Alberta Public Health Disease Management Guidelines

Streptococcal Disease Group A, Invasive

Alberta

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Health and Wellness Promotion Branch

Public Health Division

Alberta Health

Streptococcal Disease Group A, Invasive | Alberta Health, Government of Alberta

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Revision History

Revision Date	Document Section	Description of Revision
April 2023	Revision History	• Moved to beginning of document for easier clarification of changes to document
	Case definition	• Changed “Adult” to “Acute” for ARDS
	Reporting Requirements	• Changed HCP reporting to MOH from FMP to 24 hours • Changed Lab reporting to MOH from FMP to 24 hours • Added exception that reporting of throat swabs reports is not required
	Epidemiology	• Updated Incidence
	Public Health Management	• Added statement recommending public health action of cases within 24 hours. • Management of Contacts – clarified wording • Appendix 2 – removed “nose” from specimen collection list

Case Definition

Confirmed Case

- Isolation of Group A *Streptococcus pyogenes* (GAS) from a normally sterile site[(A)] with or without severe invasive disease.[(B)]

Probable Case

- Isolation of GAS from a non-sterile site and with severe invasive disease[(B)] in the absence of another identified etiology.

[(A)] Normally sterile site specimens are defined as:

- blood;
- cerebrospinal fluid (CSF);
- pleural fluid;
- peritoneal fluid;
- pericardial fluid;
- bone;
- joint fluid; or
- specimens taken during surgery, muscle/tissue collected during debridement for necrotizing fasciitis, or fluid from a deep abscess).

NOTE: A specimen taken from a non-sterile site collected during a sterile procedure is not considered a "normally sterile site".

[(B)] **Severe, invasive disease** may manifest as several conditions. These include:

- streptococcal toxic shock syndrome (STSS), which is characterized by hypotension (systolic blood pressure < 90 mm Hg in an adult and < 5th percentile for age in children) and at least TWO of the following signs:
  - renal impairment (creatine level > 177 µmol/L for adults),
  - coagulopathy (platelet count < 100,000/mm^3 or disseminated intravascular coagulation),
  - liver function abnormality (AST, ALT or total bilirubin > 2x upper limit of normal),
  - acute respiratory distress syndrome (ARDS), and/or
  - generalized erythematous macular rash that may desquamate.
- soft tissue necrosis including, necrotizing fasciitis, myositis or gangrene;
- meningitis;
- GAS pneumonia NOTE: Pneumonia with isolation of GAS from bronchoalveolar lavage (BAL) when no other cause has been identified should be regarded as a form of severe invasive disease for the purposes of public health management;
- any other life threatening condition (as determined on a case-by-case basis); and
- death.

Reporting Requirements

Health Practitioners

Health practitioners shall notify the Medical Officer of Health (MOH) (or designate) of the zone of:

- All confirmed and probable severe, invasive GAS (iGAS) cases in the prescribed form within 24 hours, and
- All other confirmed and probable iGAS cases in the prescribed form by mail, fax or electronic transfer within 48 hours.

Laboratories

All laboratories shall report all positive laboratory results* by mail, fax or electronic transfer:

- within 24 hours to the Zone MOH (or designate), and
- within 48 hours to the Chief Medical Officer of Health (CMOH) (or designate).

*Positive laboratory samples from throat swabs do not need to be reported.

NOTE: Isolates collected from a normally sterile site (i.e., invasive) may be submitted to the National Center for Streptococcus via the Alberta Public Laboratories (ProvLab) in Edmonton, Alberta for passive surveillance of emm serotyping and antimicrobial susceptibility trend analysis.

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- The MOH (or designate) of the zone where the case currently resides shall forward the initial Notifiable Disease Report (NDR) of all confirmed and probable cases to the CMOH (or designate) within two weeks of notification and the final NDR (amendment) within four weeks of notification.
- For out-of-province and out-of-country reports, the following information should be forwarded to the CMOH (or designate) by phone, fax or electronic transfer within 48 hours (two business days) including:
  - name,
  - date of birth,
  - out-of-province health care number,
  - out-of-province address and phone number,
  - positive laboratory report, and
  - other relevant clinical/epidemiological information.

Epidemiology

Etiology

Group A streptococcal (GAS) disease is caused by *Streptococcus pyogenes*, a gram positive, non-spore forming, non-motile bacterium. Distinct group A streptococcal serotypes have been identified through emm typing and emm serotyping. There are over 120 serotypes or genotypes.[1] The M protein, which is encoded by the emm gene, is an important virulence factor and is also an epidemiological marker that is used worldwide to characterize GAS isolates.[2] Certain emm types are correlated with specific manifestations of group A streptococcus disease.[2]

Clinical Presentation

Streptococcus pyogenes can cause a variety of invasive and non-invasive infections. The most frequently encountered illnesses caused by *S. pyogenes* are sore throat (strep throat) and skin infections such as impetigo or pyoderma.[1] *Streptococcus pyogenes* can also cause scarlet fever, puerperal fever, erysipelas, septicemia, cellulitis, mastoiditis, otitis media, pneumonia, peritonisilitis, wound infections, necrotizing fasciitis and streptococcal toxic shock syndrome.[3]

The symptoms preceding the onset of invasive GAS disease are variable depending on the manifestation or site of infection. Symptoms may be vague and include pain of unusual severity, swelling, fever, chills, flu-like symptoms, generalized muscle aches, generalized macular rash, bullae, nausea, vomiting, diarrhea, malaise or joint pain.[1,3,4]

Streptococcal toxic shock syndrome (STSS) and necrotizing fasciitis (NF) are the most serious manifestation of invasive GAS. STSS is caused by a toxin-producing GAS strain and is characterized by fever and hypotension along with multi-organ involvement.[1] Necrotizing fasciitis can have devastating consequences and symptoms usually include fever and a red, painful swelling of tissue which spreads rapidly.[5] NF is diagnosed when the disease spreads along the layer of tissue that surrounds the muscle (fascia). It is treated by surgical debridement of the infected tissue along with antibiotic therapy.[6]

Diagnosis

The diagnosis of a confirmed case of invasive GAS disease is made by isolating *S. pyogenes* from a normally sterile site. These include cultures from blood or other focal sites of infection such as CSF, pleural fluid, and tissues obtained in the operating room or from sites showing evidence of NF or myositis. Positive samples should be submitted by the laboratory to the National Centre for Streptococcus (NCS) for serotyping. The NCS performs M typing and molecular *emm* gene sequencing for *S. pyogenes* for routine surveillance.[7]

Molecular sequencing and susceptibility testing are helpful in characterizing outbreaks, determining disease trends and guiding appropriate clinical management of cases and contacts.

Treatment

- Laboratory testing of antimicrobial sensitivity of the GAS strain is useful in determining appropriate antibiotic therapy.
- GAS is treated with antibiotics.
- High-dose parenteral therapy is generally required for severe infections.
- Treatment may continue for two to six weeks.

Reservoir

Humans.[3]

Transmission

Transmission is generally person-to-person by large respiratory droplets or by direct contact with patients or carriers, extremely rarely through indirect contact with objects.[3]

Foodborne outbreaks of pharyngitis have been reported. This is generally a consequence of human contamination of food along with improper food preparation or refrigeration.[1]

Incubation Period

The incubation period is not clearly defined and may depend on the route of inoculation. It has been described as short, typically one to three days, but may be as long as seven days in cases of non-invasive disease.[3] In cases associated with the accidental subcutaneous inoculation of organisms, such as during childbirth or after penetrating trauma, the incubation period may be as short as 14 hours.[1]

Period of Communicability

GAS is communicable for 10–21 days in untreated, uncomplicated cases but may last for weeks or months if purulent discharge is present.[3] Transmissibility generally ends within 24 hours of starting appropriate antibiotic treatment.

Host Susceptibility

Susceptibility is universal. The development of invasive GAS disease appears to be facilitated by the presence of specific virulent strains, predisposing host factors such as younger or older age, and chronic health stresses such as HIV infection, cancer, cardiovascular disease, diabetes, respiratory disease and alcohol abuse.[7] Factors that increase the likelihood of developing STSS include age (neonates and older adults), diabetes, alcoholism, surgical procedures, penetrating trauma (e.g., insect bites, lacerations, slivers, burns), non-penetrating trauma (e.g., bruise, hematoma, muscle strain) and having varicella disease.[4]

The risk of invasive GAS infection among people living in the same household as a case is estimated to range between 0.66–2.94 per 1000.[8,9] Estimates are based on extremely small numbers of subsequent cases; however, the estimated rates are higher than the rate of sporadic disease in the general population.[7]

Immunity only develops against the specific emm type of GAS and may last for years.[3]

Incidence

Invasive GAS was put under surveillance in Alberta in 1998. A resurgence of the disease became evident in the province in 1999 and subsequently, invasive GAS was made reportable on August 1, 1999.[12]

The most common *emm* type in Alberta from 2011 to 2017 was *emm*1. In 2018 and 2019, *emm*76 and 81 replaced *emm*1 as the most common types. *Emm*49 emerged as the most common type in 2020 and 2021. In 2020, severe cases (NF, STSS and death) accounted for ~18% of total cases.

Commonly identified risk factors include substance use and addiction, homelessness, and non-surgical wounds.

Annual case counts can be accessed through Alberta Health's Interactive Health Data Application.

Public Health Management

Key Investigation

- **Public health investigation should be initiated for all iGAS cases within 24 hours of receipt of the lab report.**
- Obtain information on the clinical presentation.
- Determine whether or not specimen was collected from a normally sterile site.
- Determine if the case has severe invasive disease.
- Identify risk factors/susceptibility for acquiring disease.
- Identify close contacts. Close contacts include household and non-household contacts as well other specified contacts.
  - Household contacts are considered individuals who have spent at least four hours per day, on average, in the previous seven days **or** 20 hours per week with the case including:
    - persons living in the household, and
    - children and staff of family day homes.
  - Non-household contacts are considered individuals who have had exposure to the case during the period from seven days prior to the onset of symptoms to 24 hours after the initiation of antimicrobial therapy in the case AND are identified as:
    - individuals who share the same bed or had sexual relations with the case,
    - persons who have had direct mucous membrane contact with the oral or nasal secretions of the case (e.g., mouth-to-mouth resuscitation, open-mouth kissing but does not include kissing with closed mouth or sharing utensils, water bottles, cigarettes, etc.),
    - persons who have had direct contact with an open skin lesion of the case, or
    - injection drug users who have shared needles with the case.
- Classmates, work colleagues as well as social or sports contacts of a case are not considered contacts unless they meet the criteria for close contacts. Secondary cases in schools (kindergarten and older) and workplaces are rare.
- Child care center (excluding family day homes) attendees and staff (refer to Appendix 1).
- Long Term Care Facility (LTCF) residents and staff (refer to Appendix 2).
- Hospital patients and staff (refer to Appendix 3).

NOTE: If the case has symptoms that are clinically compatible with the illness, e.g., pharyngitis a few days before diagnosis of invasive GAS, use this symptom onset date as Day 1. If uncertain, consult the MOH.

Management of a Case

- Confirm that the case has received appropriate antimicrobial therapy.
- Contact and droplet precautions should be instituted when caring for hospitalized patients with known or suspected invasive GAS until 24 hours of effective antibiotic therapy is complete.[13]
- The infection control practitioner (or designate) should be notified immediately if a health care worker (HCW) with suspected or confirmed GAS disease (invasive or non-invasive) worked while the infection was communicable or if there is any possibility that the infection might have been occupationally acquired.

Management of Contacts

Reference [7] applies to this section.

- Chemoprophylaxis is provided to eradicate nasopharyngeal colonization of GAS and prevent secondary cases.
  - Offer chemoprophylaxis to close contacts of cases with severe invasive disease.[7] Recommended chemoprophylaxis is outlined in Table 1.
  - Offer chemoprophylaxis as soon as possible (and preferably within 24 hours of case identification/notification) but may be offered up to seven days after the last exposure unless the exposure occurred after the case has completed 24 hours of appropriate antibiotic therapy.
- Educate all close contacts of invasive GAS disease:
  - About disease transmission, appropriate personal hygiene, routine practices and contact precautions.
  - To monitor for symptoms and seek medical attention immediately if they develop symptoms of GAS within 30 days of diagnosis in the index case.
- Refer to Appendix 1 for management in child care attendees and staff.
- Refer to Appendix 2 for management in Long Term Care Facility residents and staff.
- Refer to Appendix 3 for hospital patients and staff.
- Consult with the MOH for unusual situations that do not fall under the above scenarios.
- Antibiotics for chemoprophylaxis are listed in Table 1.

Table 1: Chemoprophylaxis for iGAS[7]

Drug	Dosage[3]	Comments[3]
First generation Cephalosporins: Cephalexin	Children and adults: 25–50 mg/kg/day, to a maximum of 1g/day, in two to four divided doses x 10 days.	**First Line** • Recommended for pregnant and lactating women. • Should be used with caution in patients with allergy to penicillin. • Use of cephalosporins with nephrotoxic drugs (e.g., aminoglycosides, vancomycin) may increase the risk of cephalosporin-induced nephrotoxicity.
Erythromycin*	• Adults: 500 mg every 12 hours (base) x 10 days.	**Second Line** • Erythromycin estolate is contraindicated in persons with pre-existing liver disease or dysfunction and during pregnancy. • Sensitivity testing is recommended in areas where macrolide resistance is unknown or known to be > 10%.
Clarithromycin	• Children: 15 mg/kg/day in divided doses every 12 hours, to a maximum of 250 mg twice daily x 10 days. • Adults: 250 mg twice daily x 10 days.	**Second Line** • Contraindicated in pregnancy. • Sensitivity testing is recommended in areas where macrolide resistance is unknown or known to be ≥10%.
Clindamycin	• Children: 8–16 mg/kg/day divided into three or four equal doses x 10 days. (Not to exceed maximum of adult dose) • Adults: 150 mg every 6 hours x 10 days.	**Second Line** • Contraindicated in pregnancy and lactation. • Alternative for persons who are unable to tolerate beta-lactam antibiotics.

** Erythromycin estolate (liquid/oral suspension) for pediatric population is not available in Canada at this time.*

Preventive Measures

- Educate the public and HCWs about the modes of transmission.
- Maintain appropriate infection control practices.
- Transmission is most effectively prevented by strict adherence to good hand hygiene and other routine practices.
- Offer varicella vaccine as per the current Alberta Immunization Policy. Universal varicella immunization could potentially prevent up to 15% of all pediatric invasive GAS disease.[14]

Appendix 1: Child Care Centre Attendees and Staff

Reference 7 applies to this appendix.

Key Investigation

Investigation may be warranted if one case of invasive GAS disease with severe invasive disease occurs in a child care centre. Consideration should be taken as to:

- the nature of the facility (e.g., type of centre including size and physical structure, number and ages of children, interaction of children);
- the characteristics of the case (e.g., secondary to varicella infection);
- the potential for a source of infection within the centre including:
  - whether there has been any known streptococcal infections (e.g., other cases of invasive GAS, pharyngitis, impetigo), and
  - potential of a point source of infection;
- the presence of varicella cases within the centre in the previous two weeks; and
- the potential for a source of infection from outside the centre (e.g., exposure to a family member with GAS infection).

Management of Contacts

Chemoprophylaxis is generally not recommended when one case of invasive GAS is identified in a child care centre. When one case of invasive GAS is identified in a child care centre:

- Alert parents/guardians to the signs and symptoms of invasive GAS and advise them to seek medical attention should the child develop a febrile illness or any other clinical manifestation of GAS.
- Screening of attendees and staff is not required.
- Staff should notify public health if further cases of invasive GAS infection occur within two months.
  - 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.
  - Chemoprophylaxis may be recommended in situations where one case of invasive GAS with severe invasive disease occurs **AND**
    - a subsequent confirmed case of invasive GAS occurs in children or staff of the child care centre within one month,

    OR
    - there is a concurrent varicella outbreak in the child care centre.
- Isolates from cases occurring more than one month apart should be tested to determine strain relatedness.
  - Consultation with the microbiologist on-call is recommended.
- If a case of varicella has occurred in the child care centre within the two weeks before onset of symptoms in the index case, all attendees should be assessed for varicella vaccination history.
  - Varicella vaccination should be recommended for those without a history of prior varicella infection or vaccination as per the current Alberta Immunization Policy.
- A test of cure is not required for persons (children or staff) receiving chemoprophylaxis.

Appendix 2: Long Term Care Facility Residents and Staff

Reference 7 applies to this appendix.

Residents of long-term care facilities (LTCF) are at increased risk of morbidity and mortality due to invasive GAS disease because of their older age and/or higher prevalence of underlying conditions. When a confirmed case of invasive GAS occurs in a LTCF, there is 38% likelihood that a second positive blood culture-confirmed case of the same strain will be detected in the facility within six weeks.

Key Investigation

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

- report the case to the MOH; and
- conduct a retrospective chart review of the entire facility's residents over the previous four to six weeks for culture confirmed cases of GAS disease and suggested cases of non-invasive or invasive GAS infection, including skin and soft tissue infections (e.g., pharyngitis and cellulitis) and excluding pneumonia and conjunctivitis not confirmed by culture.

Management of Contacts

- Chemoprophylaxis is recommended for close contacts when there is invasive GAS and the case has severe invasive disease.
- Persons who share a room with a case are not considered contacts unless they meet the criteria of close contacts, i.e., the roommate has had direct mucous or non-intact skin contact with respiratory tract secretions or skin lesions of the case.
  - Contacts should be assessed on a case-by-case basis.
- HCWs are not considered contacts unless they meet the criteria of close contact (i.e., infection control practices are breached) or direct contact of mucous membranes or non-intact skin with fluid from the nose, mouth or wound of a case as described above has occurred (e.g., direct mouth to mouth resuscitation).
  - Referral of the exposed staff to their Occupational Health Department would be appropriate.
- If no excess of GAS 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 establish the absence of additional cases is warranted.

Excess of GAS Infection

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 and skin lesion cultures.
  - In LTCF with fewer than 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) suggests that screening be conducted more broadly.
- Anyone colonized with GAS should receive chemoprophylaxis.
- Non-patient care staff should be asked about possible recent GAS infections. Those with a positive history should be screened for GAS and those who are positive should be treated with antibiotics as per the recommended regimen.
- All GAS isolates should have further typing.
  - Culture for a test of cure is recommended for individuals found to have the outbreak-related strain, particularly if there is epidemiologic evidence indicating that the contact with the individual is significantly related to illness.

Definition of Excess of GAS Infection

An excess of GAS infection (or a LTCF outbreak) is defined as:

- an incidence rate of confirmed invasive GAS infection of > 1 per 100 residents per month, OR
- at least two cases of confirmed invasive GAS infection in one month in LTCF with fewer than 200 residents, OR
- an incidence rate of suggested invasive or non-invasive GAS infections of > 4 per 100 residents per month.

- Culture for a test of cure is not necessary for individuals infected with a strain of GAS not related to the outbreak.

- All GAS positive residents and staff should be re-screened, including throat and skin lesions 14 days after chemoprophylaxis has been started.
  - This should be followed 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 course, discontinue chemoprophylaxis unless the facility has an ongoing problem with GAS infection.
- Active surveillance for GAS infection should be initiated and continued for one to two months.
- Appropriate specimens should be taken for culture to rule out GAS when suspected infections are detected by active surveillance.

Appendix 3: Hospital Patients and Staff

Reference 7 applies to this appendix.

Most cases of nosocomial invasive GAS are sporadic. It is important to recognize clinical presentations compatible with invasive GAS and institute additional precautions while waiting for confirmation.

Key Investigation

- Active surveillance for early identification of outbreaks may also be effective in preventing some cases.
- Prevention of a hospital outbreak of GAS infection requires very rapid investigation and intervention once a single hospital-acquired case has been identified
- If, within one month of a confirmed invasive GAS case, one or more possibly linked invasive or non-invasive cases are identified in patients or staff, the situation should be treated as an outbreak.

Management of Cases and Contacts

- Contact and droplet precautions should be implemented when caring for patients with known or suspected invasive GAS until 24 hours of effective antimicrobial therapy is complete.

Management of HCW Exposed to GAS

- An occupational exposure of a HCW is defined as secretions from the nose, mouth, wound or skin of the infected person coming into contact with the mucous membranes or non-intact skin of the HCW within seven days before the onset of GAS until 24 hours after effective antibiotic therapy.
- If the appropriate personal protective equipment was worn, there was no occupational exposure of the HCW.
- The risk of an exposed HCW developing GAS infection and the efficacy of prophylaxis is unknown.
- HCW who have an occupational exposure to patient with severe invasive disease may be offered chemoprophylaxis**.**
- HCW who have an occupational exposure to any case of GAS should be counseled about symptoms associated with GAS and advised to seek care immediately if symptoms develop within 21 days of exposure.
- No screening, treatment, modifications of work practices or work restrictions for HCW in contact with a patient with GAS infection are required when there has not been an occupational exposure.

Management of HCW Colonized or Infected with GAS

- There are no modifications to work practices or work restrictions for HCW who are colonized with GAS and are asymptomatic if they are not epidemiologically linked to patient transmission.
- Asymptomatic colonized HCW who are epidemiologically linked to transmission of GAS to patients resulting in invasive or non-invasive disease should be offered chemoprophylaxis and should be excluded from care duties until 24 hours after the start of treatment with an effective antibiotic therapy.
- HCW with symptomatic GAS infection (invasive or non-invasive) should be offered therapy and should be excluded from patient care duties until 24 hours after the start of antibiotic therapy.
- HCW with symptomatic GAS infection and colonized HCW linked epidemiologically to an outbreak should be informed of the potential for transmission of GAS within households and be advised that symptomatic family members should seek medical evaluation.

Management of Possible or Confirmed GAS Outbreaks in Hospitals

- Detailed information on the management of possible or confirmed GAS outbreaks in hospitals can be found at www.phac-aspc.gc.ca/publicat/ccdr-rmtc/06vol32/32s2/index.html

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