used in combinations are rifampin, aminoglycosides (e.g., gentamicin), and fusidic acid (not readily available in the United States). To date, clinical studies have not documented a therapeutic benefit; recent reports have raised concern about the potential nephrotoxicity of gentamicin and about adverse drug reactions from the addition of rifampin. As a result, the use of gentamicin in combination with β-lactams or other antimicrobial agents is no longer routinely recommended for the treatment of endocarditis. Rifampin continues to be used for the treatment of prosthetic device–related infections and for osteomyelitis.

The combination of daptomycin with a β-lactam antibiotic has been successfully used to treat patients with persistent MRSA bacteremia, even those infected with isolates that exhibit reduced susceptibility to daptomycin. The combination appears to enhance the bactericidal activity of daptomycin, perhaps by reducing the bacterial cell surface charge and thus allowing more daptomycin binding.

ANTIMICROBIAL THERAPY FOR SELECTED SETTINGS

When necessary, the use of oral antistaphylococcal agents for uncomplicated skin and soft tissue infections is usually successful. For other infections, parenteral therapy is indicated.

S. aureus endocarditis is usually an acute, life-threatening infection. Thus, prompt collection of blood for cultures must be followed immediately by empirical antimicrobial therapy. For life-threatening *S. aureus* native-valve endocarditis, therapy with a β-lactam is recommended. If a MRSA strain is isolated, vancomycin (15–20 mg/kg every 8–12 h, given in equal doses up to a total of 2 g) or daptomycin (6 mg/kg every 24 h) is recommended. The vancomycin dose should be adjusted on the basis of trough vancomycin levels. Patients are generally treated for 4–6 weeks, with duration depending on whether there are complications. For prosthetic-valve endocarditis, surgery in addition to antibiotic therapy is often necessary. The combination of a β-lactam agent—or, if the isolate is β-lactam-resistant, vancomycin (30 mg/kg every 24 h, given in doses up to a total of 2 g) or daptomycin (6 mg/kg every 24 h)—with an aminoglycoside (gentamicin, 1 mg/kg IV every 8 h) and rifampin (300 mg orally or IV every 8 h) for ≥6 weeks is recommended.

For hematogenous osteomyelitis or septic arthritis in children, a 4-week course of therapy is usually adequate. In adults, treatment is often more prolonged. For chronic forms of osteomyelitis, surgical debridement is necessary in combination with antimicrobial therapy. For joint infections, a critical component of therapy is the repeated aspiration or arthroscopy of the affected joint to prevent damage from leukocytes. The combination of rifampin with ciprofloxacin has been used successfully to treat prosthetic joint infections, especially when the device cannot be removed. The efficacy of this combination may reflect enhanced activity against staphylococci in biofilms as well as the attainment of effective intracellular concentrations.

The choice of empirical therapy for staphylococcal infections depends in part on susceptibility data for the local geographic area. Increasingly, vancomycin and daptomycin are the drugs of choice for both community- and hospital-acquired infections. The increase in CA-MRSA skin and soft tissue infections has drawn attention to the need for initiation of appropriate empirical therapy. Oral agents that have been effective against these isolates include clindamycin, trimethoprim-sulfamethoxazole, doxycycline, linezolid, and tedizolid.

THERAPY FOR TOXIC SHOCK SYNDROME

Supportive therapy with reversal of hypotension is the mainstay of therapy for TSS. Both fluids and pressors may be necessary. Tampons or other packing material should be promptly removed. The role of antibiotics is less clear. Some investigators recommend a combination of clindamycin and a semisynthetic penicillin or vancomycin (if the isolate is resistant to methicillin). Clindamycin is advocated because, as a protein synthesis inhibitor, it reduces toxin synthesis in vitro. Linezolid also appears to be effective. A semisynthetic penicillin or glycopeptide is suggested to eliminate any potential focus of infection as well as to eradicate persistent carriage that might increase the likelihood of recurrent illness. Anecdotal reports document the successful use of IV immunoglobulin to treat TSS. The role of glucocorticoids in the treatment of this disease is uncertain.

THERAPY FOR OTHER TOXIN-MEDIATED DISEASES

Therapy for staphylococcal food poisoning is entirely supportive. For SSSS, antistaphylococcal therapy targets the primary site of infection.

173 Streptococcal Infections

Michael R. Wessels

Many varieties of streptococci are found as part of the normal flora colonizing the human respiratory, gastrointestinal, and genitourinary tracts. Several species are important causes of human disease. Group A *Streptococcus* (GAS, *Streptococcus pyogenes*) is responsible for streptococcal pharyngitis, one of the most common bacterial infections of school-age children, and for the postinfectious syndromes of acute rheumatic fever (ARF) and poststreptococcal glomerulonephritis (PSGN). Group B *Streptococcus* (GBS, *Streptococcus agalactiae*) is the leading cause of bacterial sepsis and meningitis in newborns and a major cause of endometritis and fever in parturient women. Viridans streptococci are the most common cause of bacterial endocarditis. Enterococci, which are morphologically similar to streptococci, are now considered a separate genus on the basis of DNA homology studies. Thus, the species previously designated as *Streptococcus faecalis* and *Streptococcus faecium* have been renamed *Enterococcus faecalis* and *Enterococcus faecium*, respectively. The enterococci are discussed in Chap. 174.

Streptococci are gram-positive, spherical to ovoid bacteria that characteristically form chains when grown in liquid media. Most streptococci that cause human infections are facultative anaerobes, although some are strict anaerobes. Streptococci are relatively fastidious organisms, requiring enriched media for growth in the laboratory. Clinicians and clinical microbiologists identify streptococci by several classification systems, including hemolytic pattern, Lancefield group, species name, and common or trivial name. Many streptococci associated with human infection produce a zone of complete (β) hemolysis around the bacterial colony when cultured on blood agar. The β-hemolytic streptococci can be classified by the Lancefield system, a serologic grouping based on the reaction of specific antisera with bacterial cell-wall carbohydrate antigens. With rare exceptions, organisms belonging to Lancefield groups A, B, C, and G are all β-hemolytic, and each is associated with characteristic patterns of human infection. Other streptococci produce a zone of partial (α) hemolysis, often imparting a greenish appearance to the agar. These α-hemolytic streptococci are further identified by biochemical testing and include *Streptococcus pneumoniae* (Chap. 171), an important cause of pneumonia, meningitis, and other infections, and the several species referred to collectively as the *viridans streptococci*, which are part of the normal oral flora and are important agents of subacute bacterial endocarditis. Finally, some streptococci are nonhemolytic, a pattern sometimes called γ *hemolysis*. Among the organisms classified serologically as group D streptococci, the enterococci are classified as a distinct genus (Chap. 174). The classification of the major streptococcal groups causing human infections is outlined in Table 173-1.

GROUP A STREPTOCOCCI

Lancefield's group A consists of a single species, *S. pyogenes*. As its species name implies, this organism is associated with a variety of suppurative infections. In addition, GAS can trigger the postinfectious syndromes of ARF (which is uniquely associated with *S. pyogenes* infection; Chap. 381) and PSGN (Chap. 338).