Streptococcal Toxic Shock Syndrome (STSS)
Investigation Guideline

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CASE DEFINITION (CDC 2010)

Clinical Description for Public Health Surveillance:
An illness with the following clinical manifestations*:

- Hypotension defined by a systolic blood pressure less than or equal to 90 mm Hg for adults or less than the fifth percentile by age for children aged less than 16 years.
- Multi-organ involvement characterized by two or more of the following:
  - Renal impairment: Creatinine greater than or equal to 2 mg/dL (greater than or equal to 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 less than or equal to 100,000/mm3 (less than or equal to 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.

* Clinical manifestations do not need to be detected within the first 48 hours of hospitalization or illness, as specified in the 1996 case definition.

Laboratory Criteria for Case Classification:
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 non-sterile 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).

LABORATORY ANALYSIS
- Specimens are not required to be sent to the Kansas Health and Environmental Laboratory (KHEL).
- Gram stains and cultures are performed routinely by commercial laboratories.
EPIDEMIOLOGY

Several million cases of non-invasive Group A strep illnesses, like strep throat and impetigo occur annually; while approximately 11,000-13,000 cases of invasive Group A streptococcus occur each year in the U.S. Streptococcal Toxic-Shock Syndrome (STSS) and necrotizing fasciitis (NF) accounted for approximately 6%-7% of those invasive cases. An estimated 1,100 and 1,600 of these invasive cases result in death. (CDC, 2016) Since the 1980’s, there has been a marked increase in the recognition and reporting of highly invasive group A streptococcal infections associated with shock and organ failure. Strains of group A streptococci isolated from patients with invasive disease have been predominantly M types 1 and 3 that produce pyrogenic exotoxin A or B or both. (Emerging Infectious Diseases, 1995) Those at highest risk of invasive disease include the elderly, immunosuppressed, persons with chronic cardiac or respiratory disease, diabetes or skin lesions (i.e. children with varicella [chicken pox], persons with penetrating trauma or surgical wounds, intravenous drug users), African-Americans, and American Indians. Children (especially elementary school age) are at highest risk of noninvasive disease. Nasal, throat, skin, anal and vaginal carriers of GAS have been responsible for nosocomial outbreaks.

DISEASE OVERVIEW

A. Agent:
   Bacterium, *Streptococcus pyogenes*, > 100 identified serological types.

B. Clinical Description:
   While GAS is most often associated with streptococcal pharyngitis/tonsillitis and streptococcal skin infections (impetigo or pyoderma), there are several invasive clinical syndromes, including pneumonia, bacteremia and meningitis. Bacteremia can develop in association with cutaneous infection (e.g., cellulitis, erysipelas, or infection of a surgical or nonsurgical wound), deep soft-tissue infection (e.g., myositis or necrotizing fasciitis), peritonitis, osteomyelitis, septic arthritis, postpartum sepsis, and neonatal sepsis. Potential complications of GAS infections include acute rheumatic fever and glomerulonephritis.

   STSS is a severe illness associated with invasive or noninvasive group A streptococcal 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%.

C. Reservoirs:
   Humans.

D. Mode(s) of Transmission:
   Bacteria are transmitted person-to-person by large droplet spread or by contact with respiratory secretions. Casual contact can result in nasopharyngeal carriage without illness. Those with acute respiratory tract infections (particularly nasal) can transmit noninvasive infection (i.e. upper respiratory infections or pharyngitis).
The invasive form of the disease is not transmitted person-to-person; it only occurs after the bacteria have infected a person and then get past the immune defenses of the person.

E. Incubation Period:
The incubation period is unknown for STSS but has been as short as 14 hours in cases associated with subcutaneous inoculation of organisms.

F. Period of Communicability:
When bacteria present in respiratory secretions or wound drainage. Cases treated with appropriate antibiotics are considered noninfectious after 24 hours of treatment.

G. Susceptibility and Resistance:
Immunity develops only against specific strains and/or exotoxins.

H. Treatment:
Treatment depends on type of infection. Penicillin is the drug of choice for uncomplicated infection. Clindamycin and cephalosporins are used as alternatives. For STSS and necrotizing fasciitis, high dose penicillin and clindamycin are recommended. For those with very severe illness, supportive care in an intensive care unit may also be needed. For persons with necrotizing fasciitis, early and aggressive surgery is often needed to remove damaged tissue and stop disease spread. Early, aggressive treatment may reduce the risk of death from invasive group A streptococcal disease.

NOTIFICATION TO PUBLIC HEALTH AUTHORITIES

Suspected cases of Streptococcal toxic-shock syndrome (STSS) shall be reported within 24 hours, except if the reporting period ends on a weekend or state-approved holiday, the report shall be made by 5:00 p.m. on the next business day after the 24-hour period.

1. Health care providers and hospitals: report to local health jurisdiction
2. Laboratories: report to KDHE - BEPHI
3. Local health jurisdiction: report to KDHE - BEPHI

Kansas Department of Health and Environment (KDHE)
Bureau of Epidemiology and Public Health Response (BEPHI)
Phone: 1-877-427-7317 Fax: 1-877-427-7318

Further responsibilities of state and local health departments to the CDC:
As a nationally notifiable condition, STSS cases require a ROUTINELY NOTIFIABLE report to the Center of Disease Control and Prevention (CDC).
1. ROUTINE reporting requires KDHE-BEPHI to file an electronic report for within the next reporting cycle. KDHE-BEPHI will file electronic reports weekly with CDC.
2. Local public health jurisdiction will report information requested in the Kansas electronic surveillance system, as soon as possible, ensuring that the electronic form is completed within 7 days of receiving a notification of a report.
INVESTIGATOR RESPONSIBILITIES

1) **Report** all confirmed, probable and suspect cases to the KDHE.
2) Begin the public health investigation within 3 days of receiving a report; completing the investigation within 7 days.
3) The goal of the **case investigation** is to collect epidemiological data as required by current surveillance objectives.
   - Contact the medical provider to collect additional information and confirm diagnosis using the current case definition.
   - The **Rapid Assessment Worksheet** will help in the confirmation of the case and with the initial organization and the collection of essential data.
   - Collect all information requested in Step 1) of case investigation.
   - Most data can be collected from the medical provider, and the patient may not need to be contacted.
   - Routine contact investigation is not needed for cases of STSS. Current surveillance objectives depend on the local health department’s assistance with confirmation of cases and collection of surveillance data.
4) **Record** data, collected during the investigation, in the KS EpiTrax system under the data’s associated [tab] in the case morbidity report (CMR).

STANDARD CASE INVESTIGATION AND CONTROL METHODS

Case Investigation

1) Contact the medical provider who reported or ordered testing of the case to obtain the following from the patient’s medical records.
   - Identify evidence of STSS based on case definition. (Refer to the **Rapid Assessment Worksheet**.)
   - Collect case’s demographic data and contacting information (birth date, county, sex, race/ethnicity, address) [Demographic]
   - Record hospitalizations: location and duration of stay [Clinical]
   - Record outcomes: survived or date of death [Clinical]
2) Were any of the following contributing/risk factors present:
   - Any surgeries 7 days prior to first positive culture? (date and provider)
   - Varicella rash:
     - If death resulted directly or indirectly from varicella infection investigate as a varicella related death. (Refer to **Varicella Disease Investigation Guideline**.)
   - Penetrating or blunt trauma?
   - Burn wounds?
   - Surgical wound or post-surgery associated infections?
   - For women, information related associated births or abortions?
3) Investigate epi-links among cases (clusters, commonalities, etc.).
   - For suspected **Outbreaks** refer to Managing Special Situations.
• For suspected cases associated to postpartum females or for postsurgical infections refer to Managing Special Situations

Contact Investigation
Contact investigation is of no practical value for routine situations.

Isolation, Work and Daycare Restrictions
There are no specific regulations related to STSS, but there are regulations for Streptococcal disease.

**K.A.R 28-1-6 for Streptococcal disease, hemolytic, including erysipelas, scarlet fever, and streptococcal sore throat:**

Control of Cases

- For each person hospitalized with a case, droplet precautions shall be followed for 24 hours following initiation of appropriate antimicrobial therapy.
- Each person with a case shall be excluded from working as a food employee, attending or working in a child care facility, and attending a school for 24 hours following initiation of appropriate antimicrobial therapy.
- For each person with a case who does not receive appropriate antimicrobial therapy, such exclusions shall be followed for 10 days following onset of symptoms.

Case Management
Report on any changes in patient status (i.e., date of death). [Clinical]

Contact Management
Contact investigation is of no practical value for routine situations.

Education
The following messages may be delivered to at risk groups:

- Keep all skin wounds clean to prevent infection. This includes:
  - Cuts, punctures or scrapes
  - Burns
  - Sores from shingles or other skin rashes
  - Insect and animal bites
  - Surgical incisions
- Signs and symptoms of infected wounds or surgical incisions that require medical attention can include fever and redness, swelling, heat, or pain at the site. Drainage of cloudy fluid or sudden opening of the wound can also suggest infection.
- Concerned contacts of STSS should also be instructed that:
  - Invasive disease is not spread person-to-person;
  - Antibiotic treatment is not an effective way to protect contacts; and
Medical attention should be sought immediately if they begin to exhibit signs and symptoms of illness.

MANAGING SPECIAL SITUATIONS

A. Outbreak Investigation:
1. Consider further investigation of any invasive cases clustered in time and place among groups that share common space (i.e. daycare, institutions)
3. Case finding, and additional case investigation will be an important part of any investigation.

B. Postpartum or post-surgical group A streptococcal (GAS) infection:
- A single case of postpartum or post-surgical group A streptococcal (GAS) infection calls for a timely investigation to assure that an asymptomatic carrier is not causing nosocomial infection(s).
- Coordinate with infection control personnel.
DATA MANAGEMENT AND REPORTING TO THE KDHE

A. Accept the case assigned to the LHD and record the date the LHD investigation was started on the [Administrative] tab.

B. Organize and collect data.
   - The Rapid Assessment Worksheet is provided to assist the investigator but can be attached to the record in EpiTrax.
   - Investigators can also collect and enter all required information directly into EpiTrax [Clinical], [Demographics], [Epidemiological], and [Notes] tabs without using the paper forms.
   - During outbreak investigations, refer to guidance from a KDHE epidemiologist for appropriate collection tools.

C. Report data collected during the investigation via EpiTrax.
   - Verify that all data requested in Rapid Assessment Worksheet has been recorded on an appropriate EpiTrax [tab], or that actions are completed for a case lost to follow-up as outlined below.
   - Some data that cannot be reported on an EpiTrax [tab] may need to be recorded in [Notes] or scanned and attached to the record.
   - Paper report forms do not need to be sent to KDHE after the information is recorded in EpiTrax. The forms should be handled as directed by local administrative practices.

D. If a case is lost to follow-up, after the appropriate attempts:
   - Indicate ‘lost to follow-up’ on the [Administration] tab with the number of attempts to contact the case recorded.
   - Record at least the information that was collected from the medical records.
   - Record a reason for ‘lost to follow-up’ in [Notes].

E. Once the investigation is completed, the LHD investigator will click the “Complete” button. This will trigger an alert to the LHD Administrator, so they can review the case before sending to the state.
   - The LHD Administrator will then “Approve” or “Reject” the CMR.
   - Once a case is “Approved” by the LHD Administrator, BEPHI staff will review the case to ensure completion before closing the case.

ADDITIONAL INFORMATION / REFERENCES


C. **Case Definitions:** [www.cdc.gov/nndss/](http://www.cdc.gov/nndss/)

D. **Kansas Regulations/Statutes Related to Infectious Disease:**[www.kdheks.gov/epi/regulations.htm](http://www.kdheks.gov/epi/regulations.htm)

E. **Additional Information (CDC):**
   - [www.cdc.gov/groupastrep/diseases-hcp/index.html](http://www.cdc.gov/groupastrep/diseases-hcp/index.html)
   - [www.cdc.gov/Features/NecrotizingFasciitis/](http://www.cdc.gov/Features/NecrotizingFasciitis/)

ATTACHMENTS

To view attachments in the electronic version:

1. Go to <View>; <Navigation Pane>; <Attachments> – OR – Click on the “Paper Clip” icon at the left.
2. Double click on the document to open.
**STSS Assessment Form**

(Please refer to the Disease Investigation Guideline for additional guidance.)

<table>
<thead>
<tr>
<th>Clinical Case Definition Criteria for STSS</th>
</tr>
</thead>
<tbody>
<tr>
<td>☐ Yes ☐ No <strong>Hypotension present</strong> (Systolic &lt; 90 mmHg for adults or &lt;5th percentile in children &lt; 16 years)</td>
</tr>
<tr>
<td>☐ Yes ☐ No <strong>2 or more of the following multi-organ manifestations present:</strong></td>
</tr>
<tr>
<td>☐ Renal impairment (As shown by one of the following below)</td>
</tr>
<tr>
<td>☐ Creatinine ≥ 2 mg/dl (≥ 177 umol/L) for adults, or</td>
</tr>
<tr>
<td>☐ Creatinine ≥ 2x the normal upper limit for age, or</td>
</tr>
<tr>
<td>☐ Creatinine &gt; 2x elevation over baseline in patients with renal disease</td>
</tr>
<tr>
<td>☐ Coagulopathy (As shown by one of the following below)</td>
</tr>
<tr>
<td>☐ Disseminated intravascular coagulation, defined by the following:</td>
</tr>
<tr>
<td>☐ Prolonged clotting times</td>
</tr>
<tr>
<td>☐ Low fibrinogen level</td>
</tr>
<tr>
<td>☐ Presence of fibrin degradation products</td>
</tr>
<tr>
<td>☐ Platelets &lt; 100,000 / mm³ (100 x 10⁶/L):</td>
</tr>
<tr>
<td>☐ Hepatic involvement (As shown by one of the following below)</td>
</tr>
<tr>
<td>☐ Alanine aminotransferase (ALT) ≥ 2x the normal upper limit, ALT level:</td>
</tr>
<tr>
<td>☐ Aspartate aminotransferase (AST) ≥ 2x the normal upper limit, AST level:</td>
</tr>
<tr>
<td>☐ Total Bilirubin ≥ 2x the normal upper limit, Total Bilirubin level:</td>
</tr>
<tr>
<td>☐ Acute respiratory distress syndrome (As shown by one of the following below)</td>
</tr>
<tr>
<td>☐ Acute onset of diffuse pulmonary infiltrates and hypoxemia in absence of cardiac failure, or</td>
</tr>
<tr>
<td>☐ Diffuse capillary leak manifested by acute onset of generalized edema, or</td>
</tr>
<tr>
<td>☐ Pleural or peritoneal effusions with hypoalbuminemia</td>
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<td>☐ Generalized erythematous macular rash that may desquamate,</td>
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<td>☐ Soft-tissue necrosis, including necrotizing fasciitis or myositis, or gangrene</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Laboratory Testing Criteria</th>
</tr>
</thead>
<tbody>
<tr>
<td>☐ Culture isolation of Group A Streptococcus.</td>
</tr>
<tr>
<td>Specimen source:</td>
</tr>
<tr>
<td>Examination of bacterial culture results:</td>
</tr>
<tr>
<td>1. Was patient on antibiotics when any culture specimens were collected: ☐ Yes ☐ No ☐ Unk</td>
</tr>
<tr>
<td>Note specimens affected by antibiotic use.</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Additional epidemiological data to collect for CONFIRMED and/or PROBABLE cases:</th>
</tr>
</thead>
<tbody>
<tr>
<td>Date of Onset of Symptoms:</td>
</tr>
<tr>
<td>Collection Date of 1st positive culture:</td>
</tr>
<tr>
<td>Hospitalized, date of admission:</td>
</tr>
<tr>
<td>Date of hospital discharge:</td>
</tr>
<tr>
<td>Was patient transferred from another hospital? ☐ Yes ☐ No If yes, specify hospital:</td>
</tr>
<tr>
<td>Was patient admitted to ICU? ☐ Yes ☐ No</td>
</tr>
<tr>
<td>Did the patient survive the infection? ☐ Yes ☐ No If NO, date of death:</td>
</tr>
<tr>
<td>STSS Rapid Assessment Form</td>
</tr>
<tr>
<td>---------------------------</td>
</tr>
</tbody>
</table>
| Where was the patient a resident at the time of the initial culture? | □ Private residence  
  □ Homeless  
  □ Group Living, specify:  
  □ Other, specify: |
| Types of infection caused by organism, besides of STSS? | □ Abscess (not skin)  
  □ Bacteremia (no focus)  
  □ Cellulitis  
  □ Chorioamnionitis  
  □ Empyema  
  □ Endocarditis  
  □ Endometritis  
  □ Meningitis  
  □ Necrotizing fasciitis  
  □ Osteomyelitis  
  □ Pericarditis  
  □ Peritonitis  
  □ Puerperal sepsis  
  □ Septic abortion  
  □ Septic arthritis |
| Did the patient survive the infection? | □ Yes  
  □ No |
| Any underlying health causes or prior illness? | □ Yes  
  □ No |
| Did the patient have surgery or any skin incision within 14 days of the first positive culture? | □ Yes  
  □ No |
| Did patient have any of the following: | □ Burns  
  □ Blunt trauma  
  □ Penetrating trauma  
  □ Varicella |
| If yes to any of the above, record the number of days prior to the first positive culture: | □ 0-7 days  
  □ 8-14 days |
| FOR FEMALE PATIENTS ONLY |
| At the time of the positive culture, was the patient: | □ Pregnant  
  □ Post-partum  
  □ Neither pregnant or post-partum  
  □ Unknown pregnancy status |
| If pregnant or post-partum, the outcome of fetus: | □ Survived, no apparent illness  
  □ Survived, clinical infection  
  □ Induced abortion  
  □ Abortion/stillbirth  
  □ Live birth/neonatal death  
  □ Still pregnant |
| If the patient delivered a baby: | □ Method of delivery:  
  □ Vaginal  
  □ C-section |
| If yes, date of delivery: | |
| Any additional information: | |