INTERNATIONAL SOCIETY FOR INFECTIOUS DISEASES

GUIDE TO INFECTION CONTROL IN THE HEALTHCARE SETTING

Streptococcus pyogenes (Group A Streptococcal Infections)

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Topic Outline

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KEY ISSUE

- Handwashing is one of the most important infection control practices for the prevention of spread of infection with *Streptococcus pyogenes* [Group A streptococcus (GAS)] (1-6).
- One healthcare-acquired postpartum or postsurgical invasive GAS infection should prompt enhanced surveillance and streptococcal isolate storage; 2 or more cases caused by the same strain of GAS should prompt an epidemiological investigation that includes the culture of specimens from epidemiologically linked healthcare workers (HCWs) (7).
- There are increasing reports of GAS in long-term care facilities. There is a need to study risk factors and guidelines to address potential clusters/outbreaks of GAS infections in this setting (7-11).
- In a larger context GAS remains a challenge in terms of best prevention strategies for developing countries.

KNOWN FACTS

- Group A streptococci frequently colonize the throat of asymptomatic persons and may also colonize the skin, rectum, and vagina (8, 9).
- Streptococcal disease is ordinarily spread by direct person-to-person contact. In cases of pharyngitis and respiratory infections, droplet nuclei of saliva or nasal secretions are the mode of spread. Crowding such as occurs in schools or military barracks favors interpersonal spread of the organism in community outbreaks. Fomites can also be a source of streptococcal transmission 8, 9).
- A variety of clinical presentations may occur, including pharyngitis, otitis media, quinsy (peritonsillar abscess), skin and soft tissue infections

(pyoderma, impetigo, erysipelas, and scarlet fever), pneumonia, and puerperal fever (8,9, 20).

- Most GAS infections are relatively mild illnesses. More recently invasive and serious GAS infections have become concerning (20).
- Invasive group A streptococcal infection is defined as isolation of GAS from a normally sterile site (e.g., blood) or by the isolation of GAS from a non-sterile site in the presence of the streptococcal toxic shock syndrome or necrotizing fasciitis (7-11, 20).
- Post-infectious complications of GAS infections include rheumatic fever with secondary aortic and mitral valve injury and glomerular nephritis. Pharyngeal strains of GAS can result in either syndrome. Infections of the skin are only associated with the acute glomerular nephritis (20).
- Streptococcal infections should be treated to limit secondary complications (20).
- Outbreaks of pharyngitis and impetigo in school-age children or in group settings are common (20).
- Clusters/outbreaks are less common, but had been described mainly in 2 healthcare settings, postpartum, and postsurgical populations. There has also been more recent interest in healthcare-associated clusters in the long-term care facility setting, where there have been growing cases identified (8, 9, 12-18).

Controversial Issues

- No controlled trials have evaluated the effectiveness of chemoprophylaxis in preventing invasive GAS disease among household contacts of persons with invasive GAS infections. Given the infrequency of these infections and the lack of a clearly effective chemoprophylaxis regimen, the available data do not support a recommendation for routine testing for GAS colonization or for routine administration of chemoprophylaxis to all household contacts of persons with invasive GAS at this time. However, in some situations, prophylaxis may be recommended for someone who is exposed to someone with an

invasive group A streptococcal infection (i.e., necrotizing fasciitis, streptococcal toxic shock syndrome). That decision should be made after individual patients talk with their doctors (7, 11, 20).

- Given the rise in cases in those 65 years of age and older and living in long-term care facilities, additional controls in these populations, including larger scale prophylaxis, may warrant discussion (but is now not common practice) (7,11).
- The global strategies for prevention of GAS on a larger scale remain complex (19).
- Updates to statistics and suggested practices is available at CDC's Streptococcal home page and related pages (20, 21)

SUGGESTED PRACTICE

- Standard precautions, including handwashing, are the most important infection control practices for the prevention of spread of infection with GAS such as minor/limited skin infections, wounds and burns, and endometritis (puerperal sepsis) (1-6, 12).
- HCWs should wear gloves and gowns for contact with the skin of patients with major lesions, wounds, and purulent discharge. Place the patient in a private room. When a private room is not available, place the patient in a room with a patient(s) who also has infection with *S. pyogenes* (cohorting). Discard the gloves after use and wash hands thoroughly between patient contacts. Contact isolation may be discontinued after 24 hours of directed antistreptococcal therapy (12).
- For GAS infections that involve the pharynx and respiratory tract, such as pneumonia and scarlet fever in infants and children, HCWs should use standard and droplet precautions, including use of a surgical mask when working within 3 feet (1 meter) of the patient. Logistically, some hospitals may want to implement the wearing of a mask to enter the room of affected patients. Place the patient in a private room. When a

private room is not available, cohorting should be used. When a private room is not available and cohorting is not achievable, maintain spatial separation of at least 3 feet (1 meter) between the infected patient and other patients and visitors. Special air handling and ventilation are not necessary, and the door may remain open (7, 12, 20).

- HCWs who are known or suspected to have infection or colonization of their respiratory tract with *S. pyogenes* should wear a mask to reduce respiratory spread of their organism (12).
- Attempt to eradicate colonization in those HCWs who are proven sources of outbreaks (description evaluation of cluster/outbreak in healthcare setting below).
- Newer typing modalities, including whole — genome sequencing (compared to traditional pulsed field gel electrophoresis [PFGE]) may be needed to elucidate epidemiology in some clusters. Even though the Lancefield M protein serotyping system over the past 60 years has been very valuable, in recent years the inherent difficulties encountered in expanding this system through conventional serologic procedures have become increasingly evident. Using a less demanding sequence based system that is predictive of Lancefield M serotypes (*emm* typing), specialized labs such as the U.S. Centers for Disease Control and Prevention (CDC) have extended the system established decades ago by Dr Rebecca Lancefield (17, 18, 20, 21).

SUMMARY / ANNOTED REVIEW OF RELEVANT TOPICS

- *Streptococcus pyogenes* (group A beta-hemolytic streptococcus) is a Gram-positive, catalase-negative cocci. It can be carried in the pharynx, skin, vagina, and rectum asymptomatically. There are a wide variety of clinically presentations of GAS. Although the most common GAS infections are mild (i.e., pharyngitis, skin infections) if left untreated there can be serious secondary sequelae, including rheumatic fever and glomerular nephritis (8, 9, 20).
- More concerning in recent years are invasive GAS infections. Invasive GAS infection is defined as isolation of GAS from a normally sterile site (e.g., blood) or by the isolation of GAS from a non-sterile site in the presence of the streptococcal toxic shock syndrome or necrotizing fasciitis (8, 20).
- Worldwide, rates of invasive disease increased from the mid-1980s to early 1990s. Rates of invasive disease have been stable over the last several years in the United States. However, there have been increases in the severity of disease, including those associated with M-1 and M-3 serotypes (*emm* types 1 and 3). Resistance to erythromycin has increased worldwide (8, 20, 21).
- By estimates from CDC, using the Active Bacterial Core Surveillance (ABCs) Report in the year 2012 there were approximately 10,700 cases of invasive GAS and 1150 deaths due to GAS infection in the United States. The case fatality rates for septic shock, streptococcal toxic shock syndrome (STSS), and necrotizing fasciitis were 45%, 38%, and 29%, respectively. The annual incidence was highest among persons aged ≥65 years (9.4/100,000) or <1 year (5.3) and among blacks (4.7/100,000). National rates remained steady over 8 years of surveillance. Factors independently associated with death included increasing age, residence in a nursing home, recent surgery, septic shock, necrotizing fasciitis, meningitis, isolated bacteremia, pneumonia, *emm* types 1 or 3, and underlying chronic illness or immunosuppression.

In a 30-valent M-protein vaccine, *emm* types accounted for 91% of isolates (8, 20, 21).

- Direct contact with patients or carriers and large respiratory droplets are the primary means of acquisition. Disease caused by *S. pyogenes* is most common in late winter and early spring. In the community setting, outbreaks of pharyngitis in school children and other congregate setting are common in these months. Contaminated hands of HCWs are an important means of transmission, particularly outside the setting of the operating room. Appropriate gloving and good handwashing techniques are important to emphasize in efforts to control an outbreak. (1-6) The addition of contact precautions for wound, skin, and soft tissue and droplet precautions for pharyngeal and respiratory infections in infants and children are appropriate infection control practices. Prompt identification and investigation of an outbreak of healthcare associated *S. pyogenes* infection will assist in its control (12).
- In the past, healthcare setting outbreaks had been described mainly in 2 populations; postpartum and postsurgical patients. GAS infections are also reported in burn patients (wound), bacteremias in the setting of intravascular catheters devices and pneumonias. More recently outbreaks in the long-term care setting have been of concern. Specifically in this setting, in addition to the traditional factors, staff turnover, compromised skin integrity in residents, a suboptimal infection control program, and lack of awareness of infections likely contributed to continued GAS transmission (8-10, 20).
- There are 2 fairly recent guidelines that are excellent resources for addressing infection control related to GAS infections and particularly in these high-risk settings, one related to an expert panel meeting by CDC in the United States and the second by Public Health Agency of Canada. Highlighted from these comprehensive guidelines are distilled below (7, 11).
- In 2000 CDC hosted a workshop to formulate recommendations for household contacts of those with invasive GAS infections and for

responding to healthcare associated clusters, including postpartum and postsurgical invasive GAS infections. The recommendations from this panel were published in 2002 (7).

- In this CDC expert panel review, a household contact is defined as a person who spent at least 24 hours in the same household as the index patient during the seven days before the onset of the case patient's symptoms. Review by the committee of 2 prospective studies that were designed to identify subsequent cases among household contacts (who were observed for a total of 66.5 million person-years) identified only 5 confirmed cases of subsequent invasive disease. There are no controlled trials that have evaluated the effectiveness of chemoprophylaxis in preventing invasive GAS disease among household contacts of persons with invasive GAS infections. In addition, antimicrobial therapy can have undesirable side effects, including adverse reactions and selection for resistant organisms (7) .
- Thus, the committee did not recommend routine screening for and chemoprophylaxis to household contacts. However, they suggested that providers and public health officials might choose to offer chemoprophylaxis to household contacts that are at an increased risk of sporadic disease [HIV infection, diabetes mellitus, varicella zoster (chickenpox) patients <10 years of age, cancer, heart disease, injection drug use, steroid use, ≥65 years of age] or mortality due to GAS (≥65 years of age). HCWs should routinely inform all household contacts of persons with invasive GAS disease about the clinical manifestations of pharyngitis and invasive GAS infection (e.g., fever, sore throat, and localized muscle pain and emphasize the importance of seeking medical attention if contacts develop such symptoms) (7).
- Given the potential for prevention of additional cases, the CDC panel recommended that even one case of postpartum or postsurgical GAS infection should prompt an epidemiological investigation by the hospital's infection control personnel, which should include enhanced surveillance and storage of GAS isolates from the index patients and

any other cases for at least 6 months. Enhanced surveillance should include one or both of the following (7):

1. review of microbiological records and autopsy reports from the previous 6 months and/or
2. review of operative, labor and delivery, and medical records from within the hospital.

- If 2 or more cases are identified within a 6-month period, they may have a common source of GAS transmission. Isolates should be compared by an appropriate typing method (i.e., PFGE, serotyping, other molecular methods). Isolates that differ probably are community acquired, but enhanced surveillance should be initiated.
- If 2 cases are found to be caused by the same strain within a 6-month period, screening of HCWs is strongly recommended to prevent further cases of serious infection. If infection-control personnel choose to screen healthcare workers, screening should be considered for HCWs who were present at deliver and for those who perform vaginal examinations before delivery (for postpartum cases) and for all HCWs present in the operating room during surgery and those who change dressings on open wounds (for postsurgical cases). If screening of HCWs is undertaken, sites from which specimens should be obtained and cultured include throat, anus, vagina, and any skin lesions. Screened HCWs may return to work pending culture results. However, HCWs identified as colonized should be suspended from patient care duties until they have received chemoprophylaxis for 24 hours and their streptococcus strains should be compared with patient strains using the same typing methods.
- If a HCW is epidemiologically linked to the case patient and the strain the HCW is carrying is the same as the strains isolated from patients, the committee suggests follow-up cultures should be done for the HCW (CDC suggestions 7-10 days after the completion of therapy). If no colonized HCW is identified or if HCWs are colonized with strains unrelated to the outbreak strain, the search for colonized HCWs could

be broadened to include those HCWs without immediate epidemiological links to all case patients. This might include, for example, HCWs who had direct contact with most but not all case patients (7, 20).

- The Public Health Agency of Canada published their Guidelines for the Prevention and Control of Invasive Group A Streptococcal Disease in October 2006. This 26-page resource adds to the previously described U.S. review in that it offers simple and clear definitions, an extensive glossary, review of the literature and references by topic area, and particular sections on GAS infection control and investigation in the childcare and long term care facilities settings. Two areas of difference from the U.S. guideline relevant for the infection control community are summarized below (11).
- The Canadian workgroup's consensus (11) on chemoprophylaxis for contacts was slightly more inclusive than the U.S. guideline above (7), in that it does suggest prophylaxis for the closest contacts of confirmed severe cases of GAS infections, including streptococcal toxic shock syndrome, soft tissue necrosis, meningitis, pneumonia, other life-threatening conditions or a confirmed case resulting in death (and did not identify the underlying conditions of the contacts as a factor as strongly as the U.S. guideline).
- For the long-term care setting, in addition to strict enforcement of standard infection control precautions, this guideline lays out what may constitute a cluster/outbreak and steps to investigate for and address a potential clusters/outbreaks. It suggests that in this setting the following should be an impetus for action:
  1. an incidence rate of culture-confirmed invasive GAS infections of >1 per 100 residents per month, or
  2. at least 2 cases of culture confirmed invasive GAS infection in one month in a facility with fewer than 200 residents, or
  3. an incidence rate of suggested invasive or non-invasive GAS infection of >4 per 100 residents per month.

- This guideline suggests when a confirmed case of GAS infection in a long-term care facility is identified that the following additional steps should be taken (11):
  1. retrospective chart review of facility's residents over the 4-6 weeks prior to the case for other culture confirmed or any suggestive cases of invasive or non-invasive GAS infection and
  2. assess the potential sources of infection from outside the facility. If an excess of these infections is identified, then the next steps would be:
     - screen patient-care staff for GAS;
     - based on size of the facility screen some or all facility residents for GAS (using a cut off of 100 beds: <100 beds screen all residents, >100 beds screen residents within the same care unit as the case);
     - offer prophylaxis for all those identified with colonization with GAS;
     - question non-patient care staff about recent GAS infection and screen those with positive history;
     - obtain genotyping of GAS isolates and "test of care" those with outbreak related strains;
     - rescreening of GAS positive residents and staff identified; and
     - active surveillance for GAS infections for 1 to 2 months. If no excess is identified, especially if there is evidence of outside source for the index case, then active surveillance alone for 2-4 weeks to establish absence of additional cases is warranted.

- In summary, handwashing is the cornerstone of infection control for GAS infections (1-6) Additional precautions including contact and droplet precautions are appropriate for use by HCWs for specific other presentations of GAS infection. For certain high-risk household contacts of GAS infection, prophylaxis maybe appropriate. For healthcare associated GAS infections enhanced surveillance, saving isolates, and screening/prophylaxis of epidemiologically-linked HCWs in certain settings may aid in prevention of further infections. Some additional

surveillance and investigation in the long-term care setting may also be appropriate when there is suspicion of clusters/breaks in this setting.

- It can be difficult to determine the number of invasive group A streptococcal disease cases that might be expected in any given area during a certain time period. CDC developed the Group A Strep Calculator to help local and state health public health officials determine if the number of invasive group A streptococcal cases seen locally are greater than what would be expected. The calculator estimates the average number of invasive group A streptococcus cases expected during a 1-month period in a region with given population characteristics and compares locally observed rates to this expected rate. More information about the Group A Strep Calculator is available at https://www.cdc.gov/groupastrep/outbreaks/calculator/index.html (10, 20)
- Several clusters have been described in the U.S. and international literature that have suggested that traditional typing protocols, such as PFGE, may not be sensitive enough to allow fine epidemiological discrimination of GAS isolates. Whole-genome sequencing presents a valid alternative that allows accurate fine scale epidemiological investigation of clusters of GAS. Examples include a postpartum GAS cluster in Australia in 2010 that used this technique to prove relatedness of *emm* 28 isolated from puerperal sepsis cases from the same hospital from isolates from other hospitals (supporting suspected patient-to-patient transmission or common sources). CDC and several other referral laboratories are available with expertise and resources to help with typing of suspected clusters (CDC strep labs: https://www.cdc.gov/streplab/m-proteingene-typing.html) (20)
- In 2005 WHO published 'A Review of the Technical Basis for the Control of Conditions Associated with Group A Streptococcal Infections' looking more from an international, global public health perspective (19). Although not completely related to healthcare associated transmission, it lays out a broader plan for GAS control. It sites that the most successful

GAS control activities have combined multiple strategies including primary prophylaxis, treatment of skin infections, health promotion, secondary prophylaxis, and RHD (rheumatic heart disease) registers. Although effective, these comprehensive programs require a substantial commitment from individuals and organizations (including ministries of health). It also suggests that in light of the current lack of a clear strategy for primary prevention of GAS infections, there is definitely a place for a safe, effective, affordable, and practical GAS vaccine. It appears likely that the vaccine most advanced in development — a multivalent, type-specific vaccine — will not provide sufficient and long-lasting protection in less developed countries, although this should be assessed. This document underscores that GAS remains a challenge throughout the world in the community and in healthcare settings.

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