TABLE 173-1 CLASSIFICATION OF STREPTOCOCCI

Lancefield Group	Representative Species	Hemolytic Pattern	Typical Infections
A	*S. pyogenes*	β	Pharyngitis, impetigo, cellulitis, scarlet fever
B	*S. agalactiae*	β	Neonatal sepsis and meningitis, puerperal infection, urinary tract infection, diabetic ulcer infection, endocarditis
C, G	*S. dysgalactiae* subsp. *equisimilis*	β	Cellulitis, bacteremia, endocarditis
D	Enterococci[a]: *E. faecalis, E. faecium*	Usually nonhemolytic	Urinary tract infection, nosocomial bacteremia, endocarditis
	Nonenterococci: *S. gallolyticus* (formerly *S. bovis*)	Usually nonhemolytic	Bacteremia, endocarditis
Variable or nongroupable	Viridans streptococci: *S. sanguis, S. mitis*	α	Endocarditis, dental abscess, brain abscess
	Intermedius or *milleri* group: *S. intermedius, S. anginosus, S. constellatus*	Variable	Brain abscess, visceral abscess
	Anaerobic streptococci[b]: *Peptostreptococcus magnus*	Usually nonhemolytic	Sinusitis, pneumonia, empyema, brain abscess, liver abscess

[a]See Chap. 174. [b]See Chap. 201.

Worldwide, GAS infections and their postinfectious sequelae (primarily ARF and rheumatic heart disease) account for an estimated 500,000 deaths per year. Although data are incomplete, the incidence of all forms of GAS infection and that of rheumatic heart disease are thought to be tenfold higher in resource-limited countries than in developed countries (Fig. 173-1).

PATHOGENESIS

GAS elaborates a number of cell-surface components and extracellular products important in both the pathogenesis of infection and the human immune response. The cell wall contains a carbohydrate antigen that may be released by acid treatment. The reaction of such acid extracts with group A–specific antiserum is the basis for definitive identification of a streptococcal strain as *S. pyogenes*. The major surface protein of GAS is M protein, which occurs in more than 100 antigenically distinct types and is the basis for the serotyping of strains with specific antisera. The M protein molecules are fibrillar structures anchored in the cell wall of the organism that extend as hairlike projections away from the cell surface. The amino acid sequence of the distal or amino-terminal portion of the M protein molecule is quite variable, accounting for the antigenic variation of the different M types, while more proximal regions of the protein are relatively conserved. A newer technique for assignment of M type to GAS isolates uses the polymerase chain reaction to amplify the variable region of the *emm* gene, which encodes M protein. DNA sequence analysis of the amplified gene segment can be compared with an extensive database (developed at the Centers for Disease Control and Prevention [CDC]) for assignment of *emm* type. This method eliminates the need for typing sera, which are available in only a few reference laboratories. The presence of M protein on a GAS isolate correlates with its capacity to resist phagocytic killing in fresh human blood. This phenomenon appears to be due, at least in part, to the binding of plasma fibrinogen to M protein molecules on the streptococcal surface, which interferes with complement activation and deposition of opsonic complement fragments on the bacterial cell. This resistance to phagocytosis may be overcome by M protein–specific antibodies; thus individuals with antibodies to a given M type acquired as a result of prior infection are protected against subsequent infection with organisms of the same M type but not against that with different M types.

GAS also elaborates, to varying degrees, a polysaccharide capsule composed of hyaluronic acid. The production of large amounts of capsule by certain strains imparts a characteristic mucoid appearance to the colonies. The capsular polysaccharide plays an important role in protecting GAS from ingestion and killing by phagocytes. In contrast to M protein, the hyaluronic acid capsule is a weak immunogen, and antibodies to hyaluronate have not been shown to be important in protective immunity. The presumed explanation is the apparent structural identity between streptococcal hyaluronic acid and the hyaluronic

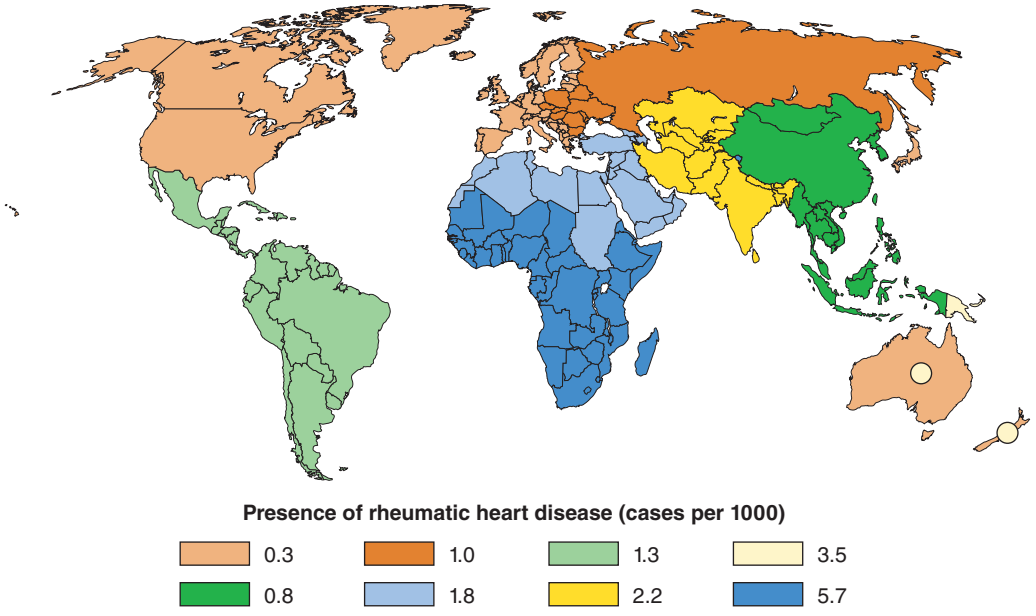

FIGURE 173-1 Prevalence of rheumatic heart disease in children 5–14 years old. The *circles* within Australia and New Zealand represent indigenous populations (and also Pacific Islanders in New Zealand). *(From JR Carapetis et al: Lancet Infect Dis 5:685, 2005, with permission.)*