

تازه های عفونت های استرپتوکوکی گروه A

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INTRODUCTION

- Group A *Streptococcus* (GAS) is a gram-positive bacterium that grows in pairs or chains and causes complete, or -hemolysis when cultured on sheep blood agar.
- GAS cause a broad spectrum of disease, from primary upper respiratory tract and skin infections to secondary complications such as acute rheumatic fever (ARF) and glomerulonephritis, as well as severe invasive illness, including toxic shock syndrome (TSS) and necrotizing fasciitis which may involve almost every organ system.
- Despite the beneficial effects of antibiotics, clinicians continue to encounter GAS disease frequently in practice.

PHARYNGITIS

- GAS pharyngitis, the most common GAS infection, occurs most often in school-age children and accounts for 15% to 30% of all cases of pharyngitis in this age group.
- Transmission results from contact with infected respiratory tract secretions and is facilitated by close contact in schools and child care centers.
- The rate of GAS transmission from an infectious case to close contacts is approximately 35%.
- The incubation period for GAS pharyngitis is 2 to 4 days.



Differential Features of Group A Streptococcus (GAS) and Viral Pharyngitis

Findings Suggestive of GAS Infection

- SYMPTOMS
 - Sore throat
 - Dysphagia
 - Fever
 - Headache
 - Abdominal pain
 - Nausea/vomiting
- SIGNS
 - Soft palate petechiae
 - Anterior cervical lymphadenopathy
 - Scarlet fever rash

Findings Suggestive of Viral Infection

- SYMPTOMS
 - Cough
 - Running nose
 - Hoarse voice
 - Diarrhea
- SIGNS
 - Stomatitis
 - Conjunctivitis

Scarlet fever

- Scarlet fever, characterized by a diffuse, erythematous, blanching, fine papular rash that resembles sandpaper on palpation, is another manifestation of GAS infection.
- Scarlet fever is caused by erythrogenic toxin-producing strains of GAS and may manifest desquamation after the rash starts to fade.
- Exudative pharyngitis may occur, but this finding also is common with viral pharyngitis.
- In children younger than 3 years, an atypical symptom complex known as streptococcosis may occur, consisting of persistent nasal congestion, rhinorrhea, low-grade fever, and anterior cervical lymphadenopathy.
- In infants, the only symptoms may be low-grade fever, fussiness, and decreased feeding.

DIAGNOSIS OF GAS

- Diagnosis of acute GAS pharyngitis requires microbiologic testing.
- The decision to test should take into consideration patient age, clinical symptoms and signs, time of year, and exposure to sick contacts who have confirmed GAS infection.
- Testing for GAS pharyngitis, therefore, is recommended for the following patients who have symptoms suggestive of GAS:
 - those who do not have symptoms or signs of viral infection,
 - those exposed to diagnosed GAS infection,
 - and those who are ill when there is a high prevalence of GAS infection in the community.
- Of note, testing of asymptomatic contacts in homes, child care centers, or schools is not indicated unless the contact is at increased risk of developing complications from GAS infection.

- Several rapid tests for GAS pharyngitis are available. The specificity of these tests generally is high (very few false-positive results), but reported sensitivities vary considerably and generally are 80% to 85% (ie, false-negatives occur).
- As with throat cultures, the sensitivity of these tests is highly dependent on the quality of the throat swab specimen, experience of the test performer, and the rigor of the culture method used for comparison.

TESTS

- Serologic testing: may be used to confirm GAS pharyngitis.
 - The antibody response occurs 2 to 3 weeks after the onset of infection, it is not useful for the diagnosis of acute GAS pharyngitis
 - Serologic testing consists of measurements of antistreptococcal antibody titers, such as antistreptolysin O and antideoxyribonuclease B.
- Rapid antigen detection test (RADT):
 - RADT is suggested for initial use in patients who are likely to have GAS pharyngitis and in those whose throat culture results will not be available for more than 48 hours.
 - RADT has a specificity of 95% and greater and a sensitivity of 65% to 90%.
- Throat Culture: the gold standard, with 90% to 95% sensitivity

TREATMENT GOALS

- Treatment of GAS pharyngitis has several goals:
 - reducing the incidence of suppurative and non suppurative complications,
 - reducing the duration and relieving symptoms and signs of infection,
 - and reducing transmission to others.

TREATMENT

- Oral penicillin V K (250 mg to 500 mg twice to three times a day for 10 d) is the antibiotic treatment of choice for GAS pharyngitis because of its efficacy, safety, and narrow spectrum.
- No GAS isolate to date has shown penicillin resistance.
- For patients who cannot swallow pills, amoxicillin (50 mg/kg, maximum 1 g, once daily for 10 d) often is used instead of oral penicillin because of its more palatable liquid formulation.
- Cephalosporins or macrolides may be used as first-line therapy in patients allergic to β -lactam antibiotics but otherwise are not recommended as first-line therapy.
- A 5-day course of the cephalosporins cefpodoxime or cefdinir or the macrolide azithromycin at a higher dose (12 mg/kg per day) is comparable in terms of clinical and bacteriologic cures to a typical 10-day course of penicillin

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- Alternative choices include a narrow-spectrum cephalosporin, amoxicillin clavulanate, clindamycin, erythromycin, clarithromycin, or an azalide such as azithromycin.
- Patients who have multiple recurrent episodes may represent a carrier state.
- Pharyngitis in carriers is likely due to intercurrent viral infection, but if a GAS carrier develops an acute illness consistent with GAS pharyngitis, treatment is indicated.
- It is estimated that up to 20% of asymptomatic school-age children may be GAS carriers.

| Antibiotic | Dose | Duration |
|--|---|-----------------|
| Penicillin V K | 250 mg bid or tid if <27 kg (60 lb); 500 mg bid or tid if >27 kg (60 lb) | 10 d |
| Amoxicillin | 50 mg/kg, maximum 1 g, once daily | 10 d |
| Benzathine penicillin G | 600,000 U if <27 kg (60 lb); 1,200,000 U if >27 kg (60 lb) | Single dose |
| For penicillin-allergic patients: | | |
| Cephalexin | 25 to 50 mg/kg per day divided bid; maximum 1 g/d | 10 d |
| Cefpodoxime | 5 mg/kg, maximum 100 mg, bid | 5 d |
| Cefdinir | 7 mg/kg bid, maximum 600 mg/d | 5 d |
| Clindamycin | 20 mg/kg per day divided tid; maximum 1.8 g/d | 10 d |
| Azithromycin | 12 mg/kg, maximum 500 mg, once daily | 5 d |
| Clarithromycin | 15 mg/kg per day divided bid; maximum 250 mg/dose | 10 d |

- GAS carriage is difficult to eradicate with conventional antimicrobial therapy.
- Several agents, including clindamycin, cephalosporins, amoxicillin-clavulanate, azithromycin, or a combination that includes either 10 days of penicillin V or IM penicillin G benzathine with rifampin for the last 4 days of treatment are more effective than penicillin alone in terminating chronic streptococcal carriage.
- Of these drugs, oral clindamycin, 20 to 30 mg/kg per day in 3 doses (maximum, 900 mg/day) for 10 days, has been reported to be most effective. Documented eradication of carriage is helpful in evaluation of subsequent episodes of acute pharyngitis; however, carriage can recur after reacquisition of GAS infection, as some individuals are “carrier prone.”

Streptococcal Non Suppurative Complications

- These include:
 - **Rheumatic fever**
 - Post-streptococcal Glomerulonephritis
 - Streptococcal Toxic Shock Syndrome
 - Pediatric Autoimmune Neuropsychiatric Disorder Associated With Group A Streptococci
 - Necrotizing Fasciitis

RHEUMATIC FEVER

- ARF is caused by previous GAS pharyngeal infection, with a latent period of 2 to 4 weeks.
- The disorder is most common among children ages 5 to 15 years.
- Currently, most cases of ARF occur in developing countries.

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- ARF presents as an acute febrile illness, with clinical manifestations that include arthritis, carditis or valvulitis, skin lesions, and neurologic disturbances.
- The arthritis, occurring in 75% of patients who have ARF, is a migratory polyarthritis, affecting several joints in rapid succession, most commonly larger joints.
- Treatment with nonsteroidal anti-inflammatory drugs (NSAIDs) or salicylates may lead to resolution, potentially blunting the migratory feature; thus, monoarticular arthritis may occur.
- The relationship between post streptococcal reactive arthritis (PSRA), a migratory arthritis that occurs after a streptococcal infection, and ARF is debated.
- Some speculate this is a separate disorder; others think PSRA is part of the clinical spectrum of ARF.

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- The diagnosis of ARF is based on the Jones criteria, which were published initially in 1944 and later revised by Jones and subsequently the American Heart Association, with the most recent revision published in 2002.
- The rate of isolation of GAS from the oropharynges of patients who have ARF is only between 10% and 20%.
- Serologic testing, which demonstrates either elevated antibody titers or rising titers with serial testing, is used more often for confirmation of infection.
- The streptozyme test measures five streptococcal antibodies:
 - antistreptolysin O (ASO),
 - antihyaluronidase(AHase),
 - antistreptokinase (ASKase),
 - Antinicotinamideadenine dinucleotidase (anti-NAD),
 - and antideoxyribonuclease B (anti-DNase B) antibodies.

Jones criteria for the Diagnosis of Acute Rheumatic Fever

Jones Criteria for the Diagnosis of Acute Rheumatic Fever

Diagnosis: Requires 2 major criteria or 1 major and 2 minor criteria plus evidence of recent group A streptococcal infection

| Major | Minor | Evidence of Recent GAS Infection |
|----------------------|--------------------------------|---|
| Carditis | Fever | Positive throat culture or RADT or Elevated or rising antistreptococcal antibody titers |
| Polyarthrititis | Arthralgia | |
| Chorea | Elevated acute phase reactants | |
| Erythema marginatum | | |
| Subcutaneous nodules | Prolonged PR interval | |

RADT_rapid antigen detection test

Table 3.58. Revised Jones Criteria (2015)

1. All patients require evidence of antecedent GAS infection for diagnosis of ARF (except in case of chorea, where evidence of antecedent GAS infection is not required).
2. To confirm an initial diagnosis of ARF, need 2 major OR 1 major and 2 minor criteria.
3. To confirm recurrent ARF diagnosis, need 2 major OR 1 major and 2 minor OR 3 minor criteria.
4. Criteria for diagnosis are dependent on whether patient is from a low-risk or a moderate-/high-risk population. Moderate- and high-risk populations include countries where ARF remains endemic (Africa, Asia-Pacific, indigenous population of Australia). The United States, Canada, and Europe are examples of low-risk areas.
5. Major and minor criteria are listed below, by risk categorization; differences for moderate-/high-risk populations are **bolded**.

Low-Risk Population

Major Criteria

- Carditis (clinical or subclinical)
- Arthritis (polyarthritis only)
- Chorea
- Subcutaneous nodules
- Erythema marginatum

Minor Criteria

- Polyarthralgia
- Fever $\geq 38.5^{\circ}\text{C}$
- ESR ≥ 60 mm/h and/or CRP ≥ 3 mg/dL
- Prolonged PR interval (in absence of carditis)

Moderate- and High-Risk Population

Major Criteria

- Carditis (clinical or subclinical)
- Arthritis (polyarthritis or **monoarthritis**, or **polyarthralgia**)
- Chorea
- Subcutaneous nodules
- Erythema marginatum

Minor Criteria

- **Monoarthralgia**
- **Fever $\geq 38^{\circ}\text{C}$**
- **ESR ≥ 30 mm/h** and/or CRP ≥ 3 mg/dL
- Prolonged PR interval (in absence of carditis)

- The carditis of ARF is a pancarditis that occurs in 50% of patients.
- Symptoms and signs include chest pain, pericardial friction rub or murmur on auscultation, and heart failure.
- Varying degrees of heart block may be seen on electrocardiography, and cardiomegaly may be noted on chest radiographs.
- Echocardiography may show a variety of findings, including valvular regurgitation or stenosis, chamber enlargement or dysfunction, and pericardial effusion.

TREATMENT OF ARF

- Treatment of ARF focuses on eradication of acute disease manifestations, and prophylaxis against future GAS infection to prevent recurrent ARF.
- Eradication of GAS requires the same antibiotic regimens that are used to treat GAS pharyngitis.
- In addition, household contacts should have throat cultures performed and be treated if the cultures are positive for GAS.
- Aspirin, administered at 80 to 100 mg/kg per day and continued until all symptoms have resolved, is the major anti-inflammatory agent used for symptom relief.

Post streptococcal Glomerulonephritis

- Poststreptococcal glomerulonephritis (PSGN) is the most common cause of acute nephritis worldwide.
- PSGN is caused by previous throat or skin infection with nephritogenic strains of GAS.
- Although the exact mechanism is unclear, antigens of nephritogenic streptococci are believed to induce immune complex formation in the kidneys.
- The latent period is 1 to 3 weeks following GAS pharyngitis and 3 to 6 weeks following GAS skin infection.
- Deposition of GAS nephritogenic antigens within the glomerular subendothelium leads to glomerular immune complex formation, which triggers complement activation and subsequent inflammation; deposition within the glomerular subepithelium leads to epithelial cell damage and subsequent proteinuria.

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- The clinical presentation of PSGN ranges from asymptomatic microscopic hematuria to a nephritic syndrome consisting of hematuria, proteinuria, edema, hypertension, and elevated serum creatinine values.
- Gross hematuria is present in up to 50% of patients. Edema occurs because of sodium and fluid retention, which may lead to secondary hypertension.
- Decreased glomerular filtration rate results in increased serum creatinine concentration; acute renal failure requiring dialysis is possible.
- Urinalysis shows hematuria with or without red blood cell casts, proteinuria, and often pyuria.
- Serum C3 complement values are low due to activation of the alternative complement pathway, and C4 and C2 values are normal to mildly decreased.

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- Diagnosis requires clinical findings of acute nephritis in the setting of a recent GAS infection.
- If throat or skin cultures are negative, confirmation of a recent GAS infection may be obtained through serologic testing.
- Low C3 is characteristic of, but not specific to, PSGN.
- Renal biopsy typically is not performed to confirm the diagnosis of PSGN.

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- Treatment for PSGN focuses on supportive management of the clinical manifestations.
- Evidence of persistent GAS infection requires antibiotic treatment.
- Proteinuria starts to resolve as the patient recovers, but at a slower rate, and may persist for up to 3 years.
- The prognosis for most children who have PSGN is excellent.
- Although rare, recurrent proteinuria, hypertension, and renal insufficiency may develop up to several years after the initial illness.

Pediatric Autoimmune Neuropsychiatric Disorder Associated With Group A Streptococci

- Pediatric autoimmune neuropsychiatric disorder associated with group A streptococci (PANDAS) describes a group of neuropsychiatric disorders, in particular obsessive compulsive disorder (OCD), tic disorders, and Tourette syndrome, that are exacerbated by GAS infection.
- GAS infection in a susceptible host is believed to lead to an abnormal immune response, with production of autoimmune antibodies that cross react with brain tissue, which leads to central nervous system manifestations.
- This proposed association is controversial, with uncertainty focused on whether the association is causal or incidental, given the rates of GAS infection and GAS carriage and the frequency of OCD and tic disorders in children.



Streptococcal Toxic Shock Syndrome

- GAS TSS is a form of invasive GAS disease associated with the acute onset of shock and organ failure.
- The pathogenesis of GAS TSS is believed to be mediated by streptococcal exotoxins that act as super antigens, which activate the immune system.
- The resultant release of cytokines causes capillary leak, leading to hypotension and organ damage.
- GAS TSS typically presents with fever and the abrupt onset of severe pain, often associated with a preced in soft-tissue infection such as cellulitis.
- GAS TSS also may present in association with other invasive GAS diseases such as necrotizing fasciitis, bacteremia, pneumonia, osteomyelitis, myositis, or endocarditis.

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- The clinical course is characterized by abrupt onset of exacerbations that are associated with GAS infection, with gradual resolution over weeks to months.
- Diagnostic criteria for PANDAS include OCD and tic disorders, including Tourette syndrome; abrupt onset in childhood; an episodic course of symptoms; and a temporal relationship between GAS infection confirmed by RADT, throat culture, or skin culture or serologic testing.
- Evaluation for GAS infection should be considered in children who present with the abrupt onset of OCD or tic disorder.

Streptococcal Suppurative Complications

Tonsillopharyngeal Cellulitis and Abscess:

Cellulitis or abscess can arise in the peritonsillar or retropharyngeal spaces.

Retropharyngeal infection is more common in younger children; peritonsillar disease occurs more commonly in older children and adolescents.

Although these infections are often polymicrobial, GAS is the predominant bacterial species due to the spread of GAS pharyngitis to adjacent structures.

Clinical manifestations and positive blood cultures.

Diagnosis is clinical and requires a high degree of suspicion because of the rapid progression of infection

Contd.

- Treatment of GAS necrotizing fasciitis includes early and aggressive surgical exploration and debridement, antibiotic therapy, and hemodynamic support if GAS TSS is present as well.
- Surgical exploration facilitates debridement of necrotic tissue and obtaining of cultures to guide antibiotic therapy.
- Repeat surgery is necessary until all necrotic tissue has been removed.
- Antibiotic therapy with penicillin G IV (300,000 U/kg per day divided every 4 to 6 h) plus clindamycin IV (13 mg/kg, maximum 600 mg, every 8 h) is recommended.
- Antibiotic therapy should continue for several days after completion of surgical debridement.

Table 3.60. Chemoprophylaxis for Recurrences of Acute Rheumatic Fever^a

| Drug | Dose | Route |
|--|---|---------------|
| Penicillin G benzathine | 1.2 million U, every 4 wk ^b ; 600 000 U, every 4 wk for patients weighing less than 27 kg (60 lb) | Intramuscular |
| OR | | |
| Penicillin V | 250 mg, twice a day | Oral |
| OR | | |
| Sulfadiazine or sulfisoxazole | 0.5 g, once a day for patients weighing 27 kg (60 lb) or less 1.0 g, once a day for patients weighing greater than 27 kg (60 lb) | Oral |
| For people who are allergic to penicillin and sulfonamide drugs | | |
| Macrolide or azalide | Variable (see text) | Oral |

Table 3.59. Duration of Prophylaxis for People Who Have Had Acute Rheumatic Fever (ARF): Recommendations of the American Heart Association^a

| Category | Duration |
|--|--|
| Rheumatic fever without carditis | 5 years since last episode of ARF or until 21 years of age, whichever is longer |
| Rheumatic fever with carditis but without residual heart disease (no valvular disease ^b) | 10 years since last episode of ARF or until 21 years of age, whichever is longer |
| Rheumatic fever with carditis and residual heart disease (persistent valvular disease ^b) | 10 years since last episode of ARF or until 40 years of age, whichever is longer; consider lifelong prophylaxis for people with severe valvular disease or likelihood of ongoing exposure to group A streptococcal infection |

سیاس فراوان از توجه شما