

Streptococcus milleri* Group (*Streptococcus anginosus*): Recovery from Intra-abdominal and Soft Tissue Sites

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ABSTRACT

One hundred thirty-three *Streptococcus milleri* group (*S. anginosus*) isolates were recovered from 487 surgical patients. The streptococci were recovered from 33 percent of intra-abdominal infection cultures (84/257), 22 percent of samples from penetrating visceral trauma (19/86), 52 percent of perirectal abscess specimens (13/25), 13 percent of nonpuerperal breast abscess cultures (8/60), and 15 percent of diabetic foot lesions (9/59). Ninety-eight percent of the *S. milleri* (131/133) were recovered as companion flora in polymicrobial cultures. The organisms were highly susceptible to the beta-lactam antibiotics. The precise pathogenic role of the *S. milleri* group (*S. anginosus*) is unknown. However, intrinsic virulence may be expressed in patients with severe infection or other predisposing factors.

Introduction

The designation *Streptococcus milleri* refers to a phenotypically heterogeneous group of organisms which have been proposed to belong to the single species *Streptococcus anginosus*. These organisms have been implicated in a multitude

of infections ranging from periodontal disease to intra-abdominal abscess.^{4,10,11,16} In the clinical laboratory, however, these organisms are often viewed generically as viridan streptococci and given little clinical significance. Selective case presentations suggest that the *Streptococcus milleri* group is associated with pyogenic infection of internal organs and may be refractory to antimicrobial therapy.^{21,31} Pyogenic intra-abdominal disease associated with *Streptococcus milleri* group has often been reported to occur follow-

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ing surgery.²⁰ While numerous clinical reports have appeared over the last 80 years implicating these organisms in human disease, to date no reports have documented the routine recovery of the *Streptococcus milleri* group from selective surgical cultures. This report studies the recovery of *Streptococcus milleri* (*Streptococcus anginosus*) from intra-abdominal and other soft tissue sites.

Materials and Methods

SPECIMEN COLLECTION AND MICROBIOLOGY

Over a 5 year period (1984–1989), routine cultures were submitted to the Surgical Microbiology Research Laboratory from a total of 487 patients on general, vascular, and trauma surgical services. All patients were participants in clinical studies which required informed consent as per institutional guidelines. Specimens submitted for culture were from intra-abdominal infections (N = 257), intraoperative peritoneal samples from penetrating trauma to the bowel (N = 86), aspirations from perirectal abscesses (N = 25), acute and chronic nonpuerperal breast abscess samples obtained by needle aspiration (N = 60), and tissue debridement from diabetic foot infections (N = 59).

All samples were transported in closed containers (fluid: Porta-a-Cul vial,* tissue: 2-ml volume vial containing 0.5 ml of Wilkins-Chalgren broth†) within 30 minutes of collection to the Surgical Microbiology Research Laboratory. The specimens were processed in an anaerobic chamber containing 80 percent nitrogen, 10 percent carbon dioxide, and 10 percent hydrogen. Tissue samples were homogenized in one-ml tissue grinders

containing Wilkins-Chalgren broth. Fluid and tissue homogenate were plated upon the following media: trypticase soy blood agar;* Columbia colistin-nalidixic blood agar, MacConkeys agar,† CDC anaerobic blood agar, phenylethyl alcohol anaerobic blood agar, and kanamycin-vancomycin anaerobic blood agar.‡ A Gram stain was made at the time of initial culture. In addition, a thioglycollate broth (supplemented with vitamin K and hemin) and chopped meat carbohydrate were inoculated and incubated at 35°C.

All plates were incubated at 35°C. Aerobic plates were inspected at 24 and 48 hours, while anaerobic plates were visually inspected at 48 and 120 hours. Aerobic and anaerobic isolates were characterized by standard methods.^{12,14} Streptococcal isolates were identified by the Rapid Strep system.§ The inoculum for the Rapid Strep system was prepared from trypticase soy agar as described by Facklam.⁷ The Rapid Strep strips were incubated according to manufacturer's instructions. Antimicrobial susceptibilities were performed using the micro-broth dilution technique.^{22,23}

Results

One hundred thirty-three *Streptococcus milleri* group isolates were obtained from 487 surgical isolates. Overall, 27 percent of the cultures yielded *S. milleri* isolates. Ninety-eight percent of the recoveries were from mixed microbial populations involving both aerobic and anaerobic isolates. Only two of the 133 isolates were from pure cultures involving perforated gastric ulcers.

In table I are shown the *S. milleri* recovery from the clinical specimens.

* BBC Microbiology Systems, Cockeysville, MD.

† Difco, Detroit, MI.

‡ Remel, Lenexa, KS.

§ Analytab Products, Plainview, NY.

TABLE I
Recovery of *Streptococcus milleri* Group from Surgical Isolates

Study Groups	# Patients	Recovery ^a	Percent Incidence ^b	Pure Culture	Mixed
Intra-abdominal	257	84	33	2	82
Perirectal	25	13	52		13
Breast abscess	60	8	13		8
Penetrating trauma	86	19	22		19
Diabetic foot	59	9	15		9
Total	487	133	27	2	131

^a Number of patients from which *S. milleri* group (*S. anginosus*) were recovered.

^b Percent recovered per study group.

Thirty-three percent of the intra-abdominal cultures were positive for *S. milleri* group. In acute penetrating abdominal wounds, *S. milleri* were recovered from 19 of 86 peritoneal fluid samples (22 percent). The organisms were recovered from 52 percent of the perirectal abscess cultures (13/25). The lowest recovery was from non-puerperal breast abscesses and diabetic foot lesions, 13 percent (8/60) and 15 percent (9/59), respectively. In table II are documented the *S. milleri* recovered in patients with intra-abdominal infection. Twenty-nine percent (29 percent) of the *S. milleri* group isolates were recovered from patients with intra-abdominal abscesses (25/84). The next most frequent diagnosis was perforated appendix (15/84) and perforated colon/diverticula, (18/84). Eleven isolates were recovered from perforated ulcers of the stomach or duodenum, while four isolates were recovered from patients with perforations of the ileum. *Streptococcus milleri* group isolates were recovered from seven patients with ischemic disease (strangulated ileum: four, mesenteric infarction: three). Four isolates were recovered from polymicrobial liver abscess cultures.

The *S. milleri* group isolates recovered from intra-abdominal and soft tissue infections demonstrated excellent sus-

ceptibility to penicillin, ampicillin, ampicillin/sulbactam, cephalothin, erythromycin, clindamycin, vancomycin, and chlordamphenicol (all isolates susceptible). Eighteen percent of the isolates were resistant to tetracycline (15/84) while eight percent were resistant to metronidazole (7/84).

Discussion

The name *Streptococcus milleri* has no official standing in the microbial tax-

TABLE II
Streptococcus milleri Group Recovery
from Intra-abdominal Infection

Diagnosis	Recovery ^a
Perforated duodenal ulcer	6
Perforated gastric ulcer	5
Perforated small bowel	4
Perforated appendix	18
Perforated colon/diverticula	15
Intra-abdominal abscess	25
Strangulated ileum	4
Cholangitis	2
Liver abscess	4
Mesenteric infarction	3
Total	84

^a Number of patients positive for *Streptococcus milleri* (*S. anginosus*) recovery.

onomy, but it has been used to describe a group of organisms that have been viewed as significant agents of purulent soft tissue infections.²⁴ This nomenclature is confusing since the organisms which fit within this broad classification are phenotypically heterogenous and may be beta-hemolytic or non-hemolytic on blood agar. Alpha hemolytic variants have been described in the literature. However, upon closer examination, many of these isolates have been shown to be beta-hemolytic.^{8,24,26} Presently, *Streptococcus anginosus*, *Streptococcus constellatus*, and *Streptococcus intermedius* are included under the unofficial *Streptococcus milleri* designation. Recent studies by Coykendall and colleagues suggest that the name *Streptococcus anginosus* should encompass all previous nomenclature.^{5,6} However, this designation is somewhat controversial since British investigators have recently shown that hemolytic activity, Lancefield grouping reactors and lactose fermentation, for all practical purpose are of little value in the accurate characterization of these strains.³³

This confusion over nomenclature and identification often extends into the clinical laboratory and could result in the organisms being overlooked or dismissed as a culture contaminant. The ecological distribution of *S. milleri* includes the upper respiratory tract, the proximal and distal regions of the alimentary tract, and the female urogenital tract.^{9,19} Reports of recovery of the *S. milleri* group from clinical samples often follows some traumatic event to the normal mucosal surfaces.^{28,34} Furthermore, the organism has been recovered from purulent soft tissue infections and may be isolated in pure or mixed culture.^{15,29,34}

In the present study, *S. milleri* group isolates were recovered from 33 percent of patients cultured for intra-abdominal infection. The precise role of this organism in intra-abdominal disease is

obscure, however, since its recovery was as a companion to a complex aerobic and anaerobic micro flora (mean microbial recovery from intra-abdominal culture was 15 isolates: five aerobes, 10 anaerobes). *Streptococcus anginosus* was recovered in pure culture from only two patients, both with a perforated gastric ulcer. The ubiquitous ecological position of these organisms in the normal alimentary tract makes it difficult to determine their relative pathogenicity in mixed intra-abdominal infections. Isolates of the *S. milleri* group were recovered as companion flora contaminating peritoneal fluid in 22 percent of patients with penetrating visceral trauma cultured within four hours after bowel injury (table I). Presently, there is little evidence suggesting that a synergistic interaction occurs between these organisms and other facultative or obligate microbial populations.³ In Europe, the *S. milleri* group is considered to be potentially significant pathogens which may be attributed to the emergence of metronidazole resistant strains in patients with intra-abdominal infections.

An empirical regimen of aminoglycoside/metronidazole, while likely to eliminate most facultative gram negative and obligate anaerobic populations, may promote the emergence of resistant *S. milleri* group in culture. Alternatively, the combination of aminoglycoside and clindamycin should provide adequate coverage (owing to *S. milleri* susceptibility to clindamycin). Nevertheless, our current knowledge of bacterial interactions which occur in polymicrobial disease is limited to only a few facultative/obligate anaerobic scenarios. Therefore, the potential importance of these organisms in intra-abdominal disease should not be dismissed.

The high frequency of *S. milleri* group recovery from perirectal disease (52 percent, 13/25) is consistent with the microbial ecology of these organisms. Perirect-

tal abscesses are often associated with a communicating fistula leading to the colonic crypts which functions to seed the distal submucosal tissues. Their relative clinical significance, however, is difficult to measure since these streptococcal isolates, like their intra-abdominal cohorts, were only a component of a luxurious polymicrobial flora which ranged from 10 to 23 isolates per patient.

An interesting finding is the recovery of *S. milleri* from non-puerperal breast abscesses and diabetic foot lesions. As in intra-abdominal disease, the streptococci were associated with a polymicrobial aerobic/anaerobic flora. The exact etiology of non-puerperal breast infections is unknown. However, analysis of microbial populations recovered in this disease suggests that oral manipulation or traumatic gynecologic procedures may play a role in nonlactating breast infections.³² Because the ecological habitat of the *S. milleri* group is conducive to an oral/genital source of infection, the recovery of this organism from purulent breast discharge is not unexpected. While a number of published reports have described *S. milleri* group recovery from skin and subcutaneous sites, few if any studies have reported on the incidence of *S. milleri* group in diabetic foot infections.^{2,13,25} While our experience suggests that the incidence of *S. milleri* group recovery in the diabetic foot patient is less than in intra-abdominal disease, the characteristic association with a polymicrobial population is similar to our penetrating trauma and intra-abdominal data.

The microbial pathogenicity of the *S. milleri* (*S. anginosus*) is poorly understood. Because the organisms were infrequently recovered in pure culture (two percent), the data suggest an intrinsically low potential for producing virulent disease. However, some strains have been shown to produce a polysac-

charide capsule and cytolytic enzymes, including collagenase, hyaluronidase, gelatinase, DNase, lecithinase, and mucopolysaccharide degrading activity, which are common to other known microbial pathogens.^{3,17,18,27,30} In the present study, *S. milleri* was frequently recovered from intra-abdominal and soft tissue infection sites as a component of a complex polymicrobial population. The isolation of *S. milleri* group from intra-abdominal and perirectal culture may in part reflect the organism's ecological position in the human alimentary tract. While the pathogenic role of the *S. milleri* group is at present speculative, because of the evolving interest in this group of organisms, one cannot dismiss the importance of tissue ischemia, microbial interactions (synergism) or previous antimicrobial therapy as factors which may potentiate their clinical significance.

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