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Guidelines for the Prevention and Control of Invasive Group A Streptococcal Disease

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Guidelines for the Prevention and Control of Invasive Group A Streptococcal Disease

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1.0 Introduction

Before the introduction of antimicrobials, morbidity from *Streptococcus pyogenes* or group A streptococcal (GAS) infection was common. The introduction of penicillin and other antibiotics resulted in a steady decline in the incidence of GAS disease through the 1970s. However, in the 1980s, there was a worldwide resurgence of GAS infection, as well as an apparent increase in virulence⁽¹⁻⁶⁾.

Because of the severity of invasive GAS disease and the increased risk of infection among close contacts of sporadic cases, these guidelines have been formulated through a consensus process to advise public health officials and clinicians about the public health management of invasive GAS cases and their close contacts. Participants involved in the consensus process are listed in Annex 1.

2.0 Objectives

These guidelines have been prepared to assist in the public health investigation and management of invasive GAS disease in Canada. They address the following:

- surveillance and reporting
- public health response to cases
- chemoprophylaxis of close contacts
- investigation and control of invasive GAS disease in long-term care facilities (LTCF) and child care centres
- laboratory issues for *S. pyogenes* (Annex 2)
- infection control issues for invasive GAS infection (Annex 3).

3.0 Surveillance of Invasive GAS Disease in Canada

Invasive GAS infection is reportable in every province and territory (P/T) in Canada. Most jurisdictions rely on passive surveillance for identification of cases. Each P/T has procedures in place for the rapid notification of cases to medical officers of health and timely reporting to the appropriate P/T public health official. Readers should refer to the case definitions specified by their respective P/T jurisdictions for the purposes of local reporting.

S. pyogenes is a Gram-positive coccus, which occurs as pairs or as chains of short to moderate size⁽⁷⁾. Invasive GAS disease is confirmed through laboratory testing of specimens taken from normally sterile sites. Local microbiology laboratories perform antibiotic susceptibility testing for clinical purposes, whereas the National Centre for Streptococcus (NCS) conducts susceptibility testing for surveillance purposes only. Some provincial public health laboratories and academic reference laboratories may perform specific molecular analyses in support of outbreak investigations; however, the NCS is the only laboratory in Canada that performs M protein typing and emm gene sequencing of S. pyogenes isolates for routine surveillance. Serotyping, molecular sequencing and antimicrobial susceptibility testing are helpful in characterizing outbreaks, determining disease trends and guiding appropriate clinical management of cases and contacts. Annex 2 provides further details on laboratory support for outbreak investigation of invasive GAS disease.

Only confirmed cases of invasive GAS disease are notifiable at the national level. Currently, some P/Ts report case-by-case data with basic core variables on a monthly basis to the Notifiable Diseases Reporting System, and others report aggregate data by age, sex and month of episode.

4.0 Epidemiology of Invasive GAS Disease in Canada

Invasive GAS disease became nationally notifiable in January 2000. The most recent year for which complete national data have been published is 2001. The overall incidence of disease in 2001 was 2.7 per 100,000 population. The highest reported incidence rates occurred among adults \geq 60 years of age (5.3 per 100,000), followed by children < 1 year of age (4.8 per 100,000) and children 1 to 4 years of age (3.6 per 100,000). Preliminary data for subsequent years show slight variation in overall incidence: 2.8 per 100,000 in 2002, 3.2 per 100,000 in 2003 and 2.6 per 100,000 in 2004 (unpublished data, Public Health Agency of Canada).

Elevated rates of invasive GAS disease have been detected among Aboriginals living in the Canadian Arctic through the population-based International Circumpolar Surveillance system. Between 2000 and 2002, no cases of invasive GAS disease were reported among non-Aboriginals in the territories, northern Quebec or northern Labrador. In contrast, among Aboriginals in northern Canada, the incidence rate of disease was 9.0 per 100,000 in 2000 (7 cases), 3.0 per 100,000 in 2001 (2 cases) and 5.0 per 100,000 in 2002 (4 cases) (9-11). Preliminary data from 2003 also indicate a higher rate of invasive GAS disease in Aboriginal (2.6 per 100,000) compared with non-Aboriginal (1.9 per 100,000) populations (seven cases overall) (12).

The NCS provides laboratory reference services for GAS associated with invasive disease. Among 2,195 isolates from blood, brain or cerebrospinal fluid (CSF) between 1993 and 1999, the most frequent M protein type identified was M1 (28%), followed by serotypes M28 (9%), M12 (8%), M3 (8%) and M4 (6%)⁽¹³⁾. With the exception of 2000-2001, M1 was consistently the most frequently encountered serotype between 1992 and 2004-2005⁽¹³⁻¹⁶⁾. The NCS also tests *S. pyogenes* isolates for antibiotic sensitivity. Of 817 isolates from all sites tested in 2004-2005, 11.1% demonstrated resistance to erythromycin, and 2.0% were resistant to clindamycin. No isolates

demonstrated resistance to penicillin, chloramphenicol or vancomycin⁽¹⁶⁾.

Clinical data for cases of invasive GAS infection are not collected nationally. Data from the Ontario GAS Study provide further information on the epidemiology of invasive disease. In cases detected by this enhanced population-based surveillance system during 1992 and 1993, the most common clinical presentations were skin or soft-tissue infections (48%), bacteremia with no septic focus (14%) and pneumonia (11%)⁽¹⁷⁾. Thirteen percent of cases were classified as streptococcal toxic shock syndrome (STSS), and 6% had necrotizing fasciitis (NF). The overall case fatality rate (CFR) was 13%, although syndrome-specific CFRs were highest among patients with STSS (81%), NF (45%) and pneumonia (33%). Overall, 44 (14%) of infections were classified as nosocomial, including 14 cases acquired in LTCF for the elderly. The risk of invasive GAS disease was significantly associated with several underlying conditions, including HIV infection, cancer, heart disease, diabetes, lung disease and alcohol abuse. Among the isolates for which serotyping was available, the most common serotypes were M1 (24%), M12 (7.4%), M4 (6.5%), M28 (6.2%) and M3 (5.8%)⁽¹⁷⁾. More recent findings from Ontario enhanced surveillance system from 1992 through 1999 demonstrate the increasing incidence of specific clinical manifestations of invasive GAS infections. The annual incidence rate of NF increased from 0.08 per 100,000 population in 1992 to 0.49 per 100,000 in 1995 $(p < 0.001)^{(18)}$. The annual incidence of GAS pneumonia increased from 0.16 per 100,000 in 1992 to 0.35 per 100,000 in 1999⁽¹⁹⁾.

Enhanced GAS surveillance in Alberta between 2000 and 2002 showed higher provincial incidence rates of disease than observed through national passive surveillance, at 5.0 (in the year 2000), 5.7 (2001) and 3.8 (2002) per 100,000, with corresponding CFRs of 10.7%, 13.2% and 6.8%, respectively. Incidence rates were highest in the metropolitan regions of Calgary (6.9 per 100,000) and Edmonton (4.8 per 100,000). Acquisition in a hospital, nursing home or LTCF was the most frequently reported risk factor (17%), followed by injection drug use (13%), pregnancy-

related risk factors (13%), varicella (12%) and cancer (11%). The most common serotypes were M1 (16%), M3 (12%) and PT2967 (10%). There was seasonal variation, the greatest number of cases occurring in the winter and early spring months⁽²⁰⁾.

5.0 Definitions

5.1 National case definition

In Canada, confirmed cases of invasive GAS disease are notifiable at the national level. Probable cases of invasive GAS disease are not nationally notifiable (Table 1).

Table 1: National Case Definition for Invasive GAS Disease (21)

	Laboratory confirmation of infection with or without clinical evidence of invasive disease.* Laboratory confirmation requires the isolation of group A streptococcus (<i>Streptococcus pyogenes</i>) from a normally sterile site.
Probable case	Invasive disease* in the absence of another identified etiology and with isolation of GAS from a non-sterile site.

*Clinical evidence of invasive disease may be manifested as several conditions. These include:

- a) STSS, which is characterized by hypotension (systolic blood pressure ≤ 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 ≤ 100,000/mm³ or disseminated intravascular coagulation)
 - iii. liver function abnormality (SGOT [AST], SGPT [ALT] or total bilirubin ≥ 2 x upper limit of normal)
 - iv. adult respiratory distress syndrome (ARDS)
 - v. generalized erythematous macular rash that may desquamate;
- b) soft-tissue necrosis, including necrotizing fasciitis, myositis or gangrene;
- c) meningitis; or
- d) a combination of the above.

SGOT = serum glutamic oxaloacetic transaminase; AST = aspartate aminotransferase; SGPT = serum glutamate pyruvate transaminase; ALT = alanine aminotransferase

A normally sterile site is defined as blood, CSF, pleural fluid, peritoneal fluid, pericardial fluid, deep tissue specimen taken during surgery (e.g. muscle collected during debridement for necrotizing fasciitis), bone or joint fluid. This does not include middle ear or superficial wound aspirates.

Pneumonia with isolation of GAS from a sterile site, or from a bronchoalveolar lavage (BAL) when no other cause has been identified, should be regarded as a form of invasive disease for the purposes of public health management; however, as BAL does not provide a sterile site specimen, the latter would not meet the national case definition and would not be nationally notifiable.

5.2 Definitions for public health management

Tables 2 and 3 provide definitions of cases and close contacts.

Table 2. Definition of Cases

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 case identified in an organiz community-based outbreak. Identify index case in an outbreak is important the characterization and matching of 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 STSS, soft-tissue necrosis (including NF, myositis or gangrene), meningitis, GAS pneumonia, other life-threatening conditions or a confirmed case resulting in death.

An epidemiologic link can be established when a person has 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, LTCF, child care centre) at or around the same time.

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

Table 3. 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 the same bed with the case or had sexual relations with the case
- Persons who have had direct mucous membrane contact with the oral or nasal secretions of a case (e.g. mouth-tomouth 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
- Selected LTCF contacts (see Section 6.3)
- Selected child care contacts (see Section 6.4)
- Selected hospital contacts (see Annex 3)

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. School classmates (kindergarten and older), work colleagues, as well as social or sports contacts of a case are not usually considered close contacts, unless they fit into one of the categories in Table 3.

An outbreak is defined as increased transmission of GAS causing invasive disease in a population. Outbreaks of invasive GAS disease do not occur in the community frequently and typically involve two cases (i.e. case-pairs) who have had close contact (17,22,23). Criteria defining the impetus for action for organization-based outbreaks or clusters are found in Table 4.

Table 4. Impetus for Action for Organization-based Outbreaks or Clusters

Long-term care facility	An incidence rate of culture-confirmed invasive GAS infections of > 1 per 100 residents per month or at least two cases of culture-confirmed invasive GAS infection in 1 month in facilities with fewer than 200 residents or an incidence rate of suggested invasive or non-invasive GAS infections of > 4 per 100 residents per month.	
Child care centre	One severe case of invasive GAS disease in a child attending a child care centre.	
Hospital	One or more linked invasive or non-invasive GAS cases in either patients or staff occurring within 1 month of an invasive GAS case (see Annex 3).	

6.0 Management of Invasive GAS Disease

The public health response to a sporadic case of invasive GAS disease, as described in Section 5.1, includes management of the case, contact identification and tracing, and maintenance of surveillance for further cases. The management of invasive GAS disease is divided into four subsections: the management of cases, contact management, management of cases occurring at LTCFs and management of cases occurring among children attending child care centres. Information about management in the hospital setting can be found in Annex 3.

6.1 Case management

Although this document is not focused on the treatment of GAS disease, where there is a strong clinical suspicion of invasive GAS disease a specimen from a normally sterile site should be obtained for culture, if possible, and empiric therapy started quickly. Confirmatory culture is important to ensure that GAS infection is diagnosed.

Laboratory testing of antimicrobial sensitivity of the GAS strain may be useful for determining appropriate antibiotic therapy. Readers should refer to treatment guidelines that address the clinical management of invasive GAS disease, which is beyond the scope of this document (24-26).

The case or a proxy for the case should be interviewed to determine close contacts.

6.2 Contact management

The cornerstone of prevention of secondary cases of invasive GAS is aggressive contact tracing to identify people at increased risk of disease (i.e. close contacts). Close contacts of an invasive GAS case may be at increased risk of secondary disease (17.22,27). It is important that they should be alerted to signs and symptoms of invasive GAS disease and be advised to seek medical attention immediately should they

develop febrile illness or any other clinical manifestations of GAS. Persons who are close contacts of cases are defined in Table 3. The recommendations for contact management in Canada are shown in Table 5. Recommended chemoprophylaxis regimens are discussed in Section 7.0.

The following were considered in determining further management of close contacts: evidence of GAS transmission, reasonable theoretical risk, limited evidence of effectiveness of chemoprophylaxis, risks and benefits of chemoprophylaxis and the number of close contacts who would need to receive chemoprophylaxis to prevent a case. The recommendations for contact management are based on expert opinion and very limited evidence.

The risk of subsequent infection in household contacts is estimated to range between 0.66 and 2.94 per 1,000, and this estimate is based on extremely small numbers of subsequent cases. Most subsequent cases in the Ontario GAS study occurred within 7 days after last contact with an infectious case.

Two population-based studies have estimated that the rate of invasive GAS infection among people living in the same household as a case is much higher than the rate of sporadic disease in the general population. The Ontario Group A Streptococcal Study estimated that the attack rate among household contacts was 2.94 per 1,000 (95% confidence interval [CI]: 0.80-7.50) (17,27). In comparison, the attack rate among household contacts estimated using data from the US Active Bacterial Core Surveillance (ABCs)/Emerging Infections Program network was 0.66 per 1,000 (95% CI: 0.02-3.67) (22). There are two major limitations of these estimates: first, household contacts and attending physicians were not asked about the use of chemoprophylaxis; and second, these attack rates are based on extremely small numbers of subsequent cases and therefore may be unstable, as exemplified by the large confidence intervals (22).

In a follow-up study of clusters identified through enhanced surveillance in England, Wales and Northern Ireland during 2003, five household clusters were identified. The clusters included two spouse pairs and three mother-neonate pairs, which is in contrast to the clusters identified in the Ontario study (three spouse pairs, one adult sibling pair) and in US ABC surveillance (one father-infant daughter pair). According to the UK data, infections in either the mother or child in the neonatal period (first 28 days of life) were considered as carrying a high risk of further cases in the mother or baby. The risk estimates for other household contacts suggested that over 2,000 close contacts would need chemoprophylaxis to prevent a subsequent case, assuming 100% effectiveness of chemoprophylaxis.

The risk of subsequent infection for nonhousehold close contacts has not been quantified, but there is a reasonable theoretical risk that invasive GAS disease can be transmitted to these persons.

There is little evidence that GAS has been transmitted to non-household close contacts after unprotected direct contact, prolonged mucous membrane contact or contact with oral or nasal secretions of a case; however, this was felt to be biologically plausible and was therefore included. Direct mucous membrane contact should be prolonged for a person to be considered this type of non-household close contact. This would include close contact, such as mouth-tomouth resuscitation or open mouth kissing, but exclude kissing with closed mouths and sharing of utensils, water bottles or cigarettes. A firefighter developed toxic shock syndrome and cellulitis within 24 hours of performing cardiopulmonary resuscitation on a child with STSS using a bag-valve mask apparatus. The close temporal relation and the isolation of the same GAS strain from the child's blood and CSF and from the hand wound of the firefighter suggest the transmission of GAS during resuscitation or while cleaning secretions from the resuscitation equipment (29).

Three Swiss studies have demonstrated the occurrence of clusters of clonal strains causing endemic or epidemic infection among injection drug users living or purchasing drugs in the same region⁽³⁰⁻³²⁾. A case report from Israel reported the occurrence of invasive GAS isolates of the same serotype in a couple who regularly shared needles for injecting drugs⁽³³⁾.

Several studies have shown that, compared with rates in the general population, rates of pharyngeal carriage of the same strain of GAS are higher among close contacts spending at least 24 hours with an index case in the week preceding onset of illness⁽³⁴⁾, among residents and staff at the LTCF of the case^(35,36) and among children sharing the same room as a case in a child care centre⁽³⁷⁻³⁹⁾. Asymptomatic pharyngeal carriage or acute streptococcal pharyngitis among such persons may contribute to the spread of invasive infection.

Decisions about chemoprophylaxis must take into account the individual and population risks and benefits of this intervention.

While prophylaxis of close contacts may be intuitively attractive, there is limited evidence that such prophylaxis is effective, and it is possible that prophylaxis may not be uniformly effective because of widespread transmission of *S. pyogenes* in the community.

The consequences of prophylaxis must also be considered. Serious adverse effects associated with the antibiotics used for prophylaxis are very rare but do occur. In addition, use of antibiotics clearly selects for antibiotic resistance and may have an impact on antibiotic resistance patterns. Finally, contact tracing and follow-up affect public health resources, which are scarce and must be directed to where they have the greatest benefit.

Based on an estimate that approximately 300 close contacts of an invasive GAS case would need to receive chemoprophylaxis to prevent one secondary case, that there would be an average of 10 contacts per case, a retail cost of \$30 per person for antibiotics and approximately 3 hours of public health nurse follow-up time per case, at \$50 per hour, the cost-effectiveness has been estimated to be \$13,500 CAD in direct health care costs per secondary case prevented. This cost-effectiveness is within the range of other recommended public health preventive measures⁽⁴⁰⁾.

On the basis of these considerations, the working group consensus is that chemoprophylaxis is indicated only for contacts at the highest risk of acquisition of the organism and of subsequent severe disease. This explains why prophylaxis is not routinely recommended for contacts of cases that are not severe (see Table 2) (e.g. bacteremia or septic arthritis). Such cases have milder disease than others with invasive GAS, and their contacts are also likely to have milder disease, as there is some degree of consistency in the type and severity of disease caused by a particular GAS strain. The level of risk may vary for different groups, and there may be individual circumstances under which different decisions regarding chemoprophylaxis may be made.

The approach for contact management and recommended chemoprophylaxis varies by country (27,28). The uncertainties in this decision-making process also explain why recommendations from various authorities will continue to differ, and as additional evidence becomes available these guidelines may need to be revisited.

Table 5. Recommendations for Contact Management

- Chemoprophylaxis should only be offered
 - to close contacts (see Table 3) of a confirmed severe case (see Table 2), that is, a 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; AND
 - 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.
- Close contacts of all confirmed cases (i.e. regardless of whether the case is a severe one) should be alerted to signs and symptoms of invasive GAS disease and be advised to seek medical attention immediately should they develop febrile illness or any other clinical manifestations of GAS infection within 30 days of diagnosis in the index case.

Follow-up of contacts

Cultures for GAS have no role in the identification of asymptomatic close contacts of sporadic cases occurring in the community. The only reason for obtaining cultures for GAS is in the diagnosis of suspected infection. There is no role for routine

culture for a test of cure for contacts receiving antibiotic chemoprophylaxis.

6.3 Long-term care facilities

Residents of LTCF are at increased risk of morbidity and mortality due to invasive GAS disease because of their older age and higher prevalence of underlying conditions (36,41-43). When a culture-confirmed case of invasive GAS disease occurs in an LTCF, there is a 38% likelihood that a second, positive blood culture-confirmed case of the same strain will be detected in the facility within 6 weeks (Dr. A. McGeer, Mount Sinai Hospital, Toronto: personal communication, July 2005). A number of outbreaks of invasive GAS infections have been documented in LTCF^(23,36,42-46). Infection is often spread through person-to-person contact, with clustering of cases by room or care unit in some instances (23,36,42,43,46). Staff may be a source of or conduit of infection either through poor infection control practices or asymptomatic carriage (35,42,44,45). However, hospital staff who are carriers are more likely to be the source of infection in outbreaks in acute care facilities, whereas outbreaks in LTCF are more often patientpropagated⁽²³⁾. In LTCF outbreaks, the implicated strain is usually widespread within the facility, and limited provision of chemoprophylaxis to close contacts is not the optimal approach.

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 (as described in Section 5.1) occurs in an LTCF such as a nursing home, the facility should
 - report the case to the local health authorities;
 - conduct a retrospective chart review of the entire facility's residents over the previous 4 to 6 weeks for culture-confirmed cases of GAS disease and any 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. An

- excess of GAS infection, or an LTCF outbreak, is defined in Table 4:
- 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 Section 7.0);
 - 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 (see Annex 2: Laboratory Support for Outbreak Investigation of Invasive GAS, for further details). 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 contact with the individual is significantly related to illness. 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 lesion(s), 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 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 2 to 4 weeks to establish the absence of additional cases is warranted.

Disease control measures for invasive GAS disease occurring in other health care settings are described in Annex 3.

6.4 Child Care Centres

For the purposes of these guidelines, child care centres include group or institutional child care centres (day care), family or home day care and pre-schools. Non-invasive GAS infection can spread easily in child care centres (CCC)⁽³⁸⁾; however, outbreaks of invasive GAS disease occurring among children attending CCC are rare. The recommendations for invasive GAS disease in CCC are therefore based on expert opinion and very limited evidence.

In two CCC outbreaks in the United States, GAS infection or carriage of the same serotype as the index case was detected in 8% to 18% of other attendees. The risk of GAS infection or carriage was associated with sharing a room with the index case and spending a greater number of hours per week at the CCC. GAS prevalence among staff was low in both outbreaks, suggesting that they did not contribute to the spread of infection (37,39).

Invasive GAS disease in children frequently occurs secondary to varicella infection^(20,47-52). Two population-based Canadian studies have shown that 15% to 25% of pediatric cases of invasive GAS disease are associated with antecedent varicella infection^(20,50). The risk is significantly increased during the 2-week period after the onset of varicella infection and may

be due to a breakdown in the skin barrier, infection through another less apparent portal, such as lesions on the oral mucosa or the respiratory tract, or immunosuppression⁽⁵⁰⁾. The National Advisory Committee on Immunization (NACI) recommends varicella vaccination for children between 12 and 18 months of age and for susceptible persons ≥ 12 months of age (53). It has been estimated that the full implementation of universal childhood varicella vaccination could prevent at least 10% of pediatric invasive GAS cases in Canada⁽⁵⁰⁾. Outbreaks of invasive GAS and varicella have been previously reported to occur concurrently among children (37,49,54). According to NACI guidelines, post-exposure use of varicella vaccine should be considered during an outbreak of varicella in a child care facility⁽⁵³⁾. Varicella vaccination of susceptible attendees may help prevent the further spread of a concurrent outbreak of invasive GAS disease (37,49)

In addition to strict enforcement of standard infection control practices⁽⁵⁵⁾, staff from the affected CCC must report to local health authorities when a confirmed case of invasive GAS disease (as described in Section 5.1) occurs in a child attending the CCC. This may be required by legislation in some provinces and territories.

Health authorities should investigate when one severe case of invasive GAS disease (see Table 2) occurs in a child attending a CCC. Investigators should take into consideration the following:

- the nature of the CCC (e.g. type of centre, 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 CCC:
 - a. whether there has been any suggested non-invasive or invasive GAS infections (e.g. other cases of invasive GAS, pharyngitis, impetigo);

- b. 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⁽²⁵⁾);
- 4. the presence of varicella cases within the CCC in the previous 2 weeks;
- the potential for a source of infection from outside the CCC (e.g. exposure to a family member with suggested non-invasive or invasive GAS infection).

The following approach should be considered in the investigation and control of invasive GAS disease when one severe case of invasive GAS disease (see Table 2) occurs in a child attending a CCC:

- 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.
- In family or home day care settings, chemoprophylaxis should be recommended for all children and staff (see Section 7.0).
- In group or institutional CCC and pre-schools, 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 CCC within 1 month or a concurrent varicella outbreak at the CCC. Cases of invasive GAS occurring among children or staff of a CCC within 1 month should be considered as part of the same cluster. Consideration could be given to testing isolates from invasive GAS cases occurring in a CCC more than 1 month apart, to determine strain relatedness. If a case of varicella has occurred in the CCC within the 2 weeks before 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 on the basis of findings that risk of GAS was significantly increased 2 weeks after

- onset of varicella infection⁽⁵⁰⁾. Varicella vaccination should be recommended for those without a history of prior varicella infection or vaccination as per the NACI guidelines⁽⁵³⁾.
- A test of cure is not warranted for persons receiving chemoprophylaxis.
- It should be emphasized that staff of the CCC must notify local public health officials if further cases of invasive GAS infection occur. This may be required by legislation in some provinces and territories.
- 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.

7.0 Recommendations for Chemoprophylaxis

The objective of chemoprophylaxis is to prevent disease in colonized individuals and in those who have recently been exposed, 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 LTCF in Canada and the United States (35,36,43,46). Further studies are needed.

First-generation cephalosporins, such as cephalexin, are the preferred antibiotic for GAS chemoprophylaxis. Second- and third-generation cephalosporins (e.g. cefuroxime axetil, cefixime) may also be considered, but they have a broader spectrum, increased likelihood of resistance and higher cost than first-generation cephalosporins^(56,57). Cephalosporins are more effective than penicillin in eradicating GAS

from pharyngeal carriers (56,58,59). A meta-analysis of 35 trials involving 7,125 pediatric patients with GAS tonsillopharyngitis showed that the bacteriologic cure rate significantly favoured cephalosporins compared with penicillin (odds ratio [OR] = 3.02, 95% CI: 2.49-3.67) after 10 days of treatment. Eight of 11 individual cephalosporins showed superior bacteriological cure rates among children. The summary OR for clinical cure rate was 2.33 (95% CI: 1.84-2.97) (60). A meta-analysis of nine randomized controlled trials with adult patients showed that the bacteriologic eradication rate was nearly two times higher for cephalosporins than penicillin for the treatment of acute GAS tonsillopharyngitis after 10 days of treatment (summary OR = 1.83, 95% CI: 1.37-2.44); the clinical cure rate also favoured cephalosporins (summary OR = 2.29, 95% CI: 1.61-3.28) (57). Cephalosporins are acceptable for penicillin-allergic patients who do not manifest immediate-type hypersensitivity to beta-lactam antibiotics (61).

The macrolides erythromycin and clarithromycin are suitable alternative agents that have been shown to be clinically effective for treatment of GAS pharyngitis (62-67). However, macrolide resistance is a concern in Canada. According to surveillance data for invasive GAS submitted to NCS, erythromycin resistance has been relatively stable over the past 4 years, ranging from 9.8 to 11.1% (14-16). In areas where macrolide resistance is either unknown or known to be $\geq 10\%$, testing of the GAS isolate is recommended to determine appropriate treatment.

Clindamycin is another alternative agent recommended for patients infected with an erythromycin-resistant strain of *S. pyogenes* who are unable to tolerate beta-lactam antibiotics⁽⁶¹⁾. A 10-day regimen of orally administered clindamycin (20 mg/kg per day) was effective in eradicating GAS from the oropharynx of persistently colonized, asymptomatic children (92%, 24/26) in a randomized, unblinded, controlled clinical trial⁽⁶⁸⁾. Gallegos et al. ⁽⁶⁹⁾ found that clindamycin regimens of either 150 mg 4 times per day or 300 mg 2 times per day were equally efficacious, with a clinical cure rate of 93% among adults with acute streptococcal tonsillitis/pharyngitis

in a double-blind, randomized, multicentre study. However, emergence of resistance would need to be monitored closely for this anti-microbial. In 2004-2005, 2.0% of GAS isolates tested for antimicrobial sensitivity at the NCS were resistant to clindamycin $^{(16)}$, as compared with 1.6% of isolates in 2003-2004 $^{(15)}$, 1.9% in 2002-2003 and 0.9% in 2001-2002 $^{(14)}$.

Oral penicillin VK (or amoxicillin in young children) may be considered for GAS chemoprophylaxis because of its proven efficacy, safety, narrow spectrum and low cost⁽⁷⁰⁾. However, penicillin is less effective in eradicating GAS from the upper respiratory tracts of chronic (asymptomatic) carriers. Carriers treated with penicillin are generally characterized by a lack of a serologic response and may account for a significant proportion of penicillin treatment failures (58,71-73). Streptococcal internalization within epithelial cells may contribute to eradication failure and persistent throat carriage (74). Some experts feel that penicillin should be considered an alternative first-line therapy, whereas other experts believe that penicillin monotherapy may be inferior on the basis of data from bacteriologic eradication in the treatment of GAS pharyngitis and in the eradication of carriage; however, the relevance of these data to chemoprophylaxis of contacts is unclear.

Azithromycin may be considered for the eradication of GAS from the pharynx using a shorter 5-day course (70,75), but Canadian evidence has shown that azithromycin may select for macrolide resistance among streptococci more strongly than erythromycin and clarithromycin, and therefore it should not be considered as a first- or second-line therapy (76).

The chemoprophylactic agents and dosages recommended for preventing disease and decreasing transmission of GAS are listed in Table 6. It is important to ensure that contacts requiring chemoprophylaxis complete the recommended course.

Table 6. Recommended Chemoprophylaxis Regimens for Close Contacts

Drug	Dosage	Comments
First-generation cephalosporins: cephalexin, cephadroxil, cephradine	First line. Children and adults: 25 to 50 mg/kg daily, to a maximum of 1 g/day in 2 to 4 divided doses × 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.
Erythromycin	Second line. Children: 5 to 7.5 mg/kg every 6 hours or 10 to 15 mg/kg every 12 hours (base) × 10 days (not to exceed maxi- mum of adult dose) Adults: 500 mg every 12 hours (base) × 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%.
Clarithromycin	Second line. Children: 15 mg/kg daily in divided doses every 12 hours, to a maxi- mum of 250 mg po bid × 10 days Adults: 250 mg po bid × 10 days	Contraindicated in pregnancy. Sensitivity testing is recommended in areas where macrolide resistance is unknown or known to be ≥ 10%.
Clindamycin	Second line. Children: 8 to 16 mg/kg daily divided into 3 or 4 equal doses × 10 days (not to exceed maximum of adult dose) Adults: 150 mg every 6 hours × 10 days	Alternative for persons who are unable to tolerate beta-lactam antibiotics.

8.0 Vaccines

Currently, there are no vaccines approved for use in Canada for the prevention of GAS infections. There are a number of vaccines under development. Recent results of a phase I trial of a multivalent vaccine in the United States have demonstrated significant increases in antibody levels to all six component M antigens used in the vaccine among healthy adult volunteers (77). Results of a phase I trial and preliminary results of a phase II trial for a multivalent vaccine in Canada have also shown high titres of antibodies to 26 targeted serotypes contained in the vaccine among healthy adult volunteers (78,79). There was no evidence of tissue cross-reactive antibodies or vaccine-related serious adverse events among participants for either vaccine.

9.0 Communications

9.1 Communication pertaining to sporadic cases

In general, it is not necessary to inform the general public of a sporadic case, even if it involves a fatality. However, it is important that a communication strategy be prepared in advance in order to address any questions that may arise among those concerned with the control measures or if approached by the media. Details of the communication strategy need to be tailored to the context of the sporadic case (e.g. liaison with school authorities is important when a case is a student). This could include information on the disease and its characteristics, local epidemiology of GAS and recommended treatment and prophylactic measures.

9.2 Communication pertaining to clusters or outbreaks

It is essential that a communication strategy be in place to provide timely information to the public or local community when a cluster or outbreak occurs. A communication strategy aimed at the health care community should also be developed. This should include the criteria and the process for reporting to public health, timely surveillance reports and updates, guidelines on early diagnosis (including signs and symptoms) and recommended treatment and prophylactic measures. It is important to involve the health care community as early as possible after the recognition of an outbreak. The need for an outbreak advisory committee comprising public health representatives, clinicians and medical laboratory personnel should be evaluated.

In addition to the principles previously described, essential elements of a communication strategy include the following:

- Wide consultation, including public health representatives, clinicians and laboratory personnel, before any decision is made;
- 2. Clearly designated responsibilities. A designated lead organization should be identified. Messages should be coordinated and consistent. The lead organization should be responsible for the announcement of the decision and the management of communications with respect to the operation of a control program;
- 3. Within each organization, one spokesperson should be responsible for communicating with the media.

10.0 Areas for Future Research

These public health guidelines for invasive GAS disease have been formulated through a consensus process involving public health officials, as well as experts in adult and pediatric infectious diseases and microbiology, and are based on limited evidence and expert opinion. Risk of subsequent infection among household contacts has been estimated on the basis

of very small numbers of subsequent cases in two studies; further studies are needed to quantify this risk more precisely. Studies should also be performed to assess the risk of subsequent infection among non-household close contacts. Although screening is generally not indicated for investigations of invasive GAS disease in CCC, it may be considered in applied research settings to provide further information on the epidemiology of GAS infections in CCC. There is a need to evaluate the efficacy of chemoprophylaxis of close contacts and the effectiveness of different approaches to prophylaxis. As additional evidence becomes available, these guidelines may need to be revisited.

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ANNEX 1

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Approved by: Public Health Agency of Canada and the Canadian Communicable Disease Control Expert Group

ANNEX 2

Laboratory Support for Outbreak Investigation of Invasive Group A Streptococcal Disease

The National Centre for Streptococcus (NCS) provides laboratory support for the investigation of clusters or outbreaks of invasive group A Streptococcus (GAS) disease. The decision to initiate this type of investigation rests with the local public health agencies. The investigation team should coordinate the shipment of isolates and required information to the NCS through its local provincial laboratory or designate laboratory. The local outbreak investigation team is asked to provide a brief written description of the event, and this should be forwarded, via the appropriate provincial laboratory or designated laboratory, to the NCS in advance of isolate submission. This facilitates a timely laboratory response. Isolates associated with outbreak investigation are given priority testing status, and reports are phoned or faxed to the submitters as soon as testing is complete. Preliminary results for isolates from an outbreak investigation should be available within 1 week.

Contact the NCS at:

Phone: (780) 407-8977; (780) 407-8937

Fax: (780) 407-8984

Email: m.lovgren@provlab.ab.ca; g.tyrrell@provlab.ab.ca

If the investigation is to include testing of contacts (i.e. characterization of non-invasive GAS isolates), arrangements for the primary culture of these specimens should be made through the local microbiology laboratories and/or the provincial laboratories. Isolates may then be forwarded to the NCS for further investigation. Submitters are encouraged to use the NCS submission form for all isolates. This document is available through the NCS Web site at www.provlab.ab.ca (Partners\National Centres\National Centre for Streptococcus\NCS Requisition Forms).

Characterization of *Streptococcus* pyogenes (GAS)

The analysis of GAS includes serologic and molecular techniques. The strain profile includes the identification of the M protein type and T protein, and anti-opacity factor testing for serum opacity factor-positive strains.

M typing

M protein is a significant virulence factor produced by GAS. It is a surface protein antigen that gives the organism the ability to resist phagocytosis as a way of evading the human immune response to infection. Traditional serologic characterization of M protein relies on an antigen-antibody reaction between the organism and M type specific antisera. The M antisera are inherently difficult to prepare (commercial reagents are not available), and consequently this specialized testing is offered in only six reference laboratories worldwide. There are 86 M protein types that have been officially classified by this serologic method. The testing is performed by immunodiffusion and, especially for less common M types, several steps may be required to classify the strain. The production of M protein is coded by the emm gene, and molecular analysis is able to classify a rapidly expanding number of emm types. The emm type corresponds to the M type (e.g. M1 = emm 1) when the strain belongs to one of the internationally recognized M types. However emm typing is able to classify a large number of strains for which traditional M antisera are not available. This makes *emm* typing a more specific tool.

T typing

T protein is not a virulence factor, but it provides an additional serologic "marker" with which to differentiate strains. A GAS strain may carry one or more T antigens, and the same T pattern may be shared by several M or *emm* types. T typing is therefore a less specific typing method than M or *emm* typing; however, there is an association between the T pattern and the specific M or *emm* type. T typing is performed by observing the antigenantibody reaction with specific T typing antisera.

SOF typing

Serum opacity factor (SOF) is an enzyme that is produced by some M/emm types. It is an apoproteinase that is named for its ability to produce opacity when an extract of the strain is mixed with mammalian serum (horse serum is typically used). Some M types are known to be SOF positive and others are typically SOF negative (e.g. M1 is always SOF negative, and M22 is typically SOF positive). The opacity factor of SOF-positive strains may be typed by neutralization of the reaction using specific antisera. This is called anti-opacity factor (AOF) typing and, with few exceptions, the AOF type is consistent with the M/emm type.

sic gene typing of M1 strains

Traditional fingerprinting techniques (e.g. pulsed field gel electrophoresis) are not specific enough to differentiate strains of the same M/emm type. However, for M1/emm 1 strains, which account for 20% to 30% of the invasive disease-causing strains each year in Canada, variation within the *sic* (streptococcal inhibitor of complement) gene may be used to provide further analysis of isolates associated with an outbreak. Utilization of this testing for specific investigations must be discussed with the NCS before isolates are sent.

Writers: Marguerite Lovgren and Gregory J. Tyrrell

Selected Readings

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ANNEX 3

Infection Control for Invasive Group A Streptococcus Infection in Hospitals

This document was developed for the use of health care workers (HCWs) to prevent the transmission of invasive group A streptococcus (GAS) in hospitals. Invasive GAS disease is defined as disease with isolation of GAS from a normally sterile site (Section 5.1 of these Guidelines). For recommendations on non-invasive GAS please refer to the Public Health Agency of Canada (PHAC) Infection Control Guideline: Routine Practices and Additional Precautions for Preventing the Transmission of Infections in Health Care – Revision of Isolation and Precaution Techniques⁽¹⁾.

The recommendations in this document are based on PHAC infection control guidelines: *Routine Practices* and Additional Precautions for Preventing the Transmission of Infections in Health Care – Revision of Isolation and Precaution Techniques⁽¹⁾, Prevention and Control of Occupational Infections in Health Care⁽²⁾ and Hand Washing, Cleaning, Disinfection and Sterilization in Health Care⁽³⁾.

Some specific recommendations in this Annex may supersede existing PHAC infection control guidelines; they are based on new evidence, expert opinion and consensus. The recommendations in this Annex have been reviewed and endorsed by the PHAC Infection Control Guidelines Steering Committee. A glossary of terms is found at the end of the Annex.

Transmission of Invasive GAS in Health Care Settings

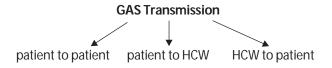
GAS is primarily spread by large droplet contact of the oral or nasal mucous membranes with infectious respiratory secretions or with exudates from wounds or skin lesions, or by direct or indirect contact of non-intact skin with exudates from skin or wounds or infectious respiratory secretions⁽¹⁾. Transmission between patients through contaminated hands and the reduction of transmission by handwashing was initially reported by Semmelweiss in 1848⁽⁴⁾. Transmission by contaminated equipment or patient care products (e.g. bidets, multi-dose injection vials) has rarely been reported⁽⁵⁾.

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, usually 1 to 3 days. The infection is communicable until 24 hours of effective antibiotic treatment has been completed.

Nosocomial infections accounted for 12% of all invasive GAS infections identified during prospective surveillance in Ontario from 1992 to 2000⁽⁶⁾. Although pre-existing GAS carriage by the patient may play a role in some cases of sporadic post-partum or postoperative infections, GAS may also be acquired from health care providers with symptomatic infection or asymptomatic carriage⁽⁵⁻⁸⁾ Hospital outbreaks of invasive GAS have been reported in a variety of patient groups (e.g. post-partum women and newborns, postoperative surgical patients, burn patients, neonatal intensive care patients, patients in geriatric wards)^(5,8). Some outbreaks have been associated with persistent carriage of GAS by asymptomatic health care providers (e.g. surgeons, obstetricians, anesthesiologists, nurses). The pharynx, vagina, rectum and/or specific areas of skin (e.g. scalp) have been sites of colonization (5,8,9). Outbreaks of GAS infection have also occurred in exposed HCWs^(5,10).

Infection Control Measures To Prevent Transmission of Invasive GAS in Health Care Institutions

The transmission of invasive GAS in hospitals and long-term care facilities is most effectively prevented by adherence to good hand hygiene and other routine practices at all times. In addition, for patients with invasive GAS infection, contact and droplet precautions are required until 24 hours of effective antibiotic therapy has been administered. As most cases of nosocomial invasive GAS are sporadic, it is important to recognize clinical presentations compatible with invasive GAS early and institute additional precautions while awaiting laboratory confirmation. 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 (6,8). For further information regarding infection control measures in long-term care facilities please see Section 6.3 of the Guidelines.



In order to effectively prevent the transmission of GAS from patient to patient, patient to HCW and/or HCW to patient, the following infection control practices are necessary:

- Consistent adherence to good hand hygiene practice.
- Use of routine practices at all times and for all patients, including wearing a surgical/procedure mask and eye protection or face shield when contamination of the mucous membranes is likely, for example when doing wound irrigation.
- In addition to routine practices at all times, applying contact and droplet precautions when caring for patients with known or suspected invasive GAS disease (Section 5.1 of the Guidelines) until 24 hours of effective

- antimicrobial therapy is complete. For the purpose of infection control, GAS pneumonia with or without a positive blood culture is considered an invasive infection, although not identified as such for reporting.
- Ensuring that HCWs promptly report illness possibly due to GAS (pharyngitis, impetigo, wound or skin infections, cellulitis) and comply with policies regarding not working when ill with a potentially communicable disease.
- Investigating clusters and identifying and treating patients and staff members with symptomatic GAS infection.
- Patients who share a room with a patient with invasive GAS are not considered as exposed and do not require prophylaxis. Unusual circumstances, e.g. the roommate has had direct mucous or non-intact skin contact with infectious respiratory tract secretions or skin lesions of an infected patient, should be assessed on a case-by-case basis.

Occupational Health Work Practices to Manage HCWs Exposed/Colonized/ Infected with GAS (invasive or noninvasive infection)

Management of HCWs exposed to GAS

- An occupational exposure of a HCW is defined as secretions from the nose, mouth, wound or skin infection of the infected case coming into contact with the mucous membranes or non-intact skin of the HCW from within 7 days before the onset of GAS until 24 hours of effective antibiotic therapy.
- If appropriate personal protective equipment was worn, there was no exposure.
- The risk of development of GAS infection in exposed HCWs and the utility and efficacy of prophylaxis for this group are unknown. HCWs who have an occupational exposure to a patient with GAS soft tissue necrosis (including necrotizing fasciitis, myositis or gangrene), toxic shock syndrome, meningitis, pneumonia, other

life threatening GAS disease or GAS disease resulting in death may be offered chemoprophylaxis (Tables 3 and 5 of the Guidelines). In this situation, screening and/or cultures for test of cure are not necessary. This recommendation differs slightly from current guidelines defined in Prevention and Control of Occupational Infections in Health Care⁽²⁾, which indicates that management may include laboratory investigation and prophylaxis as recommended by provincial/territorial guidelines. HCWs with an occupational exposure should be counselled about the symptoms associated with GAS and advised to seek care immediately if symptoms of GAS disease (skin infection, pharyngitis, unexplained fever) develop in the 21 days after exposure.

- An occupational exposure to a patient with a form of invasive GAS not listed above is not considered to pose a significant risk of serious disease in HCWs; if workers report a significant exposure to such patients, they should be counselled about the symptoms associated with GAS and advised to seek care immediately if symptoms of GAS disease (skin infection, pharyngitis, unexplained fever) develop in the 21 days after exposure.
- There are no modifications to work practices or work restrictions for HCWs exposed to GAS.
- No screening, treatment, modifications of work practices or work restrictions for HCWs in contact with a patient with a GAS infection are required when there has not been an occupational exposure.

Management of HCWs colonized or infected with GAS

- There are no modifications to work practices or work restrictions for HCWs who are colonized with GAS and are asymptomatic if they are not epidemiologically linked to patient transmission.
- Asymptomatic, colonized HCWs who are epidemiologically linked to transmission of GAS to patients resulting in invasive or non-invasive disease should be offered chemoprophylaxis (Table 6 of the Guidelines) and should be

- excluded from patient care duties until 24 hours after the start of treatment with effective anti-biotic therapy.
- HCWs 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 effective antibiotic therapy.
- HCWs with 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.
- Local public health authorities should be notified of cases of invasive GAS disease or a suspected or confirmed outbreak of GAS as required by legislation.
- Infection control and occupational health should be notified immediately of a HCW with suspected or confirmed GAS disease (invasive or non-invasive) if the HCW worked while the infection was communicable or if there is any possibility that the infection might have been occupationally acquired.
- Occupationally acquired infections should be reported to provincial/territorial ministries of labour and/or workplace safety insurance boards, as required by legislation.

Management of possible or confirmed GAS outbreaks in hospitals

- If, within 1 month of an invasive GAS case, one or more possibly linked additional invasive or non-invasive cases occur in either patients or staff, the situation should be treated as an outbreak until typing results are available.
- Occupational Health, Infection Prevention and Control, and Public Health authorities should be notified and liaise if an outbreak is suspected or confirmed.
- As part of the outbreak investigation, specimens for culture (throat, rectal, vaginal, skin lesions, stoma sites) should be obtained from HCWs and

- patients epidemiologically linked to the nosocomial GAS transmission. A thorough inspection of the skin should be done for HCWs who are epidemiologically linked to nosocomial GAS transmission and culture of lesion carried out as appropriate (there have been outbreaks associated with skin/scalp carriage)⁽⁵⁾.
- Patients and HCWs epidemiologically linked to transmission and identified as colonized by screening cultures should be promptly offered antibiotics to eradicate carriage (Table 6 of the Guidelines) (2,3). Isolates should be obtained and typed (serotyping or another equivalent method) to identify relatedness (see Annex 2: Laboratory Support for Outbreak Investigation of Invasive GAS Disease).
- HCWs who are either colonized, symptomatic or infected with GAS and epidemiologically linked to transmission should be excluded from patient care duties until 24 hours after the start of effective antibiotic therapy and assessed for fitness to work. The type of patient/physical setting/work/hygiene practices and control measures that can be used should be assessed, and a follow-up schedule established (2.3).

- Culture for a test of cure is recommended for individuals found to have the outbreak-related strain if there is epidemiologic evidence indicating that contact with the individual is linked to transmission. If the person remains colonized, investigation of the household contacts for carriage should be considered.
- HCWs and/or patients who are identified by outbreak investigations and whose isolates are identified by typing as not being part of the outbreak do not require any follow-up or test of cure cultures.
- For algorithms in cases of post-partum and post-surgical GAS disease, please refer to guidelines from the Centers for Disease Control and Prevention⁽⁸⁾.

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Glossary of Terms

Additional precautions: These precautions are required when routine practices are not sufficient to prevent transmission. They include contact, droplet and airborne precautions.

Contact precautions: Includes specific recommendations for personal protective equipment (such as gowns if clothing or forearms will have direct contact with the patient or contaminated environmental surfaces, and gloves upon entry into patient's room or bed space); proper use and disinfection of patient care equipment between patients; patient accommodation and transport.

Contact transmission: Includes direct contact, indirect contact and droplet (large droplet) transmission as described below. Although droplet transmission is a type of contact transmission, it is considered separately as it requires different precautions.

- Direct contact occurs when the transfer of microorganisms results from direct physical contact between an infected or colonized individual and a susceptible host (body surface to body surface).
- Indirect contact involves the passive transfer of microorganisms to a susceptible host via an intermediate object such as contaminated hands that are not washed between patients, contaminated instruments or other inanimate objects.

Droplet precautions: Includes specific recommendations for personal protective equipment (including masks within 1 metre of the patient); patient accommodation and transport.

Droplet transmission: Refers to large droplets, greater than or equal to 5 μ m in diameter, generated from the respiratory tract of the source patient during coughing or sneezing, or during procedures such as suctioning or bronchoscopy. These droplets are propelled a short distance, < 1 metre, through the air

and deposited on the nasal or oral mucosa of the new host.

Exposed HCW: To be considered an exposed HCW, secretions from the nose, mouth, skin lesions or wound of the infected case have to come in contact with the mucous membranes or non-intact skin of the HCW.

Hand hygiene: A general term that applies either to handwashing, an antiseptic handwash, an antiseptic hand rub, or a surgical hand antisepsis.

Mask: A barrier covering the nose and mouth to protect the mucous membranes from splashes or sprays and from microorganisms contained in large droplet particles (> 5 μ m in size). Masks may also be used by the source patient to contain large droplet particles generated by coughing or sneezing. The term mask in this document refers to surgical/procedure masks, not to special masks such as high efficiency dust/mist masks or respirators.

Nosocomial infection: An infection is considered nosocomial or hospital-acquired if the disease was neither present nor incubating at the time of hospital admission.

Routine practices: Routine practices are infection prevention and control practices for use in the routine care of all patients and are dependent on the task being performed and the health care setting. Routine practices outline the importance of handwashing before and after caring for patients; the need to use gloves, masks and eye protection or face shield, and gowns when splashes or sprays of blood, body fluids, secretions or excretions are possible; the cleaning of patient care equipment; the patient's physical environment; accommodation requirements for specific patients; management of soiled linens; and precautions to reduce the possibility of HCW exposure to bloodborne pathogens by sharp objects.

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