Invasive Group A Strep

Including Streptococcal Toxic Shock Syndrome

Disease Plan

Quick Links

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Questions about this disease plan?

Contact the Utah Department of Health Bureau of Epidemiology at 801-538-6191.

✓ CRITICAL CLINICIAN INFORMATION

Clinical Evidence

Signs/Symptoms

- Invasive group A streptococcal (GAS) infections may develop from soft tissue infections (e.g., cellulitis, erysipelas, pyoderma); less commonly from pharyngitis or pneumonia and include:
  - Sepsis
  - Necrotizing fasciitis
- Streptococcal toxic shock syndrome (STSS) may be associated with invasive or non-invasive group A streptococcal infection (most commonly a cutaneous lesion) and is characterized by:
  - Hypotension
  - Involvement of one or more of the following: renal or liver impairment, thrombocytopenia, respiratory distress, generalized erythematous macular rash
  - Abrupt onset of severe pain at site of infection
- Other serious complications of GAS infection include:
  - Acute rheumatic fever
  - Scarlet fever
  - Post-streptococcal glomerulonephritis

Mode of Transmission

- Humans are the primary reservoir for GAS. Transmission occurs through direct and indirect contact with infected secretions/objects and large respiratory droplets.

Period of Communicability

- GAS is generally communicable until 24 hours post-antibiotic treatment.

Incubation Period

- The incubation period for invasive disease depends on the site or type of infection/illness.

Laboratory Testing

Type of Lab Test/Timing of Specimen Collection

- Cultures from sterile or non-sterile sites (not performed by UPHL)

Type of Specimens

- Sterile: blood, CSF, joint, pleural, or pericardial fluid
- Non-sterile: wound, pharyngeal swab (only for STSS)

Treatment Recommendations

- Treatment depends on site/type of illness
- Treatment regimens may include clindamycin, penicillin, cefazolin and/or vancomycin.
- GAS bacteremia
  - For adults, penicillin G: 4 million units intravenously every four hours PLUS clindamycin — 900 mg intravenously every eight hours. Generally administered for a minimum of 14 days, however, treatments should be individually tailored given type of infection and response to treatment.
- Necrotizing fasciitis:
  - Early and aggressive surgical exploration and debridement of necrotic tissue
  - Empiric therapy until culture results are available should include broad-spectrum antimicrobial therapy with activity against gram-positive, gram-negative, and anaerobic organisms: a carbapenem or a beta-lactam with a beta-lactamase inhibitor PLUS clindamycin — 600–900 mg intravenously every eight hours PLUS an agent active against methicillin-resistance *S. aureus* (MRSA).

- Streptococcal Toxic Shock (STSS)
    - Empiric therapy for STSS until culture results are available: clindamycin — 900 mg intravenously every eight hours PLUS a carbapenem intravenously OR a combination drug containing penicillin and a beta-lactamase inhibitor.
    - For confirmed STSS: clindamycin — 900 mg intravenously every eight hours PLUS penicillin G — 4 million units intravenously every four hours.
    - Surgical debridement if applicable

Contact Management

Quarantine of Contacts

- None

Infection Control Procedures

- Contact and droplet precautions for first 24 hours on antibiotics

✓ WHY IS GROUP A STREP IMPORTANT TO PUBLIC HEALTH?

Invasive group A streptococcal (GAS) infections may manifest as any of several clinical syndromes identified by bacterial cultures typically found in sterile sites, such as blood, muscle, or the lungs. These bacterial infections cause severe disease and can result in death.

✓ DISEASE AND EPIDEMIOLOGY

Clinical Description

Invasive Disease
The most common presentation of this organism is a non-invasive sore throat or superficial skin infections. Invasive disease, where the organism is found in a sterile site such as tissue, blood, CSF, or body fluids, is uncommon, but can be very severe. The most common types of invasive disease include bacteremia, cellulitis, pneumonia, and meningitis. Severe cases can also present as necrotizing fasciitis. Invasive strep diseases have a rapid onset and progression.

Streptococcal Toxic Shock Syndrome (STSS)
STSS is a rare, but a serious, complication of streptococcal infection. It is frequently associated with deep soft tissue infection and is characterized by abrupt onset of severe pain at the site of infection and multi-system organ involvement. More likely portals of infection include blunt or penetrating trauma, including surgical procedures and vaginal delivery. Soft tissue infection may require surgical debridement, fasciotomy, or amputation. Shock and renal dysfunction are apparent within 4–8 hours in virtually all patients.

Causative Agent

Group A streptococci, *Streptococcus pyogenes*, are gram-positive beta-hemolytic aerobic bacteria. They can be referred to as Group A beta hemolytic strep (GABHS), GAS, or *Streptococcus pyogenes*. Group A streptococci can be further classified through their *emm* type, of which over 240 unique variants have been identified.

Differential Diagnosis

Many invasive bacterial diseases, such as *Streptococcus pneumoniae*, Group B streptococci, *Haemophilus influenzae*, meningococcal disease, etc., can have a similar presentation. For necrotizing fasciitis, the differential diagnosis can be *Staphylococcus aureus, Bacteroides fragilis, Vibrio vulnificus*, or *Clostridium perfringens.*

Laboratory Identification

Laboratory findings are based on the isolation of the organisms from affected tissues (e.g., blood, wounds).

Utah Public Health Laboratory (UPHL): UPHL does not perform routine cultures for streptococcal diseases. These tests are usually performed in clinical laboratories.

Treatment

Invasive GAS disease is serious. Treatment depends on the type or site of illness. The majority of patients will be hospitalized. Appropriate antibiotic therapy is necessary, along with supportive care. Much of the damage caused by these organisms is by toxins or inflammatory processes.

Penicillin-resistant group A streptococci have not been identified. Treatment regimens may include clindamycin, penicillin, cefazolin, cefotaxime, ceftriaxone, and/or vancomycin. Clindamycin may reduce toxin production, so it is a useful antibiotic in combination with a beta-lactam antibiotic; however, it should not be used exclusively because group A streptococci resistant to clindamycin is increasing in some geographic regions.

Case Fatality

Invasive Disease: Overall, approximately 12%

Strep TSS: Pediatric 5–10%, adult 30–80%

Necrotizing Fasciitis: 25

Reservoir

Humans are the only known reservoir. Individuals who are colonized or infected with group A streptococci in the pharynx are the likely source of the organisms. About 2–3% of adults and 15–20% of school children are colonized.

Transmission

GAS is transmitted via large respiratory droplets or direct contact with patients or carriers and rarely through indirect contact with contaminated objects.

Susceptibility

Co-morbidities, including HIV infection, diabetes, malignancy, injecting drug use, cardiac disease, varicella, acute skin breakdown and individuals with blunt and penetrating trauma are associated with an increased risk of invasive GAS disease.

Incubation Period

The incubation period for invasive disease depends on the site or type of infection/illness.

Period of Communicability

In untreated cases of pharyngitis, patients can be communicable for weeks to months, but highest transmission is typically during the first 2-3 weeks of illness. With adequate treatment, transmissibility usually ends within 24 hours.

Epidemiology

In the United States, national estimated incidence of invasive GAS disease is 4.8 cases/100,000 population per year. Persons over 65 years have the highest incidence (9.4/100,000), followed by children younger than one year (5.3/100,000). Nationally, the incidence of GAS has remained relatively stable. It is thought that there are shifts and drifts in the pathogenicity factors of GAS that result in pandemics of invasive GAS. In Utah, this disease is more prevalent between winter and early spring.

M Types 1, 12, 28, 89, and 3 cause the majority (53%) of invasive disease in cases of GAS. However, these are also commonly isolated from asymptomatic carriers, or those with pharyngitis only. Pyrogenic exotoxins, M proteins type 1 and 3, and toxic-shock toxins may act as super-antigens. For more information on M protein and emm typing visit: https://www.cdc.gov/streplab/groupa-strep/emm-background.html.

Susceptible person of invasive disease include individuals with underlying conditions (e.g., chronic pulmonary, acute skin breakdown, blunt and penetrating trauma, cardiac, liver, kidney disease or diabetes), injecting drug users, those who are immunocompromised, those with recent surgical procedures, or women who have recently given birth. Increasing age, disease syndrome (septic shock, STSS, necrotizing fasciitis, meningitis, and pneumonia), nursing home residence, and M types 1 and 3 are independent predictors of mortality. Association with varicella also increases likelihood of invasive GAS, especially in children.

Streptococcal toxic shock syndrome (STSS) affects people of all ages, most of whom do not have underlying disease. This disease is rarely preceded by strep pharyngitis. More likely portals of infection include surgical procedures and vaginal delivery. Infection can begin at a site of minor local trauma that does not have to result in a break in the skin. There is rapid development (24–72 hours) from minor non-penetrating trauma such as hematoma, deep bruises, or muscle strains. Viral infections can also provide a portal. NSAIDs can mask early symptoms or predispose patients to more severe infection. These are usually sporadic cases and not related to clusters or epidemics.

Note: Toxic shock syndrome (TSS) can be caused by two different organisms: Group A strep and Staph aureus. STSS is generally not related to tampon usage. Please review the TSS disease investigation plan for further information.

✓ PUBLIC HEALTH CONTROL MEASURES

Public Health Responsibility

- Investigate all suspect cases of disease, fill out and submit appropriate disease investigation forms.
- Provide education to the general public, clinicians, and first responders regarding disease transmission and prevention.
- Recommend routine immunization against varicella. Varicella is an important risk factor for invasive GAS disease.
- In any case of invasive GAS, assure that all contacts with varicella are carefully managed.
- Identify clusters or outbreaks of this disease. The GAS calculator (https://www.cdc.gov/groupastrep/outbreaks/calculator/index.html) may be used to determine if the number of GAS cases reported are greater than the number of expected cases.
- Identify potential post-surgical or post-partum infections that may be traced to carriers involved in direct patient care.

Prevention

- Following a case of invasive GAS disease, the risk to close cases in schools and childcare facilities is low, and chemoprophylaxis is not indicated in these settings, UNLESS there is an association with varicella.
- There may be an increased risk of invasive GAS disease among household members and other close contacts, so chemoprophylaxis, while usually not recommended, may be considered. Severe invasive GAS disease outbreaks have occurred in some closed environments, such as military bases, nursing homes, and hospitals. Considerations when contemplating chemoprophylaxis:
    - Extent of contact with an index case
    - Underlying conditions, which may increase risk (advanced age, immunosuppression, diabetes, pregnancy, varicella, etc.)
    - Costs and potential side effects of chemoprophylaxis.

Chemoprophylaxis

Chemoprophylaxis is generally not recommended. For extensive or protracted outbreaks in special close contact groups (e.g., military recruits, childcare centers, nursing homes), it may be necessary to administer antibiotic prophylaxis to the entire group to terminate spread. In these settings, the benefits of such widespread use of antibiotics should be carefully weighed against the potential side effects.

Vaccine

No vaccine is currently available.

Isolation and Quarantine Requirements

Isolation: People with streptococcal illnesses should stay home from work, school, or childcare until:

- They are afebrile **AND**
- 24 hours after starting appropriate antibiotic therapy.

Hospital: Standard body substance and droplet precautions should be followed.
Quarantine: Not applicable.

✓ CASE INVESTIGATION

Reporting

GAS is reportable in Utah and STSS is nationally reportable. Both GAS and STSS cases are usually first reported to public health from laboratory results as “Invasive Group A Strep.”

Correctly reporting cases of STSS to the CDC: If a GAS event meets the case definitions for STSS (see below) during the investigation, please amend the record to STSS and fill out the appropriate investigation form.

Invasive Group A Strep (CSTE, 1995)

Clinical Description

Invasive GAS infections may manifest as any of several clinical syndromes, including pneumonia, bacteremia in association with cutaneous infection (e.g., cellulites, erysipelas, or infection of a surgical or nonsurgical wound), deep soft-tissue infection (e.g., myositis or necrotizing fasciitis), meningitis, peritonitis, osteomyelitis, septic arthritis, postpartum sepsis (e.g., puerperal fever), neonatal sepsis, and non-focal bacteremia.

Laboratory Criteria

Isolation of GAS by culture from a normally sterile site (e.g., blood or CSF, joint, pleural, or pericardial fluid)

Case Classification

A case that is laboratory confirmed

Streptococcal Toxic Shock Syndrome (CSTE, 2010)

Clinical Description

STSS is a severe illness associated with invasive or noninvasive GAS (*Streptococcus pyogenes*) infection. STSS may occur with infection at any site, but most often occurs in association with infection of a cutaneous lesion. Signs of toxicity and a rapidly progressive clinical course are characteristic, and the case fatality rate may exceed 50%.

Clinical Case Definition

An illness with the following clinical manifestations:

- Hypotension defined by a systolic blood pressure ≤90 mm Hg for adults or less than the fifth percentile by age for children aged less than 16 years,
  AND
- Multi-organ involvement characterized by two or more of the following:
  - Renal impairment: Creatinine ≥2 mg/dL (≥177 µmol/L) for adults or greater than or equal to twice the upper limit of normal for age. In patients with preexisting renal disease, a greater than twofold elevation over the baseline level.
  - Coagulopathy: Platelets ≤100,000/mm3 (≤100 x 106 /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 greater than or equal to twice the upper limit of normal for the patient's age. In patients with preexisting liver disease, a greater than twofold increase over the baseline level.
  - Acute respiratory distress syndrome: defined by acute onset of diffuse pulmonary infiltrates and hypoxemia in the absence of cardiac failure or by evidence of diffuse capillary leak manifested by acute onset of generalized edema, or pleural or peritoneal effusions with hypoalbuminemia.
  - A generalized erythematous macular rash that may desquamate.
  - Soft-tissue necrosis, including necrotizing fasciitis or myositis, or gangrene.

Laboratory Criteria for Diagnosis

Isolation of group A *Streptococcus*

Case Classification

Probable: a case that meets the clinical case definition in the absence of another identified etiology for the illness and with isolation of group A *Streptococcus* from a nonsterile site.

Confirmed: a case that meets the clinical case definition and with isolation of group A *Streptococcus* from a normally sterile site (e.g., blood or cerebrospinal fluid or, less commonly, joint, pleural, or pericardial fluid).

Table of criteria to determine whether a case is classified

Criterion	Confirmed	Probable
Clinical Evidence		
Hypotension (systolic blood pressure ≤90 mm Hg for adults or less than the fifth percentile by age for children aged less than 16 years)	N	N
Renal impairment (creatinine ≥2 mg/dL [≥177 µmol/L] for adults, or greater than or equal to twice the upper limit of normal for age. In patients with preexisting renal disease, a greater than twofold elevation over the baseline level)	O^	O^
Coagulopathy (platelets ≤100,000/mm3 or disseminated intravascular coagulation, defined by prolonged clotting times, low fibrinogen level, and the presence of fibrin degradation products)	O^	O^
Liver involvement (alanine aminotransferase, aspartate aminotransferase, or total bilirubin levels greater than or equal to twice the upper limit of normal for the patient's age. In patients with preexisting liver disease, a greater than twofold increase over the baseline level)	O^	O^
Acute respiratory distress syndrome (defined by acute onset of diffuse pulmonary infiltrates and hypoxemia in the absence of cardiac failure; or by evidence of diffuse capillary leak manifested by acute onset of generalized edema; or pleural or peritoneal effusions with hypoalbuminemia)	O^	O^
Generalized erythematous macular rash that may desquamate	O^	O^
Soft-tissue necrosis, including necrotizing fasciitis or myositis, or gangrene	O^	O^
Laboratory Evidence		
Isolation of group A *Streptococcus* by culture from a normally nonsterile site		N
Isolation of group A *Streptococcus* by culture from a normally sterile site (e.g., blood or cerebrospinal fluid, or, less commonly, joint, pleural, or pericardial fluid)	N	

Notes:

N = All “N” criteria in the same column are Necessary to classify a case.

O = At least one of these “O” (Optional) criteria in each category (e.g., clinical evidence and laboratory evidence) in the same column—in conjunction with all “N” criteria in the same column—is required to classify a case.

O^ = For Streptococcal STSS, at least two of the clinical —“O” criteria are required to classify a case as confirmed or probable.

Case Investigation Process

- Fill out a morbidity form.
- Determine if disease meets the criteria of STSS. If so, change case to STSS and complete investigation.
- Complete appropriate investigation form.
- Determine if additional preventive measures for contacts are needed.

Outbreaks

The Utah definition for an outbreak is defined as three (3) or more epidemiologically-linked cases in unrelated people occurring at a hospital, school, or childcare facility in a 30-day period. Outbreaks may warrant additional investigation and should be reported to public health.

Identification of Case Contacts and Management

For household contacts of index patients, routine screening and chemoprophylaxis against GAS are not recommended. While unusual, local health officer or providers may recommend prevention/chemoprophylaxis (see above) to contacts that are at an increased risk of sporadic disease or mortality due to GAS.

Case contact management should be considered in prolonged outbreaks or those associated with varicella outbreak and chemoprophylaxis on case-by-case basis.

✓ REFERENCES

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✓ VERSION CONTROL

V.02.19.16: Added section describing importance of invasive Group A *Streptococcus* to Public Health; UT-NEDSS Minimum/Required Fields; Susceptibility section on acquiring Group A *Streptococcus*; updated Streptococcal Toxic Shock Syndrome Case Definition and Reference sections.

V.06/23/2017: Added “Critical Clinical Information” section. Updated “Causative Agent,” “Treatment,” “Case Mortality,” and “Epidemiology.” Amended “Reporting” and “Case Definition” sections to better delineate between GAS, STSS, and NF.

V.07.03.19: Updated “Critical Clinician Information” section. Updated the following “Disease and Epidemiology” sections – Clinical Description, STSS Description, Differential Diagnosis, Laboratory Identification, Transmission, Susceptibility, Epidemiology, Chemoprophylaxis, Public Health Responsibility, Clinical Case Definition, Identification and Case Contact Management.

✓ UT-NEDSS Minimum/Required Fields by Tab

Demographic

- First Name
- Last Name
- City
- State
- County
- Date of Birth
- Area Code
- Phone Number
- Birth Gender
- Ethnicity
- Race

Clinical

- Disease
- Onset Date
- Date Diagnosed
- Died
- Disease
- Date of Death

Laboratory

- Specimen Source

Epidemiological

- Imported From

Reporting

- Date first reported to public health

Administrative

- State Case Status (completed by UDOH)
- Outbreak Associated
- Outbreak Name

✓ Streptococcal Disease, Invasive, Group A Rules for Entering Laboratory Test Results

The following rules describe how laboratory results reported to public health should be added to new or existing events in UT-NEDSS. These rules have been developed for the automated processing of electronic laboratory reports, although they apply to manual data entry, as well.

Test-Specific Rules

Test specific rules describe what test type and test result combinations are allowed to create new morbidity events in UT-NEDSS, and what test type and test result combinations are allowed to update existing events (morbidity or contact) in UT-NEDSS.

Test Type	Test Result	Create a New Event	Update an Existing Event
Culture*	Positive	Yes	Yes
	Negative	No	Yes
	Equivocal	No	Yes

*Only specimens from sterile sites are valid for inclusion into EpiTrax.

Whitelist Rules

Whitelist rules describe how long an existing event can have new laboratory data appended to it. If a laboratory result falls outside the whitelist rules for an existing event, it should not be added to that event, and should be evaluated to determine if a new event (CMR) should be created.

Streptococcal disease, invasive, Group A Morbidity Whitelist Rule: If the specimen collection date of the laboratory result is 60 days or less after the event date, the laboratory result should be added to the morbidity event.

Streptococcal disease, invasive, Group A Contact Whitelist Rule: Never added to contact.

Graylist Rule

We often receive laboratory results through ELR that cannot create cases, but can be useful if a case is created in the future. These laboratory results go to the graylist. The graylist rule describes how long an existing event can have an old laboratory result appended to it.

Streptococcal disease, invasive, Group A Graylist Rule: If the specimen collection date of the laboratory result is 30 days before to seven days after the event date of the morbidity event, the laboratory result should be added to the morbidity event.

Other Electronic Laboratory Processing Rules

- If an existing event has a state case status of “not a case,” ELR will never add additional test results to that case. New labs will be evaluated to determine if a new CMR should be created.