to treat intra-abdominal infections have been associated with the development of *"Streptococcus milleri* group" infections. Tresadern (57) reported the development of 13 post-operative infections with *"Streptococcus milleri* group" in patients who had undergone colorectal surgery. In 6 of the 13 metronidazole and gentamicin were given as prophylaxis for surgery. He proposed that the suppression of anaerobic and enteric gram-negative organisms and the lack of activity of metronidazole and gentamicin against *"Streptococcus milleri* group" allowed its expression as a pathogen.

Madden and Hart (33), in reviewing 253 appendectomies, identified *"Streptococcus milleri* group" organisms as the pathogen in 11 of 38

children who developed infections post-operatively. Metronidazole and gentamicin were used prophylactically in 6 of 11 patients from which *"Streptococcus milleri* group" organisms were isolated. The authors claimed that the use of these agents rendered the organisms pathogenic.

One could also assume that suppression of the rest of the normal flora gave an ecologic advantage to members of the *"Streptococcus milleri* group".

Long-term use of metronidazole has also been implicated in the development of a pyogenic hepatic abscess (32). A 38-year-old male receiving metronidazole and methylprednisone for treatment of Crohn's disease developed a perianal abscess from which *Peptostreptococcus* was initially identified on culture and therapy with metronidazole was continued. Subsequently, a hepatic abscess developed from which a *"Streptococcus milleri* group" organism was isolated. Continued use of metronidazole may have selected the organism, or initial misidentification of the organism may have led to treatment with inappropriate antibiotics.

Onderdonk (58) demonstrated the persistence of *"Streptococcus milleri* group" organisms in experimental abscesses caused by these organisms and *Bacteroides fragilis* following treatment with metronidazole. It would appear that choosing antibiotics which lack activity against the *"Streptococcus milleri* group" for surgical prophylaxis or for treatment of intra-abdominal infections may promote the development of infections with this potential pathogen.

Conclusion

"Streptococcus milleri group" organisms have been implicated in various types of infections (CNS, cardiac, oropharynx, skin, abdominal) usually associated with abscess formation, either alone or in mixed culture. *"Streptococcus milleri* group" organisms are susceptible to a wide range of antibiotics including penicillins, cephalosporins, clindamycin, vancomycin and erythromycin, although surgical evacuation is often necessary for bacterial eradication. The renewed interest in this group of organisms has been due to recent reports of the *"Streptococcus milleri* group" causing intra-abdominal infections in patients treated with agents such as metronidazole and aminoglycosides which lack adequate activity. Practitioners need to gain a better understanding of the *"Streptococcus milleri* group" to aid them in recognizing and treating properly infections with this elusive pathogen.

References

1. **Guthof O:** Über pathogene "vergrunende Streptokokken". Streptokokken-Befunde bei dentogenen Abszessen und Infiltraten im Bereich der Mundhöhle. Zentralblatt für Bakteriologie, Parasitenkunde, Infektionskrankheiten, Hygiene 1956, 166: 553–564.
2. **Colman G, Williams REO:** Taxonomy of some human viridans streptococci. In: Wannamaker LW, Matsen JM (ed): Streptococci and streptococcal diseases: recognition, understanding, and management. Academic Press, New York, 1972, p. 281–299.
3. **Facklam RR:** Physiological differentiation of viridans streptococci. Journal of Clinical Microbiology 1977, 5: 184–201.
4. **Facklam RR:** The major differences in the American and British *Streptococcus* taxonomy schemes with special reference to *Streptococcus milleri.* European Journal of Clinical Microbiology 1984, 3: 91–93.
5. **Coykendall AL, Wesbecher PM, Gustafson KB:** *Streptococcus milleri, Streptococcus constellatus,* and *Streptococcus intermedius* are later synonyms of *Streptococcus anginosus.* International Journal of Systematic Bacteriology 1987, 37: 222–228.
6. **Whiley RA, Hardie JM:** DNA-DNA hybridization studies and phenotypic characteristics of strains within the *Streptococcus milleri* group. Journal of General Microbiology 1989, 135: 2623–2633.
7. **Whiley RA, Beighton D:** Emended descriptions and recognition of *Streptococcus constellatus, Streptococcus intermedius* and *Streptococcus anginosus* as distinct species. International Journal of Systematic Bacteriology 1991, 41: 1–5.
8. **Skerman VBD, McGowan V, Sneath PHA:** Approved lists of bacterial names. International Journal of Systematic Bacteriology 1980, 30: 225–420.
9. **Gallis HA:** Viridans and beta haemolytic (non group A, B, and D) streptococci. In: Mandell GL, Douglas RG, Bennett JE (ed): Principles and practice of infectious diseases. Churchill Livingstone, New York, 1990, p. 1563–1571.
10. **Gossling J:** Occurrence and pathogenicity of the *Streptococcus milleri* group. Reviews of Infectious Diseases 1988, 10: 257–285.
11. **Kambal AM:** Isolation of *Streptococcus milleri* from clinical specimens. Journal of Infection 1987, 14: 217–223.
12. **Ball LC, Parker MT:** The cultural and biochemical characteristics of *Streptococcus milleri* strains isolated from human sources. Journal of Hygiene 1979, 82: 63–78.
13. **Poole PM, Wilson G:** Occurrence and cultural features of *Streptococcus milleri* in various body sites. Journal of Clinical Pathology 1979, 32: 764–768.
14. **Whiley RA, Fraser H, Hardie JM, Beighton D:** Phenotypic differentiation of *Streptococcus intermedius, Streptococcus constellatus* and *Streptococcus anginosus* strains within the *Streptococcus milleri* Group. Journal of Clinical Microbiology 1990, 28: 1497–1501.

15. **LePennec MP, Bernardi-Grassias L:** In-vitro activity of 13 antibiotics against clinical isolates of *Streptococcus milleri.* Journal of Antimicrobial Chemotherapy 1989, 24: 618–619.
16. **Van der Auwera P:** Clinical significance of *Streptococcus milleri.* European Journal of Clinical Microbiology 1985, 4: 386–390.
17. **Shlaes DM, Lerner PI, Wolinsky E, Gopalakrishna KV:** Infections due to Lancefield group F and related streptococci *(Streptococcus milleri, Streptococcus anginosus).* Medicine 1981, 60: 197–207.
18. **Hinnebusch CJ, Nikolai DM, Bruckner DA:** Comparison of API Rapid Strep, Baxter MicroScan Rapid Pos ID panel, BBL Minitek Differential Identification System, IDS RapID STR System and Vitek GPI to conventional biochemical tests for identification of viridans streptococci. American Journal of Clinical Pathology 1991, 96: 459–463.
19. **Ruoff KL:** *Streptococcus anginosus (Streptococcus milleri):* The unrecognized pathogen. Clinical Microbiology Reviews 1988, 1: 102–108.
20. **Williams BL, McCann GF, Schoenknecht FD:** Bacteriology of dental abscesses of endodontic origin. Journal of Clinical Microbiology 1983, 18: 770–774.
21. **Wickremesinghe R, Russell C:** Viridans streptococci associated with periapical dental abscesses. Infection 1976, 4: 196–203.
22. **Murray HW, Gross KC, Masur H, Roberts R:** Serious infections caused by *Streptococcus milleri.* American Journal of Medicine 1978, 64: 759–764.
23. **Parker MT, Ball LC:** Streptococci and aerococci associated with systemic infections in man. Journal of Medical Microbiology 1976, 4: 196–203.
24. **Admon D, Ephros MA, Gavish D, Raz R:** Infection with *Streptococcus milleri.* Journal of Infection 1987, 14: 55–60.
25. **Wallis DE, Venezio FR, Montoya A, Cook FV, Scanlon PJ:** *Streptococcus* MG-*intermedius* endocarditis. Southern Medical Journal 1986, 79: 1313–1314.
26. **Levandowski RA:** *Streptococcus milleri* endocarditis complicated by myocardial abscess. Southern Medical Journal 1985, 78: 892–893.
27. **Akashi K, Ishimaru T, Tsuda Y, Nagafuchi S, Itaya R, Hayashi J, Sawae Y, Kawachi Y, Niho Y:** Purulent pericarditis caused by *Streptococcus milleri.* Archives of Internal Medicine 1988, 148: 2446–2447.
28. **Koepke JA:** Meningitis due to *Streptococcus anginosus* (Lancefield group F). Journal of the American Medical Association 1965, 193: 739–740.
29. **DeLouvois J:** Bacteriologic examination of pus from abscess of central nervous systems. Journal of Clinical Pathology 1980, 33: 66–71.
30. **Ghosh K, Duncan R, Kennedy PG:** Acute spinal epidural abscess caused by *Streptococcus milleri.* Journal of Infection 1988, 16: 303–304.
31. **Gelfand MS, Bakhtian BJ, Simmons BP:** Spinal sepsis due to *Streptococcus milleri:* two cases and review. Reviews of Infectious Diseases 1991, 13: 559–563.
32. **Hatoff D:** Perineal Crohn's disease complicated by pyogenic liver abscess during metronidazole therapy. Gastroenterology 1983, 85: 194–195.
33. **Madden NP, Hart CA:** *Streptococcus milleri* in appendicitis in children. Journal of Pediatric Surgery 1985, 20: 6–7.
34. **Reed TMS, Davidson AI:** *Streptococcus milleri* liver abscess. Lancet 1976, ii: 648–649.
35. **Brasitus TA, Cleri DJ, Szabo K:** *Streptococcus* MG-*intermedius (Streptococcus milleri)* hepatic abscess in two patients with regional enteritis. Southern Medical Journal 1983, 76: 1297–1298.
36. **Gillon JCM, Eykyn SJ, Phillips I:** Microbiology of pyogenic liver abscess. British Medical Journal 1981, 282: 819–821.
37. **Chua D, Reinhart HH, Sobel JD:** Liver abscess caused by *Streptococcus milleri.* Reviews of Infectious Diseases 1989, 11: 197–202.
38. **Gelfand MS, Hodgkiss T, Simmons BP:** Multiple hepatic abscesses caused by *Streptococcus milleri* in association with an intrauterine device. Reviews of Infectious Diseases 1989, 11: 983–987.
39. **Miller SD, Mauff AC, Koornhof HJ:** *Streptococcus milleri* causing infection in man. South African Medical Journal 1983, 63: 684–686.
40. **Cox RA, Chen K, Coykendall AL, Wesbecher P, Herson VC:** Fatal infection in neonates of 26 weeks gestation due to *Streptococcus milleri:* report of two cases. Journal of Clinical Pathology 1987, 40: 190–193.
41. **Highet AS, Warren RE, Staughton RCD, Roberts SOB:** *Streptococcus milleri* causing treatable infection in perineal hidradenitis suppurativa. British Journal of Dermatology 1980, 103: 375–382.
42. **Müller F, Von Graevenitz A, Ferber T:** *Streptococcus milleri* subcutaneous abscesses in drug addicts. Infection 1987, 55: 201.
43. **Houston BD, Crouch ME, Finch RG:** *Streptococcus* MG-*intermedius (Streptococcus milleri)* septic arthritis in a patient with rheumatoid arthritis. Journal of Rheumatology 1980, 7: 89–92.
44. **Lever AML, Owen T, Forsey I:** Pneumoarthropathy in septic arthritis caused by *Streptococcus milleri.* British Journal of Medicine 1982, 285: 24.
45. **Brook MG, Lucas RE, Pain AK:** Clinical features and management of two cases of *Streptococcus milleri* chest infection. Scandinavian Journal of Infectious Diseases 1988, 20: 345–346.
46. **Witt DJ, Craven DE, McCabe WR:** Bacterial infections in adult patients with the acquired immune deficiency syndrome (AIDS) and AIDS-related complex. American Journal of Medicine 1987, 82: 900–906.
47. **Whiley RA, Beighton D, Winstanley TG, Fraser HY, Hardie JM:** *Streptococcus intermedius, Streptococcus constellatus,* and *Streptococcus anginosus* (the *Streptococcus miller* group): association with different body sites and clinical infections. Journal of Clinical Microbiology 1992, 30: 243–244.
48. **Brook I, Walker RI:** Interaction between penicillin, clindamycin, or metronidazole and gentamicin against species of clostridia and anaerobic and facultatively anaerobic gram-positive cocci. Journal of Antimicrobial Chemotherapy 1985, 15: 31–37.
49. **Tillotson GS, Ganguli LA:** Antibiotic susceptibilities of clinical strains of *Streptococcus milleri* and related streptococci. Journal of Antimicrobial Chemotherapy 1984, 14: 557–560.
50. **Bourgalt A, Wilson WR, Washington JA:** Antimicrobial susceptibilities of species of viridans streptococci. Journal of Infectious Diseases 1979, 140: 316–321.
51. **Pulliam LRK, Porschen RK, Hadley WK:** Biochemical properties of CO_2 dependent streptococci. Journal of Clinical Microbiology 1980, 12: 27–31.

52. **Marshall R, Kaufman AK:** Production of deoxyribonuclease, ribonuclease, coagulase, and hemolysins by anaerobic gram-positive cocci. Journal of Clinical Microbiology 1981, 13: 787–788.
53. **Steffen EK, Hentges DJ:** Hydrolytic enzymes of anaerobic bacteria isolated from human infections. Journal of Clinical Microbiology 1981, 14: 153–156.
54. **Arala-Chaves MP, Higerd TB, Porto MT, Munoz J, Goust JM, Fudenberg HH, Loadholt CB:** Evidence for the synthesis and release of strongly immunosuppressive noncytotoxic substances by *Streptococcus intermedius*. Journal of Clinical Investigation 1979, 64: 871–883.
55. **Wilcox MD, Knox KW:** Surface-associated properties of *Streptococcus milleri* group strains and their potential relation to pathogenesis. Journal of Medical Microbiology 1990, 31: 259–270.
56. **Brook I, Walker RI:** The role of encapsulation in the pathogenesis of anaerobic gram-positive cocci. Canadian Journal of Microbiology 1985, 31: 176–180.
57. **Tresadern JC, Farrand RJ, Irving MH:** *Streptococcus milleri* and surgical sepsis. Annals of the Royal College of Surgeons of England 1983, 65: 78–79.
58. **Onderdonk AB, Cisneros R:** Comparison of clindamycin and metronidazole for the treatment of experimental intra-abdominal sepsis produced by *Bacteroides fragilis* and *Streptococcus intermedius*. Current Therapeutic Research, Clinical and Experimental 1985, 38: 893–898.
59. **Phillips I, Warren C, Harrison JM, Sharples P, Ball LC, Parker MT:** Antibiotic susceptibilities of streptococci from mouth and blood of patients treated with penicillin or lincomycin and clindamycin. Journal of Medical Microbiology 1976, 9: 393–404.