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Sore Throat

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Most causes of sore throat are nonbacterial and neither require nor are alleviated by antibiotic therapy (Tables 1.1, 1.2, and 1.3). Accurate diagnosis is essential: Acute streptococcal pharyngitis warrants diagnosis and therapy to ensure prevention of serious suppurative and nonsuppurative complications. Life-threatening infectious complications of oropharyngeal infections, whether streptococcal or nonstreptococcal, may manifest with mouth pain, pharyngitis, parapharyngeal space infectious extension, and/or airway obstruction (Tables 1.4 and 1.5). In many cases, the history and/or physical exam can help direct diagnosis and treatment, but the enormous number of potential causes is too large to address all of them.

VIRAL PHARYNGITIS

Most episodes of pharyngitis are caused by viruses (see Tables 1.2 and 1.3). It is difficult to clinically distinguish between viral and bacterial pharyngitis with a very high degree of precision, but certain clues may help the physician. Accompanying symptoms of conjunctivitis, rhinitis, cough, discrete ulcerations, croup, or laryngitis are common with viral infection but rare in bacterial pharyngitis.

Many viral agents can produce pharyngitis (see Tables 1.2 and 1.3). Some cause distinct clinical syndromes that are readily diagnosed without laboratory testing (Table 1.6; see also Tables 1.1 and 1.4). In pharyngitis caused by parainfluenza and influenza viruses, rhinoviruses, coronaviruses, and respiratory syncytial virus (RSV), the symptoms of coryza and cough often overshadow sore throat, which is generally mild. Influenza virus may cause high fever, cough, headache, malaise, myalgia, and cervical adenopathy in addition to pharyngitis. In young children, croup or bronchiolitis may develop. When influenza is suspected on clinical and epidemiologic grounds or confirmed by testing (polymerase chain reaction [PCR] is most accurate), specific antiviral therapy is available for treatment of patients and prophylaxis of family members. RSV is associated with bronchiolitis, pneumonia, and croup in young children. RSV infection in older children is usually indistinguishable from a simple upper respiratory tract infection. Pharyngitis is not a prominent finding of RSV infection in any age group. Parainfluenza viruses are associated with croup and bronchiolitis; minor sore throat and signs of pharyngitis are common at the outset but rapidly resolve. Infections caused by parainfluenza, influenza, and RSV are often seen in seasonal (winter) epidemics. *Many agents can be identified using multiplex or targeted PCR testing, but there is rarely reason to test outpatients and infrequent benefit to testing inpatients except to confirm and treat influenza.*

Adenoviruses can cause upper and lower respiratory tract disease, ranging from ordinary colds to severe pneumonia and multisystem disease, including hepatitis, myocarditis, and myositis. The incubation period of adenovirus infection is 2-4 days. Upper respiratory tract infection typically produces fever, erythema of the pharynx, and follicular hyperplasia of the tonsils, together with exudate. Enlargement of the cervical lymph nodes occurs frequently. When conjunctivitis occurs in association with adenoviral pharyngitis, the resulting syndrome is called **pharyngoconjunctival fever**. Pharyngitis may last as long as 7 days and does not respond to antibiotics. There are many adenovirus serotypes; adenovirus infections may therefore develop in children more than once. Laboratory studies may reveal a leukocytosis and an elevated erythrocyte sedimentation rate. Adenovirus outbreaks have been associated with swimming pools and contamination in health care workers.

The **enteroviruses** (coxsackievirus and echovirus) can cause sore throat, especially in the summer. High fever is common, and the throat is erythematous but usually not bright red; tonsillar exudate and cervical adenopathy are unusual. Symptoms resolve within a few days. Enteroviruses can also cause meningitis, myocarditis, rash, and two specific syndromes that involve the oropharynx.

Herpangina is characterized by distinctive discrete, painful, gray-white papulovesicular lesions distributed over the posterior oropharynx (see Table 1.6). The vesicles are 1-2 mm in diameter and are initially surrounded by a halo of erythema before they ulcerate. Fever may reach 39.5°C. The illness is due to enteroviruses and generally lasts less than 7 days, but severe pain may impair fluid intake and occasionally necessitates medical support.

Hand-foot-mouth disease is caused by coxsackievirus A16. Painful vesicles that ulcerate can occur throughout the oropharynx. Vesicles also develop on the palms, soles, and, less often, on the trunk or extremities. Fever is present in most cases, but many children do not appear seriously ill. This disease lasts less than 7 days.

Primary infection caused by **herpes simplex virus** (**HSV**) usually produces high fever with acute gingivostomatitis, involving vesicles (which become ulcers) throughout the anterior portion of the mouth, including the lips. There is sparing of the posterior pharynx in herpes gingivostomatitis; the infection usually occurs in young children. High fever is common, pain is intense, and intake of oral fluids is often impaired, which may lead to dehydration. In addition, HSV may

(See *Nelson Textbook of Pediatrics*, p. 2019)

TABLE 1.1 Etiology of Sore Throat

Infection
Bacterial (see Tables 1.2, 1.3)
Viral (see Tables 1.2, 1.3)
Fungal (see Table 1.3)
Neutropenic mucositis (invasive anaerobic mouth flora)
Tonsillitis
Epiglottitis
Uvulitis
Peritonsillar abscess (quinsy)
Retropharyngeal abscess (prevertebral space)
Ludwig angina (submandibular space)
Lateral pharyngeal space cellulitis-abscess
Buccal space cellulitis
Suppurative thyroiditis
Lemierre syndrome (septic jugular thrombophlebitis)
Vincent angina (mixed anaerobic bacteria–gingivitis–pharyngitis)

Irritation
Cigarette smoking
Inhaled irritants
Reflux esophagitis
Chemical toxins (caustic agents)
Paraquat ingestion
Smog
Dry hot air
Hot foods, liquids

Other
Tumor, including Kaposi sarcoma, leukemia
Granulomatosis with polyangiitis (formerly Wegener granulomatosis)
Sarcoidosis
Glossopharyngeal neuralgia
Foreign body
Stylohyoid syndrome
Behçet disease
Kawasaki syndrome
Posterior pharyngeal trauma—pseudodiverticulum
Pneumomediastinum with air dissection
Hematoma
Systemic lupus erythematosus
Bullous pemphigoid
Syndrome of periodic fever, aphthous stomatitis, pharyngitis, cervical adenitis (PFAPA)

TABLE 1.2 Infectious Etiology of Pharyngitis

Definite Causes
Streptococcus pyogenes (Group A streptococci)
Corynebacterium diphtheriae
Arcanobacterium haemolyticum
Neisseria gonorrhoeae
Epstein-Barr virus
Parainfluenza viruses (types 1–4)
Influenza viruses
Rhinoviruses
Coronavirus
Adenovirus (types 3, 4, 7, 14, 21, others)
Respiratory syncytial virus
Herpes simplex virus (types 1, 2)

Probable or Occasional Causes
Group C streptococci
Group G streptococci
Chlamydia pneumoniae
Chlamydia trachomatis
Mycoplasma pneumoniae

TABLE 1.3 Additional Potential Pathogens Associated with Sore Throat

Bacteria
Fusobacterium necrophorum (Lemierre syndrome)
Neisseria meningitidis
Yersinia enterocolitica
Tularemia (oropharyngeal)
Yersinia pestis
Bacillus anthracis
Chlamydia psittaci
Secondary syphilis
Mycobacterium tuberculosis
Lyme disease
Corynebacterium ulcerans
Leptospira species
Mycoplasma hominis

Virus
Coxsackievirus A, B
Cytomegalovirus
Viral hemorrhagic fevers
Human immunodeficiency virus (HIV) (primary infection)
Human herpesvirus 6
Measles
Varicella
Rubella

Fungus
Candida species
Histoplasmosis
Cryptococcosis

manifest as pharyngitis in adolescents. Approximately 35% of new-onset HSV-positive adolescent patients have herpetic lesions; most teenage patients with HSV pharyngitis cannot be distinguished from patients with other causes of pharyngitis. The classic syndrome of herpetic gingivostomatitis in infants and toddlers lasts up to 2 weeks; data on the course of more benign HSV pharyngitis are lacking. The differential diagnosis of vesicular-ulcerating oral lesions is noted in Table 1.6.

A common cause of a local and large lesion of unknown etiology is **aphthous stomatitis** (Fig. 1.1). *PFAPA* (periodic fever, aphthous stomatitis, pharyngitis, and cervical adenitis) is an idiopathic periodic fever syndrome that occurs predictably every 2-8 weeks. The onset of PFAPA is usually before the age of 5 years. In addition to aphthous stomatitis and pharyngitis, PFAPA is characterized by high fever lasting 4-6 days. Individual episodes resolve spontaneously but may respond

TABLE 1.4 Distinguishing Features of Parapharyngeal–Upper Respiratory Tract Infections

	Peritonsillar Abscess	Retropharyngeal Abscess (Cellulitis)	Submandibular Space (Ludwig Angina)*	Lateral Pharyngeal Space	Masticator Space*	Epiglottitis	Laryngotracheo-bronchitis (Croup)	Bacterial Tracheitis	Postanginal Sepsis (Lemierre Syndrome)
Etiology	Group A streptococci, oral anaerobes†	*Staphylococcis aureus,* oral anaerobes,† group A streptococci, "suppurative adenitis"	Oral anaerobes†	Oral anaerobes†	Oral anaerobes†	*Haemophilus influenzae* type b (rarely), group A streptococci, *Streptococcus pneumoniae*, *Staphyloccocus aureus*, and non-type b *H. influenzae*	Parainfluenza virus; influenza, adenovirus, and respiratory syncytial virus less common	*Moraxella catarrhalis, S. aureus, H. influenzae type b* or nontypable	*Fusobacterium necrophorum*
Age	Teens	Infancy, preteens, occasionally teens	Teens	Teens	Teens	2-5 yr	3 mo-3 yr	3-10 yr	Teens
Manifestations	Initial episode of pharyngitis, followed by sudden worsening of unilateral odynophagia, trismus, hot potato (muffled) voice, drooling, displacement of uvula	Fever, dyspnea, stridor, dysphagia, drooling, stiff neck, pain, cervical adenopathy, swelling of posterior pharyngeal space Descending mediastinitis (rare) Lateral neck radiograph reveals swollen retropharyngeal prevertebral space: infants, >1 × width of adjacent vertebral body (>2-7 mm); teens, > ⅓ × width of vertebral body (>1-7 mm) CT distinguishes cellulitis from abscess	Fever, dysphagia, odynophagia, stiff neck, dyspnea; airway obstruction, swollen tongue and floor of mouth (tender) Muffled voice	Severe pain, fever, trismus, dysphagia, edematous appearing, painful lateral facial (jaw) or neck swelling (induration) May lead to Lemierre syndrome	Pain, prominent trismus, fever Swelling not always evident	Sudden-onset high fever, "toxic" appearance, muffled voice, anxiety, pain, retractions, dysphagia, drooling, stridor, sitting up, leaning forward tripod position, cherry-red swollen epiglottis Usually not hoarse or coughing Lateral neck radiograph shows "thumb sign" of swollen epiglottis	Low-grade fever, barking cough, hoarseness, aphonia, stridor; mild retractions; radiograph shows "steeple sign" of subglottic narrowing on anteroposterior neck view	Prior history of croup with sudden onset of respiratory distress, high fever, "toxic" appearance, hoarseness, stridor, barking cough, tripod sitting position; radiograph as per croup plus ragged tracheal air column	Prior pharyngitis with sudden-onset fever, chills, odynophagia, neck pain, septic thrombophlebitits of internal jugular vein with septic emboli (e.g., lungs, joints), bacteremia

*Often odontogenic; check for tooth abscess, caries, tender teeth.
†*Peptostreptococcus, Fusobacterium, Bacteroides.*

TABLE 1.5 Red Flags Associated with Sore Throat

Toxic appearance
Shock
Fever >2 wk
Duration of sore throat >2 wk
Trismus
Drooling
Cyanosis
Hemorrhage
Asymmetric tonsillar swelling or asymmetric cervical adenopathy
Respiratory distress (airway obstruction or pneumonia)
Suspicion of parapharyngeal space infection
Suspicion of diphtheria (bull neck, uvula paralysis, thick membrane)
Apnea
Severe, unremitting pain
"Hot potato" voice
Chest or neck pain
Weight loss

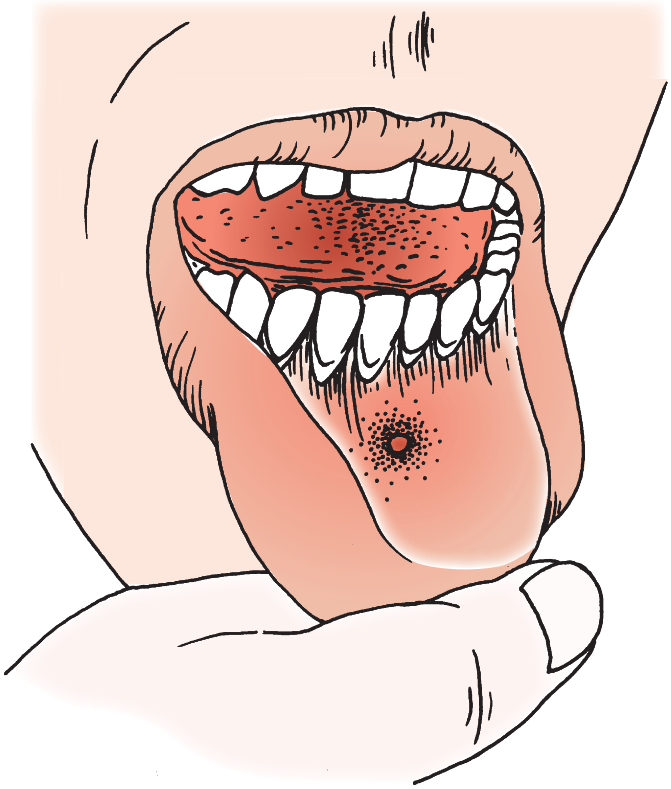

FIGURE 1.1 Aphthous stomatitis ("canker sore"). (From Reilly BM. Sore throat. In: *Practical Strategies in Outpatient Medicine*. 2nd ed. Philadelphia: WB Saunders; 1991.)

to oral prednisone or cimetidine. There are reports of improvement after tonsillectomy. In most patients PFAPA completely resolves before puberty without sequelae. The diagnosis is based on clinical criteria after excluding cyclic neutropenia, other periodic fever syndromes, infections, and malignancy.

Infants and toddlers with **measles** often have prominent oral findings early in the course of the disease. In addition to high fever, cough, coryza, and conjunctivitis, the pharynx may be intensely and diffusely erythematous, without tonsillar enlargement or exudate. The presence of **Koplik spots**, the pathognomonic white or blue-white enanthem of measles, on the buccal mucosa near the mandibular molars provides the evidence of the correct diagnosis before the rash develops. Measles can be complicated by pneumonia and encephalitis. In the United States, widespread use of the measles vaccine has virtually eliminated transmission of natural measles infection except among unvaccinated subpopulations (children <12 months old, families who have refused immunization). Most cases are imported by unimmunized visitors from countries with endemic measles.

INFECTIOUS MONONUCLEOSIS

◆ Pathogenesis

Acute exudative pharyngitis commonly occurs with infectious mononucleosis caused by primary infection with the Epstein-Barr virus (EBV). Mononucleosis is a febrile, systemic, self-limited lymphoproliferative disorder that is usually associated with hepatosplenomegaly and generalized lymphadenopathy. Acute pharyngitis may be mild or severe, with significant tonsillar hypertrophy (possibly producing airway obstruction), erythema, and impressive tonsillar exudates. Regional lymph nodes may be particularly enlarged and slightly tender. Infectious mononucleosis usually occurs in adolescents and young adults; EBV infection is generally milder or subclinical in preadolescent children. In U.S. high school and college students, attack rates are 200-800 per 100,000 per year. EBV is transmitted primarily by saliva.

◆ Clinical Features

After a 2-4 week incubation period, patients with infectious mononucleosis usually experience an abrupt onset of malaise, fatigue, fever, and headache, followed closely by pharyngitis. The tonsils are enlarged with exudates and cervical adenopathy. More generalized adenopathy with hepatosplenomegaly often follows. Fever and pharyngitis typically last 1-3 weeks, and lymphadenopathy and hepatosplenomegaly resolve over 3-6 weeks. Malaise and lethargy can persist for several months and can affect school or work performance.

◆ Diagnosis

Laboratory studies of diagnostic value include atypical lymphocytosis; these lymphocytes are primarily EBVspecific, cytotoxic T lymphocytes that represent a reactive response to EBV-infected B lymphocytes. A modest elevation of serum transaminase levels, reflecting EBV hepatitis, is common. Tests useful for diagnosis include detection of heterophile antibodies that react with bovine erythrocytes (most often detected by the monospot test) and a specific antibody against EBV viral capsid antigen (VCA), early antigen (EA), and nuclear antigen (EBNA). Acute infectious mononucleosis is usually associated with a positive heterophile test result and antibody to VCA and EA (Fig. 1.2).

The findings of acute exudative pharyngitis together with hepatomegaly, splenomegaly, and generalized lymphadenopathy suggest infectious mononucleosis. Early in the disease and in cases without liver or spleen enlargement, differentiation from other causes of pharyngitis, including streptococcal pharyngitis, is difficult. Indeed, a small number of patients with infectious mononucleosis have a throat culture positive for group A streptococci. (They are likely streptococcal carriers; see subsequent text.) An indistinguishable syndrome can occur with cytomegalovirus, but differentiation is rarely of clinical importance. Serologic evidence of mononucleosis should be sought

(See *Nelson Textbook of Pediatrics*, p. 1586)

TABLE 1.6 Vesicular-Ulcerating Eruptions of the Mouth and Pharynx

	Gingivostomatitis	Herpangina	Hand-Foot-Mouth Disease	Chickenpox	Systemic Lupus Erythematosus (SLE)	Inflammatory Bowel Disease (IBD)	Aphthous Stomatitis	Behçet Disease	Vincent Stomatitis	Recurrent Scarifying Ulcerative Stomatitis (Sutton Disease)
Etiology	Herpes simples virus (HSV I)	Cocksackievirus A, B; echovirus or HSV (rarely)	Cocksackievirus A, cocksackievirus B (rarely)	Varicella-zoster virus	Autoimmune	Autoimmune	Unknown	Unknown; vasculitis	Unknown; or anaerobic bacteria	Unknown
Location	Ulcerative vesicles of pharynx, tongue, and palate plus lesions of mucocutaneous (perioral) margin	Anterior fauces (tonsils), soft palate (uvula), less often pharynx	Tongue, buccal mucosa, palate, palms, soles, anterior oral cavity	Tongue, gingiva, buccal mucosa, marked cutaneous lesions; trunk > face	Oral, nasal mucosa; palate, pharynx, buccal mucosa	Lips, tongue, buccal mucosa, oropharynx	As in IBD	Oral (similar to IBD); genital ulcers	Gingiva; ulceration at base of teeth	Tongue; buccal mucosa
Age	Less than 5 yr	3-10 yr	1 yr-teens	Any age	Any age	Any age	Teens and adulthood	Teens, adulthood, occasionally <10 yr	Teens; if younger, consider immunodeficiency and blood dyscrasia	Teens
Manifestations	Fever, mouth pain, toxic, fetid breath, drooling, anorexia, cervical lymphadenopathy; cracked, swollen hemorrhagic gums; secondary inoculation possible (fingers, eye, skin); reactivation with long latency (any age)	Fever, sore throat, odynophagia; summer outbreaks; 6-12 lesions (2-4 mm papule) → vesicle → ulceration; headache, myalgias	Painful bilateral vesicles, fever	Fever, pruritic cutaneous vesicles, painful oral lesions	Renal, central nervous system, arthritis, cutaneous, hematologic, other organ involvement; ulcers minimally to moderately painful; may be painless	Multiple recurrences; painful ulcerations 1-2 mm, but may be 5-15 mm	Similar to IBD	Painful ulcerations (heal without scarring); uveitis, arthralgia, arthritis, lower gastrointestinal ulceration (similar to IBD); recurrences; spontaneous remissions	Fever, bleeding gums; gray membrane	Deep, large, painful ulcerations; relapsing; scarring with distortion of mucosa

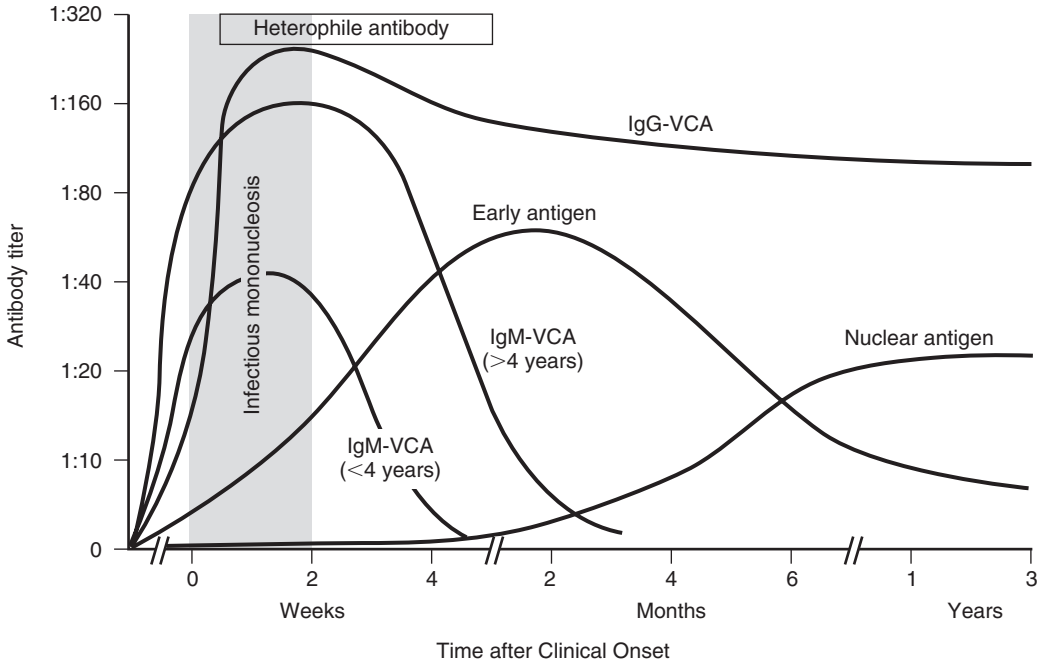

FIGURE 1.2 Schematic representation of the evolution of antibodies to various Epstein-Barr virus antigens in patients with infectious mononucleosis. The titers are geometric mean values expressed as reciprocals of the serum dilution. The minimal titer tested for viral capsid antigen (VCA) and early antigen antibodies was 1:10; for Epstein-Barr nuclear antigen, it was 1:2.5. The immunoglobulin (Ig)M response to capsid antigen was divided because of the significant differences noted according to age. (From Jenson HB, Ench Y, Sumaya CV. Epstein-Barr virus. In: Rose NR, de Macario EC, Folds JD, et al, editors. *Manual of Clinical Laboratory Immunology*. 5th ed. Washington, DC: American Society for Microbiology; 1997. p. 634-43.)

when splenomegaly or other features are present or if symptoms persist longer than expected.

Primary infection with **human immunodeficiency virus** (HIV) may produce a mononucleosis-like illness with sore throat, fever, lymphadenopathy, rash, myalgias, and hepatosplenomegaly. Early infection may be detected by viral RNA or DNA load because immunoglobulin (Ig)M or IgG titers may have not yet developed.

GROUP A STREPTOCOCCAL INFECTION

In the evaluation of a patient with sore throat, the primary concern in the United States is usually accurate diagnosis and treatment of pharyngitis caused by group A streptococci (GAS) or *Streptococcus pyogenes*, which accounts for about 15% of all episodes of pharyngitis. The sequelae of GAS pharyngitis, especially acute rheumatic fever (ARF) and acute glomerulonephritis (AGN), at one time resulted in considerable morbidity and mortality in the United States and continue to do so in other parts of the world. Prevention of ARF in particular depends on timely diagnosis of streptococcal pharyngitis and prompt antibiotic treatment. Group A streptococci are characterized by the presence of group A carbohydrate in the cell wall, and they are further distinguished by several cell wall protein antigens (M, R, T). These protein antigens, especially the M protein, a virulence factor, are useful for studies of epidemiology and pathogenesis but are not used in clinical care.

◆ Epidemiology

GAS pharyngitis is endemic in the United States; epidemics occur sporadically. Episodes peak in the late winter and early spring. Rates of GAS pharyngitis are highest among children aged 5-11 years old. Spread of GAS in classrooms and among family members is common, especially in the presence of crowded living conditions. Transmission occurs primarily by the inhalation of organisms in large droplets or by direct contact with respiratory secretions. Pets do not appear to be a frequent reservoir. Untreated streptococcal pharyngitis is particularly contagious early in the acute illness and for the first 2 weeks after the organism has been acquired, but antibiotic therapy effectively prevents disease transmission. Within 24 hours of institution of therapy with penicillin, it is difficult to isolate GAS from patients with acute streptococcal pharyngitis, and infected children can return to school.

Molecular epidemiology studies of streptococcal pharyngitis have shown that the prevalent M protein types vary among communities and over time. Numerous distinct strains of GAS can circulate simultaneously in a community during the peak season. GAS M proteins can be identified in research studies by using PCR to establish the specific M protein gene (*emm* gene); M protein identification is not available for use in clinical care. Children with streptococcal pharyngitis can serve as a local reservoir for strains that cause invasive disease (e.g., sepsis, streptococcal toxic shock syndrome, cellulitis, necrotizing fasciitis) in the same geographic area and season.

◆ Clinical Features

The classic patient presentation of acute streptococcal pharyngitis involves a sudden onset of fever and sore throat. Headache, malaise, abdominal pain, nausea, and vomiting occur frequently. *Cough, rhinorrhea, conjunctivitis, stridor, diarrhea, discrete ulcerated lesions, and hoarseness are distinctly unusual and suggest a viral etiology.*

Examination of the patient reveals marked pharyngeal erythema. Petechiae may be noted on the palate, but they can also occur in viral pharyngitis, especially mononucleosis. Tonsils are enlarged, symmetric, and red, with patchy exudates on their surfaces. The papillae of the

(See *Nelson Textbook of Pediatrics*, p. 2018)

tongue may be red and swollen, hence the designation "strawberry tongue." Anterior cervical lymph nodes are often tender and enlarged.

Combinations of these signs can be used to assist in diagnosis; in particular, tonsillar exudates in association with fever, palatal petechiae, and tender anterior cervical adenitis strongly suggest infection with GAS. However, other diseases can produce this constellation of findings, including infectious mononucleosis. Some or all of these classic characteristics may be absent in patients with streptococcal pharyngitis. Symptoms usually resolve within 5 days even in the absence of antibiotic therapy. Younger children can have a syndrome called **streptococcosis—**coryza with crusting below the nares, more generalized adenopathy, and a more chronic course. When rash accompanies the illness, accurate clinical diagnosis is easier. **Scarlet fever**, so-called because of the characteristic fine, diffuse red rash, is essentially pathognomonic for infection with group A streptococci. Scarlet fever is rarely seen in children younger than 3 years old or in adults.

Scarlet Fever

The rash of scarlet fever is caused by infection with a strain of GAS that contains a bacteriophage encoding for production of an erythrogenic (redness producing) toxin, usually erythrogenic (also called pyrogenic) exotoxin A (designated SPE A). Scarlet fever is simply GAS pharyngitis with a rash and should be explained as such to patients and their families. Although patients with the streptococcal toxic shock syndrome are also infected with GAS that produces SPE A, most GAS pharyngeal infections are not associated with development of severe invasive or systemic disease.

The rash of scarlet fever has a texture like sandpaper and blanches with pressure. It usually begins on the face, but after 24 hours, it becomes generalized. The face is red, especially over the cheeks, and the area around the mouth often appears pale in comparison, giving the appearance of circumoral pallor. Accentuation of erythema occurs in flexor skin creases, especially in the antecubital fossae (Pastia lines). The erythema begins to fade within a few days. Desquamation begins within a week of onset on the face and progresses downward, often resembling that seen after mild sunburn. On occasion, sheet-like desquamation occurs around the free margins of the fingernails; this is usually coarser than the desquamation seen with Kawasaki disease. The differential diagnosis of scarlet fever includes Kawasaki disease, measles, and staphylococcal toxic shock syndrome (Table 1.7).

◆ Diagnosis

Although signs and symptoms may strongly suggest acute streptococcal pharyngitis, laboratory diagnosis is strongly recommended, even for patients with scarlet fever (Fig. 1.3). Scoring systems for diagnosing acute GAS pharyngitis on clinical grounds have not proved very satisfactory. Using clinical criteria alone, physicians overestimate the likelihood that patients have streptococcal infection. The throat culture on blood agar plate has traditionally been used to diagnose streptococcal pharyngitis. Plating a swab of the posterior pharynx and tonsils on sheep blood agar, identifying β-hemolytic colonies, and testing them for the presence of sensitivity to a bacitracin-impregnated disk has long been the "gold standard" diagnostic test, but it takes 24-48 hours to obtain results. Rapid antigen detection tests (RADTs) that take less than 15 minutes can detect the presence of the cell wall group A carbohydrate antigen after acid extraction of organisms obtained by throat swab. RADTs are highly specific (generally >95%) when compared to throat culture. In comparison to hospital or reference laboratory throat culture results, the sensitivities of these tests are generally 75-85% and can be lower. The low sensitivity of these tests, coupled

TABLE 1.7 Differential Diagnosis of Scarlet Fever

	Scarlet Fever	Kawasaki Disease	Measles	Staphylococcal Toxic Shock Syndrome	Staphylococcal Scalded Skin Syndrome
Agent	Group A streptococci	Unknown	Measles virus	*Staphylococcus aureus*	*S. aureus*
Age range	All (peak, 5-15 yr)	Usually <5 yr	<2 yr, 10-20 yr	All (especially >10 yr)	Usually <5 yr
Prodrome	No	No	Fever, coryza, cough, conjunctivitis	Usually no	No
Enanthem	No	Occasionally	Koplik spots	No	Limited
Mouth	Strawberry tongue, exudative pharyngitis, palatal petechiae	Erythema; red, cracked lips, strawberry tongue	Diffusely red, no cracked lips	Usually normal	Erythema
Rash	Fine, red, "sandpaper," membranous desquamation, circumoral pallor, Pastia lines	Variable polymorphic; erythematous face, trunk, and diaper area; tips of fingers and toes desquamate 10–28 days after onset	Maculopapular; progressing from forehead to feet; may desquamate	Diffuse erythroderma; desquamates	Erythema, painful bullous lesions; positive Nikolsky sign; desquamates
Other	Cervical adenitis, gallbladder hydrops, fever	Coronary artery disease; fever >5 days; conjunctival (nonpurulent) injection; tender, swollen hands and feet; cervical adenopathy (size >1.5 cm); thrombocytosis; pyuria (sterile); gallbladder hydrops	"Toxic" appearance; dehydration; encephalitis, pneumonia; fever	Shock (hypotension, including orthostatic); encephalopathy; diarrhea; headache	Fever, cracked lips; conjunctivitis

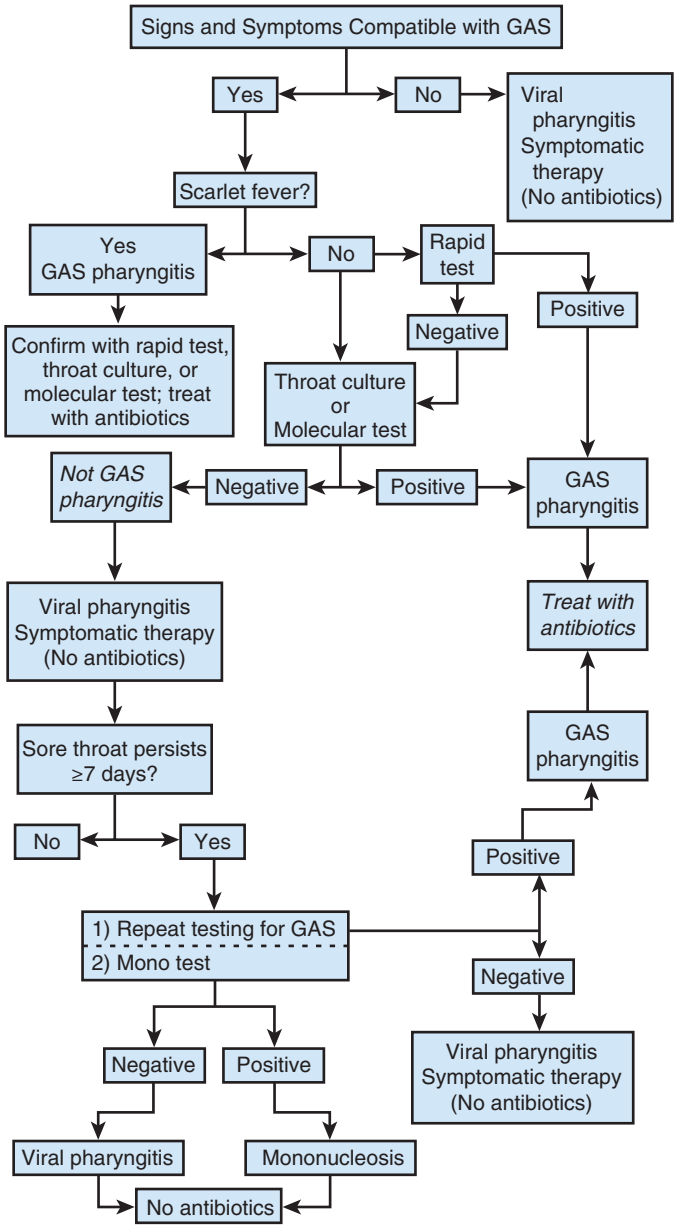

FIGURE 1.3 Management of patients with sore throat. GAS, group A streptococci.

with their excellent specificity, has led to the recommendation that two throat swabs be obtained simultaneously from patients with suspected GAS pharyngitis. One swab is used for a rapid test. When the RADT result is positive, it is highly likely that the patient has GAS pharyngitis, and the extra swab can be discarded. When the RADT is negative, GAS may nonetheless be present; thus, the extra swab should be processed for culture. The sensitivity of rapid tests can be improved by restricting testing to patients most likely to have acute GAS pharyngitis and avoiding testing patients more likely to have viral pharyngitis. This takes advantage of the spectrum effect (or spectrum bias) associated with many clinical tests including RADTs and throat cultures; the pretest probability of having the disease affects test results. One of the best validated scoring systems for children was developed by McIsaac, et al. Patients with greater likelihood of GAS infection tend to have more McIsaac criteria (fever, cervical adenopathy, tonsillar exudates, no cough, 3-15 years old), but the positive predictive value of the highest McIsaac score is only about 60% (Table 1.8). In contrast, a score ≤2 is

TABLE 1.8 Distribution of McIsaac Scores in a Study of Pediatric Patients With Pharyngitis*

McIsaac Score	Number of Patients (%)	GAS Culture-Positive† n (%)
0	42 (2%)	3 (7%)
1	200 (11%)	37 (19%)
2	576 (31%)	118 (20%)
3	552 (30%)	162 (29%)
4	365 (20%)	163 (45%)
5	113 (6%)	70 (62%)

*McIsaac criteria: Fever (temperature >38°C), tender anterior cervical adenopathy, tonsillar swelling or exudates, absence of cough, and age <15 years. One point is awarded for each criterion.
†Hospital laboratory throat culture result.
GAS, group A streptococci.
From Tanz RR, Gerber MA, Kabat W, et al. Performance of a rapid antigen detection test and throat culture in community pediatric offices: implications for management of pharyngitis. *Pediatrics.* 2009;123:437-444.

associated with a negative predictive value of about 80%. The presence of viral symptoms such as cough, rhinorrhea, conjunctivitis, laryngitis, stridor, croup, or diarrhea decreases the likelihood that the illness is due to GAS. Patients with a negative RADT result should not be treated before culture verification unless there is a particularly high suspicion of GAS infection (e.g., scarlet fever, peritonsillar abscess, or tonsillar exudates in addition to tender cervical adenopathy, palatal petechiae, fever, and recent exposure to a person with GAS pharyngitis).

Molecular "PCR-like" tests for GAS are available for use in hospital and reference laboratories. Some are cleared by the Food and Drug Administration (FDA) for use in physician office laboratories, particularly those offices that are certified to perform CLIA-moderate tests. These simplified molecular tests use methods that amplify the DNA of a specific GAS gene. They take less than 1 hour to perform and are reported to have both sensitivity and specificity ≥99% when compared to standard throat culture and PCR. They can be used as a "stand-alone" test for GAS or as a confirmatory test when the RADT is negative. There are three concerns with these molecular tests: (1) they are so sensitive it is likely they will identify more patients who are carriers than would ordinarily be identified by RADT and/or culture; (2) unless rigorous technique is followed they may be prone to contamination with exogenous GAS DNA from other swabs, a particular concern in physician offices when performed by staff who are not trained laboratory technologists; and (3) they are much more expensive than throat culture, and their costs may not be covered by all insurance plans.

Testing patients for serologic evidence of an antibody response to extracellular products of GAS is not useful for diagnosing acute pharyngitis. Because it generally takes several weeks for antibody levels to rise, streptococcal antibody tests are valid only for determining past infection. Specific antibodies that are often measured in the appropriate clinical setting include antistreptolysin O (ASO), anti-DNase B, and antihyaluronidase (AHT). When antibody testing is desired in order to evaluate a possible poststreptococcal illness, more than one of these tests should be performed to improve sensitivity.

◆ Treatment

Treatment begun within 9 days of the onset of GAS pharyngitis is effective in preventing acute rheumatic fever (ARF). Therapy does not

TABLE 1.9 Recommended Treatment Regimens for Acute Streptococcal Pharyngitis*

	Dose/Route	Duration	Frequency
Standard Treatment			
Amoxicillin	50 mg/kg up to 1000 mg/Oral	10 days	Once daily
Penicillin V	250 mg (500 mg for adolescents and adults)/Oral	10 days	bid
Benzathine penicillin G	600,000 U (weight <27 kg)/IM 1.2 million U (weight ≥27 kg)/IM	N/A N/A	Once
	Oral Dose	**Duration**	**Frequency**
Treatment for Penicillin-Allergic Patients			
Clarithromycin	15 mg/kg/day up to 500 mg/day	10 days	bid
Azithromycin†	12 mg/kg on day 1 then 6 mg/kg/d on days 2-5	5 days	Once daily
Clindamycin	21 mg/kg/day 20 mg/kg/day up to 900 mg/day	10 days	tid
Cephalosporins‡			
Cephalexin	40 mg/kg/day up to 1000 mg/day	10 days	bid
Cefadroxil	30 mg/kg/day up to 1000 mg/day	10 days	Once daily

*Based on Infectious Diseases Society of America 2012 and AAP Red Book recommendations.
†Maximum dose for children is 500 mg/day. Adult dosage: 500 mg the first day, 250 mg the subsequent 4 days.
‡First-generation cephalosporins (e.g., cephalexin and cefadroxil) are preferred but all cephalosporins are effective. Dosage and frequency vary among agents. Avoid use in patients with history of immediate (anaphylactic) hypersensitivity to penicillin or other β-lactam antibiotics.

appear to affect the risk of acute poststreptococcal glomerulonephritis (AGN). Antibiotic therapy also reduces the incidence of suppurative sequelae of GAS pharyngitis, such as peritonsillar abscess and cervical adenitis. In addition, treatment produces a more rapid resolution of signs and symptoms and terminates contagiousness within 24 hours. For these reasons, antibiotics should be instituted as soon as the diagnosis is supported by laboratory studies.

There are numerous antibiotics available for treating streptococcal pharyngitis (Table 1.9). The drugs of choice are penicillin and amoxicillin. Despite the widespread use of penicillin to treat streptococcal and other infections for many decades, resistance of GAS to penicillin or any other β-lactam antibiotic has not developed. Amoxicillin has been demonstrated to be effective in eradicating GAS when given by mouth once daily for 10 days. The convenience of once-daily dosing and palatability make amoxicillin an attractive approach despite its somewhat broader spectrum of antimicrobial activity. Penicillin can be given by mouth twice daily for 10 days or intramuscularly as a single injection of benzathine penicillin. Intramuscular benzathine penicillin alleviates concerns about patient compliance. A less painful parenteral alternative is benzathine penicillin in combination with procaine penicillin. Intramuscular procaine penicillin alone is not effective for prevention of ARF because adequate levels of penicillin are not present in blood and tissues for a sufficient time. Other β-lactams, including semisynthetic derivatives of penicillin and the cephalosporins, are at least as effective as penicillin for treating streptococcal pharyngitis. The broader spectrum of the cephalosporins and their higher cost relegate them to second-line status. The decreased dosing frequency of amoxicillin and some cephalosporins may improve patient adherence.

Patients who are allergic to penicillin can receive a cephalosporin if they have not had an immediate hypersensitivity reaction. Erythromycin or another non-β-lactam antibiotic, such as clarithromycin, azithromycin, or clindamycin, can be used. Resistance of GAS to macrolides has increased dramatically in many areas of the world where erythromycin has been widely used. Macrolide resistance also affects azithromycin and can affect clindamycin. Although this resistance has not yet emerged as a major problem in the United States, where the rate of macrolide resistance among GAS is generally 5-8%, there is much local variation. GAS resistance to clindamycin is in the range of 1-2%. Of note, both macrolide and clindamycin resistance are more common in Canada than in the United States. Sulfa drugs (including sulfamethoxazole combined with trimethoprim), tetracyclines, and chloramphenicol should not be used for treatment of acute streptococcal pharyngitis because they do not eradicate GAS.

Suppurative Complications

Antibiotic therapy has greatly reduced the likelihood of developing suppurative complications caused by spread of GAS from the pharynx or middle ear to adjacent structures. **Peritonsillar abscess** ("quinsy") manifests with fever, severe throat pain, dysphagia, "hot potato voice," pain referred to the ear, and bulging of the peritonsillar area with asymmetry of the tonsils and sometimes displacement of the uvula (Fig. 1.4; see also Table 1.4). There can be peritonsillar cellulitis without a well-defined abscess cavity. Trismus may be present. When an abscess is found clinically or by an imaging study such as a computed tomographic (CT) scan, surgical drainage is indicated. Peritonsillar abscess occurs most commonly in older children and adolescents.

Retropharyngeal abscess represents extension of an infection from the pharynx or peritonsillar region into the retropharyngeal (prevertebral) space, which is rich in lymphoid structures (Figs. 1.5 and 1.6; see also Table 1.4). Children younger than 4 years old are most often affected. Fever, dysphagia, drooling, stridor, extension of the neck, and a mass in the posterior pharyngeal wall may be noted. Surgical drainage is often required if frank suppuration has occurred. Spread of GAS via pharyngeal lymphatic vessels to regional nodes can cause **cervical lymphadenitis**. The markedly swollen and tender anterior cervical nodes that result can suppurate. Otitis media, mastoiditis, and sinusitis also may occur as complications of GAS pharyngitis. Additional parapharyngeal suppurative infections that may mimic streptococcal disease are noted in Table 1.4. Furthermore, any pharyngeal infectious process may produce **torticollis** if there is inflammation that extends

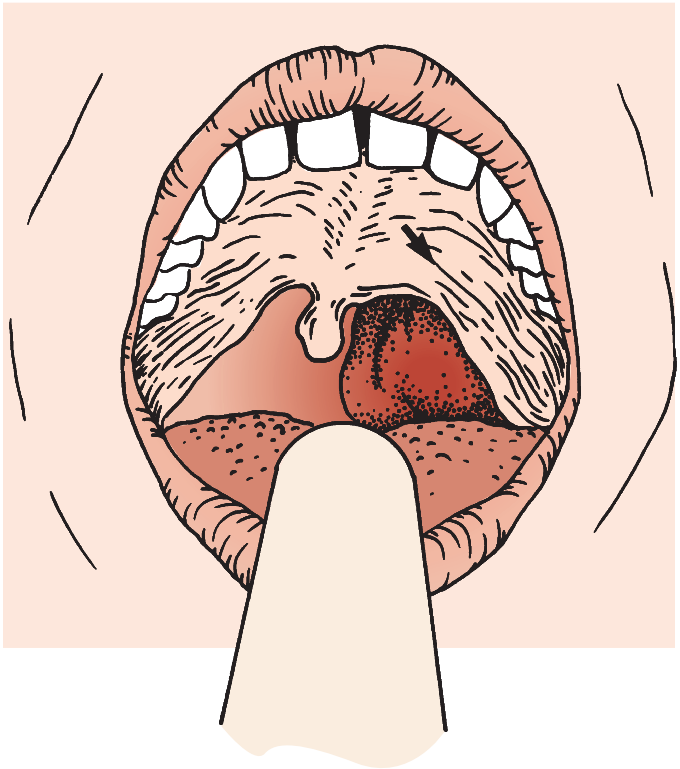

FIGURE 1.4 Peritonsillar abscess (quinsy, sore throat). The left tonsil is asymmetrically inflamed and swollen; there is displacement of the uvula to the opposite side. The supratonsillar space *(arrow)* is also swollen; this is the usual site of the surgical incision for drainage. Prominent unilateral cervical adenopathy typically coexists. (From Reilly BM. Sore throat. In: *Practical Strategies in Outpatient Medicine*. 2nd ed. Philadelphia: WB Saunders; 1991.)

to the paraspinal muscles and ligaments, producing pain, spasm, and, on occasion, rotary subluxation of the cervical spine. Oropharyngeal torticollis lasts less than 2 weeks and is not associated with abnormal neurologic signs or pain over the spinous process. Invasive sterile site or bacteremic infection with GAS is unusual as sequelae to pharyngitis.

Nonsuppurative Sequelae

Nonsuppurative complications include acute rheumatic fever (ARF), acute glomerulonephritis (AGN), and possibly reactive arthritis/synovitis. In addition, an association between streptococcal infection and neuropsychiatric disorders such as tic disorder, obsessive-compulsive disorder, and Tourette syndrome has been postulated. This possible association has been called PANDAS (pediatric autoimmune neuropsychiatric disorders associated with streptococci). The terminology has been modified to "pediatric acute-onset neuropsychiatric syndrome" (PANS) or "childhood acute neuropsychiatric syndrome" (CANS), in recognition that the etiologic role of GAS and benefit from antibiotic treatment have been difficult to establish, and it is likely that infections other than GAS infection are associated with the development, recurrence, or exacerbation of neuropsychiatric symptoms.

Therapy with an appropriate antibiotic within 9 days of onset of symptoms is highly effective in preventing ARF. Except in certain geographic areas (e.g., Salt Lake City) and populations (e.g., Hasidic Jewish communities) ARF is quite rare in North America. The impressive reduction in ARF prevalence in the United States since the mid-1960s may be related to reductions in the prevalence of so-called "rheumatogenic" GAS M types. The reason for the near disappearance of rheumatogenic types in the United States is unknown. Areas of the world with persistently high rates of ARF have different M types than the United States had in the past and has currently. AGN is not prevented by treatment of the antecedent streptococcal infection. Pharyngitis caused by one of the "nephritogenic" strains of GAS precedes

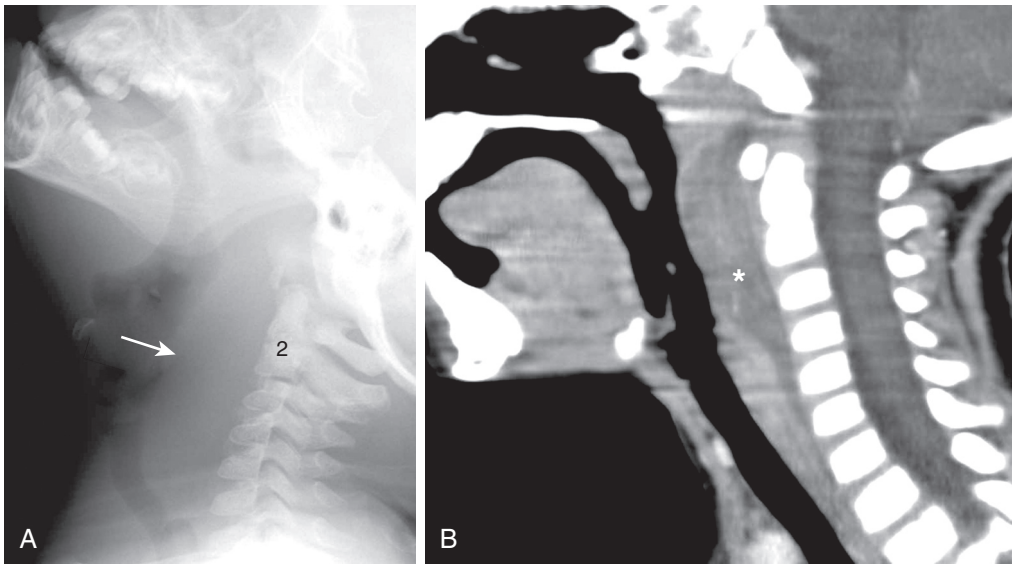

FIGURE 1.5 Retropharyngeal abscess in a 3-year-old female with sore throat and fever. *A,* Lateral soft tissue neck radiograph reveals extensive soft tissue swelling displacing the airway anteriorly from the skull base to C6 *(arrow). B,* Sagittal reconstructed contrast-enhanced computed tomography confirms thickened, enhancing retropharyngeal soft tissues indicating cellulitis. Region of hypoattenuating fluid is concerning for retropharyngeal abscess *(asterisk).* (From Lowe LH, Smith CJ. Infection and inflammation. In: *Caffey's Pediatric Diagnostic Imaging.* 12th ed. Vol 1. Philadelphia: Elsevier; 138; Figure 15.4.)

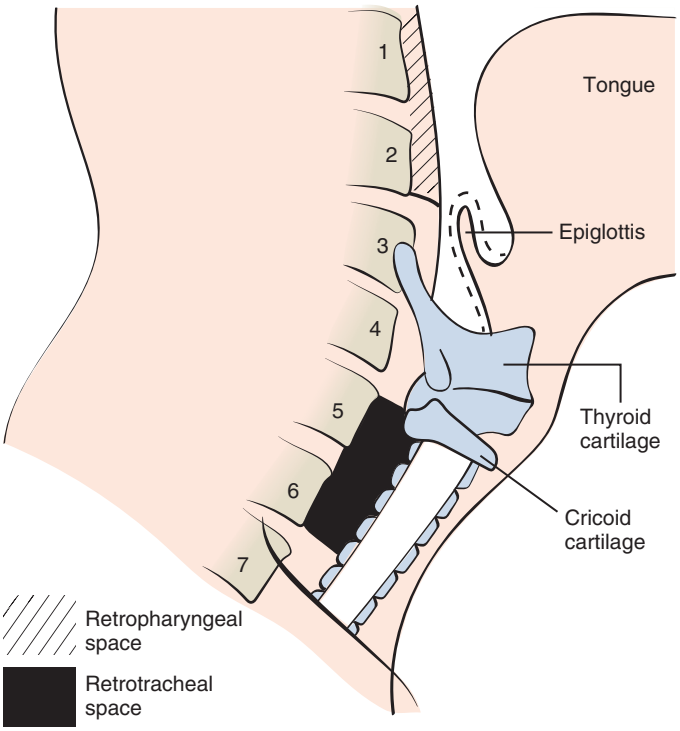

FIGURE 1.6 In an adolescent, the retropharyngeal space normally does not exceed 7 mm when measured from the anterior aspect of the C2 vertebral body to the posterior pharynx. In infants the retropharyngeal space is usually less than one width of the adjacent vertebral body. However, during crying, this distance may be three widths of the vertebral body. In addition, under normal circumstances, the retrotracheal space does not exceed 22 mm in adolescents when measured from the anterior aspect of C6 to the trachea. *Dotted lines* depict the "thumbprint" sign, noted on a lateral neck radiograph, made by a swollen epiglottis. (From Reilly BM. Sore throat. In: *Practical Strategies in Outpatient Medicine.* 2nd ed. Philadelphia: WB Saunders; 1991.)

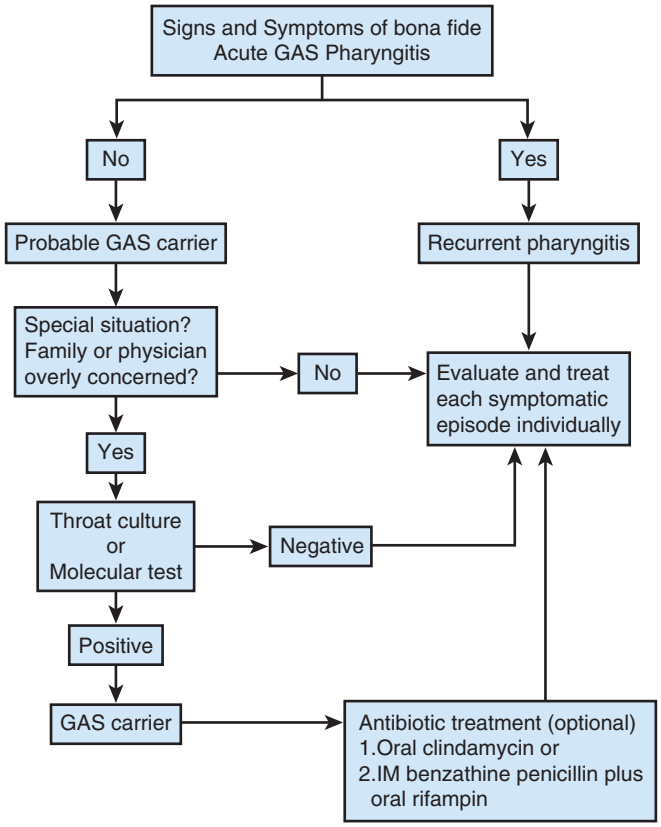

FIGURE 1.7 Management of patients with repeated or frequent positive rapid tests or throat cultures. GAS, group A streptococci; IM, intramuscular.

glomerulonephritis by about 10 days. Unlike ARF, which occurs only after GAS pharyngitis, AGN also can follow GAS skin infection.

Treatment Failure and Chronic Carriage

Treatment with penicillin cures GAS pharyngitis but does not eradicate GAS from the pharynx in as many as 25% of patients (Fig. 1.7). This causes considerable consternation among affected patients and their families. Resistance to penicillin is not the cause of treatment failure. A few such patients are symptomatic and are characterized as having clinical treatment failure. Re-infection with the same strain or a different strain is possible, as is intercurrent viral pharyngitis. Some of these patients may be chronic pharyngeal carriers of GAS who are suffering from a new superimposed viral infection; others may have been nonadherent to therapy. Many patients who continue to have positive tests for GAS despite antimicrobial treatment are asymptomatic and are identified only when follow-up throat swabs are obtained, a practice that is usually unnecessary in North America. Patients who adhered to therapy are at minimal risk for ARF. One explanation for asymptomatic persistence of GAS after treatment is that these patients are chronically colonized with GAS, were initially symptomatic because of a viral pharyngitis, and did not truly have acute streptococcal pharyngitis.

Patients who are chronically colonized with GAS are called chronic carriers. Carriers do not appear to be at risk for ARF or for development of suppurative complications, and they are rarely sources of spread of GAS in the community. There is no reason to exclude carriers from school. There is no easy way to identify chronic carriers prospectively among patients with symptoms of acute pharyngitis. The pathophysiology of chronic carriage is unknown. As resistance to penicillin is not a factor, many other causes have been hypothesized including non-adherence to antibiotic treatment, tolerance to antibiotics (suppression but lack of killing by antimicrobials), internalization of GAS by epithelial cells, and presence of β-lactamase-producing "co-pathogens," but none has been proven. The clinician should consider the possibility of chronic GAS carriage when a patient or a family member has multiple test-positive episodes of pharyngitis, especially when symptoms are mild or atypical. A culture or other test is usually positive for GAS when the suspected carrier is symptom-free or is receiving antibiotic treatment (intramuscular benzathine penicillin is recommended in order to eliminate concerns about compliance).

Carriers often receive multiple unsuccessful courses of antibiotic therapy in attempts to eliminate GAS. Physician and patient anxiety is common and can develop into "streptophobia." Unproven and ineffective therapies include tonsillectomy, prolonged administration of antibiotics, use of β-lactamase-resistant antibiotics, and culture or treatment of pets. Available treatment options for the physician faced with a chronic streptococcal carrier include the following:

1. Evaluate for GAS pharyngitis by throat swab each time the patient has pharyngitis with features that suggest streptococcal pharyngitis. Treat as acute GAS pharyngitis with amoxicillin or penicillin (or an alternative agent) each time a test is positive; this will prevent ARF if the GAS identified has been newly acquired. Avoid testing patients who do not have signs and symptoms suggestive of acute GAS pharyngitis.

2. Treating with one of the regimens effective for terminating chronic carriage.

The first option is simple, as safe as amoxicillin and penicillin, and appropriate for most patients. The second option should be reserved for particularly anxious patients; those with a history of ARF or living with someone who had it; or those living or working in nursing homes, chronic care facilities, and hospitals. Two antibiotic treatment regimens have been demonstrated in randomized trials to be effective for eradication of the carrier state:

- Intramuscular benzathine penicillin plus oral rifampin (10 mg/kg/dose up to 300 mg, given twice daily for 4 days beginning on the day of the penicillin injection)
- Oral clindamycin, given for 10 days (20 mg/kg/day up to 450 mg, divided into three equal doses)

Clindamycin is easier to use than intramuscular penicillin plus oral rifampin and may be somewhat more effective. Amoxicillin-clavulanate (40 mg amoxicillin/kg/day up to 2000 mg amoxicillin/day divided tid for 10 days) has also been used. Successful eradication of the carrier state makes evaluation of subsequent episodes of pharyngitis much easier, although chronic carriage can recur upon re-exposure to GAS.

Recurrent Acute Pharyngitis

Some patients seem remarkably susceptible to developing GAS pharyngitis. The reasons for frequent *bona fide* acute GAS pharyngitis are obscure. In contrast to chronic carriers, appropriate antibiotic treatment of each episode results in eradication of the organism.

The role of tonsillectomy in the management of patients with multiple episodes of streptococcal pharyngitis is controversial. The presence of tonsils is not necessary for GAS to infect the throat. Fewer episodes of sore throat were reported among patients treated with tonsillectomy (in contrast to patients treated without surgery) during the first 2 years after operation. Patients had experienced numerous episodes of pharyngitis over several years, and it appears that not all episodes were caused by GAS. By 2 years after tonsillectomy there was no difference between the groups in the frequency of pharyngitis. The postoperative complication rate among tonsillectomy patients was 14%. *Tonsillectomy cannot be recommended for treatment of* recurrent *pharyngitis except in unusual circumstances.* It is preferable to treat most patients with penicillin or amoxicillin whenever symptomatic GAS pharyngitis occurs. Obtaining follow-up throat specimens for culture can help distinguish recurrent pharyngitis from chronic carriage but is unnecessary in most instances.

INFECTION WITH STREPTOCOCCI THAT ARE NOT GROUP A (NON-A STREPTOCOCCI)

Certain β-hemolytic streptococci of serogroups other than group A cause acute pharyngitis. Well-documented *epidemics* of food-borne group C and group G streptococcal pharyngitis have been reported in young adults. In these situations, a high percentage of individuals who had ingested the contaminated food promptly developed acute pharyngitis, and throat cultures yielded virtually pure growth of the epidemiologically linked organism. There have been outbreaks of group G streptococcal pharyngitis among children. However, the role of non-A streptococcal organisms as etiologic agents of acute pharyngitis in *endemic* circumstances has been difficult to establish. Group C and group G streptococci may be responsible for acute pharyngitis, particularly in adolescents. However, the exact role of these agents, most of which are carried asymptomatically in the pharynx of some children and young adults, remains to be fully characterized. When they are implicated as agents of acute pharyngitis, groups C and G organisms do not appear to necessitate treatment, inasmuch as they cause self-limited infections. Acute rheumatic fever is not a sequela to these infections but acute glomerulonephritis has been documented in rare cases after epidemic group C and group G streptococcal pharyngitis.

FUSOBACTERIUM NECROPHORUM

Fusobacterium necrophorum, an anaerobic gram-negative organism, is increasingly recognized as a cause of pharyngitis in older adolescents and adults (ages 15-30 years). Prevalence in studies in Europe is reported to be about 10% in patients with pharyngitis not caused by GAS, but large surveillance studies have not been performed. In a U.S. study of students at a university health clinic, *F. necrophorum* was detected by PCR in 20.5% of patients with pharyngitis and 9.4% of an asymptomatic convenience sample; some had more than one bacterium detected by PCR of throat swabs. Many of the pharyngitis patients with *F. necrophorum* had signs and symptoms indistinguishable from patients with increased likelihood for GAS pharyngitis: About one-third had fever, one-third had tonsillar exudates, two-thirds had anterior cervical adenopathy, and most did not have cough. The symptomatic overlap of *F. necrophorum* and GAS and the presence of asymptomatic carriage could complicate the clinical assessment of sore throat in adolescents but *F. necrophorum* is difficult to culture from the throat and neither a rapid test nor PCR is available for use in clinical care.

F. necrophorum pharyngitis can be associated with development of septic thrombophlebitis of the internal jugular vein, known as Lemierre syndrome (Fig. 1.8). Approximately 80% of cases of Lemierre syndrome are due to this bacterium, but the proportion of patients infected or colonized with *F. necrophorum* who develop pharyngitis and Lemierre syndrome is unknown. Patients present initially with fever, sore throat, exudative pharyngitis, and/or peritonsillar abscess. The symptoms persist, severe neck pain and swelling develop, and the patient appears toxic. Septic shock may ensue along with metastatic complications, especially septic pulmonary emboli. Diagnosis is confirmed by computed tomography or magnetic resonance imaging of the neck and isolation of the organism on anaerobic blood culture. *F. necrophorum* is usually sensitive in vitro to penicillin, but some isolates produce β-lactamases, and treatment failure with penicillin has been reported. Many expert clinicians use metronidazole, clindamycin, a β-lactam in combination with a β-lactamase inhibitor (such as ampicillin-sulbactam), or a carbapenem. The septic thrombophlebitis of Lemierre syndrome can be polymicrobial; combination antibiotic therapy may be beneficial. Some patients require surgical debridement and/or incision and drainage. The case-fatality rate may be as high as 4-9%.

ARCANOBACTERIUM INFECTION

Arcanobacterium haemolyticum is a gram-positive rod that has been reported to cause acute pharyngitis and scarlet fever-like rash, particularly in teenagers and young adults. Detecting this agent requires special methods for culture, and it has not routinely been sought in patients with scarlet fever or pharyngitis. The clinical features of *A. haemolyticum* are indistinguishable from GAS pharyngitis; pharyngeal erythema is present in almost all patients, patchy white to gray exudates in about 70%, cervical adenitis in about 50%, and moderate fever in 40%. Palatal petechiae and strawberry tongue may also occur. The scarlatiniform rash usually spares the face, palms, and soles. The rash is erythematous and blanches; it may be pruritic and demonstrate minimal desquamation. Erythromycin appears to be the treatment of choice.

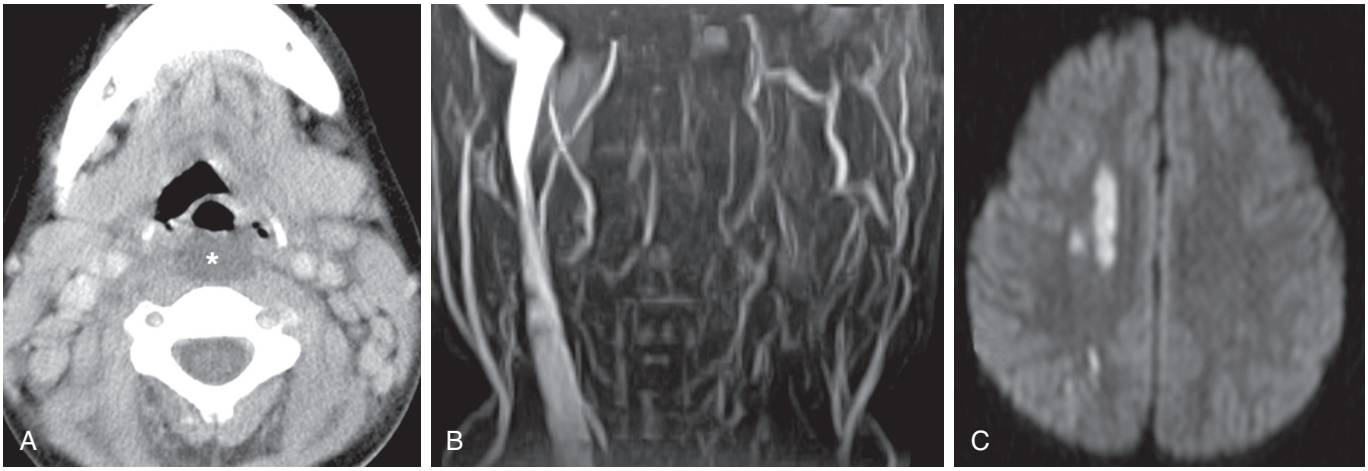

FIGURE 1.8 Lemierre syndrome (*Fusobacterium necrophorum* infection) complicated by stroke in a 6-year-old female presenting with fever, difficulty swallowing, and nuchal rigidity. *A,* Axial contrast enhanced computed tomography image shows low-attenuation retropharyngeal fluid *(asterisk). B,* Magnetic resonance imaging 2 days later, performed because of acute left arm weakness, confirms lack of left internal jugular vein patency on magnetic resonance venogram. *C,* Diffusion-weighted image of the brain reveals multiple small foci of bright signal infarction secondary to emboli from thrombophelebitis, vasospasm, or both. (From Lowe LH, Smith CJ. Infection and inflammation. In: *Caffey's Pediatric Diagnostic Imaging.* 12th ed. Vol 1. Philadelphia: Elsevier; 137; Figure 15.2.)

EPIGLOTTITIS AND BACTERIAL TRACHEITIS

Epiglottitis (or supraglottitis) is a life-threatening infection of the airway proximal to the vocal cords (Fig. 1.9; see also Fig. 1.6). Historically, it was an infection in 1-4 year-old children caused by *Haemophilus influenzae* type b. It presents with acute onset of fever and severe sore throat. This disease progresses rapidly to airway compromise. Patients are often drooling and leaning forward with the neck extended. Some patients may have stridor, but a muffled voice is more common. Management depends on establishing a secure airway by intubation and treating with antibiotics. When epiglottitis is suspected, the oropharynx should not be visualized or manipulated except in a controlled environment (intensive care unit or operating room) by someone with expertise in management of the airway who is prepared to immediately intubate the patient. Vaccination against *H. influenzae* type b has nearly eliminated this disease in childhood; however, epiglottitis caused by GAS, *Streptococcus pneumoniae*, *Staphyloccocus aureus*, and non-type b *H. influenzae* occurs occasionally.

Bacterial tracheitis (bacterial croup, bacterial laryngotracheitis) is a rare complication of viral croup. *S. aureus* is the most common superinfecting bacteria identified. Patients have a history of prolonged croup symptoms that become dramatically worse with fever and signs of airway obstruction. While sore throat may have been present at the onset of croup, it is not a prominent complaint once bacterial infection of the airway occurs. The clinical appearance of patients with bacterial tracheitis may mimic that of patients with epiglottitis.

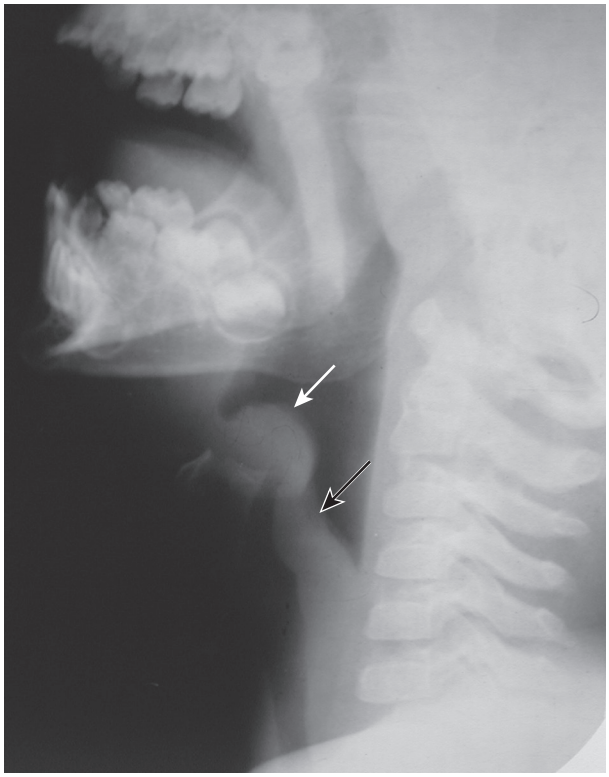

FIGURE 1.9 Epiglottis in a 5-year-old boy with respiratory distress and drooling. A lateral soft tissue neck radiograph shows a markedly thickened epiglottis *(white arrow)*, which is referred to as the "thumb" sign. The aryepiglottic folds *(black arrow)* also are thickened. (From Laya BF, Lee EY. Upper airway disease. In: *Caffey's Pediatric Diagnostic Imaging.* 12th ed. Vol 1. Philadelphia: Elsevier; 529; Figure 51.2.)

DIPHTHERIA

Diphtheria is a very serious disease that is caused by pharyngeal infection by toxigenic strains of *Corynebacterium diphtheriae.* It has become very rare in the United States and other developed countries as a result of immunization. The few diphtheria cases recognized annually in the United States usually occur in unimmunized individuals; the fatality rate is about 5%.

(See *Nelson Textbook of Pediatrics*, p. 2035)

◆ Pathogenesis

The pathogenesis of diphtheria involves nasopharyngeal mucosal colonization by *C. diphtheriae* and toxin elaboration after an incubation period of 1-5 days. Toxin leads to local tissue inflammation and necrosis (producing an adherent grayish membrane made up of fibrin, blood, inflammatory cells, and epithelial cells) and it is absorbed into the bloodstream. Fragment B of the polypeptide toxin binds particularly well to cardiac, neural, and renal cells, and the smaller fragment A enters cells and interferes with protein synthesis. Toxin fixation by tissues may lead to fatal myocarditis (with arrhythmias) within 10-14 days and to peripheral neuritis within 3-7 weeks.

◆ Clinical Features

Acute tonsillar and pharyngeal diphtheria is characterized by sore throat, anorexia, malaise, and low-grade fever. The grayish membrane forms within 1-2 days over the tonsils and pharyngeal walls and occasionally extends into the larynx and trachea. Cervical adenopathy varies but may be severe and associated with development of a "bull neck." In mild cases, the membrane sloughs after 7-10 days, and the patient recovers. In severe cases, an increasingly toxic appearance can lead to prostration, stupor, coma, and death within 6-10 days. Distinctive features include palatal paralysis, laryngeal paralysis, ocular palsies, diaphragmatic palsy, and myocarditis. Airway obstruction (from membrane formation) may complicate the toxigenic manifestations.

◆ Diagnosis

Accurate diagnosis requires isolation of *C. diphtheriae* on culture of material from beneath the membrane, with confirmation of toxin production by the organism isolated. Laboratories must be forewarned that diphtheria is suspected. Other tests are of little value.

GONOCOCCAL PHARYNGITIS

Acute symptomatic pharyngitis caused by *Neisseria gonorrhoeae* occurs occasionally in sexually active individuals as a consequence of oral-genital contact. In cases involving young children, sexual abuse must be suspected. The infection usually manifests as an ulcerative, exudative tonsillopharyngitis but may be asymptomatic and resolve spontaneously. Gonococcal pharyngitis occurs after fellatio in homosexual men and heterosexual women and is less readily acquired after cunnilingus. Gonorrhea rarely is transmitted from the pharynx to a sex partner, but pharyngitis can serve as a source for gonococcemia. Diagnosis requires culture on appropriate selective media (e.g., Thayer-Martin medium). Nucleic acid amplification tests (NAAT) may also detect the organism from pharyngeal and other sites. Examination and testing for other sexually transmitted infections and pregnancy are recommended.

CHLAMYDIAL AND MYCOPLASMAL INFECTIONS

Chlamydia species and *Mycoplasma pneumoniae* may cause pharyngitis, although the frequency of these infections is unclear. *Chlamydia trachomatis* has been implicated serologically as a cause of pharyngitis in as many as 20% of adults with pharyngitis, but isolation of the organism from the pharynx has proved more difficult. *Chlamydia pneumoniae* has also been identified as a cause of pharyngitis. Because antibodies to this organism show some cross reaction with *C. trachomatis*, it is possible that infections formerly attributed to *C. trachomatis* were really caused by *C. pneumoniae*. Diagnosis of chlamydial pharyngitis is difficult, whether by culture or serologically, and neither method is readily available to the clinician.

M. pneumoniae most likely causes pharyngitis. Serologic (positive mycoplasma IgM) or, less often, culture methods can be used to identify this infectious agent, which was found in 33% of college students with pharyngitis in one study. PCR is diagnostic but there is no need to seek evidence of these organisms routinely in pharyngitis patients in the absence of ongoing research studies of nonstreptococcal pharyngitis. The efficacy of antibiotic treatment for *M. pneumoniae* and chlamydial pharyngitis is not known, but these illnesses appear to be self-limited.

SUMMARY AND RED FLAGS

Sore throat is a common complaint. Most children with acute sore throat have a viral illness. Accurate diagnosis of acute streptococcal pharyngitis is essential because appropriate therapy ensures prevention of serious suppurative and nonsuppurative complications. Life-threatening infectious complications of oropharyngeal infections may manifest with mouth pain, pharyngitis, parapharyngeal space infectious extension, and/or airway obstruction. Other red flags are prolonged fever, prolonged sore throat, drooling, trismus, and severe, unremitting pain (see Table 1.5).

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A bibliography is available at ExpertConsult.com

(See *Nelson Textbook of Pediatrics*, p. 1493)

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