INVASIVE GROUP A *STREPTOCOCCUS* INFECTIONS

I. DESCRIPTION AND EPIDEMIOLOGY

A. Overview

Group A *Streptococcus* (GAS, *Streptococcus pyogenes*) is a gram positive, beta hemolytic aerobic bacterium. GAS can cause a wide spectrum of illness including non-invasive localized infections such as pharyngitis and more severe and invasive disease such as necrotizing fasciitis and sepsis. Humans are the only reservoir for GAS. GAS may colonize the pharynx, skin, perianal area, and vagina; colonizing GAS may or may not lead to disease. Most GAS infections are mild and self-limited. However, invasive GAS (iGAS) infections, such as bacteremia, meningitis, or empyema, are associated with high morbidity and mortality. The focus of this Communicable Disease (CD) Manual is on the public health management of iGAS infections.

B. iGAS Infections in California and the U.S.

In California, iGAS infections are not reportable as individual cases, except in the setting of iGAS meningitis, post-partum or post-surgical iGAS infections, or those that arise in a residential healthcare setting (e.g., long-term care facilities). Additionally, per California Code of Regulations (CCR) Title 17, outbreaks of any disease are reportable in the state of California, including iGAS outbreaks.

Invasive GAS infection was on the U.S. Centers for Disease Control and Prevention (CDC) National Notifiable Diseases Surveillance System (NNDSS) (https://ndc.services.cdc.gov/conditions/streptococcus-disease-invasive-group-a/) from 1995-2009. Streptococcal Toxic Shock Syndrome (STSS) is still on the NNDSS list of notifiable diseases. Neither condition is reportable in California. However, the California Emerging Infections Program conducts active population-based surveillance for iGAS infections in three Bay Area counties (Alameda, Contra Costa, and San Francisco; http://ceip.us/projects/abcs) to monitor trends and assess disease burden.

The CDC estimates that 14,000–25,000 cases of iGAS infection with 1,500 – 2,300 deaths occur annually in the United States.

C. Symptoms and Clinical Course

GAS causes a wide spectrum of illness from localized to systemic or invasive infections. Localized infections include pharyngitis and tonsillitis/strep throat; strep throat is one of the most common bacterial infections of childhood. Treatment is necessary to prevent complications such as abscess, rheumatic fever, and glomerulonephritis. Scarlet fever may also occur and is characterized by a sandpaper-like rash that is generally more appreciated by tactile touch than visually observed. GAS may cause localized skin infections such as cellulitis or erysipelas, and more invasive diseases including necrotizing fasciitis. Other iGAS infections include bacteremia; pneumonia and empyema; sepsis and septic shock, STSS; and occasionally, meningitis. GAS is also a

known cause of secondary bacterial infection following varicella infection and respiratory virus infections including influenza.

Symptoms of iGAS infections depends on the site of infection or may be non-specific, and can include fever, chills, severe pain, and myalgias. Depending on the infection, localizing symptoms may include cough (pneumonia), headache (meningitis), or pain out of proportion to any skin finding (necrotizing fasciitis).

iGAS infections are associated with high morbidity and mortality. Overall, 10-15% of iGAS infections result in death; this can be as high as 35-50% in STSS cases. Healthcare providers should have a high index of suspicion as early recognition and prompt therapy improve outcomes.

D. Transmission

GAS is most often spread by direct person-to-person transmission through contact with saliva, nasal secretions, or skin lesions of infected or colonized persons. Foodborne outbreaks have been documented following persons infected or colonized with GAS contaminating food they have prepared. Persons on antimicrobial therapy are considered non-infectious after 12 hours of appropriate antibiotic treatment (i.e., antibiotics that treat streptococcal infections). Without antibiotic therapy, risk of transmission is highest during the acute illness and decreases over three weeks. In general, persons who are symptomatic are more likely to shed GAS and potentially infect contacts, compared with persons who are colonized but do not have active infection. Hand hygiene should be stressed for ill persons and their contacts.

Most persons with localized infections are considered communicable for up to 21 days without appropriate antimicrobial therapy. However, transmission has been documented up to 28 days from last exposure in close contacts of patients with iGAS. Therefore, it is recommended that close contacts of patients with iGAS infections be monitored for signs or symptoms of infection for 30 days after the last exposure (Refer to **Section IV. B.** for details).

E. Incubation Period

The incubation period depends on the type of infection and the point of entry; for example, the incubation period is approximately 2 to 5 days for GAS pharyngitis, while hypotension can develop within 24 to 48 hours once symptoms begin in streptococcal septic shock syndrome.

F. Clinical Management

Clinical management decisions should be made by the patient's healthcare provider. iGAS infections always require prompt antimicrobial therapy and will often require intensive supportive care. For necrotizing infections, emergency surgical consultation and debridement should be pursued. For prophylaxis of contacts please see **Section IV. D.**

II. CALIFORNIA SURVEILLANCE CASE DEFINITIONS (CDPH 2019)

Most GAS infections, including iGAS infections, are not reportable in the state of California; most of these infections are sporadic and public health interventions are limited. In 2019, "Streptococcal Infections (Outbreaks of Any Type and Individual Cases in Food Handlers and Dairy Workers Only)" was removed from the CCR Title 17, Section 2500 reportable diseases list. However, GAS meningitis, healthcare-associated infections, and outbreaks remain reportable (as meningitis, and outbreaks of any disease are reportable).

Invasive GAS infection is defined as the isolation of *S. pyogenes* from a normally sterile site (e.g., blood, cerebrospinal fluid, pleural fluid, peritoneal fluid, pericardial fluid, joint fluid, surgical specimens, bone, and scrotal fluid) and may present as meningitis, pneumonia, necrotizing soft-tissue infection, or post-partum infection, among other manifestations.

In addition to GAS meningitis (e.g., isolation of *S. pyogenes* from cerebral spinal fluid) and iGAS occurring as part of an outbreak, the following healthcare-associated infections should be reported to local and state public health authorities:

- Residential healthcare-associated iGAS infections: iGAS infections that occur in patients who, in the preceding 48 hours or longer, were residents of licensed health care facilities, including skilled nursing facilities (SNFs).
- Postpartum associated iGAS infections: Infections whereby GAS is isolated from a sterile site, wound infection (e.g., Cesarean section incision) or in association with a clinical postpartum infection (e.g., endometritis) during the postpartum period (i.e., all inpatient days following delivery and the first 7 days after discharge from healthcare facility).
- Postsurgical associated iGAS infections: Infections whereby GAS is isolated from a sterile site or a surgical wound in a postsurgical patient for whom the indication for surgery was not preexisting GAS infection, during the inpatient days following surgery and 7 days after discharge from healthcare facility.

Most iGAS infections are sporadic and there are limited public health interventions for prevention and control; therefore, iGAS infections not falling into the above categories are not reportable in California.

III. iGAS CASE INVESTIGATION AND REPORTING

A. Purpose of Reporting and Surveillance

- Individual cases of iGAS are reportable in the healthcare setting (e.g., residential healthcare facilities/SNFs, postsurgical, and postpartum-associated iGAS) due to the potential for nosocomial transmission. In addition, any cause of meningitis, including those due to iGAS, is also reportable in CA.

- Any infectious disease outbreak is also reportable per CCR Title 17. Outbreaks due to iGAS and GAS should be investigated to identify potential common source(s) and evaluate risk factors and need for prophylaxis.

B. Local Health Department (LHD) General Case Investigation Guidelines

While individual iGAS cases outside the healthcare setting are not reportable, local health departments (LHDs) may learn about an increase in iGAS cases from community physicians who may notice an increase in iGAS cases in children or adults requiring hospitalization, or other populations, including among homeless individuals.

If outbreaks of GAS and iGAS are identified in healthcare facilities, schools, or congregate living facilities (e.g., barracks or dorms), or among children, public health action should be taken. The CDC recommends collecting clinical and demographic case data; investigation to identify epidemiologic links including whether or not the outbreak is facility based; and requesting laboratories to save isolates. Guidelines for investigation and control of GAS clusters and outbreaks may be found on the CDC GAS Disease Outbreaks and Public Health Response webpage (https://www.cdc.gov/groupastrep/outbreaks.html).

C. LHD Reporting

GAS infections are reportable within California only in the setting of outbreaks of GAS/iGAS, iGAS meningitis, and healthcare-associated infections (e.g., post-surgical/post-partum, long term care facility residents). For outbreaks of GAS/iGAS, healthcare providers are required to report immediately to the LHD. The LHD should report outbreaks to IDB at 510-620-3434 during business hours. Health facilities licensed by CDPH are also required per CCR Title 22 to report outbreaks and single cases of postpartum or postsurgical iGAS cases as unusual infectious disease occurrences to their respective CDPH Licensing and Certification (L&C) District Office. LHD may contact the CDPH Healthcare-Associated Infections (HAI) Program, at HAIProgram@cdph.ca.gov for consultation regarding healthcare-associated cases.

LHDs may have their own reporting requirements for GAS or iGAS.

To report outbreaks of GAS/iGAS in CalREDIE:

1. Select Outbreak from the CalREDIE home page and begin a new outbreak record.
2. In the Outbreak tab, select “Other/Unknown” for “Disease” and “Other” for “Outbreak Type”. (Note: When “Other/Unknown” is selected for “Disease”, three additional tabs [Outbreak Report, Other Outbreak Report, and Foodborne OB] will appear.)
    a. Complete as much of the form as possible. Required fields are shaded dark pink.
    b. In the “Notes/Remarks” section, please include details on investigation such as any public health actions taken including if prophylaxis was prescribed or recommended for contacts.

3. Go to the "Other Outbreak Report" tab and complete as much of the form as possible, including the number of cases, clinical case definition or syndrome, pathogen, extent of outbreak, and outbreak setting information. The "Outbreak Report" and "Foodborne OB" tabs do not need to be completed.

To report individual cases of GAS meningitis in CalREDIE, the disease being reported should be "Meningitis- bacterial (other than for *H. influenzae* (<5 years old) and *N. meningitidis*)". Upload any culture results into the electronic filing cabinet, along with a copy of the hospital discharge summary, if available. In the notes section of the Case Investigation tab, please describe patient's clinical course.

D. Laboratory Resources

GAS is classified based on its M protein. M proteins help determine virulence, and strains that lack the M protein are considered avirulent. Typing of the M protein was previously done serologically but is now performed by sequencing of the variable region of the *emm* gene. Currently, the CDPH Microbial Diseases Laboratory does not routinely offer M protein typing for *S. pyogenes*. In some situations, further laboratory characterization may be useful, e.g., in post-surgical settings to determine nosocomial transmission. Whole genome sequencing may be available at the Microbial Diseases Laboratory for these situations. CDPH will work with LHDs to determine if isolates should be collected and saved for further laboratory characterization.

Please discuss with the CDPH on-call subject matter expert (SME). Contact the SME through the Infectious Disease Branch main line 510-620-3434, if additional testing is requested.

IV. CASE MANAGEMENT AND PUBLIC HEALTH CONTROL MEASURES

A. Investigation Recommendations

In general, the goals of investigation are to identify source of transmission, ensure appropriate isolation and treatment of patients, and identify contacts who may require post-exposure prophylaxis or monitoring. Please see **Section IV. D.** for discussion of contacts and post-exposure prophylaxis.

Investigation and management of sporadic cases and outbreaks in the healthcare setting:

Long-term care settings/Skilled nursing facilities

- For iGAS infections that arise in a licensed long-term care/skilled nursing care facility, LHD may contact the HAI program at HAIprogram@cdph.ca.gov for consultation and technical assistance (including onsite infection prevention assessment). Outbreaks in these settings may span several months to years. Vigilance in identifying cases and prompt investigation are crucial as these patients tend to have very high morbidity and mortality.
- If a resident with iGAS is identified, the facility should:

  - Ensure appropriate terminal cleaning of facilities and rooms used by case.
  - Identify close contacts who may be at risk for iGAS and consider antibiotic chemoprophylaxis (please see **Section IV. D.** for more information on contact management).
  - Consider resident and staff notification as per Council for Outbreak Response: Healthcare-Associated Infections and Antimicrobial Resistance (CORHA) Framework for HAI Outbreak Notification.
  - Provide education to staff on signs/symptoms of GAS and iGAS infection, hand hygiene and other infection control practices including adherence to sick leave policies.
  - Review infection prevention practices including hand hygiene, wound care, personal protective equipment, and environmental cleaning practices.
  - Request the clinical lab save isolates and forward to local public health laboratory.
- In addition, the facility should monitor for additional cases:
  - Conduct active surveillance for additional cases and review records for prior previously unidentified cases within past 6 months. This includes review of infection control logs to identify both invasive and non-invasive cases of GAS among residents.
  - Review employee records to identify facility staff ill with invasive and non-invasive GAS infections.
  - Consider need for cohorting and screening of other residents if other cases are identified within the facility. Consider also screening available facility staff for GAS colonization.
  - Ensure that records are maintained for staffing patterns, wound care, and resident room histories to assist with outbreak investigation during the active surveillance period.
  - Continue prospective active monitoring for at least 6 months.

Acute care healthcare facilities:

- For iGAS infections that arise in the post-surgical period (during the hospital stay or up to 7 days after discharge), LHD may contact the HAI Program at HAIprogram@cdph.ca.gov for additional guidance.
- For iGAS infections that arise in the post-partum setting (up to 7 days post discharge from the hospital), any sign of sepsis is an obstetrical emergency. If either the mother or neonate has an iGAS infection, the other should be urgently offered chemoprophylaxis. Contact the HAI program as above.
- Consider patient and healthcare personnel notification as per Council for Outbreak Response: Healthcare-Associated Infections and Antimicrobial Resistance (CORHA) Framework for HAI Outbreak Notification.
- Have the clinical lab save isolates and forward to local public health laboratory.
- Identify additional cases associated with the facility (through retrospective review of records for 6 months and prospective surveillance for 6 months).

- Identify any healthcare personnel as possible asymptomatic colonized carriers/persons; review staffing rosters to identify shared personnel; and consider screening those personnel for asymptomatic carriage of GAS, especially in the postsurgical or postpartum setting.
- Identify close contacts who may be at risk for iGAS and consider antibiotic chemoprophylaxis (please see **Section IV. D.** for more information on contact management).

Investigation and management of sporadic cases outside of the healthcare setting:

A single case of iGAS is not reportable to the state. However, the LHD may be notified of a case, and public health follow up initiated, especially if the iGAS infection has an unusual presentation (e.g., travel related), involves a young child, or results in death. Potential follow-up scenarios include the following:

Household settings:

Identify any persons who had close contact to the patient within 7 days prior to infection, up to 24 hours post-appropriate antimicrobial therapy. Contacts who are considered high-risk of serious infection should be offered prophylaxis. If there are two or more cases of iGAS in a household within 30 days, offer prophylaxis to all household members. Additionally, if a high-risk contact resides in the household, consideration may be given to offering prophylaxis to the entire household in addition to the high-risk contact. See **Section IV. D.** for further instructions.

Schools, Daycares and other Childcare settings:

- The child or staff member (e.g., teachers, aides) with iGAS should be excluded for up to 24 hours post-antibiotic therapy initiation.
- Have the school notify other parents and staff and provide information on signs/symptoms of GAS/iGAS; please see **Appendix A**.
- Identify other cases of iGAS or GAS in other children or staff (e.g., asking the school to review attendance logs, discussion with school nurse). If additional cases are identified, assist the childcare setting with improved infection control procedures (See **Section IV. B.**).
- Identify any children or other contacts who may have had varicella or influenza infections within the past 14 days (within 0-14 days of case patient onset). GAS is a common bacterial cause of coinfections which can result in necrotizing fasciitis, bacteremia, and other invasive illnesses. If children or staff are identified with recent or current varicella infections, recommend varicella vaccination for post-exposure prophylaxis to children who have not been previously immunized and eligible to receive vaccination. If children or staff are identified with recent or current influenza infections within the past 14days, recommend influenza vaccination for those not previously vaccinated.
- Ensure that the childcare setting conducts surveillance for additional iGAS cases up to 30 days from the last case.

B. Infection Control Measures

- Stress hand washing and personal hygiene for both ill persons and their contacts.
- In facilities such as schools, dormitories, long-term care facilities, etc. perform enhanced terminal cleaning of bedrooms, bathrooms, and any other shared spaces where there may be many touch surfaces. A 1:10 parts bleach to water solution may be used. Additional cleaning guidance is available from the CDC.

C. Management of Cases

There are no specific applicable California codes or regulations guiding the management of cases of iGAS. All cases with GAS infection should be educated regarding disease transmission and appropriate infection control measures. Drainage and secretion precautions may be terminated following 24 hours after effective antibiotic therapy.

D. Management of Contacts:

Close Contacts

Close contacts are defined as persons who have had prolonged exposure to the iGAS patient during the 7 days prior to onset of symptoms and for up to 24 hours after the patient was started on antibiotic treatment. In general, most classmates, school staff, work colleagues, and social or sports contacts of a case are not considered close contacts with the following exceptions:

- Household contacts: person who has spent 24 hours in the same household as the patient during the seven days prior to the case patient's symptom onset
- University or boarding school attendees: students who share a kitchen in a residence hall and roommates
- Persons who have had direct mucous membrane contact with oral or nasal secretions, or contact with open skin lesion (e.g., intimate partners, contact with secretions in a healthcare setting such as CPR or suctioning without appropriate personal protective equipment)
- Children and staff of home or family run daycare centers
- Injection drug users who have shared drug paraphernalia equipment with the case
- Residents of long-term care facilities, prisons, juvenile detention, or other congregate facilities--public health should be consulted to determine which residents are most at risk based on exposure and other risk factors for iGAS

There are no specific applicable California codes or regulations guiding the management of contacts. However, close contacts of cases with iGAS should receive education about the clinical signs/symptoms of GAS infection, including iGAS, and importance of seeking care early if signs/symptoms do arise. If they fall into the high-risk category, they may be considered for post-exposure prophylaxis (below).

High Risk Contacts and Post-exposure Prophylaxis

Post-exposure prophylaxis (PEP) may be considered for some people following exposure to patients with iGAS infections to prevent subsequent illness. Although the CDC does not routinely recommend chemoprophylaxis for most household contacts* of iGAS cases, PEP may be considered for household members or other close contacts who are considered to be high risk for iGAS. This includes persons who are aged ≥65 years or <28 days (i.e., neonates) or who otherwise have an increased risk for iGAS, such as pregnant women at ≥ 37 weeks or up to 28 days postpartum, persons with diseases impacting the immune system such as HIV infection, diabetes, cancer, or heart disease; use of injection drugs, steroids, or medications to suppress the immune system; or persons with onset of influenza or varicella infection within the past 14 days.

The CDC does not recommend routine use of culture to identify household contacts who are colonized. Household contacts should watch for signs and symptoms of iGAS disease for 30 days after exposure.

*The CDC defines a household contact as a person who has spent 24 hours in the same household as the patient during the 7 days prior to the case patient's symptom onset.

CDC PEP recommendations:

Dosing information can be found at: Prevention of Invasive Group A Streptococcal disease among Household Contacts of Case Patients and among Postpartum and Postsurgical Patients: Recommendations from the Centers of Disease Control and Prevention (https://academic.oup.com/cid/article/35/8/950/330363).

Please see **Section VI, Additional Resources**, for detailed information.

E. Management of Persons Colonized with GAS (i.e., carriers):

In general, detection of carriers is not routinely recommended except in special settings (e.g., concern for nosocomial transmission).

V. APPLICABLE STATE STATUTES AND REGULATIONS

A. California Code of Regulations, Title 17, Public Health, Section 2500:

- Outbreaks of any disease, including GAS/iGAS, and individual GAS meningitis cases are reportable.
- LHDs may have their own reporting requirements for GAS and iGAS.

B. California Code of Regulations, Title 22, Division 5 Licensing and Certification of Health Facilities, Sections 70737 (ACH) and 72541 (SNF):

- Occurrences such as outbreaks and unusual occurrences which threaten the welfare, safety or health of patients, personnel or visitors in licensed healthcare facilities are reportable.

VI. ADDITIONAL RESOURCES

A. General Information/Education

- Amy E Bryant and Dennis L. Stevens. (2015). *Streptococcus pyogenes* In J.E. Bennett, R. Dolin, and M.J. Blaser Mandell, Douglas, and Bennett's Principles and Practices of Infectious diseases (pp2285-2299) Philadelphia: Churchill Livingstone.
- Factor SH, Levine OS, Schwartz B et al. Invasive group A streptococcal disease: risk factors for adults. *Emerg Infect Dis* 2003; 9(8):970-977
- CDC Group A Streptococcal (GAS) Disease webpage https://www.cdc.gov/groupastrep/index.html
- CDC GAS Disease Outbreaks and Public Health Response webpage https://www.cdc.gov/groupastrep/outbreaks.html

B. Guidelines on treatment and prevention and communicable disease control:

- American Academy of Pediatrics. [Group A Streptococcal Infections]. In: Kimberlin DW, Brady MT, Jackson MA, Long SS, eds. *Red Book: 2015 Report of the Committee on Infectious Diseases.* 30th ed. Elk Grove Village, IL. American Academy of Pediatrics, 2015:732-744.
- The Prevention of Invasive Group A Streptococcal Infections workshop Participants. Prevention of Invasive Group A Streptococcal Disease among Household Contacts of Case Patients and among Postpartum and Postsurgical Patients: Recommendations from the Centers for Disease Control and Prevention. *Clin Infect Dis* 2002; 35(8): 950-59.
- American Public Health Association. [Streptococcal]. In: Heymann, David L., ed. Control of Communicable Diseases Manual.20th Ed. Washington, DC. American Public Health Association; 2015:581–9.
- Jordan HT, Richards CL Jr, Burton DC, Thigpen MC, Van Beneden CA. Group A Streptococcal Disease in Long-Term Care Facilities: Descriptive Epidemiology and Potential Control Measures. *Clin Infect Dis*. 2007;45(6):742–52.
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- Adebanjo T, Mosites E, Van Beneden CA, Onukwube J, Blum M, Harper M, Rudolph K, Frick A, Castrodale L, McLaughlin J, Bruce MG, Gounder P.Risk factors for group A *Streptococcus* colonization during an outbreak among people experiencing homelessness in Anchorage, Alaska, 2017. *Clin Infect Dis.* 2018 May 18. [Epub ahead of print]
- Mosites E, Frick A, Gounder P, Castrodale L, Li Y, Rudolph K, Hurlburt D, Lecy KD, Zulz T, Adebanjo T, Onukwube J, Beall B, Van Beneden CA, Hennessy T, McLaughlin J, Michael B. Outbreak of invasive infections from subtype *3* group A *Streptococcus* among homeless adults — Anchorage, Alaska, 2016–2017. *Clin Infect Dis*. 2017;66(7):1068–74.
- Kobayashi M, Lyman MM, Francois Watkins LK, Toews K, Bullard L, Radcliffe RA, Beall B, Langley G, Van Beneden C, Stone ND. A cluster of group A streptococcal infections in a skilled nursing facility—the potential role of healthcare worker presenteeism. CDC: http://www.cdc.gov/hepatitis/hev/efaq.htm

C. For the Public:

CDPH Group A *Streptococcus* fact sheet

https://www.cdph.ca.gov/Programs/CID/DCDC/CDPH%20Document%20Library/GASFactSheet.pdf

VII. UPDATES

Original version finalized and completed on March 23, 2023.

Appendix A
Template Letter for School/Daycare

Dear Parent or Guardian:

The X Department of Public Health have been notified that a child/staff member at the school/daycare has been diagnosed with invasive Group A *Streptococcus* Disease (GAS). Most infections caused by GAS are mild for example, strep throat or some minor skin infections, but in some instances, disease can be more serious.

If your child has symptoms of a sore throat, fever, or skin infection in the next 30 days, we recommend that you take your child to their provider along with this letter to be assessed and tested and treated if needed. If the provider diagnoses your child with GAS infection, your child will need to stay home from school/daycare for 24 hours following the start of the antibiotics.

In very rare cases, this infection can be more serious and cause invasive disease. The risk of another case of invasive Group A *Streptococcus* disease at the school/daycare is very rare, however, it is important to know the signs and symptoms.

These symptoms include:

- High fever
- Muscle aches or pain
- Unexplained diarrhea or nausea and vomiting

If your child becomes ill with these symptoms, please seek care immediately.

At this time, it is safe for your child to continue their current routine at school as long as they feel well. We remain in contact with the school/daycare in case there are further cases.

Sincerely,

X Department of Public Health