

GROUP A STREPTOCOCCUS (GAS) – INVASIVE

Case definition

CONFIRMED CASE

Laboratory confirmation of infection with or without clinical evidence of invasive disease:

- isolation of group A streptococcus [*Streptococcus pyogenes*] from a normally sterile site [a normally sterile site is defined as: blood, cerebrospinal fluid, pleural fluid, pericardial fluid, peritoneal fluid, deep tissue specimen taken during surgery [e.g. muscle collected during debridement for necrotizing fasciitis], bone or joint fluid excluding the middle ear and superficial wound aspirates [e.g. skin and soft tissue abscesses]].

Clinical evidence of invasive disease may be manifested as one or more of several conditions:

- Soft tissue necrosis, including necrotizing fasciitis, myositis or gangrene
- Meningitis
- Streptococcal toxic shock syndrome, which is characterized by hypotension [systolic blood pressure ≤ 90 mm Hg in an adult and < 5 percentile for age for children] and at least two of the following signs:
 - Renal impairment [creatinine level ≥ 177 $\mu\text{mol/L}$ for adults]
 - Coagulopathy [platelet count $\leq 100,000/\text{mm}^3$ or disseminated intravascular coagulation]
 - Liver function abnormality [SGOT, SGPT or total bilirubin ≥ 2 x upper limit of normal]
 - Adult respiratory distress syndrome
 - Generalized erythematous macular rash that may desquamate

PROBABLE CASE

Clinical evidence of invasive disease [see clinical evidence above] in the absence of another identified etiology and with non-confirmatory laboratory evidence of infection:

- isolation of group A streptococcus from a non-sterile site

OR

- positive group A streptococcus antigen detection

Further to the case definitions, please note the following definitions for Public Health management:

Sporadic Case: A single case of invasive GAS disease occurring in a community where there is no evidence of an epidemiologic link (by person, place or time) to another case.

Index Case: The first identified in an organization- or community-based outbreak. Identifying the index case in an outbreak is important for the characterization and matching of GAS isolate strains.

Subsequent Case: A case with onset of illness occurring within 21 days and caused by the same strain as another case (including sporadic or index cases) and with whom an epidemiologic link can be established. Most subsequent cases in the community will occur within 7 days of another case.

Severe Case: Case of Streptococcal Toxic-Shock Syndrome (STSS), soft tissue necrosis (including necrotizing fasciitis, myositis or gangrene), meningitis, GAS pneumonia, other life-threatening conditions or a confirmed case resulting in death.

Causative agent

Streptococcus pyogenes, Group A Streptococcus

Source

GAS may be carried in the nasopharynx, gastrointestinal tract and on the skin of humans.

Incubation

Usually 1 to 3 days.

Transmission

Transmission occurs via large respiratory droplets or by direct contact with infected clients or carriers; rarely through contaminated objects. Person-to-person transmission occurs through exposure to secretions from wounds, nasal and oral cavities.

Communicability

Transmissibility generally ends within 24 hours of treatment. If untreated, uncomplicated cases are communicable for 10-21 days or until infection is resolved. Asymptomatic carriage is quite common (up to 15% of the population). In cases with purulent discharges, communicability extends for weeks or months

Symptoms

Symptoms preceding the onset of invasive GAS disease may include unusually severe pain, swelling, fever, chills, flu-like symptoms, myalgias, generalized macular rash, nausea, vomiting, diarrhea, malaise and joint pain.

Clinical evidence of disease may manifest as several conditions including:

- STSS
- Necrotizing Fasciitis (NF)
- Necrotizing Myositis (NM)

STSS is the most serious manifestation of invasive GAS disease. It comprises a primary site of GAS infection together with hypotension, adult respiratory distress syndrome, renal impairment, rapid onset of shock and multi-organ failure.

The most common primary site of invasive GAS infections is soft tissue, but pneumonia, septic arthritis and primary bacteremia may also occur.

Pneumonia with isolation of GAS from a sterile site, or from a bronchoalveolar lavage non-sterile site when no other cause has been identified, should be regarded as a form of invasive disease for the purposes of public health management.

Upper respiratory tract manifestations of GAS are more common with children, arthritis and pelvic infections are more common in young adults, and NF is more common in the elderly.

NF and NM alone are less severe than STSS with a mortality rate of approximately 20%. However, they may progress to STSS, which has a mortality rate of 80%.

Diagnostic testing

Throat swab, or exudate from infected area for culture

Treatment

Advice should be sought from infectious disease specialists.

PUBLIC HEALTH MANAGEMENT & RESPONSE

Case management

Follow-up of invasive GAS is a priority and the following steps must be taken **immediately**:

- [a] Contact primary care provider to obtain clinical information on case
- [b] Record age, gender and address of case
- [c] Interview case or a proxy for the case to determine close contacts.

To establish an epidemiological link, a person must have one or both of the following in common with a confirmed case:

- Contact with a common, specific individual (including confirmed or probable cases).
- Presence in the same location (e.g. school, long-term care facility, child care setting) at or around the same time.

For public health management, cases that occur subsequent to the index case with whom an epidemiologic link can be established may have acquired the disease directly from the index case or may have acquired the disease from another common source.

The public health response to a sporadic case of invasive GAS includes:

- Case management
- Contact tracing
- Maintenance of surveillance for further cases.

Case(s) in a long-term care facility:

GAS infections within long term care facilities (LTCF) are often spread through person-to-person contact, with a clustering of cases by room or care unit. Outbreaks in LTCF are often patient-propagated, whereas within acute care facilities, staff who are carriers are more likely to be the source of infection or outbreaks.

In addition to strict enforcement of standard infection control practices, the following approach may be useful in the investigation and control of invasive GAS disease in LTCF:

When a confirmed case of invasive GAS disease occurs in a LTCF such as a nursing home, the facility should:

- Report the case to the Public Health Unit within the District.
- Conduct a retrospective chart review of the entire facility's residents over

the previous 4–6 weeks, for culture-confirmed cases of GAS disease and any suggested cases of invasive or non-invasive GAS infection, including skin and soft tissue infections (e.g. pharyngitis and cellulitis) and excluding non-culture-confirmed pneumonia and conjunctivitis.

- Assess the potential for a source of infection from outside the facility (e.g. regular visits from children who have recently been ill).

If an excess of GAS infection is identified, the following actions should be considered:

- All patient care staff should be screened for GAS with throat, nose and skin lesion cultures. In LTCF with <100 beds, all residents should be screened for GAS. In LTCF with 100 beds or greater, screening can be limited to all residents within the same care unit as the infected case and contacts of the case if necessary, unless patient and care staff movement patterns or epidemiologic evidence (e.g. from the chart review) suggest that screening should be conducted more broadly.
- Anyone colonized with GAS should receive chemoprophylaxis (see below).
- Non-patient care staff should be asked about possible recent GAS infections. Those with a positive history should be screened for GAS and persons testing as positive should be treated with antibiotics as per recommended regimen.
- All GAS isolates should have further typing. Culturing for a test of cure is recommended for individuals found to have the outbreak-related strain, particularly if there is epidemiologic evidence indicating that contact with the individual is significantly related to illness.
- Culturing for a test of cure is not necessary for individuals infected with a non-outbreak-related strain of GAS.
- Re-screen all GAS-positive residents and staff including their throat and skin lesion(s) 14 days after chemoprophylaxis has been started. Follow by screening at two weeks and at four weeks after the first re-screening. If the person is found to be positive, a second course of chemoprophylaxis should be offered. If the person is still colonized after the second treatment, discontinue chemoprophylaxis unless the facility has an ongoing problem with GAS infection.
- Active surveillance for GAS infection should be initiated and continued for 1 to 2 months.
- Appropriate specimens should be taken for culture to rule out GAS when suspected infections are detected by active surveillance.

If no excess is identified, especially if there is evidence of an outside source of infection for the index case, then active surveillance alone for two to four weeks to ensure the absence of additional cases is warranted.

If the case is in a child care setting:

Child care settings include groups or institutional child care settings (day cares), family or home day care and preschools.

When a confirmed case of invasive GAS disease occurs in a child attending a child care setting, staff must report to district public health units as required by legislation.

When one severe case of invasive GAS disease occurs in a child care setting, public health practitioners should consider the following:

- 1) The nature of the setting, including the size and physical structure, number and ages of the children, type of interaction of the children.
- 2) The characteristics of the case [e.g. if the case occurred secondary to a varicella infection].
- 3) The potential for a source of infection from within the setting:
 - i. whether there has been any suggested invasive or non-invasive infections [e.g. other cases of invasive GAS, pharyngitis, impetigo]
 - ii. potential of a point source of infection [foodborne outbreaks of pharyngitis have occurred and are a consequence of human contamination of food in conjunction with improper preparation or refrigeration procedures.
- 4) The presence of varicella cases in the previous two weeks. If a case of varicella has occurred in the child care setting within the two weeks prior to onset of GAS symptoms in the index case, all attendees should be assessed for varicella vaccination history. Two weeks was chosen as the time interval based on findings that risk of GAS was significantly increased two weeks after onset of varicella infection. Varicella vaccination should be recommended for those without a history of prior varicella infection or vaccination as per the NACI guidelines; CCDR 2004; 30.
- 5) The potential for a source of infection from outside the child care setting [e.g. exposure to a family member with suggested invasive or non-invasive GAS infection.]
- 6) Parents and/or guardians of attendees should be informed of the situation, alerted to the signs and symptoms of invasive GAS disease and be advised to seek medical attention immediately should their child develop febrile illness or any other clinical manifestations of GAS.
- 7) In family or home day care settings, chemoprophylaxis should be recommended for all children and staff.
- 8) In group or institutional settings and preschools, chemoprophylaxis is generally not warranted, but may be considered in certain situations, including the occurrence of >1 case of invasive GAS disease in children or staff of the child care setting within one month or a concurrent varicella outbreak at the child care setting. Cases of invasive GAS occurring among children or staff

of a child care setting within one month should be considered as part of the same cluster. Consideration could be given to testing isolates from invasive GAS cases occurring in a child care setting more than one month apart, to determine strain-relatedness.

- 9) A test of cure is not warranted for persons receiving chemoprophylaxis.
- 10) Appropriate specimens can be taken for culture to rule out GAS when suspected infections are detected during this period; however routine screening of attendees is not recommended.

Contact tracing

Definition of Close Contacts

- Household contacts of a case who have spent at least 4 hours/day on average in the previous 7 days or 20 hours/week with the case
- Non-household persons who share sleeping arrangements with the case or had sexual relations with case
- Persons who have had direct mucous membrane contact with the oral or nasal secretions of a case [e.g. mouth-to-mouth resuscitation, open mouth kissing] or unprotected direct contact with an open skin lesion of the case
- Injection drug users who have shared needles with the case.

Susceptibility

The risk of invasive GAS is significantly associated with the following underlying conditions:

- Age >65 years
- Injection drug use
- Heart disease
- High dose steroid use immunosuppressive doses
- Diabetes Mellitus
- Cancer
- Presence of varicella infection in the 2-week period following the onset of symptoms
- Alcohol abuse
- Chronic lung disease
- Skin trauma
- HIV infection

Prophylaxis

Chemoprophylaxis is offered to prevent disease in colonized individuals and in those who have recently been exposed, thereby decreasing transmission of strain known to have caused severe infection.

Chemoprophylaxis should only be offered:

- 1) To close contacts of a confirmed severe case. A confirmed severe case is defined as a case of STSS, soft tissue necrosis (including NF, NM or gangrene), meningitis, GAS pneumonia, other life-threatening conditions or a confirmed case resulting in death;

AND

- 2) If close contacts have been exposed to the case during the period from 7 days prior to onset of symptoms in the case to 24 hours after the case's initiation of antimicrobial therapy.

Chemoprophylaxis of close contacts should be administered as soon as possible and preferably within 24 hours of case identification, but is still recommended for up to 7 days after the last contact with an infectious case.

Chemoprophylaxis for Close Contacts of Invasive GAS

Drug	Dosage	Comments
First generation cephalosporins: cephalexin, cephadroxill, cephradine	First line: Children and adults: 25 – 50 mg/kg/day, to a maximum of 1 g/day in 2 to 4 divided doses x 10 days	<p>Recommended drug for pregnant and lactating women.</p> <p>Should be used with caution in patients with allergy to penicillin.</p> <p>Use of cephalosporins with nephrotoxic drugs (e.g. aminoglycosides, vancomycin) may increase the risk of cephalosporin-induced nephrotoxicity.</p>
Erythromycin	<p>Second line: Children: 5 to 7.5 mg/kg every 6 hours or 10 to 15 mg/kg every 12 hours (base) x 10 days (Not to exceed maximum adult dose)</p> <p>Adults: 500 mg every 12 hours (base) x 10 days</p>	<p>Erythromycin estolate is contraindicated in persons with pre-existing liver disease or dysfunction and during pregnancy.</p> <p>Sensitivity testing is recommended in areas where macrolide resistance is unknown or known to be $\geq 10\%$.</p>
Clarithromycin	<p>Second line:</p> <p>Children: 15 mg /kg /day in divided doses every 12 hours to a maximum of 250 mg PO BID x 10 days</p> <p>Adults: 250 mg PO BID x 10 days</p>	<p>Contraindicated in pregnancy.</p> <p>Sensitivity testing is recommended in areas where macrolide resistance is unknown or known to be $\geq 10\%$.</p>
Clindamycin	<p>Second line:</p> <p>Children: 8 to 16 mg/kg/day divided into 3 or 4 equal doses x 10 days (Not to exceed maximum adult dose)</p> <p>Adults: 150 mg every 6 hours x 10 days</p>	<p>Alternative for persons who are unable to tolerate beta-lactam antibiotics.</p>

Exclusion

None

Education

- Practice proper hand-hygiene, especially after coughing or sneezing, and before preparing or eating foods and before and after each completed patient contact.
- Ensure all wounds are kept clean and watch for possible signs of infection such as redness, swelling, drainage and pain at the wound site. A person with signs of an infected wound, especially if fever occurs, should seek medical care immediately.

Surveillance forms

novascotia.ca/dhw/populationhealth/surveillanceguidelines/NS_Notifiable_Disease_Surveillance_Case_Report_Form.pdf

novascotia.ca/dhw/populationhealth/surveillanceguidelines/Invasive_Group_A_Strep_Case_Report_Form.pdf

REFERENCES:

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Invasive Group A Streptococcal Disease Guidelines Working Group. *Guidelines for the Prevention and Control of Invasive Group A Streptococcal (GAS) Disease*, Public Health Agency of Canada, 2006 National Advisory Committee on Immunization (NACI). *Update on Varicella*. *CCDR 2004*; 30: 1-27

cdha.nshealth.ca/pathology-laboratory-medicine

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