U.S. Centers for Disease Control and Prevention
MMWR
Morbidity and Mortality Weekly Report
Weekly / Vol. 73 / No. 32
August 15, 2024

Invasive Nontypeable *Haemophilus influenzae* Disease Outbreak at an Elementary School — Michigan, May 2023

Meghan M. Weinberg, PhD[1]; Kaitlyn Akel, MPH[2]; Oluwaseun Akinyemi, MD, PhD[2]; Thrishika Balasubramanian, MPH[1]; Heather M. Blankenship, PhD[1]; Jennifer P. Collins, MD[3]; Jim Collins, MPH[1]; Tiffany Henderson, MPH[1]; Shannon Johnson, MPH[1]; Joyce Lai, MPH[1]; Lucy A. McNamara, PhD[3]; Claudia Richardson, MD[2]; Shalabh Sharma, MS[3]; Darsheen Sheth, MBBS[2]

Abstract

In May 2023, the Detroit Health Department was notified of four cases of invasive nontypeable *Haemophilus influenzae* (Hi) disease among students attending the same elementary school and grade, all with illness onsets within 7 days. Three patients were hospitalized, and one died. Most U.S. cases of invasive Hi disease are caused by nontypeable strains. No vaccines against nontypeable or non–type b Hi strains are currently available. Chemoprophylaxis is not typically recommended in response to nontypeable Hi cases; however, because of the high attack rate (four cases among 46 students; 8.7%), rifampin prophylaxis was recommended for household contacts of patients with confirmed cases and for all students and staff members in the school wing where confirmed cases occurred. Only 10.8% of students for whom chemoprophylaxis was recommended took it, highlighting gaps in understanding among caregivers and health care providers about persons for whom chemoprophylaxis was recommended. Public health authorities subsequently enhanced communication and education to the school community, improved coordination with health care partners, and established mass prophylaxis clinics at the school. This outbreak highlights the potential for nontypeable Hi to cause serious illness and outbreaks and the need for chemoprophylaxis guidance for nontypeable Hi disease. Achieving high chemoprophylaxis coverage requires education, communication, and coordination with community and health care partners.

Introduction

After the introduction and widespread use of vaccines against *Haemophilus influenzae* (Hi) type b (Hib) in the United States for the last 30 years, the incidence of invasive Hi disease among children aged <5 years declined by >99%. Invasive Hi is now most commonly caused by nontypeable strains, which are not covered by Hib vaccines (*1*). Nontypeable Hi lacks a polysaccharide capsule and has been associated with noninvasive infections (e.g., otitis media and bronchitis) but is capable of causing invasive disease (*1*). Invasive Hi disease incidence is highest among infants and older adults; however, outbreaks are rare (*1*). Four cases of nontypeable Hi disease were reported among children aged 5–6 years who attended the same elementary school for kindergarten in Detroit, Michigan; one child died, and three others were hospitalized. Chemoprophylaxis was recommended for household contacts of the patients and for students and staff members who worked or attended class in the same school wing where the cases had occurred. The

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Detroit Health Department (DHD), in collaboration with the Michigan Department of Health and Human Services (MDHHS) and CDC, investigated the outbreak to prevent additional illnesses and assessed barriers to obtaining and taking recommended chemoprophylaxis. This activity was considered routine public health surveillance and outbreak response by MDHHS and, therefore, did not require human subjects review. This activity was reviewed by CDC, deemed not research, and was conducted consistent with applicable federal law and CDC policy.*

Investigation and Results

Identification of Outbreak

On May 1, 2023, DHD was notified of a case of invasive Hi disease in a child who died suddenly. By May 8, three additional invasive Hi disease cases were identified among students in the same school and grade, including two children from the same classroom as the index patient.

Patient Characteristics

The four cases occurred among children aged 5–6 years; all were non-Hispanic Black or African American boys. All patients had symptom onset within 7 days of each other; signs and symptoms began suddenly or worsened rapidly and included fever (four patients), myalgia (four), lethargy (four), headache (four), vomiting (two), and sore throat (two) (Table 1). None of the patients had a chronic medical condition that increases the risk for acquiring invasive Hi disease. Three patients (patients A, C, and D), including the index patient (patient A), were co-infected with at least one respiratory virus. Respiratory viruses can modulate the host immune response, and preceding respiratory infections have been associated with invasive Hi disease (*2*). The index patient died before hospitalization; the other three patients were hospitalized and recovered fully with antibiotic treatment. Using the Council of State and Territorial Epidemiologists' surveillance case definition for invasive Hi disease (*3*), the four cases were confirmed by isolation of Hi from a normally sterile site. Hi was cultured from blood (three patients) and cerebrospinal fluid (one; specimen collected 27 hours postmortem). Group A *Streptococcus* was isolated from the index patient's postmortem blood specimen.

Hi Isolate Characteristics

Whole genome sequencing (WGS) was conducted by MDHHS Bureau of Laboratories. The four Hi isolates were nontypeable (unencapsulated) and shared the same sequence type (ST-1714) with zero single nucleotide polymorphism (SNP) differences (with highly recombinant sites omitted from analysis). Additional WGS analysis conducted by CDC after the outbreak investigation found that the four isolates were within 13–39 SNPs of several isolates from an ST-1714 cluster reported in Georgia (*4*).

* 45 C.F.R. part 46. 102(l)(2), 21 C.F.R. part 56; 42 U.S.C. Sect. 241(d); 5 U.S.C. Sect. 552a; 44 U.S.C. Sect. 3501 et seq.

The *MMWR* series of publications is published by the Office of Science, U.S. Centers for Disease Control and Prevention (CDC), U.S. Department of Health and Human Services, Atlanta, GA 30329-4027.

Suggested citation: [Author names; first three, then et al., if more than six.] [Report title]. MMWR Morb Mortal Wkly Rep 2024;73:[inclusive page numbers].

TABLE 1. Clinical and laboratory characteristics of four pediatric* patients with invasive nontypeable *Haemophilus influenzae* disease — Detroit, Michigan, 2023

Patient	Signs and symptoms	Clinical encounter type	Outcome	Cerebrospinal fluid culture results	Blood culture results	Hi sequence type	Respiratory viruses detected by nucleic acid amplification
A	Fever, myalgia, lethargy, headache, sore throat, cough, rhinorrhea, abdominal pain, and difficulty breathing	Outpatient	Died	Hi†	GAS†	ST-1714	Adenovirus, RSV, coronavirus HKU1, coronavirus NL63, and RV/EV†,§
B	Fever, myalgia, lethargy, headache, vomiting, and sore throat	Inpatient	Survived	NP	Hi	ST-1714	None detected¶
C	Fever, myalgia, lethargy, headache, vomiting, rhinorrhea, and rash	Inpatient	Survived	NP	Hi	ST-1714	Adenovirus and SARS-CoV-2
D	Fever, myalgia, lethargy, headache, diarrhea, and cough	Inpatient	Survived	NP	Hi	ST-1714	RV/EV§

Abbreviations: GAS = group A streptococcus; Hi = nontypeable *Haemophilus influenzae*; NP = not performed; RSV = respiratory syncytial virus; RV/EV = rhinovirus/enterovirus.
* All patients were aged 5–6 years and attended the same elementary school and grade.
† Specimens were collected 27 hours postmortem.
§ Assay does not differentiate between rhinovirus and enterovirus.
¶ Influenza A, influenza B, RSV, and SARS-CoV-2 were tested for and not detected. Testing for additional pathogens was not performed.

Public Health Response

Routine Student Illness Surveillance

In the days immediately after the death of the index patient, school officials reported a substantial increase in reports of ill students and concerned families and staff members. Other schools within the district reported an increase in student absenteeism for unidentified illnesses, initially making it difficult to assess the scope of the outbreak.

Enhanced Illness Surveillance

To supplement routine surveillance and identify additional potential Hi disease cases, DHD requested that school administrators throughout the district notify public health officials of all cases of reportable communicable diseases or illnesses and encourage symptomatic students and staff members to seek health care. A health alert was distributed to health care providers to inform them of the outbreak and to recommend testing for Hi and other circulating pathogens for patients with clinically compatible illnesses. Through the enhanced school surveillance, public health authorities were notified of 126 ill persons from 38 schools (including 42 persons from the affected school). Attempts were made to contact all ill persons to administer a standardized questionnaire about signs and symptoms, risk factors, and potential epidemiologic links to other cases. One of the four detected cases was reported via this surveillance: patient D had recently been discharged from an emergency department with a viral syndrome diagnosis, and DHD strongly encouraged the family to seek medical attention again because the patient's health was not improving. The patient was admitted to a local hospital, and Hi bacteremia was confirmed through blood culture. All four cases were reported via routine laboratory and provider-based public health surveillance.

Chemoprophylaxis Recommendations

Recommendations for chemoprophylaxis to prevent Hi disease cases are typically limited to close contacts of patients with Hib† disease and, sometimes, Hi type a (Hia) disease (*5*,*6*). In this outbreak, however, based on the unusually high attack rate (four cases among 46 students; 8.7%) and that the four cases occurred among students from both of the school's two kindergarten classrooms, DHD recommended chemoprophylaxis after the third case was reported. Rifampin was recommended for all household contacts of patients with invasive Hi disease (i.e., 13 contacts of three patients; the number of household contacts for one patient was unknown) and for all 186 students and an unknown number of staff members in the wing of the school where the confirmed cases occurred. In a letter and a virtual meeting, school administrators and DHD updated the school community about the outbreak, explained the rationale for chemoprophylaxis, and advised eligible persons to seek prophylaxis from their primary care provider or the school health center if they did not have a provider.

Chemoprophylaxis Coverage and Barriers

DHD and MDHHS contacted caregivers of patients and eligible students to determine whether rifampin prophylaxis

† For cases of invasive Hib disease, and sometimes Hia, rifampin chemoprophylaxis is recommended for all household contacts in households with members aged <4 years who are not fully vaccinated or members aged <18 years who are immunocompromised, regardless of their vaccination status. Chemoprophylaxis is recommended in child care facility settings when two or more cases of invasive Hib disease have occurred within 60 days of one another and unimmunized or underimmunized children attend the facility.

was initiated. Among the four households with cases, one household completed chemoprophylaxis, one preferred to discuss chemoprophylaxis with their primary care provider, one experienced difficulty obtaining the prescription, and one declined chemoprophylaxis. Among 186 eligible students, the caregivers of 102 (54.8%) were interviewed; 11 (10.8%) students were reported to have started or completed chemoprophylaxis within 18 days after chemoprophylaxis was recommended to them. An additional 19 (18.6%) caregivers expressed interest in chemoprophylaxis but had not obtained the prescription or the antibiotic by the time of interview. Among the 91 students who had not started or completed chemoprophylaxis at the time of interview, reasons provided by caregivers for not taking chemoprophylaxis included not being aware of the recommendation (nine; 9.9%), not having time to obtain the chemoprophylaxis (nine; 9.9%), waiting for an appointment with their primary care provider (nine; 9.9%), thinking it was unnecessary because their child was not symptomatic or they did not want their child to take antibiotics (eight; 8.8%), and needing more information or being undecided (eight; 8.8%) (Table 2).

In response to identified barriers, the school distributed additional educational materials highlighting the importance of chemoprophylaxis, and DHD collaborated with health care partners to establish clinics within the school, including clinics that operated during nonbusiness hours. DHD also received reports of health care providers incorrectly counseling families that chemoprophylaxis was unnecessary and that children were protected by Hib vaccine,[§] highlighting misunderstandings among caregivers and providers and prompting DHD to send a second health alert to the health care community. No additional cases were reported for the remainder of the school year.

TABLE 2. Reasons* for not initiating chemoprophylaxis reported by interviewed caregivers of children who were recommended to receive chemoprophylaxis because of potential exposure to nontypeable *Haemophilus influenzae*† (N = 91) — Detroit, Michigan, 2023

Reason	No. (%)
Interested but had not obtained by the time of interview	19 (21)
Not aware of chemoprophylaxis recommendation	9 (10)
Did not have time to obtain chemoprophylaxis	9 (10)
Waiting for appointment with primary care provider	9 (10)
Did not think it was necessary or did not want child taking antibiotics	8 (9)
Needed more information or undecided	8 (9)
Primary care provider advised against or said not necessary	5 (6)
Did not have primary care provider	4 (4)
Difficulty obtaining chemoprophylaxis	4 (4)
Needed transportation assistance	3 (3)
Wanted to talk with primary care provider about chemoprophylaxis	3 (3)
Did not know where to obtain chemoprophylaxis	1 (1)
Reason not provided	32 (35)

* Some caregivers mentioned multiple reasons.
† Interviews occurred 5–18 days after chemoprophylaxis was recommended.

Discussion

Nontypeable Hi is currently the most common cause of invasive Hi disease in the United States; however, secondary transmission is uncommon, and outbreaks are rare (*1*). Hib vaccines do not provide protection against nontypeable Hi, and no vaccines against nontypeable strains are currently available. This invasive Hi disease outbreak at an elementary school highlights the potential for nontypeable Hi to cause secondary cases (*7*) and severe disease outside the typical highest-risk age groups (i.e., <1 year and ≥65 years). Co-infection with respiratory viruses (*2*), decreased exposure to Hi because of COVID-19 nonpharmaceutical interventions and subsequent decreased mucosal immunity (*8*), or strain characteristics might have contributed to the high secondary attack rate.

This outbreak also highlights the need for guidance concerning chemoprophylaxis for nontypeable Hi disease. Although the actual chemoprophylaxis coverage during this outbreak is unknown, only 11% of those interviewed reported taking chemoprophylaxis. This finding might be an underestimate because it does not include students who might have started chemoprophylaxis after the interview. In addition, this finding might not be representative of all persons who were recommended to take prophylaxis because the caregivers of 84 (45.2%) of the 186 students who were advised to take prophylaxis did not respond to public health outreach, and school staff members for whom prophylaxis was recommended were not interviewed because public health resources were limited. During interviews, caregivers reported interest in chemoprophylaxis but described multiple difficulties in obtaining it, highlighting accessibility challenges and gaps in health care provider awareness about the outbreak and understanding of the importance of chemoprophylaxis for nontypeable Hi disease. Community trust in the medical establishment was not assessed, so its contribution to low chemoprophylaxis coverage could not be evaluated. Coverage might have been improved had conveniently located mass prophylaxis clinics been rapidly established, and communication with the school community and health care providers been better coordinated.

The epidemiology of ST-1714 has not been characterized nationally. Although the outbreak isolates are closely related to an ST-1714 clonal strain reported among adults in Atlanta, Georgia, epidemiologic differences are notable: the Georgia cluster primarily occurred among adult men living with HIV, with septic arthritis as an unusually common presentation (*4*).

[§] Hib vaccine is not protective against nontypeable Hi.

Summary

What is already known about this topic?

Most U.S. cases of invasive *Haemophilus influenzae* (Hi) disease are caused by nontypeable strains. No vaccines against nontypeable or non–type b Hi strains are currently available.

What is added by this report?

Four invasive nontypeable Hi disease cases occurred among young children in an elementary school in Detroit, Michigan. Three patients were hospitalized, and one died. Chemoprophylaxis was recommended for the patients' household contacts and for students and staff members in the school wing where cases occurred. Only 11% of students for whom chemoprophylaxis was recommended took it; misinformation among caregivers and health care providers and difficulty obtaining chemoprophylaxis contributed to low coverage.

What are the implications for public health practice?

Nontypeable Hi can cause outbreaks among young children; therefore, chemoprophylaxis guidance is needed. Achieving high chemoprophylaxis coverage requires education, communication, and coordination with community and health care partners.

Implications for Public Health Practice

Nontypeable Hi can cause serious illness and outbreaks among young children; therefore, chemoprophylaxis guidance for nontypeable Hi disease is needed. Achieving high chemoprophylaxis coverage requires education, communication, and coordination with community and health care partners. Expanded WGS of nontypeable Hi isolates is needed to better understand the epidemiology of ST-1714 nationally and to detect future clusters and outbreaks.

Acknowledgments

James Barber, Smeralda Bushi, Ebone Colbert, Mat Myers, Sarah Pruett, Briana Putrus, Rosalyn Schaefer, Division of Communicable Disease, Michigan Department of Health and Human Services; Kelly Jones, Rebecca Kramer, Arianna Miles-Jay, Bureau of Laboratories, Michigan Department of Health and Human Services; Nikita Cargins, Robert Dunne, Christina Floyd, Kelvin Freeman, Denise Fair Razo, Detroit Health Department; Denise Cade, Alycia Meriweather, Wakeita Winston, Detroit Public Schools Community District; Sheila Clay, Jonnie Hamilton, Ascension Michigan Community Health; Nicole Croom, Wayne County Medical Examiner Office; Basim Asmar, Children's Hospital of Michigan; Daya Marasini, Basanta Wagle, Bacterial Meningitis Laboratory, CDC.

Corresponding author: Oluwaseun Akinyemi, Oluwaseun.Akinyemi@detroitmi.gov.

[1]Michigan Department of Health and Human Services; [2]Detroit Health Department, Detroit, Michigan; [3]Division of Bacterial Diseases, National Center for Immunization and Respiratory Diseases, CDC.

All authors have completed and submitted the International Committee of Medical Journal Editors form for disclosure of potential conflicts of interest. No potential conflicts of interest were disclosed.

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