



Health and
Wellness

Prince Edward Island Guidelines for the Management and Control Invasive Group A Streptococcal Disease

March 2018

Department of Health and Wellness
Chief Public Health Office

Invasive Group A Streptococcal Disease

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Case Definition (1)

Confirmed Case

- The isolation of group A streptococcus (GAS) (*Streptococcus pyogenes*) from a normally sterile site¹. Confirmed cases may or may not have severe invasive disease².

Probable Case

- Clinical evidence of invasive disease² in the absence of another identified etiology and with isolation of GAS from a non-sterile site.

Reporting Requirements

Health Practitioners

Health practitioners, shall, in accordance with the [Notifiable Diseases and Conditions and Communicable Diseases Regulations](#) of the Prince Edward Island (PEI) [Public Health Act \(2\)](#) report all confirmed and suspected cases by phone, as soon as suspected or when the result is known, to the Chief Public Health Officer (CPHO) (or designate) not later than 1 hour after observation (as per the [PEI Reporting Notifiable Diseases, Conditions, and Events Regulations](#)) (3). This includes all confirmed and probable cases of invasive GAS disease causing any of the following:

- Necrotizing Fasciitis (NF),
- Streptococcal Toxic Shock Syndrome (STSS), or
- Death.

¹ Normally sterile sites are defined as blood, cerebrospinal fluid (CSF), pleural fluid, peritoneal fluid, pericardial fluid, bone, joint fluid, or specimens taken during surgery (e.g. muscle 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 it **not** considered a “normally sterile site”.

² Severe invasive disease may manifest as streptococcal toxic shock syndrome (STSS), which is characterized by hypotension (systolic blood pressure ≤ 90 mm Hg in an adult and $< 5^{\text{th}}$ percentile for children), and at least two of the following signs: renal impairment (creatinine level ≥ 177 $\mu\text{mol/L}$ for adults), coagulopathy (platelet count $< 100,000/\text{mm}^3$ or disseminated intravascular coagulation), liver function abnormality (AST, ALT, or total bilirubin ≥ 2 x the upper limit of normal), adult respiratory distress syndrome (ARDS), generalized erythematous macular rash that may desquamate. Severe invasive disease may manifest also manifest as soft tissue necrosis (including necrotizing fasciitis, myositis, or gangrene), meningitis, GAS pneumonia (NOTE: pneumonia with isolation of GAS from bronchoalveolar lavage when no other cause has been identified should be regarded as a severe form invasive disease for the purposes of public health management), other life threatening conditions (as determined on a case-by-case basis), and death (1).

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Laboratories

The Provincial Laboratory shall, in accordance with the PEI *Public Health Act* (2), report all positive laboratory results by phone and mail, fax or electronic transfer, as soon as the result is known, to the CPHO (or designate) not later than 1 hour after observation (as per the [PEI Reporting Notifiable Diseases, Conditions, and Events Regulations](#)) (3).

Etiology (4)

Group A streptococcal (GAS) disease is caused by *Streptococcus pyogenes* (*S. pyogenes*), a gram-positive, β -hemolytic bacterium. Distinct GAS serotypes have been identified through *emm* typing. There are over 240 serotypes or genotypes. 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. Certain *emm* types are correlated with specific manifestations of GAS disease.

Clinical Presentation (4)

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. *Streptococcus pyogenes* can also cause scarlet fever, puerperal fever, erysipelas, septicemia, cellulitis, mastoiditis, otitis media, pneumonia, peritonitis, wound infections, necrotizing fasciitis, and streptococcal toxic shock syndrome.

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.

Streptococcal toxic shock syndrome (STSS) and necrotizing fasciitis (NF) are the most serious manifestations of invasive GAS. Streptococcal toxic shock syndrome is caused by a toxin-producing GAS strain and is characterized by fever and hypotension along with multi-organ involvement. Necrotizing fasciitis can have devastating consequences and symptoms, usually including fever and red and painful swelling of tissues which spreads rapidly. Necrotizing fasciitis 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.

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Diagnosis (5)

Samples submitted to the Provincial Laboratory for routine culture will identify GAS by isolating *S. pyogenes* (exceptions to this include samples that are only being tested for MRSA, VRE, or fungal cultures as these samples require different media). *Invasive* GAS is determined by the site of collection, and is only a concern in normally sterile sites (see [case definition](#)). If a culture is positive for invasive GAS, the CPHO is notified. The sample is then sent to the National Microbiology Laboratory for molecular *emm* gene sequencing for routine surveillance.

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

Epidemiology

Reservoir

The reservoir is humans (4).

Transmission

Transmission is generally person-to-person by large respiratory droplets or by direct contact with a case or carrier. It is highly unlikely to occur through indirect contact with objects (4).

Foodborne outbreaks of pharyngitis have been reported. This is generally a consequence of human contamination of food along with improper food preparation or refrigeration (4).

Incubation Period

The incubation period is not clearly defined and may depend on the route of inoculation. It has been described as short, typically 1 – 3 days, but may be as long as 7 – 10 days in cases of non-invasive disease (4).

Period of Communicability (4)

GAS is communicable for 10 – 21 days in untreated uncomplicated cases of impetigo, but may last for weeks or months if purulent discharge is present or in cases of GAS pharyngitis. With adequate treatment, transmissibility is generally terminated within 24 hours.

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Host Susceptibility

Susceptibility to GAS bacteria is universal. The development of invasive GAS (iGAS) 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. Skin breakdown also poses a risk for iGAS infection, this includes children with varicella, surgical procedures, penetrating trauma (e.g., insect bite, laceration, sliver, burn), or non-penetrating trauma (e.g., bruise, hematoma, muscle strain) (5).

The risk of iGAS infection among people living in the same household as a case is estimated to range between 0.66 – 2.94 per 1,000. 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 (5).

Immunity only develops against the specific M type of GAS and may last for years.

Occurrence

General

Prior to widespread antimicrobial availability, morbidity from *Streptococcus pyogenes* or GAS infection was common. A decline in the incidence of GAS was seen steadily up to the 1970s with the introduction of penicillin and other antibiotics. However, in the 1980s, there was a worldwide resurgence in GAS as well as an increase in virulence (5). Globally, it is difficult to estimate disease burden due to scarce disease registries, passive surveillance reliance, and a general under-reporting of cases. It is best estimated that there are 1.78 million new cases of iGAS each year (6). Currently there is no vaccine to prevent iGAS.

Canada (7)

National surveillance of iGAS began in January 2000, and it became nationally notifiable in 2002 (1). Published and unpublished national data between 2009 and 2014 reports an overall increase in incidence of disease from a low of 4 per 100,000 in 2009 to high of 4.7 per 100,000 in 2013. The highest incidence is typically in infants less than one year of age. In 2014, there were 1,457 cases of invasive *S. pyogenes* isolates in Canada. The dominant strains have been *emm1* and *emm89*.

Prince Edward Island

From 2006 – 2015 cases on PEI have ranged from 0 to 8 new cases per year (8).

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Control

Management of a Case

- The Provincial Microbiology Laboratory reports all cases of iGAS to the CPHO. The CPHO evaluates the case to determine if it is severe.
- Report confirmed or suspected clinical cases of invasive infection to CPHO not later than 1 hour after observation (See [Reporting Requirements](#))⁴.
- Confirm that the case has received appropriate antimicrobial therapy⁴.
- Institute contact and droplet precautions when caring for hospitalized patients with known or suspected invasive GAS until 24 hours after effective antibiotic therapy has been completed⁴.
- Based on the severity of the infection, the CPHO will pursue information on close contacts of the case and arrange for prophylactic treatment (see [Management of Contacts](#) section).

Treatment of a Case

- Management includes antibiotic therapy, surgical debridement (if appropriate), and management of septic shock (if applicable)⁴.
- See skin and soft tissue empiric guidelines (www.healthpei.ca/src/microbiology) for empiric therapy and comments on IVIG and / or Infectious Diseases Involvement⁴.
- Once group A streptococcus is identified as the sole pathogen then IV antibiotics can be tailored to typically Penicillin IV, cefazolin (if any type I Penicillin allergy); clindamycin can be discontinued after a total of 3-5 days⁴.

Management of Contacts

- Educate all close contacts of invasive GAS infection about disease transmission, appropriate personal hygiene, routine practices, contact precautions, and symptoms of infection. Advise them to seek medical attention immediately if they develop a febrile illness or another clinical manifestation of GAS within 30 days of diagnosis of a case³. Close contacts include:
 - Household contacts of a case who have spent at least 4 hours per day on average in the previous 7 days, or 20 hours per week with the case;
 - Non-household contacts who share sleeping arrangements;
 - Sexual contacts;

³ To be completed by Public Health Nursing.

⁴ Primary Health Care Provider

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- Persons who have had direct mucous membrane contact with 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; and
- Selected long-term care facility (LTCF), childcare centre, and hospital contacts.
- Offer chemoprophylaxis to close contacts of cases with **severe invasive disease** (see definition page 2)⁵. Recommended chemoprophylaxis is outlined in [Annex A](#).
 - Chemoprophylaxis is provided to eradicate nasopharyngeal colonization of GAS and to prevent secondary cases.
 - Chemoprophylaxis should be administered as soon as possible and preferably within 24 hours of case identification but may be offered up to 7 days after the last exposure.
 - Chemoprophylaxis is **not** required if exposure occurred after the case has completed 24 hours of appropriate antibiotic therapy.
- Refer to [Annex B](#) for management in child care attendees and staff.
- Refer to [Annex C](#) for management in long-term care facility (LTCF) residents and staff.
- Refer to [Annex D](#) for management of hospital patients and staff.
- Consult with the CPHO for unusual situations that do not fall under the above scenarios.

Preventative Measures

- Educate the public and Health Care Workers 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 the varicella vaccine to those who are eligible, as per the current PEI [Childhood immunization schedule](#) or [Adult immunization schedule](#). Universal varicella immunization could potentially prevent up to 15% of all paediatric invasive GAS disease.

⁵ CPHO for community contacts, employee health for occupational exposure

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References

1. **Public Health Agency of Canada.** Invasive Group A Streptococcal. [Online] Public Health Agency of Canada, May 2008. [Cited: March 30, 2017.] http://www.phac-aspc.gc.ca/publicat/ccdr-rmtc/09vol35/35s2/Strep_A-eng.php.
2. **Prince Edward Island Legislative Council Office.** Prince Edward Island Public Health Act. [Online] December 15, 2016. [Cited: February 15, 2017.] https://www.princeedwardisland.ca/sites/default/files/legislation/p-30_1.pdf.
3. **PEI Department of Health and Wellness.** It's the Law: Reporting Notifiable Diseases, Conditions, and Events. [Online] PEI Department of Health and Wellness. [Cited: March 8, 2017.] https://www.princeedwardisland.ca/sites/default/files/publications/notifiable_diseases_final_feb_12_2014_1.pdf.
4. **Heymann, David.** Streptococcal Diseases. *Control of Communicable Diseases Manual (20th Ed)*. Washington, D.C. : American Public Health Association Press, 2015.
5. **Public Health Agency of Canada .** Guidelines for the Prevention and Control of Invasive Group A Streptococcal Disease. [Online] 2006. [Cited: March 06, 2017.] <http://www.phac-aspc.gc.ca/publicat/ccdr-rmtc/06vol32/32s2/index-eng.php>.
6. **Sanyahumbi, Amy, et al., et al.** Global Disease Burden of Group A Streptococcus. [book auth.] Joseph Ferretti, Dennis Stevens and Vincent Fischetti. *Streptococcus Pyogenes: Basic Biology to Clinical Manifestations*. Oklahoma City : University of Oklahoma Health Sciences Center, 2016.
7. **Public Health Agency of Canada.** National Laboratory Surveillance of Invasive Streptococcal Disease in Canada. [Online] December 2014. [Cited: March 6, 2017.] <http://www.healthycanadians.gc.ca/publications/drugs-products-medicaments-produits/2013-streptococcus/alt/surveillance-streptococca-eng.pdf>.
8. **PEI's Chief Public Health Office.** Promote, Prevent, Protect - PEI CPHO Report: Health for all Islanders. [Online] 2016. http://www.gov.pe.ca/photos/original/cpho_report2016.pdf.
9. **Wolters Kluwer.** Evidence-Based Clinical Decision Support at the Point of Care. *UpToDate*. [Online] <http://www.uptodate.com/home>.

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Annex A: Chemoprophylaxis Dosing Chart for iGAS Contacts

Drug	Dosage	Comments
First Generation Cephalosporin: Cephalexin	Children and adults: 25 – 50 mg/kg/day, to a maximum of 1g/day, in 2 – 4 divided doses x 10 days.	First Line Recommended for pregnant and lactating women. Should be used with caution in patients with allergies to penicillin. Use of cephalosporins with nephrotoxic drugs (e.g., aminoglycosides, vancomycin) may increase the risk of cephalosporin-induced nephrotoxicity.
Erythromycin	Children: 5 – 7.5 mg/kg every 6 hours or 10 – 15 mg/kg every 12 hours (base) x 10 days. (Not to exceed maximum of adult dose). 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.
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.
Clindamycin	Children: 8 – 16 mg/kg/day divided into 3 or 4 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 pregnant and lactating women. Alternative for persons who are unable to tolerate beta-lactam antibiotics.

Source: Canadian Pediatric Society. (2016). *Invasive Group A Streptococcal Disease: Management and Chemoprophylaxis*. Retrieved on March 10, 2017 from <http://www.cps.ca/documents/position/Invasive-group-A-streptococcal-disease>.

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Annex B: Management of Childcare Centre Attendees and Staff

Chemoprophylaxis is generally not recommended when one case of invasive GAS (iGAS) is identified in a child care centre.

- When one case of iGAS is identified in a child care centre:
 - Alert parents/guardians to the signs and symptoms of iGAS and advise them to seek medical attention should the child develop a febrile illness or any other clinical manifestation of iGAS.
 - Screening of attendees and staff is not required.
 - Staff should notify public health if further cases of iGAS infection occur within 1 – 2 months.
 - Appropriate specimens can be taken for culture to rule out GAS when suspected infections are detected during this period; however routine screening of the attendees is not recommended.
 - Chemoprophylaxis may be recommended in situations where one case of iGAS with **severe invasive disease**⁴ occurs **AND**
 - A subsequent confirmed case of iGAS occurs in children or staff of the child care centre within 1 month
- OR**
 - There is a concurrent varicella outbreak in the child care centre.
- Isolates from cases occurring more than 1 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 2 weeks before onset of iGAS symptoms in an iGAS 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 [PEI Childhood Immunization Schedule](#).
- A test for cure is not required for persons (children or staff) receiving chemoprophylaxis.

⁴ **Severe invasive disease** includes; case of STSS, soft tissue necrosis (including NF, myositis or gangrene), meningitis, GAS pneumonia, other life-threatening conditions, or a confirmed case resulting in death.

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Annex C: Management of Long-Term Care Facility Residents and Staff⁽⁵⁾

Residents of long-term care facilities (LTCFs) are at increased risk of morbidity and mortality due to invasive GAS (iGAS) disease because of their older age and/or higher prevalence of underlying conditions. When a confirmed case of iGAS 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 6 weeks.

Management of Contacts

- Chemoprophylaxis is recommended for close contacts when there is iGAS and the case has **severe invasive disease**⁵.
- Persons who share a room with a case are not considered contacts unless they meet the criteria of close contacts (e.g., 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.
- Health care workers (HCWs) are not considered contacts unless they meet the criteria of close contact (e.g., infection control practices are breached, or there has been direct contact of mucous membranes or non-intact skin with fluid from the nose, mouth or wound of a case as described above, such as direct mouth-to-mouth resuscitation).
- Referral of the exposed staff to their Occupational Health Department would be appropriate.

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

- An incidence rate of confirmed iGAS infection of >1 per 100 residents per month,
- At least two cases of confirmed iGAS infection in one month in a LTCF with fewer than 200 residents, OR
- An incidence rate of suspected invasive or non-invasive GAS infections of >4 per 100 residents per month.

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 LTCFs with fewer than 100 beds, all residents should be screened for GAS.
 - In LTCFs with 100 beds or more, 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 be conducted more broadly.
- Anyone colonized with GAS should receive chemoprophylaxis.

⁵ **Severe invasive disease** includes; case of STSS, soft tissue necrosis (including NF, myositis or gangrene), meningitis, GAS pneumonia, other life-threatening conditions, or a confirmed case resulting in death.

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- 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 testing/typing.
 - Culture for a test of cure is recommended for cases found to have the outbreak-related strain, particularly if there is epidemiologic evidence indicating that contact with the case is significantly related to illness.
 - Culture for a test of cure is not necessary for cases 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 2 weeks and at 4 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 1 – 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 a case, then active surveillance alone for 2 – 4 weeks to establish the absence of additional cases is warranted.

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Annex D: Management of Hospital Patients and Staff

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

Management of Cases and Contacts

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

Management of HCW Exposed to GAS

- An occupational exposure of a health care worker (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 a HCW within 7 days before the onset of GAS until up to 24 hours after effective antibiotic therapy has been completed.
- If the appropriate personal protective equipment was worn, then there was no occupational exposure of the HCW.
- The risk between an exposed HCW developing GAS infection and the efficacy of prophylaxis is unknown at this time.
- HCWs who have an occupational exposure to a case with severe invasive disease⁶ may be offered chemoprophylaxis.
- HCWs who have an occupational exposure to any case of GAS should be counselled about symptoms associated with GAS and be advised to seek care immediately if symptoms develop within 21 days of exposure.
- No screening, treatment, modifications of work practices, or work restrictions for a HCW in contact with a case with a GAS infection are required when there has not been an occupational exposure.

Management of a HCW Colonized or Infected with GAS

- HCWs with a symptomatic GAS infection and colonized HCWs 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 <https://www.canada.ca/en/public-health/services/reports-publications/canada-communicable-disease-report-ccdr/monthly-issue/2006-32/canada-communicable-disease-report.html>

⁶ **Severe invasive disease** includes; case of STSS, soft tissue necrosis (including NF, myositis or gangrene), meningitis, GAS pneumonia, other life-threatening conditions, or a confirmed case resulting in death.