Streptococcus intermedia, Streptococcus constellatus, and Streptococcus anginosus (the Streptococcus milleri group): Association with Different Body Sites and Clinical Infections

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The associations of Streptococcus intermedia, S. constellatus, and S. anginosus (the three species of the S. milleri group) with clinical infections and sites of isolation were investigated by using a simple biochemical scheme to identify a collection of 153 clinical isolates. S. intermedia was associated with abscesses of the brain and liver, while both S. anginosus and S. constellatus were isolated from a wider range of sites and infections. S. anginosus strains predominated in both genitourinary and gastrointestinal sources and exhibited a wider range of phenotypes, particularly in the ability to ferment mannnitol and/or raffinose.

Streptococcus intermedia, S. constellatus, and S. anginosus (collectively referred to as the S. milleri group) form part of the normal flora of the mouth, gastrointestinal tract, and genitourinary tract and are often associated with purulent infections (5, 12).

Despite increasing awareness of their clinical significance, the classification, nomenclature, and identification of the S. milleri group has, until recently, remained confused (4), preventing demonstration of clear associations between particular species and specific sites of isolation and disease conditions. However, recent genetic and phenotypic studies in our laboratories have shown that the S. milleri group consists of three distinct species, S. intermedia, S. constellatus, and S. anginosus, that can be differentiated phenotypically from each other and from other viridans group streptococci (1) by a short scheme of biochemical tests (9–11). Consequently, we were able to identify and characterize a large number of these bacteria isolated from a wide variety of clinical sources, and this enabled us to determine associations between types of infection and particular species.

We obtained 153 strains of the S. milleri group from different laboratories in the United Kingdom and abroad. These included 18 strains from head and neck sites; 21 from the central nervous system (CNS); 20 from brain abscesses; 1 from cerebrospinal fluid; 12 from respiratory tracts; 24 from gastrointestinal tracts; 9 from other abdominal or pelvic sites; 44 from genitourinary sources; 19 from skin, soft tissues, and bone; and 4 from blood cultures (unspecified clinical backgrounds).

All strains were tested for production of α-galactosidase, β-galactosidase, α-glucosidase, β-glucosidase, β-N-acetylglactosaminidase, β-N-acetylglucosaminidase, sialidase, and β-D-fucosidase by using 4-methylumbelliferyl-linked fluorogenic substrates in microtitration trays as described previously (10). Acid production from the carbohydrates amygdalin, arbutin, inulin, lactose, mannitol, melibiose, N-acetylglucosamine, sorbitol, and raffinose and tests for hydrolysis of esculin and arginine were performed in microtitration trays by the method of Beighton et al. (2). Hyaluronidase production was tested for by the rapid plate method of Smith and Willett (8). The hemolytic reactions were determined on Columbia agar (GIBCO Europe Ltd., Paisley, Scotland) containing 5% (vol/vol) defibrinated horse blood. Lancefield grouping was performed with the Streptococcal Grouping Kit (UNIPATH Ltd., Basingstoke, Hants, England), in accordance with the manufacturer's instructions, on those strains received without accompanying serological data. Assignment of strains to either S. anginosus, S. constellatus, or S. intermedia was done on the basis of the identification scheme of Whiley et al. (10).

Table 1 shows the numbers of strains of the three species identified in each of the broad clinical categories. The results demonstrate a marked association of S. intermedia with infections involving the CNS, although this species, previously shown to be the species of the S. milleri group most commonly isolated from liver abscesses and dental plaque (10), exhibited an otherwise relatively limited clinical distribution, being identified infrequently from respiratory and gastrointestinal tracts and not at all from genitourinary sources. Conversely, S. anginosus was noticeably the most frequently identified of the three species from gastrointestinal tracts, as well as from genitourinary sources, and was identified commonly from most of the other broad clinical categories, except for the CNS. S. constellatus was also frequently identified among strains from most of the clinical categories, except for the CNS, but did not predominate in any particular broad clinical category, with the possible exception of the respiratory tract.

S. intermedia and S. constellatus strains exhibited the same relatively homogeneous set of biochemical test reactions as we have reported previously (10). However, we found a greater diversity of fermentation reactions among the strains of S. anginosus studied here than we had previously found. All strains of the S. milleri group, except one, which was identified as an S. intermedia strain, that fermented either raffinose or mannnitol or both were identified as S. anginosus strains (54 strains fermented both sugars, 1 fermented mannnitol only, and 6 fermented raffinose only). The distribution of these broadly fermentative S. anginosus

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strains was of interest, as 35 (88%) of 40 strains from genitourinary sources fermented one or both sugars, as did 10 (53%) of 19 strains from gastrointestinal tracts, 2 (50%) of 4 strains from other abdominal and pelvic sites, and 7 (70%) of 10 strains from skin, soft tissue, or bone. This contrasts with the absence of these broadly fermentative strains among S. anginosus isolates from the head and neck, CNS, and respiratory tract. Within the gastrointestinal tract, these broadly fermentative strains formed the majority of S. anginosus strains, i.e., 9 (64%) of 14 strains from the rectal mucosa of patients with colitis and 2 (100%) of 2 strains from perianal sources, but were absent among S. anginosus strains from the upper gastrointestinal tract.

The biochemical characteristics of the three species did not differ markedly from the data previously reported in our preliminary study of 157 strains (including 58 from normal dental plaque) (10). The increased proportion of S. anginosus strains which produced β-galactosidase and fermented mannitol and/or raffinose was largely due to the inclusion in this study of 40 isolates from genitourinary sources.

Earlier investigations into the associations between clinical distribution and particular species or subgroups within the S. milleri group have been hampered by the inability of investigators to recognize these three species because of frequent use of characteristics which are unreliable for identification of S. intermedius, S. anginosus, and S. constellatus (10), namely, possession of a Lancefield group antigen, the type of hemolysis produced, and the ability to ferment lactose (3, 6, 7). With this study, the increase in the total number of strains in the S. milleri group examined from clinical sources since our previous report (10) has more clearly demonstrated associations of these species with particular types of clinical conditions and provides a stimulating basis for future investigations into the possible routes of entry of these bacteria, their ability to colonize particular anatomical sites, and potential virulence factors.

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REFERENCES