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Outbreak of a Rare Subtype of Group A *Streptococcus* — Alaska, 2016–2017

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Introduction

Group A *Streptococcus* (GAS) is a gram-positive bacterium that is transmitted from person-to-person through respiratory droplets and skin contact. GAS asymptomatically colonizes various body sites, including the oropharynx, non-intact skin, genital mucosa, and rectum. It can also cause a range of illnesses, from mild disease like strep throat or impetigo, to severe invasive disease such as sepsis, necrotizing fasciitis, streptococcal toxic shock syndrome (STSS), and pneumonia. There are over 200 molecular subtypes of GAS, which are based on sequences of a portion of the *emm* gene which encodes the bacterial cell surface M virulence protein (*emm* types).[1] In Alaska, the Alaska Section of Epidemiology (SOE) and the Centers for Disease Control and Prevention (CDC) Arctic Investigations Program (AIP) jointly conduct surveillance for cases of invasive GAS (iGAS). During 2011–2016, 60–90 cases, representing 8–10 *emm* types, were identified each year.[2] In general, Alaska has a higher incidence of iGAS than the rest of the United States (11.4 vs. 4.8 per 100,000 persons in 2015, respectively).[3,4]

Invasive GAS outbreaks have been reported in healthcare settings and long-term care facilities throughout the United States.[5-8] Increases in the number of iGAS cases caused by a single *emm* type have also been identified in community settings.[9-11] For healthcare-associated outbreaks, CDC guidelines recommend testing staff who are linked to infected patients and decolonizing those who are found to carry GAS.[12] For sporadic, non-outbreak cases of invasive disease, CDC recommends that providers consider offering chemoprophylaxis to all household members at increased risk for contracting a secondary case of invasive disease (e.g., persons aged ≥65 years; those who use intravenous drugs; American Indian/Alaska Native people; and those with diabetes, cancer, or human immunodeficiency virus (HIV) infection).[12] However, the guidelines do not address responding to community iGAS outbreaks.

In 2016, cases of iGAS caused by a rare subtype, *emm26.3*, were identified in Alaska through routine surveillance. In contrast to the sporadic cases of iGAS that had been detected in Alaska in the past, cases of *emm26.3* iGAS were clustered temporally and geographically. The *emm26.3* subtype was first documented in 2000 in Kenya, and it has been an occasional source of invasive disease in the Middle East; *emm26.3* iGAS had not been identified in Alaska prior to 2016.[1,2]

This report describes the investigation of an ongoing outbreak of *emm26.3* iGAS in Alaska.

Methods/Results

iGAS is a reportable condition in Alaska. Clinical laboratories forward GAS isolates to the AIP laboratory, which conducts confirmatory testing, molecular typing, and antimicrobial susceptibility testing. A case of iGAS is defined as the isolation of GAS from a normally sterile site in a person living in Alaska. Isolates from a nonsterile site are counted if the patient was diagnosed with necrotizing fasciitis or STSS. For each case, AIP collects additional information on clinical presentation and outcomes through medical records reviews. During routine surveillance, the molecular typing and medical records review at AIP can occur up to 2 months after the case is first reported by a clinical laboratory.

Initial identification of emm26.3 GAS

In April 2016, the AIP laboratory identified a case of *emm26.3* iGAS through a query of the CDC *Streptococcus* laboratory database.[13] The case occurred in February 2016 in a patient living in a village near Fairbanks.

Early Investigation

By July 2016, 11 cases of *emm26.3* iGAS had been identified in Fairbanks and the surrounding villages. Nine (82%) patients had underlying alcohol-use disorders; two (18%) patients died. The patients' medical records indicated that they lived in a number of different communities in the

Interior region and no links between patients were identified.

During July–August 2016, three cases of *emm26.3* iGAS were detected in Anchorage. All three cases occurred in persons experiencing homelessness. In consultation with CDC subject matter experts in Atlanta, SOE, AIP, and the Municipality of Anchorage Department of Health and Human Services (MOA) launched an investigation to evaluate sources of transmission and characterize the clinical and epidemiological features of *emm26.3* iGAS.

Beginning in September 2016, AIP implemented enhanced surveillance methods for iGAS whereby molecular typing and medical records review were completed within 2 weeks of an identified case. At this time, a sporadic case of *emm26.3* iGAS was also identified in the Yukon-Kuskokwim (YK) Delta region.

To ascertain risk factors for disease and the clinical characteristics of *emm26.3* iGAS, patient medical records were reviewed using a standard chart abstraction form. Medical records of persons admitted to Fairbanks Memorial Hospital, the Alaska Native Medical Center, or Alaska Regional Hospital with infections caused by a non-*emm26.3* GAS subtype within the same month as the outbreak-associated case were also reviewed. The *emm26.3* iGAS cases were compared with non-*emm26.3* iGAS cases using Chi square and linear regression analysis.

In October 2016, a rapid increase in the number of *emm26.3* iGAS cases was detected in Anchorage. By the end of October, seven additional cases had been identified. At this point, the mean age of patients with *emm26.3* iGAS in Anchorage was 52 years; 70% were male, 90% were homeless, and 70% had recent history of alcohol misuse.

Phase 1 Response

Beginning in October 2016, *emm26.3* iGAS patients in Anchorage were interviewed using a questionnaire. Information was requested regarding the locations that patients had frequented the month before becoming ill and their close contacts. Close contacts were defined as persons who shared drinking containers or utensils, or were close enough to hug or touch. Close contacts were offered a letter to bring to their healthcare provider explaining the situation and the recommended chemoprophylaxis.

On November 29, 2016, a Public Health Advisory was sent out to local hospitals describing the outbreak.[14] Flyers and fact sheets were distributed with signs and symptoms of GAS infection to staff and clients at several facilities providing services to persons experiencing homelessness.

On December 5, 2016, voluntary testing for GAS colonization was offered in the shelter that was most commonly mentioned in the patient interviews (Shelter A). Oropharyngeal and skin swab specimens were tested for GAS at the Alaska State Public Health Laboratory (ASPHL). Positive specimens were forwarded to the AIP laboratory for confirmation and molecular subtyping.

Concurrently with the other outbreak response actions, healthcare providers at Shelter A's onsite clinic agreed to increase the hours of operation in order to promote early identification of cases. From December 12, 2016 through January 15, 2017, the Alaska Native Medical Center and Alaska Regional Hospital supported enhanced wound surveillance by donating laboratory services to culture wound swabs taken by the clinic.

By the end of December, 26 cases of *emm26.3* iGAS had been identified in Anchorage. Of the 16 (61%) patients who were located and agreed to be interviewed, 14 (88%) had received services at Shelter A and 5 (31%) provided information about their close contacts. For those contacts with sufficient follow-up information, a letter was provided that they were instructed to take to their healthcare provider, which outlined CDC's recommendations for chemoprophylaxis.

A total of 132 Shelter A guests and 5 staff volunteered to participate in a GAS colonization survey. Of the shelter guests, 11 (8%) had GAS colonization by any *emm*-type and six (5%) were carrying *emm26.3* GAS. No shelter staff were found to be colonized with GAS. Guests who were positive for any type of GAS were contacted and offered antibiotic chemoprophylaxis.

Local hospital volunteers extended the Shelter A clinic hours for approximately 1 month to help promote early identification of potentially infected wounds. Of the 6 clinic patients receiving a wound culture, one was found to be carrying *emm26.3*.

Despite the implementation of these targeted interventions, the number of invasive cases detected in January exceeded the number in detected in December (Figure). Upon further discussion with subject matter experts at CDC-Atlanta, the outbreak investigation team developed a revised response plan.

Phase 2 Response

The objective of the revised response was to decrease the bacterial colonization of all persons experiencing homelessness by offering a single dose of antibiotics and distributing skin antiseptic to persons using showering facilities in shelters. Given concerns about compliance with a multi-day course of antibiotics, 1 gram of azithromycin in a single dose was determined to likely be the safest, most cost-effective, and most logistically feasible option for this situation.[15-17] A team from CDC Atlanta traveled to Anchorage to help evaluate the intervention.

During February 13–17, teams of 10–12 physicians, pharmacists, nurses, and public health staff visited six homeless services sites that were most commonly mentioned in patient interviews. At each site, the intervention team approached clients to provide information about the outbreak and discuss the risks and benefits of taking azithromycin. Clients who consented to take azithromycin were evaluated by a clinical provider for potential contraindications and drug-drug interactions before they received azithromycin.

The intervention team also offered clients the opportunity to participate in a baseline GAS colonization survey. We interviewed consenting participants regarding their risk factors for GAS colonization and obtained oropharyngeal and non-intact skin (e.g., wounds, dermatitis, and insect bites) swabs to test for GAS colonization. The AIP laboratory tested the swab specimens for GAS identification and molecular subtype determination. We evaluated risk factors for GAS colonization using logistic regression.

We provided 300 individual-sized bottles of chlorhexidine to homeless showering facilities to replace soap.

The intervention team repeated the colonization survey after 4 weeks to determine if the intervention affected colonization prevalence and to guide further intervention if the Phase 2 response was not successful in reducing the number of cases.

Over the course of eight intervention events at six homeless services sites, the response teams evaluated 484 candidates for chemoprophylaxis and dispensed a single dose of azithromycin (1 g) to 394 (81%) of the persons evaluated.

During the week of the intervention, two new iGAS cases were detected at one of the intervention sites. The response team returned to this site the following week to again offer the antibiotic chemoprophylaxis intervention.

A total of 289 participants volunteered to be tested for GAS colonization at baseline (concurrent with the administration of the antibiotic). Of these participants, 12 (4%) were colonized with *emm26.3* GAS. GAS colonization was associated with sharing blankets (odds ratio [OR]: 3.7; 95% Confidence Interval [CI] 1.7–8.4) and sharing drink containers (OR: 3.4; 95% CI: 1.5–7.7).

In March 2017, 298 participants volunteered to be tested for GAS colonization during follow-up testing at the same sites. Of these participants, 98 (33%) were repeat participants from the baseline survey. Overall, 4 (1%) participants were colonized with *emm26.3* at follow-up. None of the participants who had received the antibiotics were still colonized with *emm26.3* at follow-up.

Despite the efforts to distribute chlorhexidine to showering facilities, a small proportion (25%) of participants recalled seeing the antiseptic available, and fewer (12%) participants reported using it.

Between February 18 and April 1, 2017, 5 additional cases of *emm26.3* GAS invasive disease were identified throughout Alaska; one was in a patient experiencing homelessness.

Summary Characteristics of Cases

Overall, 54 cases of *emm26.3* iGAS were identified statewide between February 2016 and April 1 2017: 11 cases were detected in Fairbanks from February 2016 to July 2016, 41 cases were detected in Anchorage from July 2016 to April 2017, and two cases were detected in the Yukon-Kuskokwim Delta in September 2016 and March 2017. Overall, 38 (70%) patients were diagnosed with underlying alcohol use disorders. In Anchorage, 35 (85%) patients were experiencing homelessness. Of the six who were not currently homeless, four (67%) had potential contact with homeless services or persons.

Of the 54 patients with *emm26.3* iGAS infection, 39 (72%) had an initial clinical presentation of cellulitis or skin abscess. All were hospitalized; 28 (52%) were diagnosed with sepsis or septic shock, five (9%) with STSS, and 14 (26%) with necrotizing fasciitis. Limb- or life-threatening complications of iGAS were observed in eight patients (three patients required limb amputations and five patients died). The median length of stay in the hospital was 11 days (range: 1–107 days).

The clinical characteristics of *emm26.3* iGAS cases were more severe compared to other *emm* types that were hospitalized in Alaska at the same time (Table). Patients with *emm26.3* were more likely to have a diagnosis of sepsis, necrotizing fasciitis, or STSS (p=0.02). Patients with *emm26.3* also had a longer hospital stay (Table).

The *emm26.3* isolates from invasive disease cases were susceptible to all tested antimicrobials, including penicillin, erythromycin, ceftriaxone, tetracycline, chloramphenicol, and levofloxacin.

Discussion

This large iGAS outbreak was caused by a novel *emm* type (*emm26.3*) and disproportionately affected persons experiencing homelessness and alcoholism. Due to the numerous challenges associated with controlling the outbreak, a novel chemoprophylaxis strategy was undertaken. After the intervention, case counts and colonization decreased.

This is the first outbreak of iGAS to be identified in Alaska since GAS surveillance began in 2000. The *emm26.3* subtype appears be more virulent than other iGAS subtype cases over the same time period (and during previous years).[2] This could be due to unique biological characteristics of this strain or low population immunity to the new strain. When a novel GAS type is introduced into a population with low immunity, outbreaks and more severe sequelae have been shown to occur.[11]

Cases associated with *emm26.3* were first detected in Fairbanks but did not appear to be epidemiologically-linked to each other. Once the bacteria was introduced into a vulnerable population living in close quarters in Anchorage, the number of cases dramatically increased. Although we did not identify direct epidemiological links between invasive cases, risk factor data suggested that sharing drinking containers or blankets was more common among those carrying the bacteria.

Recent outbreaks of iGAS are reported to have occurred among homeless persons globally, commonly affecting persons using injection drugs.[18-20] However, this outbreak commonly affected persons who were diagnosed with underlying alcohol misuse, rather than injection drug use.

To control this outbreak, we initially attempted a targeted response by testing staff and residents and offering GAS-positive persons one of three recommended chemoprophylaxis courses. After this targeted intervention, case counts did not decrease. Therefore, we subsequently offered chemoprophylaxis to as many people in the homeless community as possible. We opted to offer 1 gram of azithromycin as a single dose based on previous GAS colonization studies.[17] The number of *emm26.3* cases declined considerably in February through March 2017 as compared to monthly counts during October 2016 through January 2017.

We will continue to monitor cases of *emm26.3* iGAS and implement further control measures, as necessary. Health care providers should maintain a high index of suspicion for *emm26.3* iGAS infection among Anchorage patients experiencing homelessness and alcoholism.

Recommendations

1. Invasive GAS is reportable to SOE by both laboratories and providers (7 AAC 27.005 and .007). Invasive cases include all infections where GAS is isolated from a normally sterile site. Isolation of GAS from a non-sterile site, if accompanied by a diagnosis of necrotizing fasciitis or streptococcal toxic shock syndrome, is also reportable. Call 907-269-8000, or fax reports to 907-561-4239. Detailed information about all reportable conditions is available at: http://dhss.alaska.gov/dph/Epi/Pages/pubs/conditions/default.aspx
2. Health care providers should evaluate whether patients with iGAS have household members or close contacts who are at increased risk for invasive disease and consider offering them chemoprophylaxis (e.g., persons who are aged ≥65 years, have certain pre-existing conditions such as cancer or diabetes, or have certain concurrent infections such as chickenpox or HIV; see Table 2 in Reference 12 for a complete list).[12]
3. Healthcare providers should report suspected or confirmed clusters of iGAS to SOE at 907-269-8000. Cases diagnosed among patients who are post-surgical, postpartum, or living in a congregate setting such as a long-term care facility or homeless shelter, are of particular concern as special interventions and precautions may be necessary to control an outbreak in these settings.[21]

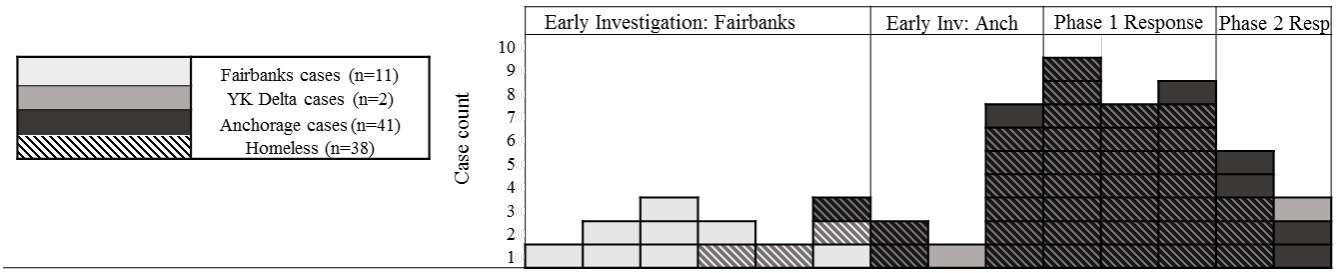
Table. Clinical Characteristics of Patients Diagnosed with *emm26.3* Invasive GAS Compared to Patients Diagnosed with Invasive GAS Caused by Other *emm* Types — Alaska 2016–2017

Characteristic	***emm26.3* cases (N=54)**	**Non-*emm26.3* cases (N=47)**	***P* value* for difference**
Age, mean (SD)	53 (11)	45 (22)	**<0.001**
Male sex, n (%)	37 (69%)	29 (62%)	0.57
Diagnoses, n (%)			
Cellulitis	33 (61%)	18 (38%)	**0.03**
Sepsis	28 (52%)	18 (38%)	0.17
Streptococcal Toxic Shock Syndrome	5 (9%)	3 (6%)	0.59
Necrotizing fasciitis	14 (26%)	5 (11%)	**0.05**
Pneumonia	7 (13%)	2 (6%)	0.27
Pharyngitis	1 (2%)	0 (0%)	0.35
Septic Arthritis	3 (6%)	3 (6%)	0.86
Length (days) of hospital stay, median (SD)	11 (22)	6 (10)	**0.02**
Admitted to ICU, n (%)	20 (37%)	12 (25%)	0.19
Required intubation, n (%)	4 (7%)	4 (9%)	0.86
Died, n (%)	5 (9%)	2 (4%)	0.32

Abbreviations: ICU- Intensive Care Unit; SD- standard deviation

**P values from Pearson's Chi square test or Fisher's exact test if expected counts ≤5*

Figure. Cases of Invasive Group A *Streptococcus emm* Subtype 26.3 and Response Activity Timeline (N=54) — Alaska, 2016–2017



Response Activity Timeline (2016–2017)	Feb	Mar	Apr	May	Jun	Jul	Aug	Sep	Oct	Nov	Dec	Jan	Feb	Mar
iGAS cases identified through routine *emm*-typing at AIP lab														
Two deaths occur in Fairbanks														
Consult with CDC-Atl regarding rare emm type														
Initial Fairbanks interviews														
Cases detected in Anchorage homeless community														
AIP increases frequency of *emm*-typing														
Outbreak investigation initiated														
Review of medical records to compare *emm*26.3 to other types and identify risk factors for *emm*26.3														
Interview patients to identify close contact and provide chemoprophylaxis														
Consult with CDC-Atl regarding increased case counts														
Public Health Alert Network message to providers														
Provide education materials to shelter guests and staff to improve early identification of cases														
Test shelter guests and staff for GAS skin and throat colonization														
Collaborate with Providence Hospital, South Central Foundation to increase shelter clinic hours for early identification/care access														
Shelter clinic increases surveillance for wound infections														
Consult with CDC-Atl as case counts remain high														
Launch single dose azithromycin intervention														
Team from Atlanta evaluates baseline GAS colonization and risk factors														
Chlorhexidine distributed to homeless shower facilities														
Revisited intervention site with cluster of cases to provide full course chemoprophylaxis														
Follow-up evaluation of GAS colonization and risk factors														

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