Invasive group A streptococcal infection and toxic shock syndrome: Epidemiology, clinical manifestations, and diagnosis

AUTHOR: Dennis L Stevens, MD, PhD
SECTION EDITORS: Michael R Wessels, MD, Morven S Edwards, MD
DEPUTY EDITOR: Keri K Hall, MD, MS

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INTRODUCTION

Group A *Streptococcus* (GAS; *Streptococcus pyogenes*) is an aerobic gram-positive coccus that causes a broad array of infections. GAS is most commonly associated with pharyngitis or skin and soft tissue (non-necrotizing) infection; these are not typically associated with invasive infection.

Less commonly, GAS causes invasive disease; invasive GAS infection refers to infection in the setting of culture isolation of GAS from a normally sterile site (most commonly blood; less commonly pleural, pericardial, joint, or cerebrospinal fluid) [1,2].

Forms of invasive GAS infection include [1,3,4]:

- Necrotizing soft tissue infection (see "Necrotizing soft tissue infections")
- Pregnancy-associated infection (see "Pregnancy-related group A streptococcal infection" and "Postpartum endometritis")
- Bacteremia (may occur in association with or in the absence of another infection)
- Respiratory tract infection

Toxic shock syndrome (TSS) occurs as a complication of invasive GAS disease in approximately one-third of cases [5].

The epidemiology, clinical manifestations, and diagnosis of invasive GAS infection will be reviewed here. Issues related to treatment and prevention of invasive GAS infection are discussed separately. (See "Invasive group A streptococcal infection and toxic shock syndrome: Treatment and prevention".)

Issues related to GAS bacteremia in children are discussed separately. (See "Invasive group A streptococcal infections in children".)

EPIDEMIOLOGY

Incidence — In resource-rich settings, there are an estimated 3.5 cases of invasive GAS infection per 100,000 persons, with a case-fatality rate of 30 to 60 percent [1,4,6-9].

Invasive infections associated with GAS have been reported with increasing frequency, predominantly from North America and Europe [5,6,9-24]. In the United States, the incidence of invasive GAS infections increased in the late 1980s. Thereafter, the incidence was stable from mid-1990s until 2012 but has increased subsequently (average annual rate of 3.8 per 100,000 for 2005 to 2012; rate of 4.8 to 5.8 per 100,000 for 2014 to 2016) [6,23]. In late 2022 and 2023, several European countries (including the United Kingdom, Ireland, France, the Netherlands, and Sweden) reported increased rates of invasive infections in tandem with notable increases in scarlet fever [25,26]. (See "Invasive group A streptococcal infections in children", section on 'Incidence'.)

In general, invasive GAS infection may occur in patients of any age. The incidence is highest in adults >50 years of age, followed by young children (particularly those <1 year of age) [27-35]. Most patients are not immunosuppressed (see 'Risk factors' below). Since the 1980s, an increase in the frequency of invasive GAS disease has occurred among patients 20 to 35 years of age. This change likely reflects increased frequency of two presentations of infection: (1) pregnancy-associated GAS infections and (2) deep infection at the site of muscle injury or blunt trauma, in the absence of a clear portal of entry [36-39].

The factors responsible for the increase in incidence of invasive GAS infection are not fully understood. Alterations in the distribution of GAS strain M types, together with an increasing prevalence of toxin-producing strains, may be responsible [5,40-43]. About half of invasive GAS infections are caused by a limited number of GAS M types (1, 3, 4, 6, and 28); the remaining half are caused by a variety of strains, including nontypeable strains [2,5,40-42,44,45]. All GAS strains

isolated from invasive infections produce a toxin called NADase [45]. All M-1 strains (the most common isolate from patients with bacteremia since 1985) produce NADase, whereas M-1 strains isolated prior to 1985 (when invasive GAS infections were less prevalent) did not produce NADase [45]. (See "Group A streptococcus: Virulence factors and pathogenic mechanisms", section on 'M and M-like proteins'.)

Risk factors — Risk factors associated with development of invasive GAS infection include [5,27,32,35,40,46-58]:

- Minor trauma, including injuries resulting in hematoma, bruising, or muscle strain
- Use of nonsteroidal anti-inflammatory drugs (NSAIDs)
- Recent surgery
- HIV infection
- Other viral infection (eg, influenza, varicella)
- Intravenous drug use
- Homelessness
- Postpartum state
- Burns
- Obesity
- Peripheral vascular disease
- Malignancy
- Corticosteroid use
- Diabetes mellitus and other forms of immunosuppression
- Cardiac disease

There has been controversy regarding an association between NSAIDs and necrotizing fasciitis with concomitant bacteremia. NSAID use for relief of pain associated with a traumatic injury may mask presenting symptoms (delaying diagnosis) or serve as an independent predisposing factor for more severe infection [5]. NSAIDs may inhibit neutrophil function, suppress fever, and augment cytokine release [59]. Studies of experimentally induced muscle injury have demonstrated that NSAIDs (particularly nonselective cyclo-oxygenase [COX] inhibitors) increase the likelihood of GAS necrotizing fasciitis/myonecrosis at the site of injury and enhance bacteremia; in addition, use of COX inhibitors reduced the efficacy of antibiotics including penicillin or clindamycin [60]. It has been demonstrated that GAS homes to the site of experimentally induced muscle injury; this process may be enhanced 10-fold by administration of NSAIDs [61].

In one study including 100 patients with GAS bacteremia, 62 were intravenous drug users (IDUs); the majority had a clear portal of entry on the skin related to IDU [55]. Among the 38

patients who were not IDUs, 24 had an underlying disease and 12 were immunosuppressed (5 due to HIV infection). In population-based studies, HIV has been identified as a predisposing factor for invasive GAS in 4 percent of cases [56]. Another study of invasive GAS infection noted IDU in only 10 percent of cases; the prevalence of GAS bacteremia was relatively high and infection occurred in association with necrotizing fasciitis, myositis, and shock [5]. A survey of invasive GAS soft tissue infections in IDUs between 1998 and 2003 identified 44 cases of invasive disease; bacteremia occurred in 61 percent of cases [62].

Risk factors for invasive GAS infection in children are discussed separately. (See "Invasive group A streptococcal infections in children", section on 'Predisposing factors'.)

Risk factors for progression from invasive GAS infection to TSS are not well defined. Failure to recognize the condition (resulting in delays in antibiotic administration and surgical debridement) is a potentially important risk factor. In addition, it has been suggested that major histocompatibility complex class II haplotypes may influence host susceptibility to development of TSS [63].

Outbreaks — Invasive GAS infection usually occurs sporadically; however, clusters and outbreaks of invasive GAS infection have occurred in nursing homes and among patients treated in inpatient and outpatient settings [64-69]. In 2008, a cluster of 11 severe GAS infections was reported in a long-term acute care hospital in New Mexico [70]. Between 2009 and 2010, a cluster of 23 cases (including 13 invasive infections) occurred in a skilled nursing facility in Pennsylvania [71]. There has been an epidemic of invasive cases of GAS in Canada largely among people who are homeless, caused by a rare strain of GAS (*emm74*) [72]. It is likely that serologically distinct GAS strains that contain sufficient virulence factors to cause invasive infection will continue to emerge. Lapses in infection control practices likely allow ongoing transmission, highlighting the importance of adherence to control measures.

MICROBIOLOGY

GAS is an aerobic gram-positive coccus that releases exotoxins that act as superantigens; these toxins are capable of activating the immune system by bypassing the usual antigen-mediated immune response sequence, resulting in the release of large quantities of inflammatory cytokines. Virulence factors and other aspects of GAS pathogenesis are discussed separately. (See "Group A streptococcus: Virulence factors and pathogenic mechanisms".)

Streptococcal TSS occurs most frequently in the setting of infection due to GAS. Group B, group C, and group G streptococci have also been associated with TSS. (See "Group B streptococcal

infections in nonpregnant adults" and "Group C and group G streptococcal infection".)

Streptococcus suis has emerged as a cause of streptococcal toxic shock-like syndrome [73]. Although this pathogen is traditionally associated with bacterial meningitis, a highly pathogenic strain has emerged with the ability to induce production of massive quantities of proinflammatory cytokines. (See "Epidemiology of community-acquired bacterial meningitis in adults".)

INVASIVE GAS INFECTION (IN ABSENCE OF TOXIC SHOCK)

The most common portals of entry for GAS are the skin, vagina, and pharynx.

Forms of disease — Forms of invasive GAS disease include necrotizing soft tissue infection, pregnancy-associated infection, bacteremia, and pneumonia [4].

Necrotizing soft tissue infection — Necrotizing soft tissue infection may include involvement of the epidermis, dermis, subcutaneous tissue, fascia, and muscle. Necrotizing infection most commonly involves the extremities (lower extremity more commonly than upper extremity), particularly in patients with diabetes and/or peripheral vascular disease. Necrotizing infection usually presents acutely (over hours); rarely, it may present subacutely (over days). Rapid progression to extensive destruction can occur, leading to systemic toxicity, limb loss, and/or death.

GAS is one of several causes of necrotizing skin infections, but this is the classic syndrome of invasive GAS infection. TSS occurs as a complication of necrotizing soft tissue infection in approximately half of cases [4,67].

Issues related to necrotizing soft tissue infection are discussed further separately. (See "Necrotizing soft tissue infections" and "Surgical management of necrotizing soft tissue infections".)

Pregnancy-associated infection — Invasive GAS infection associated with pregnancy (also referred to as puerperal GAS sepsis or postpartum GAS infection) is an important cause of maternal and infant mortality [36,74].

Most cases of puerperal GAS sepsis occur during the first 48 to 72 hours after delivery [36]. In approximately 20 percent of cases, invasive GAS infection occurs during late pregnancy (prior to onset of labor or rupture of membranes). Invasive GAS infection can also occur after discharge from the hospital. Patients with puerperal sepsis due to GAS typically present with fever and abdominal pain.

Postpartum endometritis can be caused by a number of organisms, including GAS; GAS endometritis can progress to puerperal sepsis. Postpartum endometritis should be suspected in the setting of fever and uterine tenderness following childbirth.

Issues related to puerperal sepsis and postpartum endometritis are discussed further separately. (See "Pregnancy-related group A streptococcal infection" and "Postpartum endometritis".)

Bacteremia — GAS bacteremia usually occurs in association with infection at a primary site [40,41].

- The most common source of GAS bacteremia is skin and soft tissue infection; forms include cellulitis/erysipelas, surgical wound infection, varicella virus infection, and burns [33,35]. Clinical manifestations of these conditions are discussed further separately. (See "Cellulitis and skin abscess: Epidemiology, microbiology, clinical manifestations, and diagnosis" and "Clinical features of varicella-zoster virus infection: Chickenpox" and "Assessment and classification of burn injury".)

- GAS bacteremia may also occur in the setting of necrotizing soft tissue infection, pregnancy-associated infection, or respiratory tract infection. (See 'Necrotizing soft tissue infection' above and 'Pregnancy-associated infection' above and 'Less common manifestations' below.)

In some cases, GAS bacteremia occurs in the absence of a clear localizing source. Symptoms may be nonspecific and include fever, chills, and fatigue. Among older patients, diabetes and peripheral vascular disease may serve as predisposing factors for isolated GAS bacteremia. Additional risk factors (among children and older adults) include malignancy and immunosuppression [2].

Less common manifestations — Uncommonly, GAS can cause pneumonia; in some cases, multilobular diffuse disease may develop [75]. Pleural effusion (particularly left-sided effusion) can also occur; when present, pleural effusion associated with GAS pneumonia often represents an empyema [76]. Among adults with pneumonia due to GAS, bacteremia occurs in approximately 80 percent of cases [77].

GAS bacteremia has been associated with suppurative complications of pharyngitis such as peritonsillar abscess and with extension of infection into the sinuses, middle ear, and mastoids. (See "Complications of streptococcal tonsillopharyngitis", section on 'Suppurative complications'.)

GAS bacteremia is rarely associated with uncomplicated pharyngitis or nonsuppurative complications of pharyngitis. (See "Group A streptococcal tonsillopharyngitis in children and adolescents: Clinical features and diagnosis" and "Complications of streptococcal tonsillopharyngitis", section on 'Nonsuppurative complications'.)

Other (relatively uncommon) manifestations of invasive GAS infection include septic arthritis, osteomyelitis, peritonitis, and meningitis [3].

Diagnosis — Invasive streptococcal infection should be suspected in patients with signs of systemic illness (such as fever) in the setting of skin or soft tissue infection; it should also be suspected in pregnant and postpartum women in the setting of high fever or rapid onset of fever. GAS bacteremia may occur in the absence of a clear localizing source.

The diagnosis of invasive GAS infection is established via positive culture for GAS from a normally sterile site (most commonly blood; less commonly pleural, pericardial, joint, or cerebrospinal fluid) [2,3].

For patients with suspected invasive GAS infection, blood cultures (at least two sets) should be obtained (ideally prior to antibiotic administration). In addition, cultures should be collected from clinically relevant sites. For patients with skin or soft tissue infection, a wound culture should be obtained. Patients who undergo debridement should have debrided material sent for culture. Postpartum women should have endometrial aspiration for Gram stain and culture. Patients with pneumonia should have throat and sputum culture; in addition, patients who undergo thoracentesis should have pleural fluid sent for culture and pleural fluid chemistries. (See "Epidemiology, clinical presentation, and diagnostic evaluation of parapneumonic effusion and empyema in adults".)

Recovery of GAS from blood cultures usually takes 8 to 24 hours. Gram stain of involved tissue demonstrating gram-positive cocci in pairs and chains can provide an early diagnostic clue in many cases.

Susceptibility testing should be pursued for clindamycin and oxazolidinones (linezolid and tedizolid), given the importance of these agents in suppression of toxin production. (See "Invasive group A streptococcal infection and toxic shock syndrome: Treatment and prevention", section on 'General principles'.)

TOXIC SHOCK SYNDROME

Streptococcal TSS is a complication of invasive GAS disease characterized by shock and multiorgan failure; it occurs as a result of capillary leak and tissue damage due to release of inflammatory cytokines induced by streptococcal toxins.

Epidemiology — Streptococcal TSS develops in up to one-third of patients with invasive GAS disease [7,78]. The rate of TSS among patients with necrotizing fasciitis is approximately 50 percent [4,5,67]. TSS occurs among all age groups, and most patients with TSS are not immunosuppressed [12,33-35,42,43,79].

No portal of entry is identified in up to 45 percent of patients with streptococcal TSS [5].

Clinical features — Streptococcal TSS consists of invasive GAS infection (isolation of GAS from a normally sterile body site) associated with early onset (eg, within hours) of shock and organ failure, with hypotension and tachycardia. Hypotension frequently persists despite aggressive therapy [5]. Fever is common; hypothermia may be present. Altered mental status occurs in about half of cases. An influenza-like syndrome characterized by fever, chills, myalgia, nausea, vomiting, and diarrhea occurs in about 20 percent of patients [52]. A diffuse, scarlatina-like erythema occurs in about 10 percent of cases [17].

Symptoms of underlying invasive GAS infection may be present. Most commonly, patients with streptococcal TSS present with pain at the site of minor trauma (such as a bruise, strained muscle, or sprained ankle); the discomfort typically precedes physical findings of infection [5]. Subsequently, clinical manifestations include localized swelling and erythema, followed by ecchymoses and sloughing of skin [5,67]. Deep infection (such as necrotizing fasciitis or myonecrosis) may develop within 24 to 72 hours. (See 'Necrotizing soft tissue infection' above.)

In patients without soft tissue findings (about 20 percent of cases), a variety of clinical manifestations may be observed. The clinical presentation of TSS may mimic pneumonia, myocardial infarction, myocarditis, pericarditis, peritonitis, cholecystitis, perihepatitis, pelvic inflammatory disease, or endophthalmitis [5,80-82].

End-organ manifestations include renal failure, hepatic failure, acute respiratory distress syndrome, and disseminated intravascular coagulation [5,17]. Adrenal infarction leading to adrenal insufficiency (Waterhouse-Friderichsen syndrome) has been described [83].

Renal dysfunction occurs among nearly all patients within 48 to 72 hours. Elevation of serum creatinine concentration precedes development of hypotension in 40 to 50 percent of cases [5]. Hypotension, myoglobinuria, and hemoglobinuria (due to toxin-induced hemolysis) may further contribute to acute renal failure. Many patients require dialysis for up to three weeks. In

patients who survive, the serum creatinine concentration returns to baseline within four to six weeks.

Laboratory studies may demonstrate leukocytosis with significant left shift [5]. The serum creatinine concentration is frequently elevated [5]. Other laboratory findings include hypoalbuminemia, hypocalcemia, and elevated serum creatine kinase concentration, which suggests the presence of necrotizing fasciitis or myositis [5].

Blood cultures are positive for GAS in approximately 60 percent of cases [5].

Diagnostic criteria — Streptococcal TSS should be suspected in patients presenting with shock in the absence of a clear etiology. The diagnosis of streptococcal TSS is established based on the clinical criteria and culture findings.

Clinical criteria for streptococcal TSS include [17,84]:

- Hypotension (systolic blood pressure ≤90 mmHg in adults or <5th percentile for age in children <16 years)
- Multiorgan involvement characterized by two or more of the following:
  - Renal impairment – In adults, creatinine ≥2 mg/dL (177 micromol/L); in children, ≥2 times the upper limit of normal for age; in patients with pre-existing renal disease, ≥2 times elevation over baseline
  - Coagulopathy – Platelets ≤100,000/mm^3 (100 x 10^6/L) or disseminated intravascular coagulation, defined by prolonged clotting times, low fibrinogen level, and the presence of fibrin degradation products
  - Liver involvement – Alanine aminotransferase, aspartate aminotransferase, or total bilirubin levels ≥2 times the upper limit of normal for the patient's age; in patients with pre-existing liver disease, ≥2 times elevation over baseline
  - Acute respiratory distress syndrome
  - Erythematous macular rash, may desquamate
  - Soft tissue necrosis (eg, necrotizing fasciitis, myositis, or gangrene)

A probable diagnosis of TSS may be made for cases that meet the above clinical criteria (in the absence of another identified etiology for the illness) with isolation of GAS from a nonsterile site (eg, throat, vagina, skin lesion).

A confirmed diagnosis of TSS may be made for cases that meet the above clinical criteria, with isolation of GAS from a normally sterile site (eg, blood, cerebrospinal fluid, joint fluid, pleural fluid, pericardial fluid, peritoneal fluid, tissue biopsy, or surgical wound).

For patients with suspected TSS, blood cultures (at least two sets) should be obtained, and cultures should be collected from clinically relevant sites. (See 'Diagnosis' above.)

Differential diagnosis — The differential diagnosis for abrupt onset of shock in a previously healthy individual includes:

- Staphylococcal TSS – Staphylococcal TSS should be suspected in otherwise healthy individuals with rapid onset of fever, rash, hypotension, and multiorgan system involvement; relevant risk factors include recent tampon use, recent surgery, and recent infection (involving skin or soft tissue or other site). The diagnosis is established based on clinical and laboratory criteria. (See "Staphylococcal toxic shock syndrome".)

- Gram-negative sepsis – Clinical manifestations of gram-negative sepsis include fever, hypotension, and respiratory failure. In gram-negative sepsis, renal failure develops after hypotension; in GAS TSS, renal impairment frequently precedes hypotension. The diagnosis of gram-negative sepsis is established by culture. (See "Gram-negative bacillary bacteremia in adults".)

- Typhoid fever – Clinical manifestations of typhoid include fever, relative bradycardia, pulse-temperature dissociation, and abdominal pain. In typhoid fever, the white blood count is usually normal or low; in GAS TSS, it is usually normal or elevated with a marked left shift. The diagnosis of typhoid fever is established by culture. (See "Enteric (typhoid and paratyphoid) fever: Epidemiology, clinical manifestations, and diagnosis".)

- Rocky Mountain spotted fever (RMSF) – Clinical manifestations of RMSF include fever, headache, and rash; in GAS TSS, headache is rare and rash is present in only 10 percent of patients. In RMSF, the rash is most often petechial; in GAS TSS, the rash is diffusely erythematous. The diagnosis of RMSF is based on clinical symptoms. (See "Epidemiology, clinical manifestations and diagnosis of Rocky Mountain spotted fever".)

- Meningococcemia – Clinical manifestations of meningococcemia include sudden onset of fever, nausea, vomiting, headache, and petechial rash. Symptoms of meningitis in GAS TSS are infrequent. The diagnosis of meningococcemia is established by culture. (See "Clinical manifestations of meningococcal infection".)

- *Streptococcus pneumoniae* infection – Clinical manifestations of *S. pneumoniae* infection include respiratory symptoms and development of lobar consolidation and/or empyema, although pneumococcal bacteremia without apparent respiratory tract infection can occur, particularly in children. Pneumonia and empyema also can occur with GAS TSS. The diagnosis of *S. pneumoniae* infection is established via culture. (See "Invasive pneumococcal (Streptococcus pneumoniae) infections and bacteremia in adults".)

- Kawasaki disease – Kawasaki is a vasculitis that occurs in children, characterized by systemic inflammation manifested by fever and mucocutaneous involvement. The diagnosis is established based on clinical history and supported by laboratory findings. (See "Kawasaki disease: Clinical features and diagnosis".)

- COVID-19 multisystem inflammatory syndrome – There have been reports of multisystem inflammatory syndrome possibly associated with COVID-19 with clinical features similar to those of TSS, Kawasaki disease shock syndrome and/or Kawasaki disease (eg, abdominal pain, gastrointestinal symptoms, myocarditis), and laboratory findings associated with increased inflammation (eg, elevated C-reactive protein, erythrocyte sedimentation rate, and ferritin). Some, though not all, of these patients have tested positive for SARS-CoV-2. (See "COVID-19: Multisystem inflammatory syndrome in children (MIS-C) clinical features, evaluation, and diagnosis".)

- Leptospirosis – Clinical manifestations of leptospirosis include fever, rigors, myalgia, headache, and abdominal symptoms. Conjunctival suffusion is one of the most reliable distinguishing features of leptospirosis since it rarely occurs with any other infectious illness. The diagnosis of leptospirosis is established via serologic testing. (See "Leptospirosis: Epidemiology, microbiology, clinical manifestations, and diagnosis".)

- Heat stroke – Clinical manifestations of heat stroke include core body temperature >40°C with associated central nervous system dysfunction. Additional manifestations (which may also be observed in the setting of GAS TSS) include dehydration with evidence of renal impairment, hypotension, and sunburn-type erythema. The history of heat exposure is helpful in distinguishing these two illnesses. (See "Severe nonexertional hyperthermia (classic heat stroke) in adults".)

SOCIETY GUIDELINE LINKS

Links to society and government-sponsored guidelines from selected countries and regions around the world are provided separately. (See "Society guideline links: Skin and soft tissue

infections".)

SUMMARY AND RECOMMENDATIONS

- **Invasive versus non-invasive disease** – Group A *Streptococcus* (GAS; *Streptococcus pyogenes*) is a gram-positive coccus that causes a broad array of infections. GAS is most commonly associated with pharyngitis or skin and soft tissue (non-necrotizing) infection; these are not typically associated with invasive infection. Less commonly, GAS causes invasive disease; invasive GAS infection refers to infection in the setting of culture isolation of GAS from a normally sterile site (most commonly blood; less commonly pleural, pericardial, joint, or cerebrospinal fluid). (See 'Introduction' above.)

- **Incidence and risk factors** – In resource-rich settings, there are an estimated 3.5 cases of invasive GAS infection per 100,000 persons, with a case-fatality rate of 30 to 60 percent. The incidence of invasive GAS infection is increasing; the factors responsible are not fully understood. Invasive GAS infection may occur in patients of any age; the incidence is highest in adults >50 years of age, followed by young children (particularly those <1 year of age). Most patients are not immunosuppressed. Invasive GAS infection usually occurs sporadically; however, clusters and outbreaks of invasive GAS infection have occurred. (See 'Epidemiology' above.)

- **Invasive syndromes** – Clinical syndromes of invasive GAS infection (in absence of toxic shock) include necrotizing soft tissue infection, pregnancy-associated infection, bacteremia, and less common manifestations. GAS bacteremia usually occurs in association with infection at a primary site; the most common source is skin and soft tissue infection. In some cases, GAS bacteremia occurs in the absence of a clear localizing source. (See 'Invasive GAS infection (in absence of toxic shock)' above.)

- **Diagnosis** – Invasive streptococcal infection should be suspected in patients with signs of systemic illness (such as fever) in the setting of skin or soft tissue infection. It should also be suspected in pregnant and postpartum women in the setting of high fever or rapid onset of fever. The diagnosis of invasive GAS infection is established via positive culture for GAS from a normally sterile site (most commonly blood; less commonly pleural, pericardial, joint, or cerebrospinal fluid). (See 'Diagnosis' above.)

- **Toxic shock syndrome** – Streptococcal toxic shock syndrome (TSS) is a complication of invasive GAS disease characterized by shock and multiorgan failure; it occurs as a result of capillary leak and tissue damage due to release of inflammatory cytokines induced by

streptococcal toxins. In general, invasive GAS disease is complicated by TSS in approximately one-third of cases; necrotizing soft tissue infection is complicated by TSS in approximately half of cases. (See 'Toxic shock syndrome' above.)

- **Clinical manifestations** – Streptococcal TSS may present with a range of clinical features; these include hypotension, tachycardia, and fever. Hypothermia may be present. Altered mental status occurs in about half of cases. An influenza-like syndrome characterized by fever, chills, myalgia, nausea, vomiting, and diarrhea occurs in about 20 percent of patients. A diffuse, scarlatina-like erythema occurs in about 10 percent of cases. In addition, symptoms of underlying invasive GAS infection may be present. (See 'Clinical features' above.)

- **Diagnosis** – Streptococcal TSS should be suspected in patients presenting with shock in the absence of a clear etiology. The diagnosis is established based on the clinical criteria and culture findings. Clinical criteria for streptococcal TSS include (1) hypotension (systolic blood pressure ≤90 mmHg in adults or <5th percentile for age in children <16 years) and (2) multiorgan involvement, characterized by two or more of the following: renal impairment, coagulopathy, liver involvement, acute respiratory distress syndrome, erythematous macular rash (may desquamate), and/or soft tissue necrosis (eg, necrotizing fasciitis, myositis, or gangrene). (See 'Diagnostic criteria' above.)

  A probable diagnosis of TSS may be made for cases that meet the above clinical criteria (in the absence of another identified etiology for the illness) with isolation of GAS from a nonsterile site (eg, throat, vagina, skin lesion). A confirmed diagnosis of TSS may be made for cases that meet the above clinical criteria, with isolation of GAS from a normally sterile site (eg blood, cerebrospinal fluid, joint fluid, pleural fluid, pericardial fluid, peritoneal fluid, tissue biopsy, or surgical wound). (See 'Diagnostic criteria' above.)

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