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Multistate Outbreak of Respiratory Infections Among Unaccompanied Children, June 2014–July 2014

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Background. From January 2014–July 2014, more than 46 000 unaccompanied children (UC) from Central America crossed the US–Mexico border. In June–July, UC aged 9–17 years in 4 shelters and 1 processing center in 4 states were hospitalized with acute respiratory illness. We conducted a multistate investigation to interrupt disease transmission.

Methods. Medical charts were abstracted for hospitalized UC. Nonhospitalized UC with influenza-like illness were interviewed, and nasopharyngeal and oropharyngeal swabs were collected to detect respiratory pathogens. Nasopharyngeal swabs were used to assess pneumococcal colonization in symptomatic and asymptomatic UC. Pneumococcal blood isolates from hospitalized UC and nasopharyngeal isolates were characterized by serotyping and whole-genome sequencing.

Results. Among 15 hospitalized UC, 4 (44%) of 9 tested positive for influenza viruses, and 6 (43%) of 14 with blood cultures grew pneumococcus, all serotype 5. Among 48 nonhospitalized children with influenza-like illness, 1 or more respiratory pathogens were identified in 46 (96%). Among 774 nonhospitalized UC, 185 (24%) yielded pneumococcus, and 70 (38%) were serotype 5. UC transferring through the processing center were more likely to be colonized with serotype 5 (odds ratio, 3.8; 95% confidence interval, 2.1–6.9). Analysis of core pneumococcal genomes detected 2 related, yet independent, clusters. No pneumococcus cases were reported after pneumococcal and influenza immunization campaigns.

Conclusions. This respiratory disease outbreak was due to multiple pathogens, including *Streptococcus pneumoniae* serotype 5 and influenza viruses. Pneumococcal and influenza vaccinations prevented further transmission. Future efforts to prevent similar outbreaks will benefit from use of both vaccines.

Keywords. unaccompanied children; *Streptococcus pneumoniae*; influenza; outbreak; vaccination.

Unaccompanied children (UC), who are often from Central America, cross the US–Mexico border daily. UC apprehended by US Customs and Border Protection (CBP) can be referred to the US Department of Health and Human Services' (HHS) Office of Refugee Resettlement (ORR); most UC stay in ORR-funded care provider programs, including shelter facilities, until they are released to US sponsors who care for them while their immigration cases proceed. From January 2014 to July 2014, more than 46 000 UC entered the United States compared with approximately 16 800 for all of 2013 [1], precipitating a humanitarian crisis. The holding capacity at Border Patrol stations was exceeded, and the duration of stay at stations lengthened while additional shelter space was identified. Three temporary ORR-funded shelters were opened to accommodate the surge.

To relieve crowding at border stations, a CBP Processing Center was opened in Nogales, Arizona. UC aged 12–17 years were eligible to be transferred from Nogales to temporary shelters if they were medical cleared by HHS-deployed clinicians and received immunizations against measles, mumps, rubella, varicella, meningococcal disease, diphtheria, and pertussis. Pneumococcal vaccine is not routinely recommended for adolescents in any country, and influenza vaccine is not given during the interseasonal period. In Central America, many countries recently introduced 10-valent and 13-valent pneumococcal conjugate vaccine (PCV10, PCV13) in their infant immunization programs [2].

In July 2014, 4 children who had transited through the Nogales CBP Processing Center and were placed at a temporary ORR shelter at Naval Base Ventura County (NBVC) in California were hospitalized with acute respiratory illnesses, including pneumonia. Additional cases were reported at shelters in other states, signaling a possible widespread outbreak. There were no

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reports of any unusual increase in influenza activity or pneumococcal disease in surrounding communities [3]. However, seasonal influenza viruses and other respiratory viruses were circulating in the UC's countries of origin [4]. Because adolescents are typically at low risk for hospitalization from respiratory infections and because 4 such cases were identified at NBVC within 1 week, ORR requested the assistance of local, state, and federal partners to determine the magnitude and etiology of the outbreak, identify epidemiological risk factors for severe respiratory illness, and provide disease control recommendations.

PATIENTS AND METHODS

The investigation took place during July 2014–August 2014 at 3 temporary shelters (NBVC; Joint Base San Antonio–Lackland [JBSA–L], Texas; and US Army Garrison Fort Sill, Oklahoma) as well as 1 standard shelter in Baytown, Texas. Medical records were reviewed from an additional patient who was hospitalized from the Nogales CBP Processing Center.

Facility Descriptions

Nogales CBP Processing Center was established in June 2014 to temporarily house UC (approximate average duration of stay, ≤7 days). During June 2014–July 2014, 4809 UC transited through Nogales, with a maximum census of approximately 1200. The facility was a large, open-air warehouse. Children were housed by age and sex in separate areas that were divided by chain link fencing and contained mattresses side-by-side on the floor. Portable toilets were used for bathroom facilities. The facility had limited ability to isolate sick children. Medical screening and vaccine administration were initiated to clear children to be sent to a temporary shelter. From Nogales, UC could be sent to a temporary shelter if they were aged 12–17 years and medically cleared and vaccinated, or to 1 of nearly 100 standard shelters. UC were also being transferred to standard shelters directly from CBP stations.

Temporary shelters on NBVC, JBSA–L, and Fort Sill were opened during May 2014–June 2014, with maximum capacities of approximately 575, 1200, and 1200 UC, respectively. On-site medical clinics and isolation areas were staffed 24 hours a day. The standard shelter in Baytown had a capacity of 168 UC. All children at the standard shelter received medical screening within 48 hours of arrival. Healthcare providers reported selected illnesses or symptoms of concern, but surveillance for severe respiratory disease was not performed consistently across shelters.

Investigation of Hospitalized Episodes of Acute Respiratory Illness

Medical record reviews were conducted among hospitalized UC with acute respiratory illness to gather demographic, epidemiological, and clinical information. Blood cultures, Binax NOW urinary pneumococcal antigen test, influenza rapid tests, and other diagnostic tests (eg, rhinovirus, respiratory syncytial virus, Group A *Streptococcus*) were performed at the treating physician's discretion.

Influenza-like Illness Investigation

Influenza-like illness (ILI) was defined as a measured temperature ≥100°F plus cough or sore throat with onset during June 2014–July 2014. ILI cases were found through routine medical screening (Baytown, NBVC, JBSA–L, Fort Sill), self-reporting (Baytown, NBVC, JBSA–L, Fort Sill), and active screening for ILI (ie, all children were seen at the clinic) at 1 facility (NBVC) during 25 June 2014–1 August 2014. Active screening was only conducted at 1 facility where the outbreak was first recognized. It was part of the early outbreak response but was not logistically feasible at all facilities. Assenting UC with ILI were interviewed, and nasopharyngeal (NP) and oropharyngeal (OP) specimens were collected [5]. Epidemiologic data, including transit histories, were collected from the interviews and CBP-maintained apprehension and transfer database files. Shelter medical chart reviews were completed where available. Hospitalized cases were not included as ILI cases.

Pneumococcal Colonization Assessment

Because a significant proportion of hospitalized cases had blood cultures positive for *Streptococcus pneumoniae* (pneumococcus) serotype 5, which is rarely a cause of disease or colonization in US adolescents, a pneumococcal colonization assessment was conducted. An additional NP swab was collected to assess pneumococcal colonization among all assenting symptomatic and asymptomatic UC at NBVC (18 July 2014) and Baytown (24 July 2014) and among a convenience sample at JBSA–L and Fort Sill (28 July 2014). To identify potential transit exposures, additional data were collected using CBP-maintained apprehension and transfer database files.

Laboratory Investigation

Available pneumococcal isolates from blood cultures of hospitalized patients were obtained for serotyping. For ILI cases, NP and OP swabs were analyzed using TaqMan Array Card (TAC, Life Technologies), which is a real-time polymerase chain reaction (PCR) platform that simultaneously detects multiple respiratory agents, including adenovirus, enteroviruses, influenza A and B viruses, parainfluenza viruses (1–4), rhinoviruses, Group A *Streptococcus*, *Haemophilus influenzae*, *Mycoplasma pneumoniae*, *Staphylococcus aureus*, *S. pneumoniae*, *Chlamydophila pneumoniae*, *Bordetella pertussis*, *Legionella* spp., coronaviruses, respiratory syncytial virus, and human metapneumovirus [6]. Influenza- and enterovirus-positive samples were confirmed and typed by real-time reverse transcriptase PCR and viral protein 1 reverse transcription PCR followed by Sanger sequencing, respectively [7, 8].

To assess pneumococcal colonization, calcium alginate NP specimens were collected; placed into skim milk, tryptone, glucose, and glycerin media; and kept at −70°C during transport. NP specimens were inoculated into enrichment broth

media, incubated for 6 hours, subcultured onto blood-agar plates, and incubated overnight [9]. *Streptococcus pneumoniae* colonies were identified using bile solubility and optochin susceptibility and serotyped by Quellung reaction. Blood isolates of *S. pneumoniae*, all serotype 5, from hospitalized children and a systematic stratified sample of colonization strains by shelter were further characterized using multilocus sequence typing (MLST), serotyping, antimicrobial susceptibility testing [10], and core genome comparisons using whole genome sequencing generated by the Illumina MiSeq sequencing platform [11].

Statistical Analyses

Frequencies of demographic and clinical characteristics among hospitalized cases and pathogens among ILI cases were calculated. Pneumococcal serotypes identified in colonization specimens were categorized according to those included in PCV10 (1, 4, 5, 6B, 7F, 9V, 14, 18C, 19F, 23F) and PCV13 (PCV10 serotypes plus 3, 6A, and 19A). We evaluated the bivariate association of the UC's transit exposures with pneumococcal colonization (for all serotypes and serotype 5) by calculating prevalence ratios (PRs) and 95% confidence intervals (CIs). Data analyses were conducted using SAS 9.3 (SAS Institute, Inc., Cary, North Carolina).

Ethics

Protocol and case investigation forms were reviewed at the Centers for Disease Control and Prevention (CDC) and determined to be public health response and not research; thus, institutional review board review was not required. Written informed consent was obtained from ORR, the legal custodian of UC, and UC provided verbal assent. All interviews were conducted in Spanish.

RESULTS

Investigation of Hospitalized Episodes of Acute Respiratory Illness

We identified 15 hospitalized patients in 4 states (Figure 1); hospitalizations occurred from June 17 2014–19 July 2014 (Figure 2). At the time of admission, 7 (47%) patients were at NBVC, 3 (20%) at Fort Sill, 2 (13%) each at Baytown and JBSA–L, and 1 (7%) at Nogales. The median age of hospitalized patients was 15 years (range, 13–17); 12 (80%) were male. Fourteen (93%) patients had radiographically confirmed pneumonia, and 6 (43%) patients received care in the intensive care unit. Median duration of hospitalization was 8 days (interquartile range, 3–19), and no patients died. Many patients originated from El Salvador (47%) and Guatemala (33%); had transited through Reynosa, Mexico (40%); were apprehended near Hidalgo, Texas (53%); and were processed through Nogales, Arizona (71%) (Table 1). Median journey time was 8 days (range, 3–31) between start of migration and apprehension in the United States and 13 days (range, 2–28) from apprehension to symptom onset.

Of 15 hospitalized patients, 14 (93%) had blood cultures collected (Table 1); 6 (43%) were positive for *S. pneumoniae*, and all pneumococcal blood isolates were characterized as serotype 5 MLST 289 (ST289). Nine (60%) of the 15 hospitalized patients

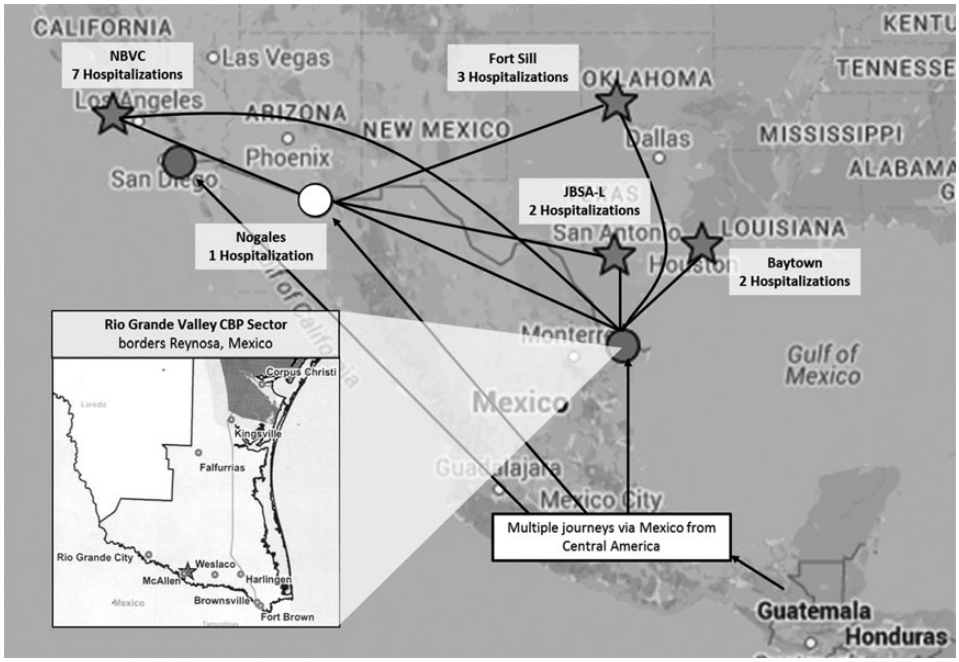

Figure 1. Geographic distribution of hospitalizations among unaccompanied children in multiple states during June 2014–July 2014. Black lines represent common journey paths. Stars represent shelters. White dot represents the US Customs and Border Protection (CBP) Processing Center. Gray dots represent border crossing areas. Abbreviations: JBSA–L, Joint Base San Antonio-Lackland; NBVC, Naval Base Ventura County.

were tested for influenza viruses; of these, 4 (44%) were positive: influenza A (3) and influenza B (1) virus. Two hospitalized patients were positive for both *S. pneumoniae* and influenza virus.

Influenza-like Illness Investigation

A total of 140 children had ILI across all 4 shelters. Among 48 (34%) children with ILI who had available specimens, 1 or more respiratory pathogens were detected in 46 (96%; Table 2). The most frequently identified bacteria were *H. influenzae* (n = 29, 60%), *S. pneumoniae* (n = 22, 46%), and Group A *Streptococcus* (n = 7, 15%). Rhinoviruses (n = 21, 44%), enteroviruses (n = 18, 38%), and influenza (n = 13, 27%) were the most commonly detected viruses. Six children (13%) had codetections with both influenza virus and *S. pneumoniae*.

Pneumococcal Colonization Assessment

Among 977 UC approached, 812 (83%) assented to NP swab collection; 774 (95%) had adequate bacterial growth (Table 3). Twenty-four percent (n = 185) of children were colonized with pneumococcus; NBVC and Fort Sill had the highest and lowest colonization rates of 31% and 11%, respectively. Six (0.1%) children had multiple pneumococcal serotypes. Serotype 5, included in both PCV10 and PCV13, was the most frequent colonizing serotype (n = 70, 38%). Fifty-six percent and 48% of pneumococci were contained in the PCV13 and PCV10 vaccines, respectively.

Risk Factors for Pneumococcal Colonization

In the bivariate analysis, any pneumococcal colonization among UC was associated with transiting through the Mexico border arrival location of Camargo, Mexico (PR, 2.2; 95% CI, 1.21–4.2), and the US border arrival locations of Brownsville, Texas (PR, 2.3; 95% CI, 1.4–3.8), Rio Grande City, Texas (PR, 1.8; 95% CI, 1.1–2.9), and Nogales CBP Processing Center, Arizona (PR, 1.7; 95% CI, 1.3–2.3; Table 4). Only transit through Nogales, Arizona, was associated with pneumococcal colonization with serotype 5 (PR, 3.8; 95% CI, 2.1–6.9).

Whole Genome Sequencing of Pneumococcal Serotype 5 Strains and Viral Subtyping

Analysis of the core genome of pneumococcal serotype 5 strains detected 2 related, yet independent, clusters, primarily differentiated by a resistance-conferring recombination event that encompassed the *folA* gene. These 2 distinct multilocus ST289 clusters were found among the 6 blood pneumococcal isolates and a sample of 31 NP pneumococcal isolates. One cluster was identified among 2 blood isolates and 10 NP isolates. A second cluster was identified among 4 blood isolates and 21 NP isolates. There was no association between cluster type and facility location or country of origin. Typing of available enterovirus-positive NP/OP specimens revealed 2 enterovirus types: EV-C105 (n = 16) and EV-C117 (n = 2); none were EV-D68. Among 13 influenza-positive NP/OP specimens, 8 (62%) were positive for only influenza A (H1N1)pdm09, 4 (31%) were positive for only influenza B, and 1 (8%) was positive for both influenza A(H1N1)pdm09 and influenza B.

Immunization Campaigns

As a result of the preliminary clinical, epidemiological, and laboratory findings, ORR instituted CDC's recommendation to

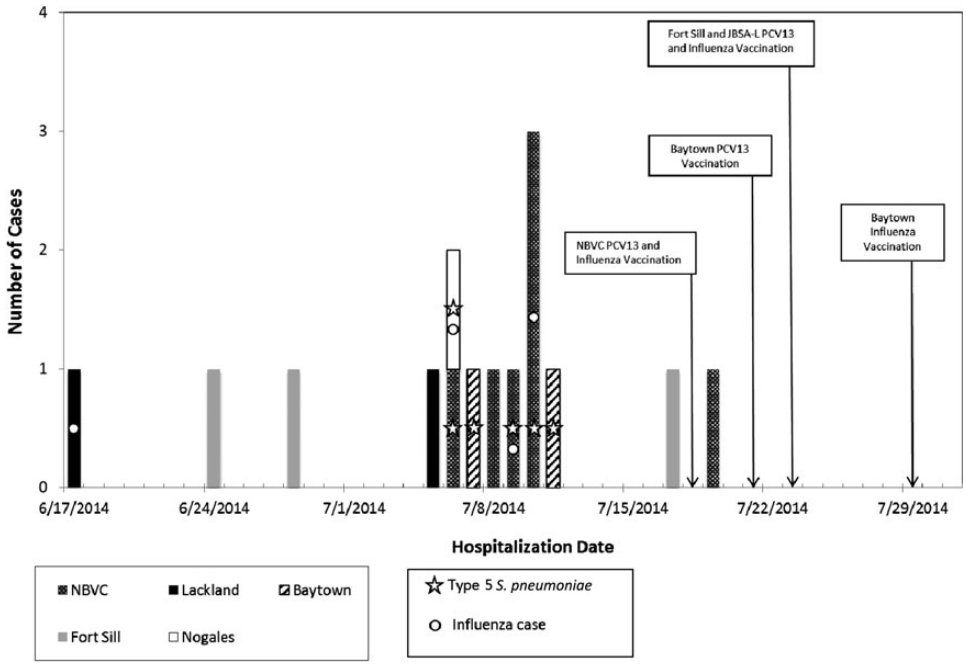

Figure 2. Temporal distribution of hospitalizations among unaccompanied children in multiple states during June 2014–July 2014. Abbreviations: JBSA–L, Joint Base San Antonio-Lackland; NBVC, Naval Base Ventura County; PCV13, 13-valent pneumococcal conjugate vaccine.

Table 1. Characteristics of Hospitalized Cases With Acute Respiratory Illness Among Unaccompanied Children in US Customs and Border Protection and Office of Refugee Resettlement Facilities, Multiple States, June 2014–July 2014

Characteristic	Total N = 15	Naval Base Ventura County n = 7	Baytown n = 2	Joint Base San Antonio n = 2	Fort Sill n = 3	Nogales n = 1
Country of origin, no. (%)[a]						
El Salvador	7 (47)	4 (57)	1 (50)	2 (100)	0 (0)	0 (0)
Guatemala	5 (33)	3 (43)	0 (0)	0 (0)	2 (67)	0 (0)
Honduras	2 (13)	0 (0)	1 (50)	0 (0)	1 (33)	0 (0)
Mexico border arrival location, no. (%)[a]						
Reynosa	6 (40)	3 (43)	0 (0)	1 (50)	2 (67)	0 (0)
Cananea	1 (7)	1 (14)	0 (0)	0 (0)	0 (0)	0 (0)
Sonoyta	1 (7)	0 (0)	0 (0)	0 (0)	1 (33)	0 (0)
US border arrival location, no. (%)[a]						
Hidalgo, Texas	8 (53)	3 (43)	2 (100)	1 (50)	2 (67)	0 (0)
Lukeville, Arizona	1 (7)	0 (0)	0 (0)	0 (0)	1 (33)	0 (0)
Nogales, Arizona	1 (7)	1 (14)	0 (0)	0 (0)	0 (0)	0 (0)
First CBP sector, no. (%)[a]						
Rio Grande Valley sector, Texas	11 (73)	5 (71)	2 (100)	2 (100)	2 (67)	0 (0)
Tucson sector, Arizona	1 (7)	1 (14)	0 (0)	0 (0)	0 (0)	0 (0)
Transit through Nogales CBP Processing Center, Arizona (n = 14), no. (%)	10 (71)	6 (100)	0 (0)	1 (50)	2 (67)	1 (100)
Median time from leaving country to US apprehension (IQR; n = 9), days	8 (3–31)	16 (7–31)	8 (7–8)	3 (N/A)	18 (8–27)	N/A
Median time from US apprehension to symptom onset (IQR; n = 10), days	13 (2–28)	9 (2–13)	13 (5–20)	24 (19–28)	19 (N/A)	12 (N/A)
Clinical lab results						
Streptococcus pneumoniae isolated from blood, n/tested (%)	6/14 (43)	3/7 (43)	2/2 (100)	0/1 (0)[b]	0/3 (0)	1/1 (100)
Influenza positive swab, n/tested (%)	4/9 (44)	2/5 (40)	0/1 (0)	1/1 (100)	0/1 (0)	1/1 (100)
Influenza A types, n (%)	3 (75)	1 (50)	. . .	1 (100)	. . .	1 (100)
Influenza B types, n (%)	1 (25)	1 (50)	. . .	. . .	. . .	. . .
S. pneumoniae and influenza A or B coinfection, n/tested for both (%)	2/8 (25)	1/5 (20)	0/1 (0)	. . .	0/1 (0)	1/1 (100)
Respiratory syncytial virus positive swab, n/tested (%)	0/4 (0)	0/4 (0)	. . .	. . .	. . .	. . .
Rhinovirus positive swab, n/tested (%)	1/1 (100)	. . .	. . .	1/1 (100)	. . .	. . .

Abbreviations: CBP, US Customs and Border Protection; IQR, interquartile range; NA, not applicable.

[a] Missing data for country of origin (n = 1), Mexico border arrival location (n = 7), US border arrival location (n = 5), and first CBP sector (n = 3).

[b] One Joint Base San Antonio-Lackland case had a positive Binax *S. pneumoniae* urine antigen test performed on pleural fluid.

vaccinate all UC with PCV13. Previous work with the US Food and Drug Administration resulted in extension of the expiration date of specific formulations of 2013–2014 influenza vaccines, which were administered to UC. Those in shelters with associated hospitalized cases were vaccinated during 18 July–29 July. No additional respiratory hospitalizations were detected after the immunizations were implemented.

DISCUSSION

We report evaluation of an outbreak of acute respiratory infections among UC from Central America at 3 temporary shelters, 1 standard shelter, and 1 CBP processing center in 4 states. This outbreak occurred among adolescents, an age group that typically has a low incidence of hospitalization due to respiratory infections [12, 13]. Multiple respiratory pathogens may have contributed to this outbreak. Among hospitalized children, *S. pneumoniae* (all characterized as serotype 5) and influenza viruses were most commonly detected. Among children with mild illness (ie, ILI) who were screened in shelters, rhinovirus, enterovirus, and influenza viruses A and B were commonly identified. We found high rates of pneumococcal colonization overall and specifically with serotype 5, which is rarely a cause of disease and colonization in US adolescents [14].

Several factors likely contributed to this outbreak. Children living in the Central American countries from which UC migrated have higher rates of respiratory illness [15] and increased rates of serotype 5 pneumococcal disease [16] compared with their US-born counterparts. UC did not benefit from PCV13 programs in El Salvador, Honduras, or Guatemala because each country introduced infant vaccination only recently (2010, 2011, and 2012, respectively) [17]. Adolescents would not have been vaccinated, and vaccine use among infants would not have reached levels adequate to confer herd protection to adolescents [18]. The influenza season started in Central

Table 2. Pathogens Detected From Unaccompanied Children With Influenza-like Illness Within Facilities Across Multiple States, July 2014–August 2014

Pathogens, no. (%)[a]	Total N = 48	Naval Base Ventura County n = 30	Baytown n = 6	Joint Base San Antonio-Lackland n = 4	Fort Sill n = 8
Haemophilus influenzae	29 (60)	21 (70)	2 (33)	3 (75)	3 (38)
Staphylococcus pneumoniae	22 (46)	17 (57)	1 (17)	3 (75)	1 (13)
Rhinoviruses	21 (44)	15 (50)	2 (33)	2 (50)	2 (25)
Enterovirus C105	16 (33)	10 (33)	2 (33)	1 (25)	3 (38)
Enterovirus C117	2 (4)	2 (7)	0 (0)	0 (0)	0 (0)
Group A *Streptococcus*	7 (15)	6 (20)	0 (0)	0 (0)	1 (13)
Influenza A(H1N1)pdm09 virus	8 (17)	5 (17)	1 (17)	1 (25)	1 (13)
Influenza B virus	4 (8)	4 (13)	0 (0)	0 (0)	0 (0)
Influenza A(H1N1)pdm09 virus and influenza B virus codetections	1 (2)	1 (3)	0 (0)	0 (0)	0 (0)
Adenovirus	4 (8)	3 (10)	0 (0)	0 (0)	1 (13)
Staphylococcus aureus	3 (6)	3 (10)	0 (0)	0 (0)	0 (0)
Parainfluenza viruses[b]	1 (2)	1 (3)	0 (0)	0 (0)	0 (0)
Mycoplasma pneumoniae	2 (4)	1 (3)	0 (0)	1 (25)	0 (0)
S. pneumoniae and influenza A or B codetections	6 (13)	4 (13)	1 (17)	1 (25)	0 (0)
Any virus	39 (81)	27 (90)	4 (67)	2 (50)	6 (75)
Any bacteria	36 (75)	27 (90)	2 (33)	4 (100)	3 (38)
Any pathogen	46 (96)	30 (100)	5 (83)	4 (100)	7 (88)

[a] Pathogens tested for using the TaqMan Array Card included adenovirus, enteroviruses, influenza A/B viruses, human metapneumovirus, parainfluenza viruses, rhinoviruses, respiratory syncytial virus, human coronaviruses, *Streptococcus pneumoniae*, Group A *Streptococcus, Haemophilus influenzae, Staphylococcus aureus, Bordetella pertussis, Legionella* spp., *Mycoplasma pneumoniae,* and *Chlamydophila pneumoniae*. Indeterminate TaqMan Array Card (TAC) results were classified as negative. Influenza- and enterovirus-positive samples from TAC were confirmed and typed by viral protein 1 reverse transcription polymerase chain reaction and then followed by Sanger sequencing.

[b] Parainfluenza virus type 4 only.

Table 3. *Streptococcus pneumoniae* Colonization in Multiple States, July 2014–August 2014

Serotype, no. (%)	Total N = 774	Naval Base Ventura County n = 383	Baytown n = 104	Joint Base San Antonio-Lackland n = 119	Fort Sill n = 168
Any type	185 (24)	118 (31)	14 (14)	34 (29)	19 (11)
PCV10 types[a]	88 (48)	65 (55)	4 (29)	11 (32)	8 (42)
PCV13 types[a]	103 (56)	75 (64)	4 (29)	16 (47)	8 (42)
Individual serotypes	N = 192[b]	N = 121	N = 14	N = 34	N = 23
005	70 (37)	58 (48)	2 (14)	5 (15)	5 (22)
003	14 (7)	10 (8)	0 (0)	4 (12)	0 (0)
013	8 (4)	6 (5)	1 (7)	1 (3)	0 (0)
23A	8 (4)	4 (3)	1 (7)	3 (9)	0 (0)
35B	7 (4)	5 (4)	0 (0)	1 (3)	1 (4)
16F	6 (3)	2 (2)	1 (7)	1 (3)	2 (9)
28A	5 (3)	2 (2)	2 (14)	1 (3)	0 (0)
07F	4 (2)	2 (2)	1 (7)	1 (3)	0 (0)
10A	4 (2)	2 (2)	0 (0)	2 (6)	0 (0)
008	3 (2)	2 (2)	1 (7)	0 (0)	0 (0)
037	3 (2)	1 (1)	0 (0)	1 (3)	1 (4)
09V	3 (2)	1 (1)	0 (0)	1 (3)	1 (4)
10F	3 (2)	0 (0)	2 (14)	0 (0)	1 (4)
18C	3 (2)	0 (0)	0 (0)	3 (9)	0 (0)
18F	3 (2)	3 (2)	0 (0)	0 (0)	0 (0)
19F	3 (2)	2 (2)	0 (0)	0 (0)	1 (4)
35F	3 (2)	2 (2)	0 (0)	0 (0)	1 (4)
Other types[c]	33 (17)	16 (13)	3 (21)	7 (21)	7 (30)
Nontypeable	9 (5)	3 (2)	0 (0)	3 (9)	3 (13)

Abbreviations: PCV10, 10-valent pneumococcal conjugate vaccine; PCV13, 13-valent pneumococcal conjugate vaccine.

[a] PCV10 types include 4, 6B, 9V, 14, 18C, 19F, 23F, 1, 5, 7F; PCV13 types include 4, 6B, 9V, 14, 18C, 19F, 23F, 1, 5, 7F, 3, 6A, 19A.

[b] Some children had more than 1 serotype.

[c] Serotypes that tested positive among 2 unaccompanied children (UC) included 4, 20, 34, 38, 9N, 11A, 18A, 19A, 23F, 22F/22A, 33F/33A/37. Serotypes that tested positive among 1 UC included 2, 13, 7C, 12F, 15A, 17F, 19B, 23B, 33F, 35A, 7F/7A, and nonvaccine type.

Table 4. Association Between Travel History and Colonization With *Streptococcus pneumoniae* and Serotype 5 *S. pneumoniae* Among Unaccompanied Children

Transit History	All *Streptococcus pneumoniae* (%)	PR (95% CI)[a]	*Streptococcus pneumoniae* Serotype 5 (%)	PR (95% CI)[a]
Country of origin	N = 184		N = 69	
Honduras	55 (30)	Referent	19 (28)	Referent
Guatemala	74 (40)	0.8 (.6–1.1)	20 (29)	0.60 (.3–1.1)
El Salvador	53 (29)	0.94 (.7–1.3)	29 (42)	1.48 (.9–2.6)
Other country	2 (1)	1.05 (.3–3.5)	1 (2)	1.52 (.2–9.8)
Mexico border arrival location	N = 64		N = 25	
Reynosa	49 (77)	Referent	21 (84)	Referent
Camargo	6 (9)	2.2 (1.2–4.2)	3 (12)	2.6 (.9–7.6)
Matamoros	4 (6)	1.8 (.8–4.0)	1 (4)	1.0 (.2–7.0)
Other Mexico border arrival location	*5 (8)*	0.9 (.4–2.0)	0 (0)	0.2 (.0–3.2)[a]
US border arrival location	N = 112		N = 40	
Hidalgo, Texas	66 (59)	Referent	24 (60)	Referent
Rio Grande City, Texas	12 (11)	1.8 (1.1–2.9)	5 (13)	2.0 (.8–4.9)
Brownsville, Texas	8 (7)	2.3 (1.4–3.8)	3 (8)	2.4 (.8–6.9)
Other border arrival location	26 (23)	1.1 (.8–1.7)	8 (20)	1.0 (.4–2.0)
CBP sector	N = 110		N = 39	
Rio Grande Valley sector, Texas	91 (83)	Referent	34 (87)	Referent
Tucson sector, Arizona	10 (9)	1.3 (.8–2.2)	3 (8)	1.1 (.3–3.2)
Other CBP sector	9 (8)	0.7 (.4–1.3)	2 (6)	0.4 (.1–1.6)
Transit through Nogales CBP Processing Center, AZ	123/185 (67)	1.7 (1.3–2.3)	57/70 (81)	3.8 (2.1–6.9)

Abbreviations: CBP, Custom Border Patrol; CI, confidence interval; PR, prevalence ratio.

[a] Common prevalence ratio reported. To avoid undefined results, logit estimator used a correction of 0.5 in every cell for the tables that contained a zero cell.

America just before this outbreak recognition [19]. Influenza and other respiratory viruses can cause primary viral pneumonia [12, 20], and secondary bacterial infections or coinfections can also occur [21]. Influenza infection can increase pneumococcal colonization density [22], possibly predisposing UC to severe pneumococcal and other respiratory infections. While influenza vaccination is available in these countries, there is limited use in adolescents [23]. Overall, the identification of multiple subtypes of different pathogens suggests that this outbreak was propagated through enhanced person-to-person transmission rather than a point source exposure.

We observed that transit through the Nogales CBP Processing Center was significantly associated with overall pneumococcal colonization and serotype 5 colonization, suggesting potential enhanced transmission at that facility, similar to other outbreaks that occur among populations that experience crowded living conditions and physical stress [24]. Serotype 5 is among the most invasive pneumococcal serotypes; thus, it is not surprising that severe disease occurred in the setting of a relatively high prevalence of colonization [25–27]. If serotype 5 carriage was also high among US adolescents at the time of the outbreak, we would have expected some evidence of an epidemic in the local population. However, no cases of invasive pneumococcal disease serotype 5 among US adolescents aged 12–17 years have been reported to US surveillance since 2008 [28]. Lastly, this outbreak is unique due to the social circumstances of UC. Many UC fled their home countries because of violence [29]. The "toxic stress" that results from such events has been associated with increased frequency of febrile illness as well as alterations in innate and adaptive immunity [30]. While our data are inadequate to specifically assess crowding before crossing the US border, some UC reported traveling (eg, by bus and train) and living in crowded housing while waiting to cross the border and in CBP stations.

None of these explanations exclude the possibility that there is currently an unrecognized epidemic of serotype 5 pneumococcal disease in Central America, a region where the serotype 5 ST289 strain is thought to be widely distributed [16]. In the absence of robust surveillance for severe pneumococcal disease in Central America, the possibility of an ongoing epidemic cannot be excluded [31, 32]. The appearance of 2 serotype 5 strains as determined by whole genome sequencing suggests the possibility that the strains originated in Central America.

Our investigation has some limitations. Hospitalized children were tested for respiratory pathogens at the discretion of the treating physician, so there was no systematic testing for all respiratory pathogens. ILI case ascertainment, subsequent testing, and the ability to interview all hospitalized children were incomplete because some children had been placed in standard shelters or with sponsors before the investigation began. Although we were able to estimate the total number of children who transited through Nogales Processing Center (n = 4809),

which gives some estimate of children at risk, we were not able to determine an exact denominator of children at all facilities because children were transitioning through these facilities daily and the total number of children with mild illness was unknown; thus, we cannot calculate an exact attack rate. Pneumococcal colonization might have been underestimated if UC who had contact with hospitalized cases had transitioned out of facilities in the interim. UC previously colonized with serotype 5 might have also cleared the organism by the time they were approached for evaluation. Lastly, no single electronic database was available to provide transit histories, so data on UC movements and time spent at shelters were often incomplete, limiting our ability to conduct multivariate analyses.

The data were gathered rapidly during this outbreak, which led to several public health interventions. First, the high rates of serotype 5 pneumococcal disease and colonization, influenza circulation, and crowded housing led to a recommendation to vaccinate UC with PCV13 and influenza vaccine between seasonal influenza vaccine availability. No cases were reported after vaccination (Figure 2). Second, infection control practices were reviewed and strengthened. Facility administrative policies were reviewed, current CDC recommendations were reemphasized in all facilities [33, 34], syndromic surveillance and reporting systems were implemented, hand hygiene and respiratory etiquette were encouraged, and isolation and management of ill UC were continued. Overcrowding in shelters and processing centers should be avoided as much as possible since this can predispose settings to infectious disease outbreaks [35, 36].

CONCLUSION

This outbreak of respiratory disease was due to multiple pathogens, including *S. pneumoniae* serotype 5, influenza viruses, and other agents, and affected a vulnerable, high-risk migrant population. While PCV13 and influenza vaccinations and ongoing infection control practices appear to have interrupted this outbreak, continued use of vaccines, strengthening syndromic surveillance and reporting systems, and avoidance of overcrowded facilities are interventions that can help detect and prevent future outbreaks among UC in the United States.

Notes

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