Streptococcus milleri causing infection in man

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Summary

We describe the microbiological and morphological characteristics of 151 strains of *Streptococcus milleri* isolated during the course of routine bacteriological investigations. Although these strains formed a fairly heterogeneous group, several constant features were identified which typify the species.

Strept. milleri emerged as a major cause of pyogenic infection, clinical disease being characterized by localized collections of pus in almost every organ system. Bacteraemia due to *Strept. milleri* was a significant indicator of the presence of an occult abscess. Endocarditis was rare.

The penicillins or erythromycin remain the drugs of choice for treating infections caused by this organism.

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The viridans streptococci have only recently been assigned to five well-defined species[1,2] based on a system of key biochemical reactions.[3,4] One species, *Streptococcus milleri,* has emerged as an important pathogen in man,[5] and is now recognized as a major cause of pyogenic infection, bacteraemia and occasionally endocarditis.[2,6,7]

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At the Central Public Health Laboratories in London *Strept. milleri* was found to be the species of viridans streptococcus most frequently associated with pyogenic infections (68%), in contrast to its low incidence (8%) in infective endocarditis.[8] *Strept. milleri* has most frequently been isolated from purulent lesions in the liver, central nervous system, lungs, appendix, pleural cavity and pelvis, as well as from peritoneal fluid in cases of peritonitis.

A total of 151 strains of *Strept. milleri* initially isolated during the course of routine bacteriological investigations were examined culturally, antigenically and biochemically in our laboratories. We report this large series to describe further the microbiological and morphological characteristics of this important organism.

Materials and methods

Source of material. Isolates examined in this study comprised significant or pure cultures of *Strept. viridans* obtained from the bloodstream, collections of pus in intra-abdominal and intrathoracic viscera, peritoneal and pleural cavities, the central nervous system, subcutaneous tissue and infected bone (Table I). These cultures were obtained from our central and peripheral laboratories.

Bacteriological methods. All cultures were confirmed to be streptococci according to the criteria of Cowan and Steele.[9] Each isolate was examined for colonial form, odour and haemolysis on horse blood agar after overnight aerobic incubation at 37°C. Growth was compared aerobically, anaerobically and in the presence of 10% carbon dioxide. Individual isolates were examined for growth on 40% bile agar and for hydrolysis of aesculin.

Biochemical characteristics. Species identification was made according to the scheme of Watkins *et al.*[4]

Lancefield grouping. Latex particles coated with specific antisera to groups A, B, C, D, F and G (Streptex; Wellcome) were used to agglutinate overnight cultures in serum broth or enzyme-treated cultures from blood agar plates.

Clinical information. The attending physician was required to complete a questionnaire on the clinical status of each patient.

TABLE I. DISTRIBUTION OF PURULENT LESIONS CAUSED BY *STREPT. MILLERI*

Site and lesion	No. of isolates	Site and lesion	No. of isolates
Head and neck	**7**	**Pelvis**	**8**
Brain abscess	**3**	**Pelvic abscess**	**3**
Subdural empyema	**1**	**Endometritis**	**1**
Thyroid abscess	**1**	**Chronic vaginitis**	**2**
Chronic sinusitis	**2**	**Osteomyelitis**	**12**
Thorax	**12**	**Wound sepsis**	**15**
Purulent pneumonia	**3**	**Abscess**	**25**
Empyema	**7**	**Bloodstream**	**11**
Lung abscess	**1**	**Skin, subcutaneous**	
Traumatic pericarditis	**1**	**sepsis**	**24**
Abdomen	**18**	**Unknown**	**21**
Peritonitis	**5**		
Subphrenic abscess	**2**		
Appendix abscess	**11**		

Information requested included details of presenting symptoms and signs, relevant laboratory investigations, underlying disease or predisposing factors and therapy.

Results

Microbiological characteristics. *Strept. milleri* was found to be a minute colony-forming organism with a marked preference for, or dependence upon, the presence of added CO_2. Most cultures were noted to have a pleasant, distinctive odour. Thirty-one strains (21%) of *Strept. milleri* were α-haemolytic, 76 strains (50%) were ß-haemolytic and 44 strains (29%) were non-haemolytic. A Lancefield group antigen was detected mainly in the ß-haemolytic strains. There was an overall preponderance of strains belonging to Lancefield group F (70%), with fewer strains belonging to groups G (8%), C (3%) and A (1%). Eighteen per cent of all isolates proved ungroupable. In all groups the majority of strains hydrolysed arginine (150 out of 151) and gave a positive Voges-Proskauer (VP) reaction (145 out of 151). Aesculin was generally hydrolysed by all strains except those which belonged to group F (38% positive). Growth was generally inhibited by 40% bile agar and the production of peroxide was rare (Table II).

Clinical characteristics. Clinical details were unavailable for 27 of the 151 patients (18%). Of the remaining 124 patients 60 (48%) had internal collections of pus, 12 (10%) had osteomyelitis, 38 (31%) had skin or subcutaneous abscesses, 8 (6%) had febrile bacteraemia and 6 (5%) had proven infective endocarditis. Purulent lesions were widespread throughout the body (Table I).

Discussion

The 151 strains of streptococci which we have designated as *Strept. milleri* appear to form a large and fairly heterogeneous group. Constant within this group, however, are several features which serve to typify the species. These include a marked preference for, or dependence upon, the presence of CO_2, a characteristic honey-like odour, inhibition of growth by 40% bile agar, hydrolysis of arginine and aesculin and a positive VP reaction.

We believe that these easily determined characteristics are sufficiently distinctive for the preliminary identification of most strains of *Strept. milleri* by routine diagnostic laboratories. This should result in a better appreciation of the pathological significance of this important organism. Clinical infections due to *Strept. milleri* were characterized by the presence of localized pus in almost every organ system. This may be related to the widespread distribution of the organism on the body's surface,[5,10] including the mouth, throat, gastro-intestinal tract and vagina. This suggests that infection with this organism may arise by local invasion of *Strept. milleri* from an area in which it is normally found. It may also explain our findings of a very high incidence of subcutaneous sepsis caused by this organism following human bites, a feature not previously described.

Abdominal lesions were caused mainly by ß-haemolytic strains and a particular association was noted between appendix abscesses and isolates belonging to group F, a finding previously suggested by Poole and Wilson.[11] Parker and Ball[5] have suggested an association between purulent abdominal lesions and abdominal injury or bowel disease; this may explain the large number of cases of postoperative abdominal wound sepsis with or without peritonitis which we found in the present study. Bacteraemia and endocarditis were uncommon and were caused mainly by α-haemolytic strains. These observations are in accordance with the descriptions of both British[8] and American[3] workers.

Assessment of the clinical features of infection with *Strept. milleri* was less complete than we would have liked. This was largely due to the paucity of information submitted with specimens and the very poor response on the part of clinical staff to our questionnaire. We nevertheless believe that this study highlights both the microbiological characteristics of this bacterium and the role it plays in the pathogenesis of pyogenic infections of man.

No study has been done to establish the drug of choice for treatment of infections caused by *Strept. milleri*. We are presently investigating the antimicrobial susceptibility of the organism to identify more clearly which antimicrobial agents are most effective. Until these results become available the penicillins or erythromycin remain the favoured drugs for treating sepsis caused by this organism.

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TABLE II. BIOCHEMICAL CHARACTERISTICS OF 151 STRAINS OF *STREPT. MILLERI*

	Lancefield group				
	A	C	F	G	Not groupable
No. of isolates	1	5	106	12	27
Growth on 40% bile	0	0	5	0	0
Fermentation					
Pyruvate	0	0	0	0	0
Arabinose	0	0	0	0	0
Mannitol	0	0	1	0	0
Raffinose	0	1	1	0	0
Sorbitol	0	0	1	0	0
Hydrolysis					
Starch	0	0	0	0	0
Arginine	1	5	105	12	27
Aesculin	1	5	40	10	15
Voges-Proskauer test	1	5	103	12	24
Production of H_2O_2	0	0	0	0	0
Synthesis of					
Dextran	0	0	1	0	0
Laevan	0	0	0	0	0
Gelatin liquefaction	0	0	0	0	0

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