acid of mammalian connective tissues. The capsular polysaccharide may also play a role in GAS colonization of the pharynx by binding to CD44, a hyaluronic acid–binding protein expressed on human pharyngeal epithelial cells.

GAS produces a large number of extracellular products that may be important in local and systemic toxicity and in the spread of infection through tissues. These products include streptolysins S and O, toxins that damage cell membranes and account for the hemolysis produced by the organisms; streptokinase; DNAses; SpyCEP, a serine protease that cleaves and inactivates the chemoattractant cytokine interleukin 8, thereby inhibiting neutrophil recruitment to the site of infection; and several pyrogenic exotoxins. Previously known as erythrogenic toxins, the pyrogenic exotoxins cause the rash of scarlet fever. Since the mid-1980s, pyrogenic exotoxin–producing strains of GAS have been linked to unusually severe invasive infections, including necrotizing fasciitis and the streptococcal toxic shock syndrome (TSS). Several extracellular products stimulate specific antibody responses useful for serodiagnosis of recent streptococcal infection. Tests for these antibodies are used primarily for detection of preceding streptococcal infection in cases of suspected ARF or PSGN.

CLINICAL MANIFESTATIONS

Pharyngitis Although seen in patients of all ages, GAS pharyngitis is one of the most common bacterial infections of childhood, accounting for 20–40% of all cases of exudative pharyngitis in children; it is rare among those under the age of 3. Younger children may manifest streptococcal infection with a syndrome of fever, malaise, and lymphadenopathy without exudative pharyngitis. Infection is acquired through contact with another individual carrying the organism. Respiratory droplets are the usual mechanism of spread, although other routes, including food-borne outbreaks, have been well described. The incubation period is 1–4 days. Symptoms include sore throat, fever and chills, malaise, and sometimes abdominal complaints and vomiting, particularly in children. Both symptoms and signs are quite variable, ranging from mild throat discomfort with minimal physical findings to high fever and severe sore throat associated with intense erythema and swelling of the pharyngeal mucosa and the presence of purulent exudate over the posterior pharyngeal wall and tonsillar pillars. Enlarged, tender anterior cervical lymph nodes commonly accompany exudative pharyngitis.

The differential diagnosis of streptococcal pharyngitis includes the many other bacterial and viral etiologies (Table 173-2). Streptococcal infection is an unlikely cause when symptoms and signs suggestive of viral infection are prominent (conjunctivitis, coryza, cough, hoarseness, or discrete ulcerative lesions of the buccal or pharyngeal mucosa). Because of the range of clinical presentations of streptococcal pharyngitis and the large number of other agents that can produce the same clinical picture, diagnosis of streptococcal pharyngitis on clinical grounds alone is not reliable. The throat culture remains the diagnostic gold standard. Culture of a throat specimen that is properly collected (i.e., by vigorous rubbing of a sterile swab over both tonsillar pillars) and properly processed is the most sensitive and specific means of definitive diagnosis. A rapid diagnostic kit for latex agglutination or enzyme immunoassay of swab specimens is a useful adjunct to throat culture. While precise figures on sensitivity and specificity vary, rapid diagnostic kits generally are >95% specific. Thus a positive result can be relied upon for definitive diagnosis and eliminates the need for throat culture. However, because rapid diagnostic tests are less sensitive than throat culture (relative sensitivity in comparative studies, 55–90%), a negative result should be confirmed by throat culture.

TREATMENT GAS PHARYNGITIS

In the usual course of uncomplicated streptococcal pharyngitis, symptoms resolve after 3–5 days. The course is shortened little by treatment, which is given primarily to prevent suppurative complications and ARF. Prevention of ARF depends on eradication of the organism from the pharynx, not simply on resolution of symptoms, and requires 10 days of penicillin treatment (Table 173-3). A first-generation cephalosporin, such as cephalexin or cefadroxil, may be substituted for penicillin in cases of penicillin allergy if the nature of the allergy is not an immediate hypersensitivity reaction (anaphylaxis or urticaria) or another potentially life-threatening manifestation (e.g., severe rash and fever).

TABLE 173-2 INFECTIOUS ETIOLOGIES OF ACUTE PHARYNGITIS

Organism	Associated Clinical Syndrome(s)
Viruses	
Rhinovirus	Common cold
Coronavirus	Common cold
Adenovirus	Pharyngoconjunctival fever
Influenza virus	Influenza
Parainfluenza virus	Cold, croup
Coxsackievirus	Herpangina, hand-foot-and-mouth disease
Herpes simplex virus	Gingivostomatitis (primary infection)
Epstein-Barr virus	Infectious mononucleosis
Cytomegalovirus	Mononucleosis-like syndrome
HIV	Acute (primary) infection syndrome
Bacteria	
Group A streptococci	Pharyngitis, scarlet fever
Group C or G streptococci	Pharyngitis
Mixed anaerobes	Vincent's angina
Arcanobacterium haemolyticum	Pharyngitis, scarlatiniform rash
Neisseria gonorrhoeae	Pharyngitis
Treponema pallidum	Secondary syphilis
Francisella tularensis	Pharyngeal tularemia
Corynebacterium diphtheriae	Diphtheria
Yersinia enterocolitica	Pharyngitis, enterocolitis
Yersinia pestis	Plague
Chlamydiae	
Chlamydia pneumoniae	Bronchitis, pneumonia
Chlamydia psittaci	Psittacosis
Mycoplasmas	
Mycoplasma pneumoniae	Bronchitis, pneumonia

TABLE 173-3 TREATMENT OF GROUP A STREPTOCOCCAL INFECTIONS

Infection	Treatment[a]
Pharyngitis	Benzathine penicillin G (1.2 mU IM) *or* penicillin V (250 mg PO tid or 500 mg PO bid) × 10 days (Children <27 kg: Benzathine penicillin G [600,000 units IM] *or* penicillin V [250 mg PO bid or tid] × 10 days)
Impetigo	Same as pharyngitis
Erysipelas/cellulitis	Severe: Penicillin G (1–2 mU IV q4h) Mild to moderate: Procaine penicillin (1.2 mU IM bid)
Necrotizing fasciitis/myositis	Surgical debridement *plus* penicillin G (2–4 mU IV q4h) *plus* clindamycin[b] (600–900 mg IV q8h)
Pneumonia/empyema	Penicillin G (2–4 mU IV q4h) *plus* drainage of empyema
Streptococcal toxic shock syndrome	Penicillin G (2–4 mU IV q4h) *plus* clindamycin[b] (600–900 mg IV q8h) *plus* IV immunoglobulin[b] (2 g/kg as a single dose)

[a]Penicillin allergy: A first-generation cephalosporin, such as cephalexin or cefadroxil, may be substituted for penicillin in cases of penicillin allergy if the nature of the allergy is not an immediate hypersensitivity reaction (anaphylaxis or urticaria) or another potentially life-threatening manifestation (e.g., severe rash and fever). Alternative agents for oral therapy are erythromycin (10 mg/kg PO qid, up to a maximum of 250 mg per dose) and azithromycin (a 5-day course at a dose of 12 mg/kg once daily, up to a maximum of 500 mg/d). Vancomycin is an alternative for parenteral therapy. [b]Efficacy unproven, but recommended by several experts. See text for discussion.