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Communicable Disease Control Invasive Group A Streptococcal Disease September 2017

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1.0 CLINICAL INFORMATION

Invasive Group A streptococcal (invasive GAS) disease is caused by *S. pyogenes*, a Gram-positive coccus. Certain strains of *S. pyogenes* are associated with severe invasive disease. This increases the likelihood that a secondary case from a severe invasive index case will also be more severe. Clinical evidence of severe invasive disease may be manifested as: streptococcal toxic shock syndrome (STSS); soft-tissue necrosis, including necrotizing fasciitis (NF), myositis or gangrene; meningitis; or death directly attributable to GAS in a confirmed case. Invasive GAS disease is confirmed through laboratory testing of specimens taken from normally sterile sites. In the post-partum scenario iGAS occurring within 7 days of hospital discharge or giving birth is considered puerperal fever.

Clinical presentation:

48 per cent soft tissue infection

14 per cent bacteremia without focus

11 per cent pneumonia

6 per cent for NF

13 per cent for STSS

Case fatality rate (CFR): Overall is 15-20 per cent; the CFR for STSS may be 30-70 per cent. Mortality is reduced by early diagnosis with surgical intervention for NF, antibiotic treatment, supportive management, intravenous immune globulin (IVIG) for STSS.

Mode of transmission: Primarily by large droplet contact of the oral or nasal mucous membranes with infectious respiratory secretions or with exudates from wounds or skin lesions, or by direct or indirect contact of non-intact skin with exudates from skin or wound or infectious respiratory secretions. Transmission by contaminated equipment or patient care products has rarely been reported.

Incubation period: The incubation period for invasive GAS infection has not been determined. The incubation period for non-invasive GAS infection varies according to the clinical syndrome, but is usually one to three days.

Period of communicability: In untreated cases 10-21 days. Transmissibility generally ends within 24 hours of appropriate antibiotic therapy. There are few data on subsequent (i.e. secondary) cases of severe invasive GAS disease. Evidence indicates an increased risk of invasive GAS disease in household contacts of a case. The risk of subsequent infection in household contacts is estimated to range between 0.66 and 2.94 per 1,000. However, this estimate is based on extremely small numbers of subsequent cases. The risk of subsequent infection for non-household close contacts has not been quantified, but there is a reasonable theoretical risk that invasive GAS disease can be transmitted to these persons.

Evidence to-date suggests that the use of prophylaxis in close contacts may prevent severe illness. These guidelines have been prepared to assist in the public health management of close contacts of cases of **severe** invasive GAS disease.

2.0 EPIDEMIOLOGY

The majority of cases occur sporadically, but nosocomial, long-term care facility (LTCF), daycare/preschool, community, educational facility and household outbreaks have been documented. Invasive GAS is most common during winter months.

Age specific rates are highest in adults ≥ 60 years of age and in children less than four years of age. Other risk factors for invasive disease include: HIV/AIDS, cancer, heart and lung disease, diabetes, IDU and alcohol abuse, and varicella infection.

Invasive GAS disease became nationally notifiable in January 2000. Overall incidence of invasive GAS cases in Canada have increased significantly from 2009 to 2014. The most recent year for which complete national data has been published is 2014. The overall incidence of disease in 2014 was 5.14 per 100,000 population. The average annual incidence rate between 2009 and 2014 was highest in infants < 1 year of age, followed by those aged 60 and greater (Public Health Agency of Canada, 2014).

The International Circumpolar Surveillance (ICS) system has identified increased rates of invasive GAS disease among Indigenous persons living in the Canadian Arctic (Public Health Agency of Canada, 2006). Between 2006 and 2013, the annual incidence rate among Indigenous people ranged between 2.25 and 20.44 per 100,000. In contrast, the incidence rate among non-Indigenous people in Northern Canada was between 0 and 6.80 per 100,000. The overall case fatality ratio (CFR) during this time period was 7.8% where all but one of the fatal cases was identified as Indigenous (Public Health Agency of Canada, 2016).

Historically, Yukon has seen low numbers of iGAS cases. From 2006 to 2012 (a seven-year period), a total of five cases, or an incidence rate of 2.12 per 100,000, were reported. However, from 2013 to 2016 (a four-year period), a total of 10 cases, or an incidence rate of 6.40 per 100,000, were reported. 2015 saw the highest number of iGAS cases in Yukon with 4 confirmed cases including 1 infant death (10.71 per 100,000). Whether this recent trend reflects random variation or a true increase, remains to be seen, but the recent increase does correspond to higher incidence rates of iGAS identified in Northern populations (Public Health Agency of Canada, 2016).

During 2015 a small cluster of severe postpartum GAS infections triggered further investigation into pregnancy associated GAS cases. Further investigation supported by the Canadian Field Epidemiology Program revealed elevated community GAS activity in the period before and following the cluster as evidenced by emergency room discharge diagnosis (including streptococcal pharyngitis and scarlet fever) and laboratory testing (Internal document, 2016). Although increased community prevalence of GAS has been associated with increased iGAS cases, our analysis did not show an overlap of emm types between the community outbreak strains and the cluster strains. Community GAS activity has returned to average levels since 2016.

3.0 CASE DEFINITIONS

3.1 Case definitions for surveillance of invasive GAS disease

INVASIVE GAS SURVIELLANCE	DEFINITION	REPORTABLE
Confirmed case	Laboratory confirmation of infection with or without clinical evidence (see Subsection 3.2) of invasive disease: <ul style="list-style-type: none"> • isolation of Group A streptococcus (<i>Streptococcus pyogenes</i>) from a normally sterile site¹ (blood, CSF, 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]) OR • demonstration of <i>S. pyogenes</i> DNA by an appropriately validated nucleic acid test (NAT) from a normally sterile site. 	Yes
Probable Case	Clinical evidence of severe invasive disease (see Subsection 3.2) in the absence of another identified aetiology and with non-confirmatory laboratory evidence of infection: <ul style="list-style-type: none"> • isolation of Group A streptococcus from a non-sterile site², OR • positive group A streptococcus antigen detection 	Yes

Notes regarding GAS pneumonia:

- GAS pneumonia is a confirmed case only when the isolate is from a sterile site (e.g., aspiration from an empyema, blood culture).
- Providing no other cause has been identified, GAS pneumonia is a probable/clinical case when the isolate is from sputum or a bronchoalveolar lavage (BAL), as sputum and BAL are not considered sterile site specimens.
- When the GAS isolate is from sputum or a BAL, regard GAS pneumonia as a form of severe invasive disease for the purposes of public health management.

¹ When fetal demise or infant death occurs in association with a puerperal infection, isolation of group A streptococcus from the placenta, amniotic fluid and/or endometrium is also considered confirmatory for both the mother and the fetus/infant. **Puerperal infection is defined as: postpartum iGAS occurring while the mother is still in hospital or within 7 days of hospital discharge or giving birth.**

² Non-sterile sites include: throat, sputum, bronchoalveolar lavage (BAL), vagina, superficial skin lesion, middle ear, or superficial abscess or wound specimens (e.g., aspirate or from incision and drainage). Incision and drainage of superficial soft tissue abscesses from which specimens identify GAS is not considered an episode of invasive disease, unless associated with other signs/symptoms of iGAS.

3.2 Types of cases

Severe case ¹	Case of STSS ² , soft-tissue necrosis (including NF ³ , myositis or gangrene), meningitis, GAS pneumonia, or death directly attributable to GAS infection including fetal/infant death and clinical evidence of maternal illness compatible with iGAS.
Sporadic case	A single case 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 case identified in an organization- or community-based outbreak.
Subsequent case	A case with onset of illness occurring within 21 days and caused by the same strain as a previous case and with whom an epidemiologic link can be established. Most subsequent cases in the community will occur within seven days of a previous case.

- 1 Only severe cases warrant chemoprophylaxis of close contacts.
- 2 Streptococcal toxic shock syndrome (STSS) is characterized by hypotension (systolic blood pressure \leq 90 mmHg in adults or $<$ 5th percentile for age in children) **and at least two** of the following signs:
 - (i) **renal impairment:** creatinine level \geq 177 μ mol/L for adults
 - (ii) **coagulopathy:** (platelet count \leq 100,000/mm³ or disseminated intravascular coagulation
 - (iii) **liver function abnormality:** serum glutamic oxaloacetic transaminase (SGOT), aspartate aminotransferase (AST), serum glutamate pyruvate transaminase (SGPT), alanine aminotransferase (ALT) or total bilirubin \geq 2x upper limit of normal
 - (iv) **adult respiratory distress syndrome (ARDS)**
 - (v) **generalized erythematous macular rash** that may desquamate
- 3 NF (necrotizing fasciitis) may or may not be associated with STSS. NF is characterized by isolation of Group A streptococci (*Streptococcus pyogenes*) from a normally sterile body site or taken under sterile conditions from deep tissue (aspirate or deep tissue exploratory) **AND** at least one of the following:
 - (i) histopathologic diagnosis: necrosis of superficial fascia and polymorphonuclear infiltrate and edema of reticular dermis, subcutaneous fat and/or superficial fascia (this should be distinguished from necrosis that occurs within an abscess);
OR
 - (ii) clinical diagnosis: gross fascial edema and necrosis found at surgery or frank necrosis on physical examination.

4.0 MANAGEMENT OF INVASIVE GAS DISEASE

The public health response to a sporadic case of invasive GAS disease includes management of the case, contact identification and tracing, and maintenance of surveillance for further cases.

4.1 Case management

Where there is a strong clinical suspicion of invasive GAS disease, a specimen from a normally sterile site should be obtained for culture and empiric therapy started immediately.

Laboratory testing of antimicrobial sensitivity of the GAS strain may be useful for determining appropriate antibiotic therapy.

4.2 Contact management

4.2.1 Close contacts

- In order to be considered a close contact, there must have been exposure 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.
- Children and staff of group day care centres, school classmates (kindergarten and older), work colleagues, and social or sports contacts of a case are **not** usually considered close contacts, unless they fit into one of the categories in Table 1.

Table 1: Definition of close contacts

• Household contacts of a case who have spent at least four hours/day on average in the previous 7 days or 20 hours/week with the case
• Non-household persons who share the same bed with the case or had sexual relations with the case
• Persons (including HCW) 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
• Children and staff of family or home day care centres

Discuss the management of the contacts of every case of **severe** invasive GAS with the Medical Officer of Health. Chemoprophylaxis is indicated only for close contacts of cases presenting with clinical evidence of **severe** invasive GAS disease. [See Subsection 3.2.](#)

Chemoprophylaxis is not routinely recommended for contacts of cases that are not severe (such as bacteremic illness or septic arthritis cases). Such cases have milder disease than others with invasive GAS. Their contacts are also likely to have milder disease as there is consistency in the type and severity of disease caused by a particular GAS strain.

The purpose of chemoprophylaxis is to reduce the risk of subsequent episodes of severe disease in close contacts. This may also contribute to reducing transmission of GAS to others.

Administer chemoprophylaxis as soon as possible and preferably within 24 hours of case identification. However, it is still recommended for up to seven days after the last contact with a severe invasive case. This recommendation is based on the finding that most subsequent cases occur within seven days after the last contact with a case.

4.3 Special settings

Table 2 outlines the criteria for special settings that warrant further investigation and consideration of chemoprophylaxis.

Table 2: Special settings

Group Child Care Centres	Children and staff of group child care centres and pre-schools when there is: <ul style="list-style-type: none"> • Occurrence of a confirmed or probable iGAS case, followed by a 2nd confirmed or probable iGAS case or a non-invasive case (e.g., pharyngitis, impetigo, wound or skin infections, cellulitis) within one month or <ul style="list-style-type: none"> • A case of varicella two weeks prior to a case of GAS or within one month of a case of GAS ^{1,2}
Long-term care facility	<ul style="list-style-type: none"> • An incidence rate of culture-confirmed invasive GAS infections of > one per 100 residents per month or • At least two cases of culture-confirmed invasive GAS infection in one month in facilities with fewer than 200 residents or • An incidence rate of suspected invasive or non-invasive GAS infections of > four per 100 residents per month
Hospital	Patients and staff of hospitals when there is: <ul style="list-style-type: none"> • Occurrence of a confirmed or probable iGAS case, followed by a 2nd confirmed or probable iGAS case or a non-invasive case (e.g., pharyngitis, impetigo, wound or skin infections, cellulitis) within one month

¹ Assess children and staff for varicella susceptibility and offer varicella vaccine as needed.

² Recommend chemoprophylaxis for individuals with acute varicella.

For recommended actions in the above situations, refer to Subsections 6.3, 6.4 and Annex 3 of the Public Health Agency of Canada Guidelines for the Prevention and Control of Invasive Group A Streptococcal Disease available 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>

4.4 Recommendations for chemoprophylaxis

Chemoprophylaxis is only recommended for close contacts of **severe** invasive disease. The objective of chemoprophylaxis is to prevent infection in colonized individuals and disease in those who have recently been infected, thereby decreasing transmission of a strain known to cause severe infection.

The recommendations for chemoprophylaxis regimens have been extrapolated from treatment guidelines for acute GAS pharyngitis and evidence from clinical trials for the eradication of pharyngeal GAS colonization. Currently, there are no studies that have specifically assessed the effectiveness of chemoprophylaxis for the prevention of subsequent cases of invasive GAS disease, although antibiotic prophylaxis has been successfully used for outbreak control in LTCFs in Canada the United States. See Table 3.

A test of cure is not warranted for persons receiving chemoprophylaxis.

The cost of chemoprophylaxis is not covered by Yukon Communicable Disease Control.

Table 3: Recommended chemoprophylaxis regimens for close contacts

Drug	Dosage	Comments
FIRST LINE REGIMEN		
First-generation cephalosporins: cephalexin, cephadroxil, cephhradine	Children and adults: 25 to 50 mg/kg daily, to a maximum of 1 g/day in 2 to 4 divided doses x 10 days	Recommended drug 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.
SECOND LINE REGIMENS		
Erythromycin	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 of adult dose). Adults: 500 mg every 12 hours (base) x 10 days	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 per cent. ¹
Clarithromycin	Children: 15 mg/kg daily in divided doses every 12 hours, to a maximum of 250 mg po bid x 10 days Adults: 250 mg po bid x 10 days	Contraindicated in pregnancy. Sensitivity testing is recommended in areas where macrolide resistance is unknown or known to be ≥ 10 per cent. ¹
Clindamycin	Children: 8 to 16 mg/kg daily 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	Alternative for persons who are unable to tolerate beta-lactam antibiotics.

¹ Since 2002, erythromycin and clarithromycin resistance for iGAS isolates has exceeded 10% in BC (data from the National Streptococcal Laboratory)

5.0 LABORATORY INVESTIGATION PROCEDURES

Identification of virulence factors and strain type in cases of invasive GAS is important for determining trends, tracking virulence changes, and further characterizing time or place of clustered cases.

Upon identification of a case of invasive GAS, Whitehorse General Hospital Laboratory will forward the isolate to the National Microbiology Lab (NML) for emm (gene that codes for M type surface protein) typing, T-agglutination typing and detection of GAS exotoxins.

Note: Include clinical information (e.g. signs of severity) if isolated from non-sterile source as non-invasive isolates will not be typed by the reference laboratory unless part of an investigation or if the clinical information is included.

6.0 REPORTING

Use the "Invasive Group A Streptococcal Disease: Case Report Form" to record details of the clinical features of the case. YCDC will fax the most current version of this form to the reporting health facility for completion after notification of the case. Fax a copy of the form back to YCDC at (867) 667-8349.

7.0 AUTHORITY

Yukon Public Health and Safety Act (2002). Available at: www.gov.yk.ca/legislation/acts/puhesa.pdf

8.0 REFERENCES

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9.0 CONTACT INFORMATION

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