antimicrobial use; (2) decrease the development of resistance within patients and populations; (3) reduce the incidence of adverse effects; and (4) control costs.

Infections caused by resistant pathogens result in significant morbidity and mortality as well as increased health care costs. Antimicrobial stewardship programs are typically multidisciplinary and often include infectious disease physicians, clinical pharmacists (usually with special training in infectious disease), clinical microbiologists, information systems specialists, infection prevention and control practitioners, and epidemiologists. These teams employ a variety of approaches to achieving the program's goals.

Established strategies of antimicrobial stewardship programs include (1) prospective audit of antimicrobial use, with intervention and feedback; (2) formulary restriction; and (3) preauthorization. *Prospective audit and feedback* are usually undertaken by an infectious disease physician or a pharmacist. In this process, orders for broad-spectrum antimicrobials (e.g., carbapenems) or high-impact agents (e.g., linezolid, daptomycin) are reviewed on a regular basis for appropriateness. In circumstances in which an antimicrobial is used in the absence of an appropriate indication, the stewardship program team intervenes and recommends an alternative to the primary team caring for the patient. This process has been successful in several quasi-experimental studies, resulting in declines in use of broad-spectrum drugs and decreases in adverse events, such as *C. difficile* infection. *Formulary restriction* is the inclusion of a limited set of antimicrobial agents in a hospital formulary for the purpose of limiting indiscriminant use of antimicrobials in the absence of demonstrated benefit. Such restriction coincidentally serves to reduce costs. *Preauthorization* is the practice of requiring clinicians to obtain approval before using selected antimicrobials. Approval may be provided electronically with sophisticated Computerized Provider Order Entry (CPOE) software, after specific criteria for use are met, or after communication with an infectious disease specialist as designated by the stewardship program. These strategies have led to a decrease in *C. difficile* infections and to improvements in drug susceptibility patterns.

Additional strategies used in specific health-care settings are guidelines and pathways, dose optimization, parenteral-to-oral conversion, and de-escalation of therapy. Antimicrobial stewardship is an evolving area and an increasingly active area of research aimed at identifying the best practices. The IDSA, in collaboration with several other professional organizations, has published guidelines for developing institutional antimicrobial stewardship programs (*www.idsociety.org/Antimicrobial_Agents/*).

SECTION 5 DISEASES CAUSED BY GRAM-POSITIVE BACTERIA

171 Pneumococcal Infections

David Goldblatt, Katherine L. O'Brien

In the late nineteenth century, pairs of micrococci were first recognized in the blood of rabbits injected with human saliva by both Louis Pasteur, working in France, and George Sternberg, an American army physician. The important role of these micrococci in human disease was not appreciated at that time. By 1886, when the organism was designated "pneumokokkus" and *Diplococcus pneumoniae*, the pneumococcus had been isolated by many independent investigators, and its role in the etiology of pneumonia was well known. In the 1930s, pneumonia was the third leading cause of death in the United States (after heart disease and cancer) and was responsible for ~7% of all deaths both in the United States and in Europe. While pneumonia was caused by a host of pathogens, lobar pneumonia—a pattern more likely to be caused by the pneumococcus—accounted for approximately one-half of all pneumonia deaths in the United States in 1929. In 1974, the organism was reclassified as *Streptococcus pneumoniae*.

MICROBIOLOGY

Etiologic Agent Pneumococci are spherical gram-positive bacteria of the genus *Streptococcus*. Within this genus, cell division occurs along a single axis, and bacteria grow in chains or pairs—hence the name *Streptococcus*, from the Greek *streptos*, meaning "twisted," and *kokkos*, meaning "berry." At least 22 streptococcal species are recognized and are divided further into groups based on their hemolytic properties. *S. pneumoniae* belongs to the α-hemolytic group that characteristically produces a greenish color on blood agar because of the reduction of iron in hemoglobin (Fig. 171-1). The bacteria are fastidious and grow best in 5% CO_2 but require a source of catalase (e.g., blood) for growth on agar plates, where they develop mucoid (smooth/shiny) colonies. Pneumococci without a capsule produce colonies with a rough surface. Unlike that of other α-hemolytic streptococci, their growth is inhibited in the presence of optochin (ethylhydrocupreine hydrochloride), and they are bile soluble.

In common with other gram-positive bacteria, pneumococci have a cell membrane beneath a cell wall, which in turn is covered by a polysaccharide capsule. Pneumococci are divided into serogroups or serotypes based on capsular polysaccharide structure, as distinguished with rabbit polyclonal antisera; capsules swell in the presence of specific antiserum (the Quellung reaction). The most recently discovered serotypes, 6C, 6D, and 11E, have been identified with monoclonal antibodies and by serologic, genetic, and biochemical means, respectively. The currently recognized 93 serotypes fall into 21 serogroups, and each serogroup contains two to five serotypes with closely related capsules. The capsule protects the bacteria from phagocytosis by host cells in the absence of type-specific antibody and is arguably the most

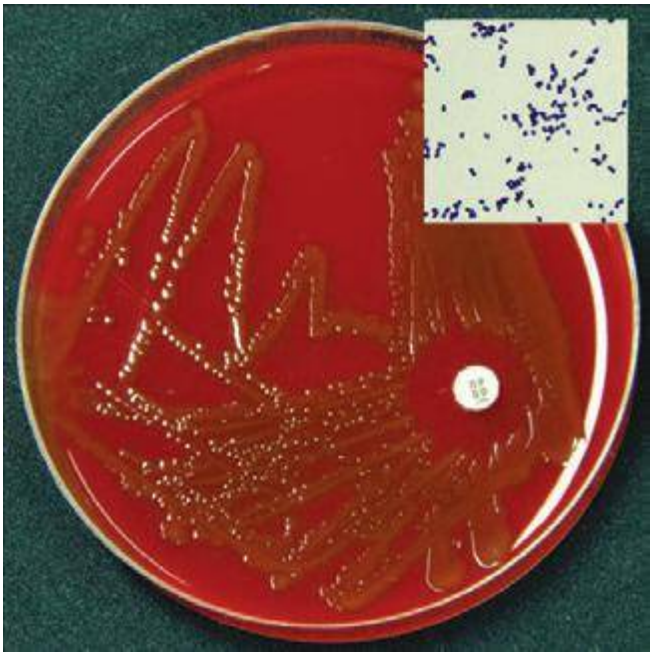

FIGURE 171-1 Pneumococci growing on blood agar, illustrating α hemolysis and optochin sensitivity (zone around optochin disk). *Inset:* Gram's stain, illustrating gram-positive diplococci. *(Photographs courtesy of Paul Turner, Shoklo Malaria Research Unit, Thailand.)*