Invasive Group A Streptococcal Necrotizing Fasciitis, Necrotizing Myositis and Toxic Shock Syndrome

Manitoba Health
Public Health

Communicable Disease Control Unit

Case Definition

1) **Group A Streptococcal** (GAS) **Necrotizing Fasciitis** (NF) **and Myositis** (NM), also known as "flesh-eating disease", as defined by the presence of both of the following:
    - laboratory diagnosis of Group A streptococcal organisms (*Streptococcus pyogenes*) from the affected area;
    - necrosis of fascia/muscle at the affected area;
2) **Streptococcal Toxic Shock Syndrome** (STSS) as defined by isolation of Group A streptococcal organisms, hypotension (systolic BP ≤90 mm Hg in adults or <5th percentile for age in children), and two or more of the following:
    - renal impairment (creatinine ≥177 umol/L);
    - coagulopathy (platelet count ≤100 x 10^9 or disseminated intravascular coagulation);
    - liver function abnormality (AST, ALT or total bilirubin levels ≥2x upper limit of normal for age);
    - adult respiratory distress syndrome (ARDS);
    - generalized erythematous macular rash that may desquamate.

    N.B. Toxic shock syndrome can also be caused by *Staphylococcus aureus*, and is also reportable.

Reporting Requirements

- All cultures positive for GAS organisms from blood, CSF, surgical tissue specimens, and other normally sterile body fluids are reportable by laboratory.
- All cases of Necrotizing Fasciitis and Myositis, and STSS caused by GAS (as well as *S. aureus*) as described above, are reportable by attending health care professional.
- Streptococcal disease that is invasive but does not meet the above surveillance case definitions is not reportable.

Clinical Presentation/Natural History

The manifestations preceding the onset of invasive GAS disease may be vague and may include:

- pain of unusual severity (out of proportion to the clinical findings)
- swelling
- fever, chills
- flu-like symptoms
- generalized muscle aches
- generalized macular rash
- bullae
- nausea, vomiting, diarrhea
- malaise
- joint pain

STSS is the most serious manifestation of invasive GAS disease. It comprises a primary site of GAS infection together with hypotension, adult respiratory distress syndrome (ARDS), renal impairment, rapid onset of shock and multi-organ failure. Toxic shock syndrome due to *Staphylococcus aureus* infection has a similar clinical picture. The most common primary site of invasive GAS infections is soft tissue but pneumonia, septic arthritis, and primary bacteremia may also occur. Upper respiratory tract manifestations of invasive GAS infections are more common in children, arthritis and pelvic infections are more common in young adults, and NF is more common in the elderly.

NF and NM alone are less severe infections than STSS, with a mortality rate of approximately 20%. However, they may progress to STSS, which has a mortality rate of up to 80%. Survivors may be left with severe long-term disability.

Etiology

A history of minor injury, blunt or penetrating trauma, surgery, and breaks in the skin or mucous membranes (sores, scratches, eczema, blisters, chicken pox, etc.) may be noted in cases of invasive GAS disease. The development of invasive GAS disease appears to be facilitated by the presence of specific virulent strains, predisposing host factors such as older age, and chronic health stresses such as HIV infection, cancer, cardiovascular disease, respiratory disease and alcohol abuse. However, the disease can occur in otherwise healthy children, adolescents and adults. Persons with STSS usually do not have a preceding illness such as pharyngitis.

Epidemiology

Reservoir: Humans. Nasal carriers are particularly likely to transmit disease. In populations where impetigo is prevalent, Group A streptococci may be recovered from the normal skin for one to two weeks before skin lesions develop; the same strain may appear in the throat (without clinical evidence of throat infection) late in the course of the skin infection.

Anal, vaginal, skin and pharyngeal carriers have been responsible for nosocomial outbreaks of serious streptococcal infection, particularly among post-surgical patients. Identification of the carrier often involves intensive epidemiologic and microbiologic investigation; eradication of the carrier state is often difficult and may require multiple courses of various antibiotics.

Transmission: By large respiratory droplets or direct contact with patients or carriers, rarely by indirect contact through objects.

Person-to-person transmission occurs through exposure to secretions from wounds, and nasal or oral cavities, such as occurs through nosocomial transmission or close contact. The common routes of entry for beta-hemolytic streptococci (mainly Group A) are the nasopharynx, wounds (including surgical), and the skin.

Casual contact rarely leads to infection.

Exposures to urine or feces do not pose a risk. Transmission from fomites is not thought to be a concern. Dried streptococci reaching the air via contaminated items (floor dust, lint from bed clothing, handkerchiefs) are viable but apparently noninfectious for mucous membranes and intact skin.

Occurrence:

General: There is limited information on the background incidence of these diseases, the frequency of secondary disease transmission and the benefits of prophylactic therapy for contacts. This makes the development of public health management guidelines difficult. Thus, these guidelines should be regularly reviewed and revised as necessary, when published evidence provides better direction.

In the United States, an estimated 10,000 to 15,000 cases of severe GAS infections occur each year, 5-19% of which (between 500 and 1,500 cases) develop necrotizing fasciitis.

Manitoba: Reporting of cases of invasive GAS disease began in late 1995 in response to a request by Manitoba Health, after an outbreak of severe forms of this disease in the fall and winter of 1995/1996.

Between September 1995 and October 2000 there were 52 cases of IGAS disease reported to Manitoba Health that met one of the case definitions: 35 cases of NF, one case of NM and 16 cases of STSS. The male to female ratio was approximately 1:1. The average age was 55.4 years, with 31 persons older than 50 years of age. The case fatality rate was 36.5%.

Incubation Period: Short, usually one to three days, rarely longer.

Susceptibility and Resistance: Invasive GAS disease has come under increased attention during the last several years as the result of apparent changes in incidence and severity. Cases of STSS and necrotizing fasciitis/myositis have increased in otherwise healthy persons and have been associated with severe outcomes such as death and limb loss.

Antibacterial immunity develops only against the specific M-type of Group A streptococcus and may last for years. Immunity against toxins (especially pyrogenic exotoxin A) is vital for recovery from invasive GAS disease.

No gender or racial differences in susceptibility have been identified.

Period of Communicability: With adequate therapy, transmissibility is generally within 24 to 48 hours.

Persons with untreated streptococcal pharyngitis may carry the organism in the pharynx for weeks or months, usually in decreasing numbers. The infectivity of these carriers decreases sharply two to three weeks after onset of infection.

Diagnosis

See **Case Definition**. The diagnosis described is for the purposes of public health reporting and follow-up. Diagnosis is based on clinical presentation and the surveillance case definitions.

Key Investigations

- All organisms associated with reported cases should be sent to Cadham Provincial Laboratory (CPL). CPL will send the isolate and its accompanying form to the National Streptococcal Reference Laboratory in Edmonton for M and T type characterization.
- Only confirmed cases of NF, NM or STSS are referred by Manitoba Health for public health follow-up; i.e., positive laboratory reports for GAS are not referred for public health follow-up unless they are confirmed cases of NF, NM or STSS.

Control

Management of Cases:

- Individual case management and nosocomial infections are not addressed in detail here. The *Invasive Group A Streptococcal Disease: Information Sheet for Physicians* by Manitoba Health (see **Additional Resources**) can assist with case management. **Advice should be sought from surgical/infectious disease specialists and infection control practitioners.**
- Preventing death and improving the outcome depends on prompt and appropriate surgical intervention and antimicrobial therapy including intravenous penicillin and clindamycin. GAS has remained very sensitive to penicillin but experimental evidence suggests that the use of clindamycin may decrease mortality through more efficient bacterial killing and inhibition of toxin synthesis. Ampicillin can be used as an alternative to intravenous penicillin when it is not available.
- Information regarding new potential treatment regimens currently under study that may be beneficial for persons with invasive disease, such as intravenous immune globulin (IVIG) for STSS, may be obtained via an infectious disease specialist from Canadian Blood Services.
- No special infection control measures other than Routine Practices as defined in the Health Canada document, Routine Practices and Additional Precautions for Preventing the Transmission of Infection in Health Care, are required. Cases with major wounds where drainage cannot be contained by dressings should be placed on Contact Precautions until 24 hours of appropriate antibiotic therapy has been received. The use of Droplet Precautions for streptococcal invasive disease is not recommended.

Management of Contacts:

- Definitive data to guide the management of contacts is presently lacking.
- There are limited data on the occurrence of secondary cases of GAS infection following a case of severe invasive GAS disease. In an isolated geographic setting in southern Ontario, an increased risk of invasive GAS disease in close contacts of patients with STSS or NF/NM was measured at about 200 times greater than the general population. However, similar observations have not been confirmed anywhere else in North America. There have been no known secondary cases of invasive GAS infections documented in contacts of patients with necrotizing fasciitis/myositis or streptococcal toxic shock syndrome (STSS) in Manitoba since the initiation of data collection in March 1996.

A) Definition of Contacts

Contacts are persons who fit the criteria in one of the following two categories:

A1) Household Contacts

Anyone living in the same household as the case within the seven days prior to the onset of illness in the case.

A2) Close Contacts

Persons who share sleeping arrangements.

Persons who have had **direct** mucous membrane contact with the oral or nasal secretions of a case. Examples of situations where close contact can occur are:

- day care centres
- persons travelling together
- persons performing mouth-to-mouth resuscitation
- close friends or frequent social contacts

Persons who have shared a hospital room, workplace, or schoolroom setting are **not** considered contacts unless the above-described exposures/activities have occurred. Exposure to urine, feces and fomites do **not** pose a risk.

B) Time Period of the Contact

Contact must have occurred between seven days prior to the onset of illness in the index case, to the time of institution of infection control precautions, or 24 hours after the implementation of appropriate antimicrobial therapy.

These guidelines are based on an estimated maximum incubation period for GAS disease of seven days.

C) Testing of Contacts

There is no need for swabbing or testing of asymptomatic contacts.

D) Specific Measures

Further studies are needed to better establish the rate of secondary spread, understand organism and host factors that contribute to the risk of invasive infection, identify short course antimicrobial regimens that may be used for prophylaxis, and assess the economic burden of invasive GAS infections. However, based on current knowledge, the following interventions are the present recommendations for the management of contacts where there is a case of STSS, GAS necrotizing soft tissue infection or death. Each situation will require individual assessment. **Physicians may wish to consult with public health professionals or infectious diseases specialists.**

D1) Symptomatic Contacts

Symptomatic contacts present with an illness consistent with GAS infection including pharyngitis, scarlet fever, cellulitis, erysipelas, inflamed joints, bursitis, impetigo, abscess, etc. All symptomatic contacts should be referred to their physician for treatment of a presumed GAS infection with penicillin, erythromycin, or a first-generation cephalosporin.

D2) Asymptomatic Contacts

Based on present evidence, treatment/prophylaxis is **not** recommended at this time. Administration of prophylaxis to asymptomatic contacts should only be considered in the event of the occurrence of a secondary epidemiologically-linked case of invasive GAS infection, which defines an outbreak. **In this instance, public health professionals and/or infectious diseases specialists should be consulted.**

D3) Long-term Care Facility Contacts

Since cases of invasive GAS have been associated with outbreaks in long-term care facilities, and the strain may be widespread within the facility, the following recommendations are unique to this setting.

When a case of STSS or NF/NM occurs in a resident of a long-term care facility,

the facility should take the following steps in consultation with public health:

- Review resident records from the last two months for any recent cases of infection consistent with GAS such as pharyngitis, pneumonia, cellulitis, conjunctivitis, etc.
- Assess the potential for a source of infection from outside the facility such as regular visits from children who have recently been ill.
- Follow reporting requirements for streptococcal invasive disease.

If an excess of GAS infection is identified (an incidence rate of possible GAS infections greater than two per 100 residents per month or at least two cases in one month in long-term care facilities with less than 100 residents) the following action should be taken:

- All residents and health care staff on the units where cases have been identified should be screened for GAS with throat, nose, and skin lesion swabs for culture.
- Anyone colonized with GAS should receive prophylaxis.
- Staff on remaining unaffected units and non-resident care staff should be questioned about possible recent GAS infections and swabbed if a positive history is obtained. Those with positive cultures should be treated with an appropriate antibiotic.
- Active surveillance for GAS infections should be undertaken and continued for four to eight weeks, including appropriate specimens for GAS cultures when suspect infection occur.

If no excess of GAS infection is identified, especially with evidence of an outside source of infection for the index case, then active surveillance alone for two to four weeks to ensure the absence of further cases is justified.

E) **Antibiotics for Prophylaxis**

Although penicillin has been the standard antibiotic treatment of GAS infections, the success rate for eradication of the organism in cases of pharyngitis treated for 10 days is less than 90%. A course of a first-generation cephalosporin results in eradication of GAS from the pharynx in up to 95% of patients with acute GAS pharyngitis. A 10-day course of cephalexin or erythromycin, in cephalosporin allergic individuals, should therefore be used for GAS prophylaxis. Penicillin may be used as an alternative.

In the event that prophylactic antimicrobial therapy is prescribed, the following drug regimens are recommended:

Cephalexin:

Children:	25-30 mg/kg/day PO in divided doses (maximum 500 mg/dose)
Adults:	250 mg PO q6h or 500 mg PO q12h

Alternative regimen:

Penicillin VK:

Children:	25-30 mg/kg/day PO in divided doses (maximum 300 mg/dose)
Adults:	300 mg PO q6h

Or, in penicillin or cephalosporin allergic patients:

Erythromycin:

Children:	25-30 mg/kg/day PO in divided doses (estolate suspension) tablets (maximum 500 mg/dose)
Adults:	250 mg PO q6h (base)

Duration of prophylaxis is 10 days. Culturing for a test of cure is not recommended.

Management of Outbreaks:

- All contacts should be managed as per this protocol.

Preventive Measures:

- Educate the public and health workers about modes of transmission; about the relationship of streptococcal infection to acute rheumatic fever, Sydenham's chorea, rheumatic heart disease and glomerulonephritis; and about the necessity for prompt diagnosis and completion of the full course of antibiotic therapy prescribed for streptococcal infections.

Additional Resources

For health care professionals:

- Information for Physicians on Invasive Group A Streptococcal Infections.
- Questions and Answers: Necrotizing Fasciitis/Myositis (also known as "Flesh-eating Disease"). Available from Audiovisual and Publications Department, Manitoba Health, telephone (204) 786-7112, fax (204) 772-7213.