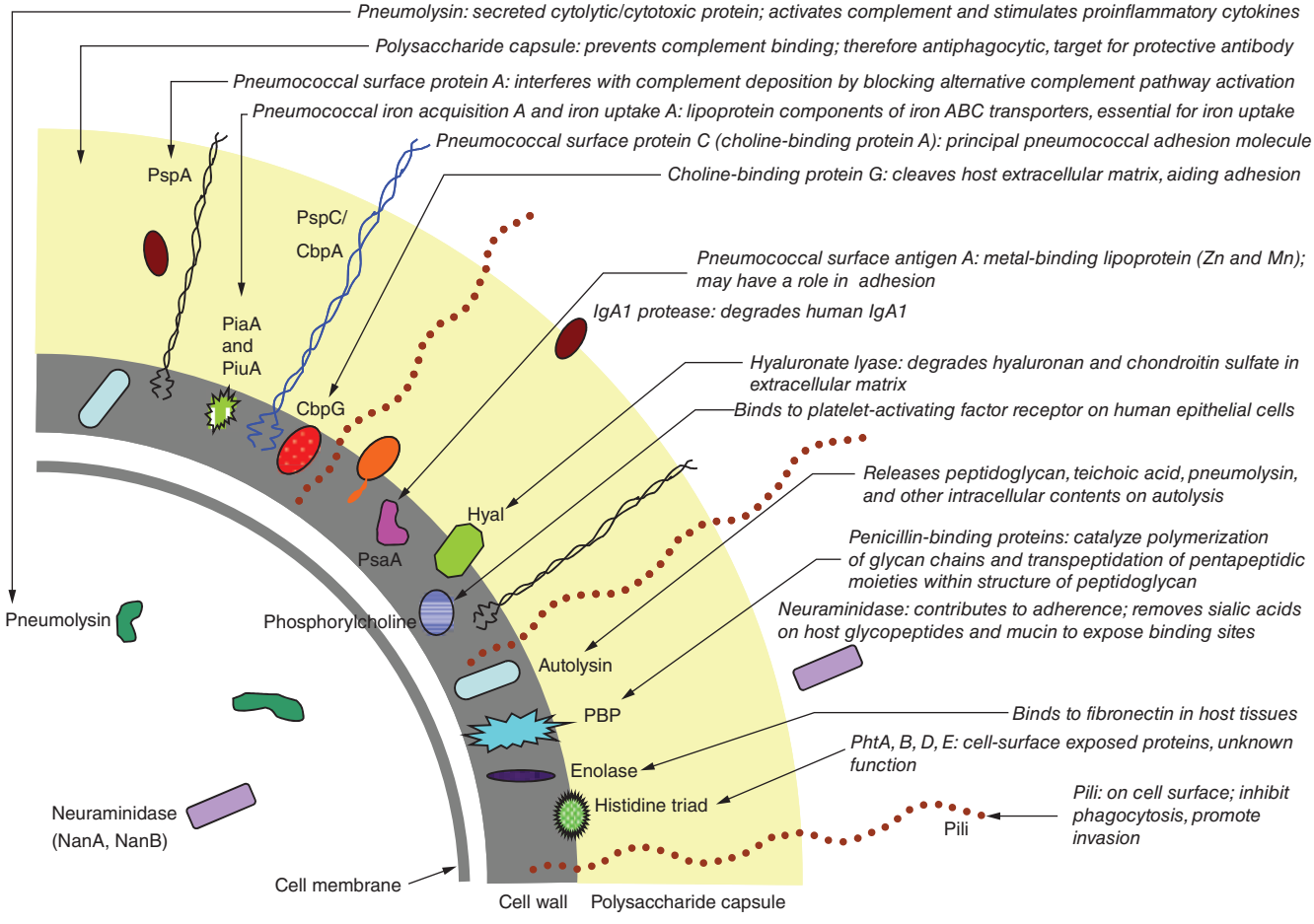

FIGURE 171-2 **Schematic diagram of the pneumococcal cell surface, with key antigens and their roles highlighted.**

important determinant of pneumococcal virulence. Unencapsulated variants tend not to cause invasive disease.

Virulence Factors Within the cytoplasm, cell membrane, and cell wall, many molecules that may play a role in pneumococcal pathogenesis and virulence have been identified (Fig. 171-2). These proteins are often involved in direct interactions with host tissues or in concealment of the bacterial surface from host defense mechanisms. Pneumolysin is a secreted cytotoxin thought to result in cytolysis of cells and tissues, and LytA enhances pathogenesis. A number of cell wall proteins interfere with the complement pathway, thus inhibiting complement deposition and preventing lysis and/or opsonophagocytosis. The pneumococcal H inhibitor (Hic) impedes the formation of C3 convertase, while pneumococcal surface protein C (PspC), also known as choline-binding protein A (CbpA), binds factor H and is thought to accelerate the breakdown of C3. PspA and CbpA inhibit the deposition of or degrade C3b. The numerous pneumococcal proteins thought to be involved in adhesion include the ubiquitous surface-anchored sialidase (neuraminidase) NanA, which cleaves sialic acid on host cells and proteins, and pneumococcal surface adhesin A (PsaA). Pili recently recognized by electron microscopy also may play an important role in binding to cells. Some of the antigens mentioned above are potential vaccine candidates (see "Prevention," below).

Although the capsule surrounding the cell wall of *S. pneumoniae* is the basis for categorization by serotype, the behavior and pathogenic potential of a serotype may also be related to the genetic origin of the strain. Molecular typing is therefore of considerable interest. Initially, techniques such as pulsed-field gel electrophoresis were used to determine genetic relatedness; such techniques have been superseded by sequencing of housekeeping genes to define a clone (multilocus sequence typing, MLST). For *S. pneumoniae*, alleles at each of the loci *aroE*, *gdh*, *gki*, *recP*, *spi*, *xpt*, and *ddl* are sequenced and compared with all of the known alleles at that locus. Sequences identical to a known allele are assigned the same allele number, whereas those differing from any known allele—even at a single nucleotide site—are assigned new numbers. Software for assignment of alleles at each locus is available on the pneumococcal MLST website (*spneumoniae.mlst.net*), and the allelic profile of each isolate and its consequent sequence type are generated. With the advent of high-throughput and relatively inexpensive sequencing techniques, whole-genome sequencing will soon supersede MLST.

EPIDEMIOLOGY

Pneumococcal infections remain a significant global cause of morbidity and death, particularly among children and the elderly. Rapid and dramatic changes in the epidemiology of this disease during the past decade in several developed countries followed the licensure and routine childhood administration of pneumococcal polysaccharide–protein conjugate vaccine (PCV). With PCV introduction in developing and middle-income countries, additional profound changes in pneumococcal ecology and disease epidemiology are likely. The disease burden and serotype distribution in the PCV era may be different than expected because of concomitant secular trends in pneumococcal disease, the impact of antibiotic use on pneumococcal strain ecology, and surveillance system attributes that can themselves affect analysis of epidemiologic features.

Serotype Distribution Not all pneumococcal serotypes are equally likely to cause disease; serotype distribution varies by age, disease syndrome, and geography. Geographic differences may be driven by variation in the burden of disease rather than by true serotype distribution differences. Most data on serotype distribution are related to pediatric invasive pneumococcal disease (IPD, defined as infection of a normally sterile site); much less information on global distribution is available for disease in adults. Among children <5 years of age, five to seven serotypes cause >60% of IPD cases in most parts of the world, seven serotypes (1, 5, 6A, 6B, 14, 19F, and 23F) account for ~60% of cases in all areas of the world, but in any given region these