Streptococcal Infections:

https://www.msdmanuals.com/professional/infectious-diseases/gram-positive-cocci/staphylococcal-infections

Streptococci are gram-positive aerobic organisms that cause many disorders, including pharyngitis, pneumonia, wound and skin infections, sepsis, and endocarditis. Symptoms vary with the organ infected. Sequelae of infections due to group A beta-hemolytic streptococci may include rheumatic fever and glomerulonephritis. Most strains are sensitive to penicillin, but macrolide-resistant strains have recently emerged.

(See also Pneumococcal Infections, Rheumatic Fever, and Tonsillopharyngitis.)

Classification of streptococci

Three different types of streptococci are initially differentiated by their appearance when they are grown on sheep blood agar:

- Beta-hemolytic streptococci produce zones of clear hemolysis around each colony.
- Alpha-hemolytic streptococci (commonly called viridans streptococci) are surrounded by green discoloration resulting from incomplete hemolysis.
- Gamma-hemolytic streptococci are nonhemolytic.

Subsequent classification, based on carbohydrates in the cell wall, divides streptococci into 20 Lancefield groups A through H and K through V (see table Lancefield Classification*). Viridans streptococci form a separate group that is difficult to classify. In the Lancefield classification, enterococci were initially included among the group D streptococci but are now classified as a separate genus even though they do express Lancefield group D antigens. Some streptococci such as Streptococcus pneumoniae are alpha-hemolytic, ie, they are a type of viridans streptococci, and do not express Lancefield antigens. Lancefield groups K through V are streptococcal species of limited virulence that can cause infections in immunocompromised people.

TABLE

Lancefield Classification*

Virulence factors

Many streptococci elaborate virulence factors, including streptolysins, DNAases, and hyaluronidase, which contribute to tissue destruction and spread of infection. A few strains release exotoxins that activate certain T cells, triggering release of cytokines, including tumor necrosis factor-alpha, interleukins, and other immunomodulators. These cytokines activate the complement, coagulation, and fibrinolytic systems, leading to shock, organ failure, and death.

Diseases Caused by Streptococci

The most significant streptococcal pathogen is *S. pyogenes*, which is beta-hemolytic and in Lancefield group A and is thus denoted as group A beta-hemolytic streptococci (GABHS).

The **most common acute diseases due to GABHS** are

- Pharyngitis
- Skin infections

In addition, delayed, nonsuppurative complications (rheumatic fever, acute glomerulonephritis) sometimes occur ≥ 2 weeks after infection.

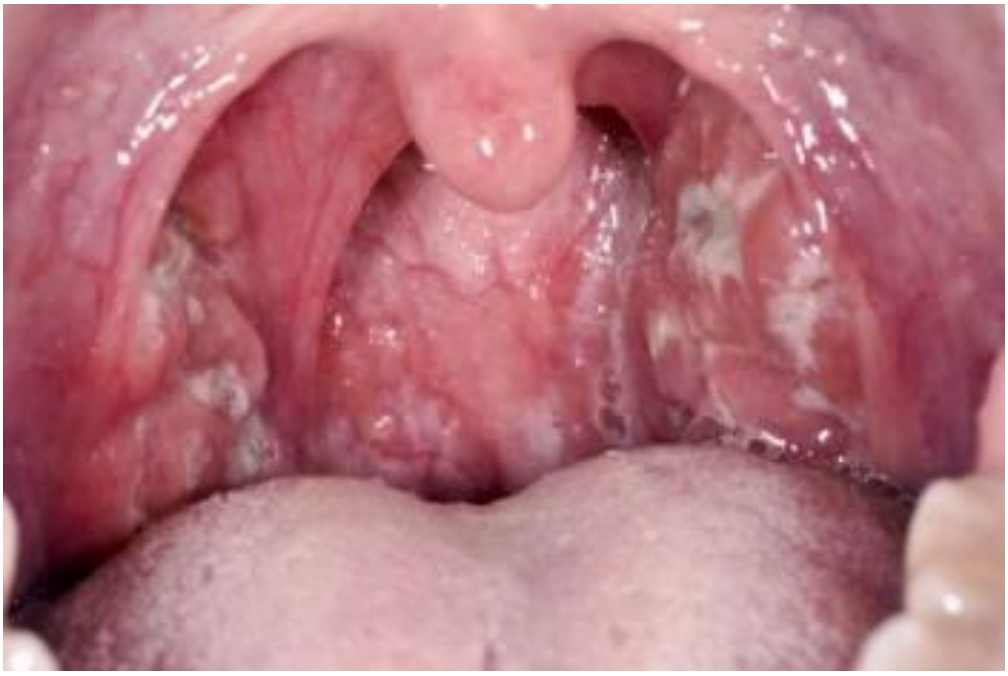
GABHS can spread through the affected tissues and along lymphatic channels (causing lymphangitis) to regional lymph nodes (causing lymphadenitis). GABHS can also cause local suppurative complications, such as peritonsillar abscess, otitis media, sinusitis, and bacteremia. Suppuration depends on the severity of infection and the susceptibility of tissue.
Other serious GABHS infections include septicemia, puerperal sepsis, endocarditis, pneumonia, and empyema.

Disease caused by other streptococcal species is less prevalent and usually involves soft-tissue infection or endocarditis (see table Lancefield Classification*). Some non-GABHS infections occur predominantly in certain populations (eg, group B streptococci in neonates and postpartum women).

Streptococcal pharyngitis

Streptococcal pharyngitis is usually caused by GABHS. About 20% of patients present with sore throat, fever, a beefy red pharynx, and a purulent tonsillar exudate. The remainder have less prominent symptoms, and the examination resembles that of viral pharyngitis. The cervical and submaxillary nodes may enlarge and become tender. Streptococcal pharyngitis can lead to peritonsillar abscess. Cough, laryngitis, and stuffy nose are not characteristic of streptococcal pharyngeal infection; their presence suggests another cause (usually viral or allergic).
An asymptomatic carrier state may exist in as many as 20%.

Streptococcal Pharyngitis



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The pharynx is erythematous, and the tonsils have purulent exudates.

DR P. MARAZZI/SCIENCE PHOTO LIBRARY

Scarlet fever

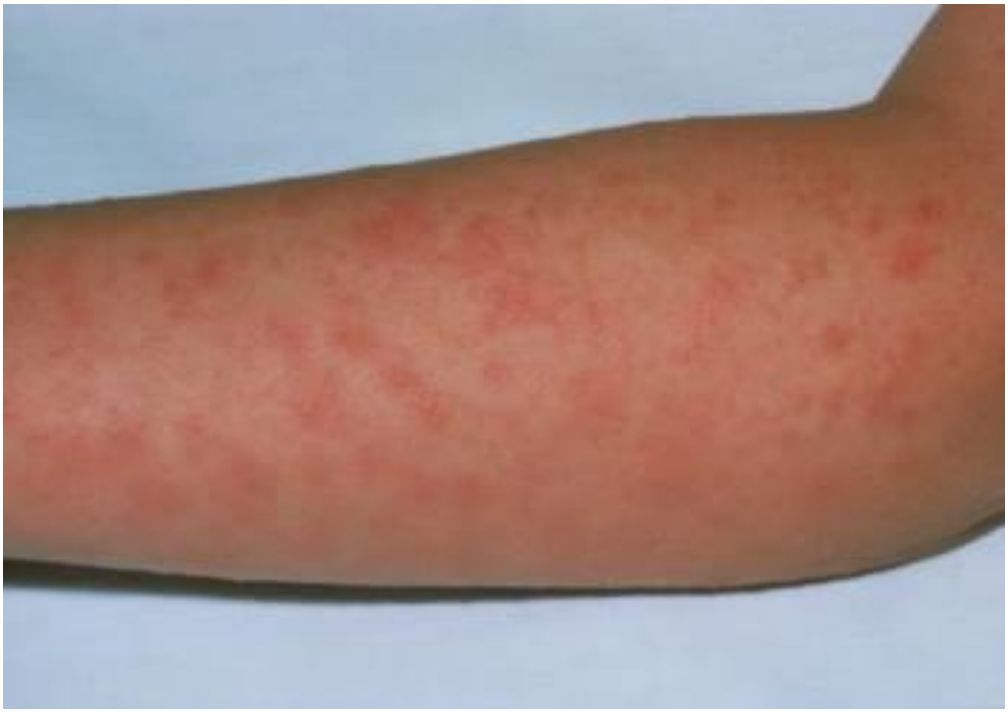
Scarlet fever is uncommon today, but outbreaks still occur. Transmission is enhanced in environments that result in close contact among people (eg, in schools or day care centers).

Scarlet fever, a predominantly childhood disease, usually follows a pharyngeal streptococcal infection; less commonly, it follows streptococcal infections at other sites (eg, the skin). Scarlet

fever is caused by group A streptococcal strains that produce an erythrogenic toxin, leading to a diffuse pink-red cutaneous flush that blanches with pressure.

The rash is seen best on the abdomen or lateral chest and as dark red lines in skinfolds (Pastia lines) or as circumoral pallor. The rash consists of characteristic numerous small (1- to 2-mm) papular elevations, giving a sandpaper quality to the skin. The upper layer of the previously reddened skin often desquamates after fever subsides. The rash usually lasts 2 to 5 days.

Scarlet Fever



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The classic scarlet fever rash initially appears as tiny red papules on the chest and abdomen. Papules may then spread over the body. The rash resembles sunburn, feels like rough sandpaper, and lasts about 2 to 5 days.

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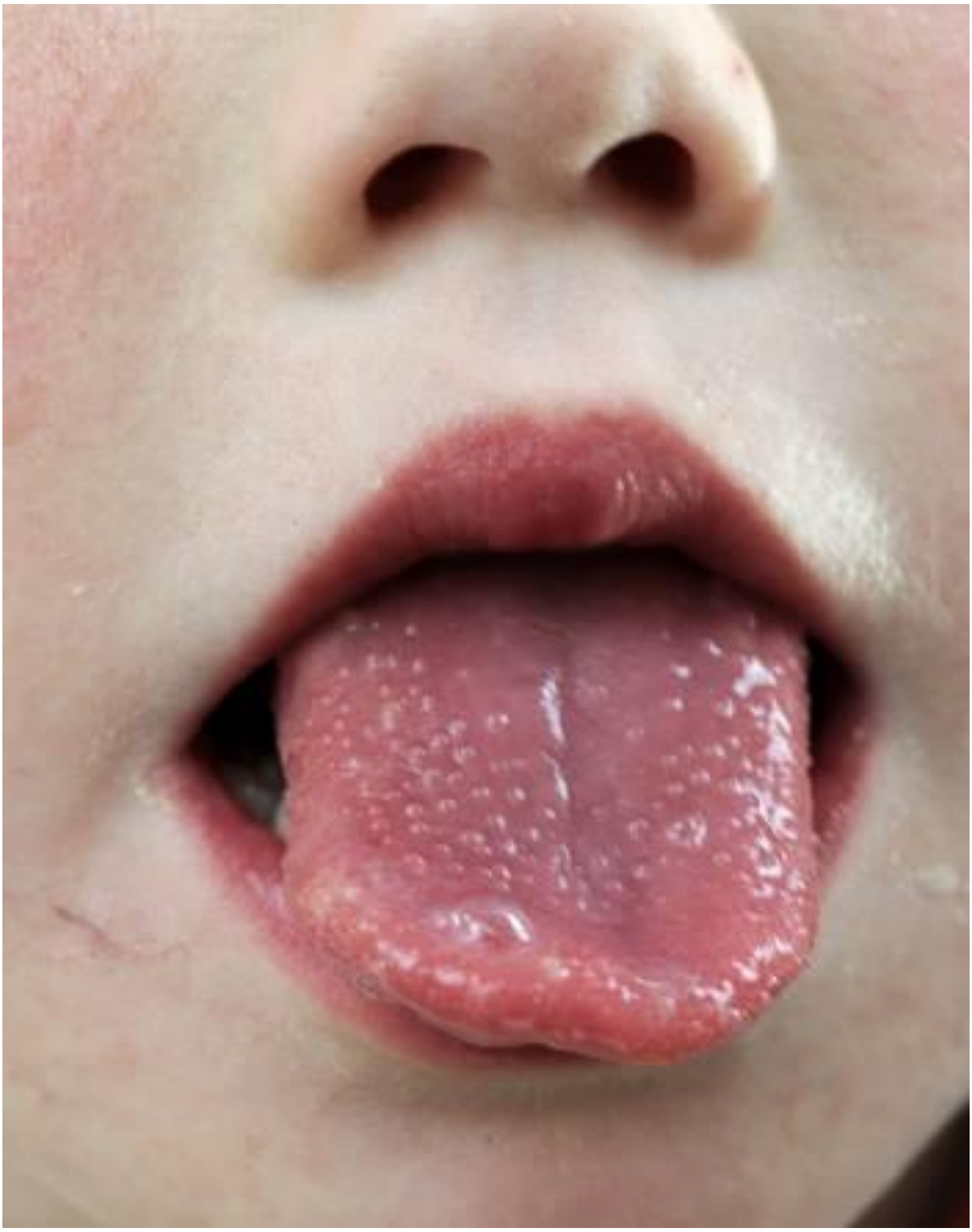
A strawberry tongue (inflamed papillae protruding through a bright red coating) also occurs and must be differentiated from that seen in toxic shock syndrome and Kawasaki disease.

Strawberry Tongue (Child)



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This tongue is erythematous with prominent papillation.

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Other symptoms are similar to those in streptococcal pharyngitis, and the course and management of scarlet fever are the same as those of other group A infections.

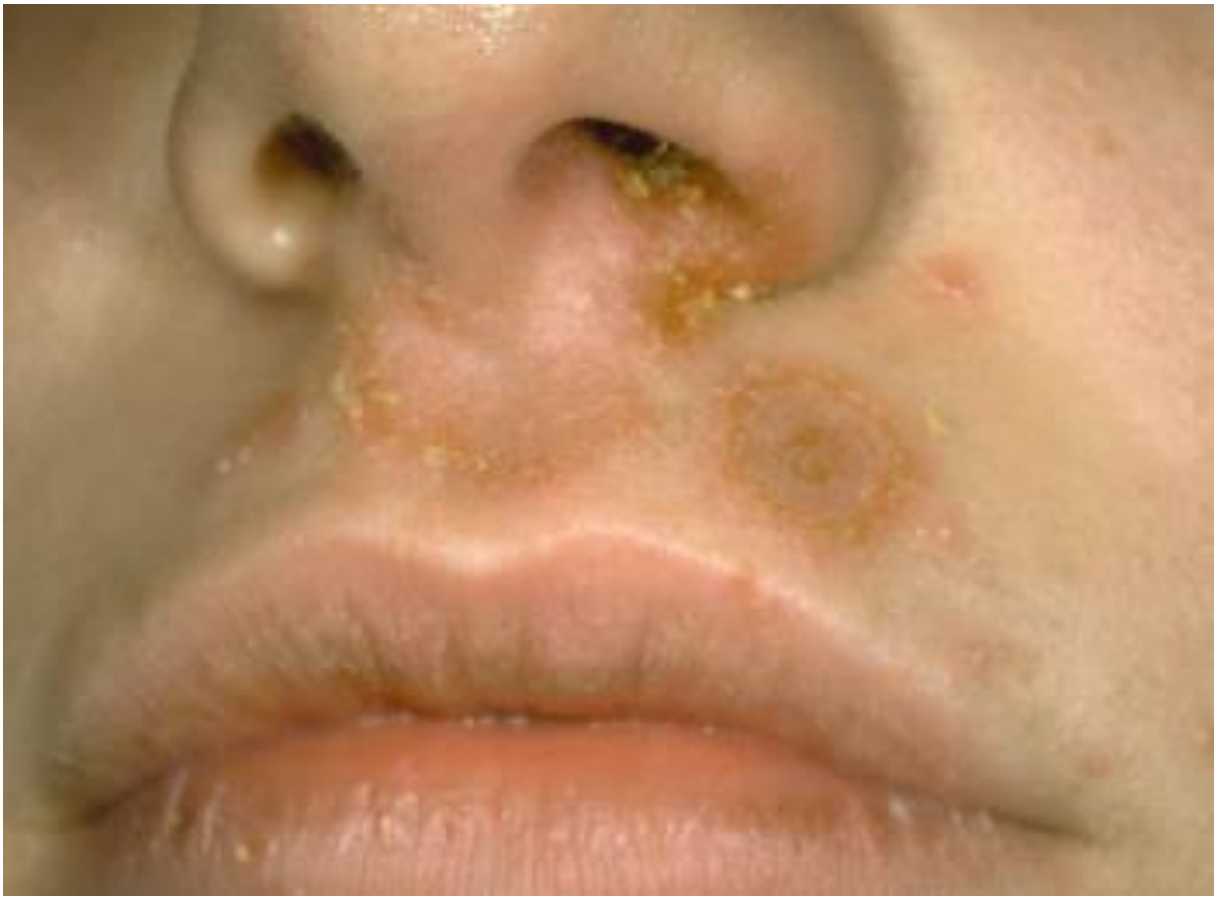
Streptococcal skin infections

Skin infections include

- Impetigo
- Erysipelas
- Cellulitis

Impetigo is a superficial skin infection that causes crusting or bullae.

Impetigo



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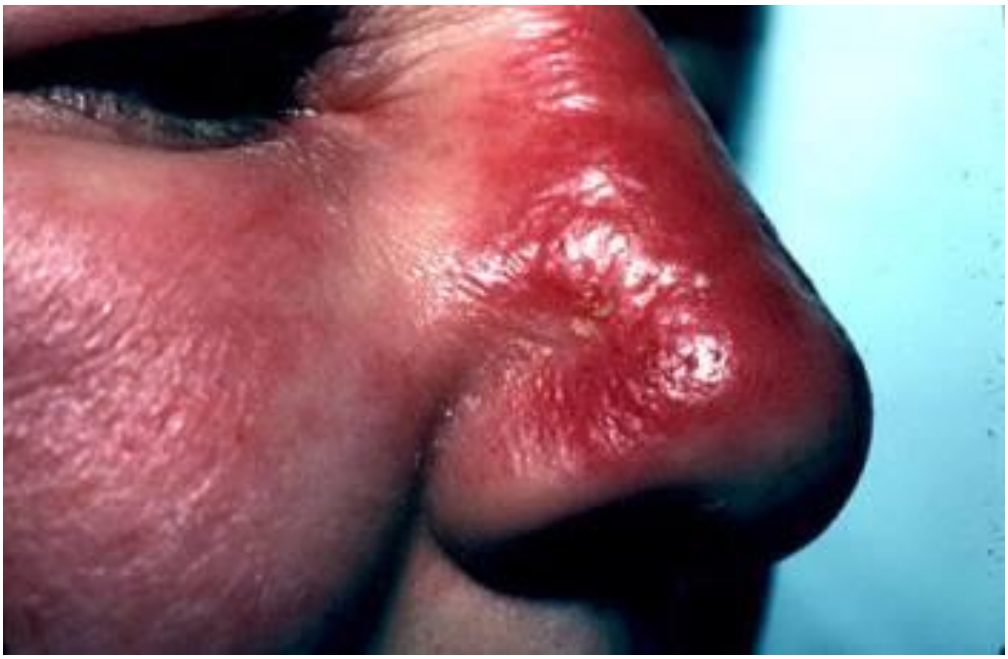
In impetigo, clusters of vesicopustular or bullous lesions form, rupture, and develop a honey-colored crust.

Image courtesy of Thomas Habif, MD.

Erysipelas is a superficial cellulitis that also involves the lymphatics. Patients have shiny, red, raised, indurated lesions with distinct margins. It is most often caused by GABHS, but other streptococcal and nonstreptococcal organisms are sometimes involved.

Erysipelas (Face)



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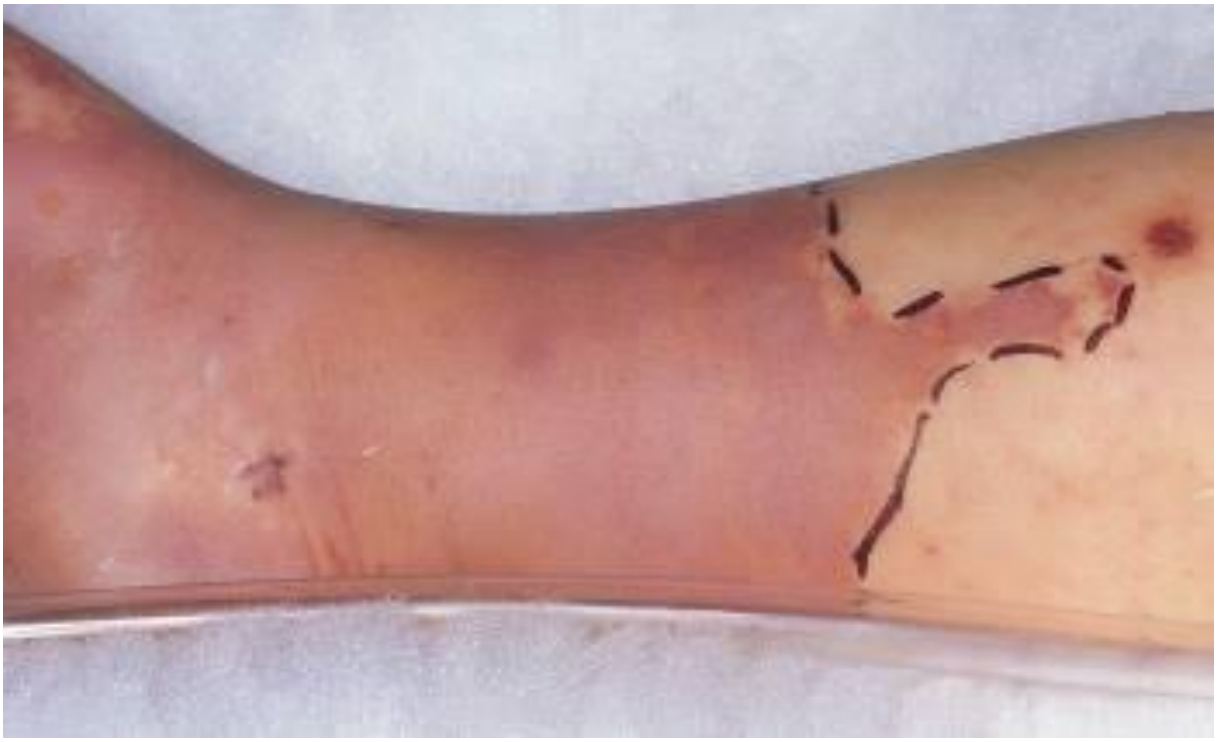
Erysipelas is characterized by shiny, raised, indurated, and tender plaque-like lesions with distinct margins.

Image provided by Thomas Habif, MD.

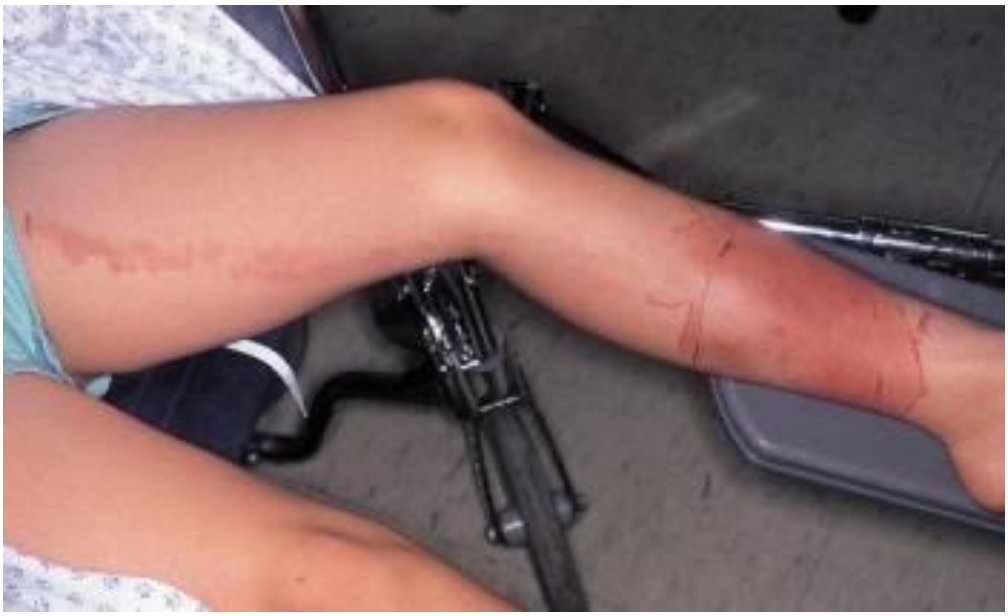
Cellulitis involves the deeper layers of skin and may spread rapidly because of the numerous lytic enzymes and toxins produced mainly by group A streptococci.

Manifestations of Streptococcal Cellulitis



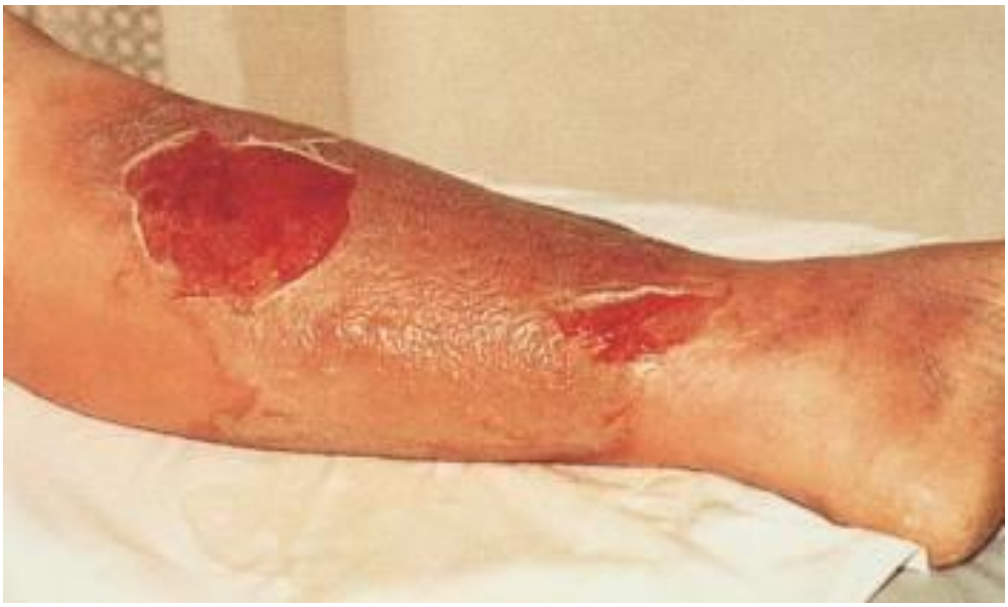
Streptococcal Cellulitis

This photo shows the focal redness and swelling, usually accompanied by warmth and tenderness, characteristic of focal cellulitis. Note the clinician has marked the border of the cellulitis with a pen, to facilitate recognition of spread or resolution.



Streptococcal Cellulitis with Accompanying Lymphangitis

This photo shows the focal redness and swelling of the lower leg, usually accompanied by warmth and tenderness, characteristic of focal cellulitis. The clinician has marked the border of the cellulitis with a pen, to facilitate recognition of spread or resolution. Note the line of redness extending up the thigh due to lymphangitis.



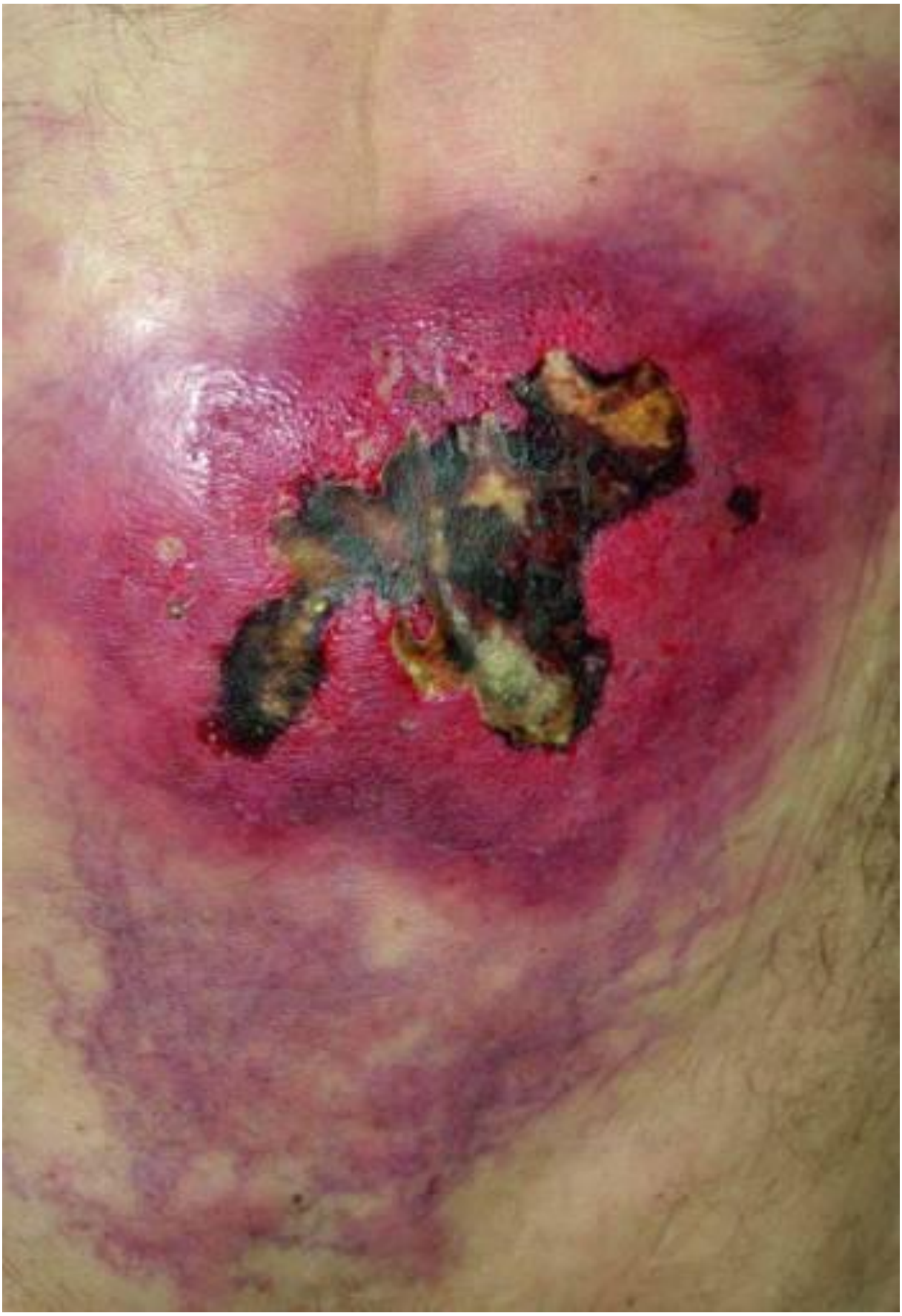
Streptococcal Cellulitis with Accompanying Tissue Necrosis

Necrotizing fasciitis

Necrotizing fasciitis due to *S. pyogenes* is a severe dermal (and sometimes muscle) infection that spreads along fascial planes. Inoculation originates through the skin or bowel.
Necrotizing fasciitis is prevalent among IV drug abusers.

Formerly known as streptococcal gangrene and popularized as the flesh-eating bacteria, the same syndrome may also be polymicrobial, involving a host of aerobic and anaerobic flora, including *Clostridium perfringens*. Polymicrobial infection is likely when the source is the bowel (eg, after intestinal surgery, bowel perforation, diverticulitis, or appendicitis).
Symptoms of necrotizing fasciitis begin with fever and exquisite localized pain out of proportion to physical findings; pain increases rapidly over time and is often the first (and sometimes only) manifestation. Diffuse or local erythema may be present. Thrombosis of the microvasculature causes ischemic necrosis, leading to rapid spread and disproportionally severe toxicity. In 20 to 40% of patients, adjacent muscles are invaded. Shock and renal dysfunction are common. Mortality is high, even with treatment.

Group A Streptococci (Necrotizing Fasciitis)



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This photo shows life-threatening infection of the subcutaneous fat and muscles by streptococci (group A), causing widespread necrosis involving the lower back.

Streptococcal toxic shock syndrome

Streptococcal toxic shock syndrome, similar to that caused by *S. aureus*, may result from toxin-producing strains of GABHS and occasionally from other streptococci. Patients are usually otherwise healthy children or adults with skin and soft-tissue infections.

Delayed complications of streptococcal infection

The mechanism by which certain strains of GABHS cause delayed complications is unclear but may involve cross-reactivity of streptococcal antibodies against host tissue.

Rheumatic fever, an inflammatory disorder, occurs in < 3% of patients in the weeks after untreated GABHS pharyngitis. It has become much less common in developed countries but is still common in developing countries. Diagnosis of a first episode is based on a combination of arthritis, carditis, chorea, specific cutaneous manifestations, and laboratory test results (Jones criteria — see Table: Modified Jones Criteria for a First Episode of Acute Rheumatic Fever (ARF)*).

One of the most important reasons for treating GABHS pharyngitis (strep throat) is to prevent rheumatic fever.

Poststreptococcal acute glomerulonephritis is an acute nephritic syndrome following pharyngitis or skin infection due to a certain limited number of nephritogenic strains of GABHS (eg, M protein serotypes 12 and 49). After a throat or skin infection with one of these strains, about 10 to 15% of patients develop acute glomerulonephritis. It is most common among children, occurring 1 to 3 weeks after infection. Nearly all children, but somewhat fewer adults, recover without permanent renal damage. Antibiotic treatment of GABHS infection has little effect on development of glomerulonephritis.

PANDAS syndrome (pediatric autoimmune neuropsychiatric disorder associated with group A streptococci) refers to a subset of obsessive disorders or tic disorders in children that is thought to be exacerbated by GABHS infection.

Certain forms of **psoriasis** (eg, guttate) may also be related to beta-hemolytic streptococcal infections.

Diagnosis of Streptococcal Infections

- Culture
- Sometimes rapid antigen tests or antibody titers

Streptococci are readily identified by culture on a sheep blood agar plate.

Rapid antigen-detection tests that can detect GABHS directly from throat swabs are available (ie, for point-of-care use). Many tests use enzyme immunoassay, but more recently, tests using optical immunoassay have become available. These rapid tests have high specificity (> 95%) but vary considerably in sensitivity (55% to 80 to 90% for the newer optical immunoassay test). Thus, positive results can establish the diagnosis, but negative results, at least in children, should be confirmed by culture. Because streptococcal pharyngitis is less common among adults and adults are unlikely to have poststreptococcal complications, many clinicians do not confirm a negative rapid screening result in adults by culture unless use of a macrolide is being considered; in such cases, culture with susceptibility testing to detect macrolide resistance should be done.

Demonstrating **antistreptococcal antibodies** in serum during convalescence provides only indirect evidence of infection. Antistreptococcal antibody tests are not useful in diagnosing acute GABHS infection because antibody first develops several weeks after GABHS infection begins and a single

high antibody titer is more likely to reflect a long antecedent infection. Antibodies are most useful in diagnosis of poststreptococcal diseases, such as rheumatic fever and glomerulonephritis. Antistreptolysin O (ASO) and antideoxyribonuclease B (anti-DNase B) titers begin to increase about 1 week after the GABHS infection and peak about 1 to 2 months after the infection. Both titers may remain elevated for several months, even after uncomplicated infections. Titers are measured in the acute phase and the convalescent phase, 2 to 4 weeks later; a positive result is defined as a ≥ 2-fold increase in the titer. A single titer greater than the upper limit of normal suggests an antecedent streptococcal infection or high streptococcal endemicity in the community. The ASO titer increases in only 75 to 80% of infections. For completeness in difficult cases, any one of the other tests (antihyaluronidase, antinicotinamide adenine dinucleotidase, antistreptokinase) can also be used.

Penicillin given within the first 5 days for symptomatic streptococcal pharyngitis may delay the appearance and decrease the magnitude of the ASO response.

Patients with streptococcal pyoderma usually do not have a significant ASO response but may have a response to other antigens (ie, anti-DNAase, antihyaluronidase).

CLINICAL CALCULATOR:

Centor Strep Pharyngitis Criteria With McIsaac Modification

Treatment of Streptococcal Infections

- Usually penicillin

Pharyngitis

(See also the Infectious Diseases Society of America's Practice Guidelines for the Diagnosis and Management of Group A Streptococcal Pharyngitis and the American Heart Association's guidelinePreventing Rheumatic Fever.)

Ordinarily, pharyngeal GABHS infections, including scarlet fever, are self-limited. Antibiotics shorten the course in young children, especially those with scarlet fever, but have only modest effect on symptoms in adolescents and adults. However, antibiotics help prevent local suppurative complications (eg, peritonsillar abscess), otitis media, and rheumatic fever.

Penicillin is the drug of choice for pharyngeal GABHS infections. No isolate of GABHS has shown penicillin resistance clinically. However, some streptococcal strains appear to have in vitro tolerance to penicillin (ie, significantly decreased bactericidal effect of penicillin); the clinical significance of such strains is unclear.

A single injection of benzathine penicillin G 600,000 units IM for small children (< 27 kg) or 1.2 million units IM for children weighing ≥ 27 kg, adolescents, and adults usually suffices.

Oral drugs may be used if the patient can be trusted to maintain the regimen for the required 10 days. Choices include

- Penicillin V 500 mg (250 mg for children < 27 kg) orally every 12 hours
- Amoxicillin 50 mg/kg (maximum 1 g) once a day for 10 days (which is an effective substitute for penicillin V)

Oral narrow-spectrum cephalosporins (eg, cephalexin, cefadroxil) are also effective and can be used unless patients have an anaphylactic reaction to penicillin. Azithromycin can be used for a 5-day course of therapy, although macrolides are inactive against *Fusobacterium necrophorum*, a common cause of pharyngitis in adolescents and adults. Delaying treatment 1 to 2 days until

laboratory confirmation increases neither the duration of disease nor the incidence of complications.

When penicillin and a beta-lactam are contraindicated, choices include

- Clindamycin 600 mg (6.7 mg/kg for children) orally every 8 hours
- Erythromycin or clarithromycin 250 mg (7.5 mg/kg for children) orally every 12 hours for 10 days
- Azithromycin 500 mg (15 mg/kg for children) once a day for 5 days

Because resistance of GABHS to macrolides has been detected, some authorities recommend in vitro confirmation of susceptibility if a macrolide is to be used and there is macrolide resistance in the community. Clindamycin 6.7 mg/kg orally every 8 hours is preferred in children who have relapses of chronic tonsillitis, possibly because of the following:

- Clindamycin has good activity against penicillinase-producing staphylococci or anaerobes coinfecting the tonsillar crypts and inactivating penicillin G.
- It appears to halt exotoxin production more rapidly than other drugs.

Amoxicillin/clavulanate is also effective.

Trimethoprim/sulfamethoxazole (TMP/SMX), some of the fluoroquinolones, and tetracyclines are unreliable for treating GABHS infection.

Sore throat, headache, and fever can be treated with analgesics or antipyretics. Aspirin should be avoided in children. Bed rest and isolation are unnecessary. Close contacts who are symptomatic or have a history of poststreptococcal complications should be examined for streptococci.

Skin infection

Cellulitis is often treated without doing a culture because isolating organisms can be difficult. Thus, regimens effective against both streptococci and staphylococci are used; for example, one of the following may be used:

- Dicloxacillin or cephalexin if methicillin-resistant *Staphylococcus aureus* (MRSA) is not likely
- TMP/SMX, linezolid, minocycline, or clindamycin if MRSA is suspected
  (see treatment of cellulitis)

Necrotizing fasciitis should be treated in an intensive care unit. Extensive (sometimes repeated) surgical debridement is required. A recommended initial antibiotic regimen is a beta-lactam (often a broad-spectrum drug until etiology is confirmed by culture) plus clindamycin. Although streptococci remain susceptible to beta-lactam antibiotics, animal studies show that penicillin is not always effective against a large bacterial inoculum because the streptococci are not rapidly growing and may lack penicillin-binding proteins, which are the target of penicillin activity.

Other streptococcal infections

For treating **groups B, C, and G infections,** drugs of choice are

- Penicillin
- Ampicillin
- Vancomycin

Cephalosporins or macrolides are usually effective, but susceptibility tests must guide therapy, especially in very ill, immunocompromised, or debilitated people and in people with foreign bodies at the infection site. Surgical wound drainage and debridement as adjuncts to antimicrobial therapy may be lifesaving.

S. gallolyticus (formerly *S. bovis*) is relatively susceptible to antibiotics. Although vancomycin-resistant *S. gallolyticus* isolates have been reported, the organism remains susceptible to penicillin and aminoglycosides.

Most **viridans streptococci** are susceptible to penicillin G and other beta-lactams. Resistance is growing, and therapy for such strains should be dictated by results of in vitro susceptibility tests.

Key Points

- **The most significant streptococcal pathogen is *S. pyogenes*, which is denoted as group A beta-hemolytic streptococci (GABHS).**
- **The 2 most common acute diseases due to GABHS are pharyngitis and skin infections.**
- **Delayed nonsuppurative complications, including rheumatic fever and poststreptococcal glomerulonephritis, can occur.**
- **Rapid antigen tests (ie, for point-of-care use) are very specific but not highly sensitive; confirm negative results using culture, at least in children.**
- **A penicillin or cephalosporin is preferred for pharyngitis; because macrolide resistance is increasing, susceptibility testing is recommended if that class of drugs is used.**

More Information

The following are some English-language resources that may be useful. Please note that THE MANUAL is not responsible for the content of these resources.

- Infectious Diseases Society of America: Practice Guidelines for the Diagnosis and Management of Group A Streptococcal Pharyngitis
- The American Heart Association (AHA): Preventing Rheumatic Fever: A New Guideline from the AHA