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Possible Airborne Person-to-Person Transmission of *Mycobacterium bovis* — Nebraska 2014–2015

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Mycobacterium bovis, one of several mycobacteria of the *M. tuberculosis* complex, is a global zoonotic pathogen that primarily infects cattle. Humans become infected by consuming unpasteurized dairy products from infected cows (*1*,*2*); possible person-to-person airborne transmission has also been reported (*3*). In April 2014, a man in Nebraska who was born in Mexico was determined to have extensive pulmonary tuberculosis (TB) caused by *M. bovis* after experiencing approximately 3 months of cough and fever. Four months later, a U.S.-born Hispanic girl from a nearby town who had been ill for 4–5 months was also determined to have pulmonary TB caused by *M. bovis*. The only social connection between the two patients was attendance at the same church, and no common dietary exposure was identified. Both patients had pulmonary cavities on radiography and acid-fast bacilli (AFB) on sputum-smear microscopy, indicators of being contagious (*4*). Whole-genome sequencing results of the isolates were nearly indistinguishable. Initial examination of 181 contacts determined that 39 (22%) had latent infection: 10 (42%) of 24 who had close exposure to either patient, 28 (28%) of 100 who were exposed to one or both patients in church, and one (2%) of 57 exposed to the second patient at a school. Latent infection was diagnosed in six contacts on follow-up examination, 2 months after an initial negative test result (*4*), for an overall latent infection rate of 25%. No infected contacts recalled consuming unpasteurized dairy products, and none had active TB disease at the initial or secondary examination. Persons who have *M. bovis* TB should be asked about consumption of unpasteurized dairy products (*2*), and contact investigations should follow the same guidance as for *M. tuberculosis* TB (*4*).

In April 2014, patient A, a man aged 42 years who was born in Mexico sought care for cough, fever, weight loss, and progressive debilitation over approximately 3 months. He had arrived in Nebraska from Mexico in 2010, and initially he worked on a dairy farm* and later in construction. No information was collected regarding his prior employment in Mexico, but he did report frequent consumption of raw milk. Chest radiography was consistent with advanced TB with cavities; numerous AFB were reported from sputum-smear microscopy. The result from nucleic acid amplification testing of sputum was positive for *M. tuberculosis* complex. The isolate was resistant both to pyrazinamide (PZA), which suggested that the

* Nebraska dairies have been free of *M. bovis* infections since 1978. In recent years, *M. bovis* infections have been detected sporadically among Nebraska beef herds (late 1990s, 2005, 2009, and 2013) and an elk herd (2009) (Nebraska Department of Agriculture, unpublished data, June 29, 2015). No persons in this investigation were thought to have had contact with these sources. The whole-genome sequencing results for all veterinary *M. bovis* isolates from Nebraska are distinct from those of both patients' isolates.

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infection was caused by *M. bovis*, and to low-concentration isoniazid (INH) (*5*). His treatment regimen was adjusted in consultation with national experts in drug-resistant TB. He recovered slowly and remained isolated at home until results from sputum smears were negative for AFB in August.

In June 2014, patient B, a Hispanic girl aged 16 years, who was born in Nebraska to Mexican parents, sought medical care after 2–3 months of cough. She initially received treatment for presumed bronchitis and allergies, without chest radiography. She remained ill through late July, when radiography revealed a pulmonary cavity and her sputum smear had numerous AFB. *M. bovis* resistant to PZA was identified after culture confirmation. She had never traveled outside the United States and was unaware of having consumed any dairy products from Mexico. She recovered quickly and remained in isolation at home until late September. The only social connection between patients A and B was regular attendance at the same church. The patients knew one another but their interactions were reported to be minimal.

Contact investigations were conducted in accordance with published guidelines (*4*) focusing on household contacts of both patients, community contacts at both the church and patient B's school, coworkers of patient A, and persons who spent extended periods in a vehicle with him. Potentially exposed health care workers were notified for follow-up at their respective facilities with a request to report infections to the health department if identified. Tuberculin skin tests (TST) and interferon gamma release assays (IGRA) were used for testing U.S.-born and foreign-born contacts, respectively; IGRA was used for all members of the church, where the majority of contacts were foreign born. Contacts whose initial results were negative, but whose exposure to either patient had ended <2 months before testing, were retested after 8–12 weeks, because immune sensitivity might not be detectable during this period after new infection (*4*). Persons who had positive test results indicating infection had chest radiographs to exclude active TB disease and thus establish latent infection (*4*).[†] All contacts were asked about their country of birth except those at a school attended by patient B where all were assumed to have been born in the United States. Midway through the investigation, after *M. bovis* was recognized as the causative agent, contacts who had positive test results were also asked about travel abroad and consumption of unpasteurized dairy products from Mexico.

[†] Tuberculosis infection is "a condition in which microorganisms [i.e., *M. tuberculosis* complex] have entered the body and typically have elicited immune responses" and "includes both latent infection and TB disease." Latent infection "is an asymptomatic condition that follows the initial infection; the infection is still present but is dormant (and believed not to be currently progressive or invasive)" and "might progress to TB disease." "[Active] TB disease is determined by finding anatomic changes caused by advancing infection (e.g., shadows from infiltrates on a chest radiograph) or by noting symptoms (e.g., malaise, feverishness, or cough), and typically by both." http://www.cdc.gov/mmwr/preview/mmwrhtml/rr5415a2.htm.

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Twenty-four persons had extended close exposure to either patient and were regarded as high-priority contacts (*4*); among these, 10 (42%) had positive results at initial testing (Table 1). Two were non-Hispanic U.S.-born contacts of patient A who did not attend the church. Among 11 high-priority contacts of patient B, seven were family members who were also potentially exposed to patient A at the church. Among patient B's five siblings, four were born in the United States, had never traveled abroad, and did not recall consuming dairy products from Mexico; three of these four siblings were infected. Patient B's eldest sibling and mother, both of whom were born in Mexico, were also infected but neither had active TB disease and thus would not have been infectious. Among 100 church members (excluding patient B and high-priority contacts of either patient), 28 (28%) had latent infection, including five U.S.-born children. Among 57 school contacts, one U.S.-born child was infected. No infections among exposed health care workers were reported.

Among 77 persons for whom retesting was indicated, 56 (73%) were retested, and six (11%) were determined to have latent infection (Table 2). During the interval between the first and second tests, none had traveled abroad or recalled eating unpasteurized dairy products from Mexico. No school contacts were retested, because their exposure had ended the previous May. No infected contacts had active TB disease, and all were offered a 4-month rifampin preventive regimen.[§]

Patient A's bacterial isolate, grown at a private hospital laboratory from a sputum sample collected April 24, 2014, was sent to the Nebraska Public Health Laboratory to facilitate genotyping at the Michigan state laboratory and first-line drug susceptibility testing at Associated Regional and University Pathologists, Inc.; second-line drug susceptibility testing was conducted at CDC. Patient B's isolate was cultured by Nebraska Public Health Laboratory from a sputum sample collected during early August, and it was similarly sent for first- and second-line drug susceptibility testing and genotyping. Routine genotyping results of both patients' isolates were indistinguishable. In late September 2014, both patients' isolates were sent to the United States Department of Agriculture National Veterinary Services Laboratories (NVSL) where whole-genome sequencing was performed. Results suggested that the two patients' isolates were closely related; phylogenetic comparisons differed by only three single nucleotide polymorphisms (SNPs). The sequences did not match others in NVSL's library, but the isolates shared a common ancestor with isolates from five cattle in Mexico.[¶]

Discussion

M. bovis primarily causes disease in cattle but also infects deer and other mammals (*1*). The human diseases caused by *M. bovis* and *M. tuberculosis* (i.e., the human variant) are clinically indistinguishable, and cases caused by both are reported in U.S. TB surveillance (*1*,*2*,*6*,*7*).[**] Treatment differs, however, because *M. bovis* is inherently resistant to PZA, which is part of the routine initial TB treatment regimen (*5*). Bovine tuberculosis eradication programs and routine pasteurization of milk products have led to marked declines in *M. bovis* TB in humans (*1*), which accounted for 1.6% of U.S. TB cases in 2014 (*6*), with regional differences (*2*,*6*–*8*).

Human *M. bovis* disease is typically attributed to consumption of unpasteurized milk (or dairy products made from unpasteurized milk) in or imported from countries with affected cattle herds (*1*,*2*,*7*,*8*). Person-to-person airborne transmission of *M. bovis* has been reported infrequently, with uncertainty remaining about dietary exposures (*3*). Findings from contact investigations and a population study regarding infectiousness of *M. bovis* compared with *M. tuberculosis* are inconclusive (*4*,*9*,*10*).[††]

Standard nucleic acid amplification test methods detect the *M. tuberculosis* complex without distinguishing between *M. tuberculosis* and *M. bovis*. Although these species can be distinguished by routine genotyping, biochemical characterization and drug susceptibility testing, which generally provide results earlier, have been historically used and can increase the index of suspicion for *M. bovis*. Whole-genome sequencing can be used to identify species and investigate transmission. NVSL sequences genomes for all U.S. *M. bovis* animal isolates, a convenience sample of cattle isolates from Mexico, and human isolates upon request.[§§]

[§] In August 2015, a U.S.-born 11-year-old niece of patient A, who reported exposure to him only at the church, became ill with shortness of breath and cough. During the church contact investigation, she and her parents were determined to have latent infection, but they had stopped taking rifampin after only 2 months. A presumptive diagnosis of TB disease caused by *M. bovis* was made, and treatment was started in September 2015, based on clinical findings, including a new pulmonary infiltrate (*4*,*6*). Results from sputum-smear microscopy, nucleic acid amplification test, and culture were negative.

[¶] These cattle included four dairy cows in Nuevo León and one steer in Durango, Mexico. On the basis of whole-genome sequencing of 15 less related cattle isolates in Group 13, this *M. bovis* strain appears to be disseminated throughout Mexico but has not been identified in U.S.-origin cattle. Isolates in this group of the SB0121 family are believed to have evolved on the Iberian Peninsula.

[**] Genotyping results from CDC's National TB Genotyping Service for the isolates from 96 TB patients with culture-confirmed disease in Nebraska during 2006–2013 indicated that all were *M. tuberculosis*.

[††] Infectious TB "refers either to TB disease of the lungs or throat, which has the potential to cause transmission to other persons, or to the patient who has TB disease." http://www.cdc.gov/mmwr/preview/mmwrhtml/rr5415a2.htm.

[§§] NVSL has sequenced 97% of *M. bovis* isolates from affected U.S. cattle herds since 1997 and 90% from feeder and feedlot cattle (both imported and domestic) since 2000. The oldest isolate sequenced is from 1991, but isolates were not consistently archived from affected herds until 1997. NVSL sequences the *M. bovis* isolates from all animal species; the size of the database is approximately 2,500 sequences.

TABLE 1. Investigation setting and results of initial testing* of contacts (N = 181) exposed to one or both of two *Mycobacterium bovis* tuberculosis patients, by United States versus foreign birth — Nebraska, 2014

	Test results negative			Test results positive			
	Foreign-born	U.S.-born	Total negative	Foreign-born	U.S.-born	Total positive	Total tested
Investigation setting†	No. (%)	No. (%)	No. (%)	No. (%)	No. (%)	No. (%)	No.
High-priority contacts of patient A	3 (23)	5 (38)	8 (62)	3 (23)	2§ (15)	5 (38)	13
High-priority contacts of patient B	2 (18)	4 (36)	6 (55)	2 (18)	3¶ (27)	5 (45)	11
Church	43 (43)	29 (29)	72 (72)	23 (23)	5** (5)	28 (28)	100
Patient B's school	NA	NA	56 (98)	0 (0)	1** (2)	1 (2)	57
Total	**NA**	**NA**	**142 (78)**	**28†† (15)**	**11 (6)**	**39§§ (22)**	**181**

Abbreviation: NA = not available.

* Tuberculin skin tests and interferon gamma release assays (IGRA) were used for testing U.S.-born and foreign-born contacts, respectively; IGRA was used for all members of the church where the majority of contacts were foreign born.

† The counts in the four categories of settings are mutually exclusive. Among the 13 high-priority contacts of patient A, 11 did not attend the church. Among the remaining two who were also potentially exposed to patient B at the church, one tested positive (patient B's grandfather). Among the 11 high-priority contacts of patient B, all were also potentially exposed to patient A at the church. Patients A and B were not counted as contacts for any setting.

§ Non-Hispanic U.S.-born adults exposed at patient A's residence.

¶ Three Hispanic siblings of patient B (aged 7, 9, and 10 years).

** Six U.S.-born children. Unknown travel and dietary history.

†† Countries of birth are Mexico (n = 26), Guatemala (n = 1), and Philippines (n = 1).

§§ All 39 persons testing positive reported no knowledge of a prior positive TB test result, but information was lacking to verify the accuracy of their recall.

TABLE 2. Investigation setting and results of follow-up testing* performed 8–12 weeks after last potential exposure and after an initial negative result for contacts (N = 56) of one or both of two *Mycobacterium bovis* tuberculosis patients — Nebraska, October 2014

	Test results negative	Test results positive	Total
Investigation setting†	No. (%)	No. (%)	No.
High-priority contacts of patient A	0 (0)	1§ (100)	1
High-priority contacts of patient B	1 (25)	3¶ (75)	4
Church	49 (96)	2 (4)	51
Total	**50 (89)**	**6** ** **(11)**	**56**

* An interferon-gamma release assay was used for testing at the church where foreign-born persons predominated and for other foreign-born contacts. Tuberculin skin tests were used for U.S.-born contacts.

† Follow-up testing was not necessary for contacts at patient B's school because the end of their exposure was >2 months before the investigation.

§ Non-Hispanic U.S.-born individual exposed at patient A's residence who reported no international travel at any time and no consumption of Mexico-origin unpasteurized dairy products. This person had no affiliation with the church or the school and reported no contact with patient B, who resided in a different town.

¶ All three were patient B's family members who were also potentially exposed to patient A at the church.

** All six denied both international travel and consumption of Mexico-origin unpasteurized dairy products in the interim. Among these, three were foreign born (two high-priority contacts of patient B and one church member).

Patient A might have been infected from consuming unpasteurized dairy products originating in Mexico. The timing of the illnesses, relatedness of the *M. bovis* isolates, and common church attendance suggest that patient B might have acquired infection from patient A. Findings from the contact investigations suggest possible airborne transmission, because approximately one third of the infections could not be explained by potential exposure in countries where *M. tuberculosis* complex infections are common. Consumption of imported contaminated dairy products could not be excluded, but locally produced dairy products were unlikely to be contaminated with *M. bovis*.

The findings in this report are subject to at least four limitations. This investigation illustrates typical challenges of investigating human *M. bovis* infections. First, the incubation period has not been well studied, but it potentially ranges from months to years and might obscure ascertainment of time and nature of exposure. Second, dietary history details could be forgotten during the interim, or consumers might be unaware of the origin or pasteurization status of dairy products they consumed. Third, TST and IGRA are based on cellular immune response and cannot distinguish between old or recent infections, or whether the cause is *M. tuberculosis* or *M. bovis*. Persons from countries where both types of infection are prevalent could be infected by either species. The variable incubation period for *M. bovis* notwithstanding, the six persons whose results changed from negative to positive were probably infected only in the weeks before being examined. Finally, despite not documenting conversion in the first five U.S.-born high-priority contacts who were infected, this observed proportion of latent infections (29% [five of 17]) upon initial testing exceeds the expected background prevalence of latent infection of <2% for persons born in the United States.

An evidence base to aid epidemiologic interpretation of whole-genome sequencing results from isolates with few differences in SNPs has not been established for *M. bovis* or *M. tuberculosis*. Maintenance of patient A's isolate in culture for approximately 5 months could have provided opportunity for accrual of the additional SNPs. Airborne transmission from either patient was plausible based on disease characteristics

Summary

What is already known about this topic?

Mycobacterium bovis, a zoonotic pathogen of cattle, causes tuberculosis in persons who consume unpasteurized contaminated dairy products. Airborne person-to-person transmission has been suspected but is difficult to confirm.

What is added by this report?

A large contact investigation around two patients with *M. bovis* pulmonary tuberculosis and the findings from molecular epidemiology strengthen the evidence for person-to-person transmission of *M. bovis* infection.

What are the implications for public health practice?

The persistence of *M. bovis* in cattle internationally and the failure to pasteurize dairy products in many locations means that further infections in humans should be anticipated. Persons with *M. bovis* infections should be asked about foodborne exposures. Contact investigations for *M. bovis* disease should be conducted using the same methods as for *M. tuberculosis* disease.

(i.e., pulmonary cavities and AFB on sputum smears) and contact findings.

This report adds to the evidence for airborne person-to-person spread of *M. bovis* (*3*,*9*,*10*). Whole-genome sequencing is an emerging tool for investigating transmission. Public health responses to *M. bovis* pulmonary TB should be the same as those for *M. tuberculosis* TB, with additional inquiries about consumption of unpasteurized dairy products. The ongoing incidence of *M. bovis* TB in humans substantiates the need to control bovine tuberculosis globally and to pasteurize all milk and dairy products.

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Cluster of Ebola Virus Disease Linked to a Single Funeral — Moyamba District, Sierra Leone, 2014

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As of February 17, 2016, a total of 14,122 cases (62% confirmed) of Ebola Virus Disease (Ebola) and 3,955 Ebola-related deaths had been reported in Sierra Leone since the epidemic in West Africa began in 2014 (*1*). A key focus of the Ebola response in Sierra Leone was the promotion and implementation of safe, dignified burials to prevent Ebola transmission by limiting contact with potentially infectious corpses. Traditional funeral practices pose a substantial risk for Ebola transmission through contact with infected bodies, body fluids, contaminated clothing, and other personal items at a time when viral load is high; however, the role of funeral practices in the Sierra Leone epidemic and ongoing Ebola transmission has not been fully characterized (*2*). In September 2014, a sudden increase in the number of reported Ebola cases occurred in Moyamba, a rural and previously low-incidence district with a population of approximately 260,000 (*3*). The Sierra Leone Ministry of Health and Sanitation and CDC investigated and implemented public health interventions to control this cluster of Ebola cases, including community engagement, active surveillance, and close follow-up of contacts. A retrospective analysis of cases that occurred during July 11–October 31, 2014, revealed that 28 persons with confirmed Ebola had attended the funeral of a prominent pharmacist during September 5–7, 2014. Among the 28 attendees with Ebola, 21 (75%) reported touching the man's corpse, and 16 (57%) reported having direct contact with the pharmacist before he died. Immediate, safe, dignified burials by trained teams with appropriate protective equipment are critical to interrupt transmission and control Ebola during times of active community transmission; these measures remain important during the current response phase.

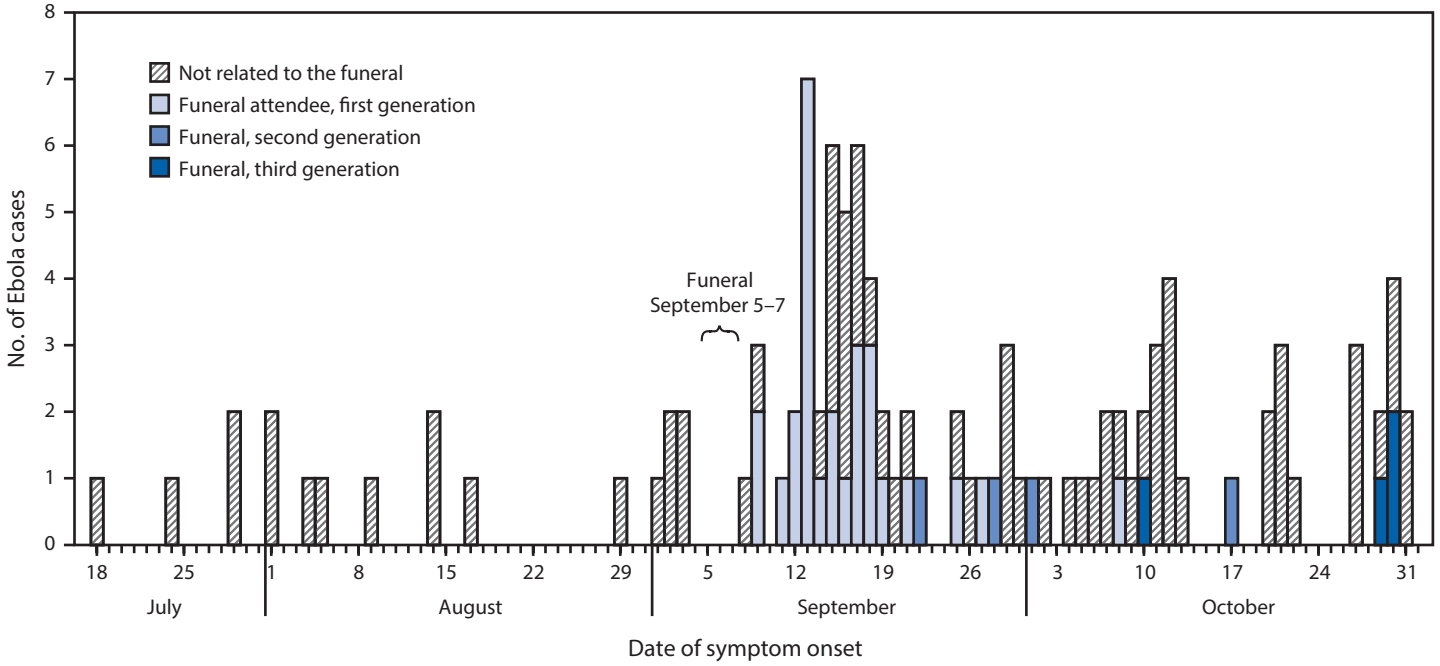
The Sierra Leone Ministry of Health and Sanitation and CDC conducted a retrospective analysis of laboratory-confirmed Ebola cases in Moyamba during July 11–October 31, to investigate the increase in cases in September 2014, determine the source and risk factors, and recommend prevention and control measures. The Moyamba District Health Management Team (DHMT) received and responded to alerts from health workers, contact tracers, and community members regarding ill persons, possible Ebola cases, and unexplained deaths. Interviewers completed standardized case investigation forms with patients or proxies regarding demographics, symptoms, illness onset, and potential exposures during the month before illness onset, including contact with ill persons, persons with suspected Ebola, and corpses, plus funeral attendance, hospital or traditional healer visits, and travel history. Laboratory technicians collected whole blood from living patients with suspected Ebola and oral swab specimens from corpses and sent the samples to a centralized laboratory for testing.

A suspected case was defined as 1) the occurrence of fever and at least three of 12 symptoms (i.e., vomiting, headache, nausea, diarrhea, difficulty breathing, fatigue, abdominal pain, loss of appetite, muscle or joint pain, unexplained bleeding, difficulty swallowing, and hiccups) in any person; or 2) any sudden, unexplained death. A confirmed case was defined as a suspected case with a positive laboratory test result by reverse transcription–polymerase chain reaction (RT-PCR) test specific for Ebola virus. If RT-PCR results from blood specimens collected <72 hours after symptom onset were negative or indeterminate, additional specimens were collected for repeat diagnostic testing. Paper case investigation forms and laboratory results were entered into the Sierra Leone Viral Hemorrhagic Fever database. Descriptive statistics were calculated using statistical software.

Confirmed Cases of Ebola

Among 281 suspected Ebola cases in Moyamba District during July 11–October 31, a total of 109 (39%) were confirmed; among these patients, 40 died (case fatality rate = 37%). The median age of patients with suspected Ebola was 30 years (range = 11 months–84 years), and 59% were male. Incidence peaked during the week of September 13–19 at 32 confirmed cases (Figure 1). Overall, during the month before becoming ill, 78 (72%) patients with confirmed Ebola reported having contact with a known or suspected Ebola patient (alive or dead) or ill person. Forty-two (39%) had attended a funeral, 36 (33%) had carried or touched a corpse at a funeral, 10 (9%) had traveled, and eight (7%) had visited a hospital or traditional healer. Among 78 patients with confirmed Ebola who reported contact, 23 (29%) had contact with a corpse, 26 (33%) had contact with a live patient, and 29 (37%) had contact with an Ebola patient both while the patient was alive and after the patient had died.

FIGURE 1. Confirmed Ebola cases (N = 108), by date of symptom onset and relation to a pharmacist's funeral* — Moyamba District, Sierra Leone, July 18–October 31, 2014



* Excludes case in one funeral attendee for whom date of symptom onset was unknown.

Attendees at a Single Funeral

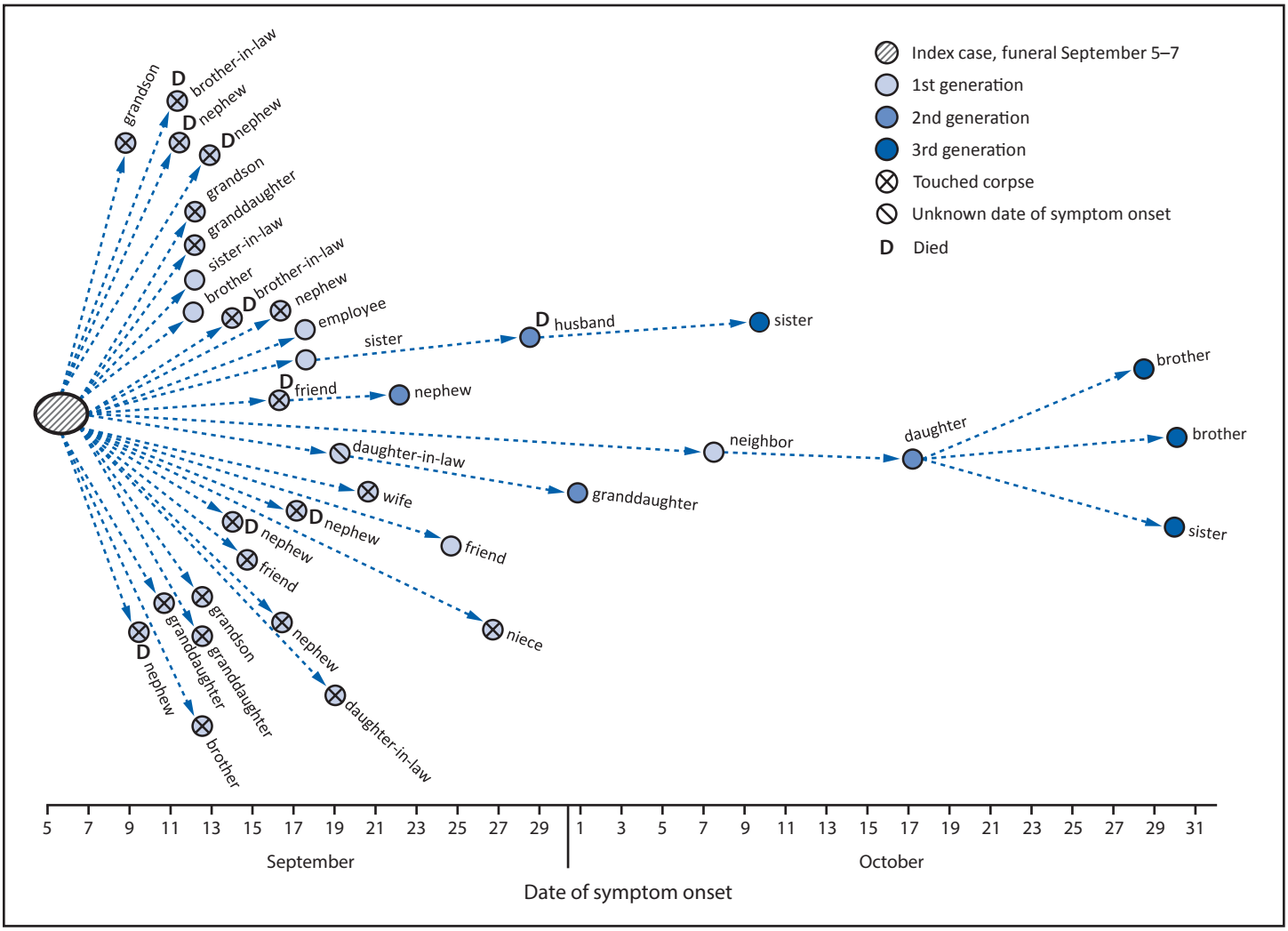
During September 5–7, 28 persons who were later confirmed to have Ebola attended the 3-day funeral of a prominent pharmacist in Moyamba; patients developed symptoms a median of 9 (interquartile range = 7–12) days after the funeral (Figure 2). The pharmacist was buried by relatives rather than by a district Ebola burial team, and his death was not investigated; consequently, no epidemiologic records exist regarding his exposures and illness, although anecdotal reports suggested he had treated an Ebola patient from a neighboring village. Among the 28 persons who attended the funeral and later developed Ebola, 23 (82%) were family members and 18 (64%) were male. Eight (29%) of these patients, all of whom were male and had touched the corpse, died and were buried by the district Ebola burial team. The case fatality rate among men was 44%; no deaths occurred among women (p = 0.02). Among the 28 Ebola patients who had attended the funeral, 16 (57%) reported having had direct contact with the pharmacist for days (August 25–September 1) before the funeral, and 21 (75%) carried or touched his corpse at the funeral. Subsequent contact with funeral attendees likely led to eight known additional confirmed cases (four in the second generation, including one death, and four in the third generation) (Figure 2).

Because the pharmacist was suspected to have died from Ebola, Moyamba DHMT engaged the local village chiefs, youth leaders, the community health officer, and others to ensure community support of rapid response measures. Moyamba DHMT conducted case investigations, traced contacts, and established quarantine in the town in mid-September 2014, closing local businesses and providing food support to residents for 21 days. District surveillance officers conducted daily active case finding. A youth leader convened a neighborhood watch, consisting of local, trained youths, who observed contacts of the pharmacist both inside and outside quarantine for Ebola symptoms every day, to support contact tracers and security. DHMT notified the community health officer to be on high alert for Ebola patients at the clinic or in the community; the community health officer notified DHMT soon after when children from the pharmacist's home became symptomatic. Only two identified contacts of the pharmacist were lost to follow-up.

Discussion

A single, traditional funeral likely led to a sharp increase in Ebola cases in a previously low-incidence district in Sierra Leone, suggesting a substantially higher rate of secondary transmission from one patient than the basic Ebola virus reproduction number of 2.53 estimated for the outbreak in Sierra Leone (*4*). A high number of secondary cases might be explained by a high viral load in the primary patient, the type of contact, timing of contact (e.g., while a patient was alive or dead), the number of persons exposed, or a combination

FIGURE 2. Chain of Ebola transmission involving 28 attendees at a pharmacist's funeral (1st generation patients) and eight epidemiologically linked cases, by date of symptom onset — Moyamba District, Sierra Leone, September 5–October 30, 2014



of these factors. An investigation of the 1995 Ebola outbreak in Kikwit, Democratic Republic of the Congo, identified 38 secondary cases linked to one patient who had many visitors while hospitalized (*5*).

Eight men with confirmed Ebola who attended this funeral died. The high case fatality rate among men might be explained by more intense or prolonged contact with the corpse by the male funeral attendees. According to traditional funeral practices in Sierra Leone, family and friends of the same sex are often responsible for preparing, washing, and clothing the body (*6*). Funerals pose a substantial risk for Ebola transmission for several reasons. First, the risk for transmission might increase with viral load, which is often highest in nonsurvivors, especially during the later stages of disease progression and at death (*7*). Second, the traditional practices of washing, preparing, and touching the body include direct, prolonged contact with the corpse. Finally, funerals attract family, friends, and colleagues from various locations. Attendance is important to demonstrate respect, establish land rights, and determine whether widows will return to their community of origin (*6*). Travelers who are exposed and become infected can establish new chains of transmission when they return to their original communities.

This report highlights the potential for high levels of transmission from a single patient or event and underscores the importance of vigilant Ebola surveillance and response. At least 36 Ebola cases and nine deaths might have been prevented had the pharmacist had a safe, medical burial. The DHMT's comprehensive and targeted response, including rapid community engagement, quarantine, and active surveillance through daily house-to-house visits and formation of a youth neighborhood watch, likely led to the prompt identification of cases and limited transmission beyond the four cases in the second generation and the four cases in the third generation.

Summary

What is already known about this topic?

Ebola Virus Disease (Ebola) is transmitted person-to-person through direct contact with blood, body fluids, or contaminated clothing and other personal items of symptomatic or deceased patients. Traditional funeral practices, including washing and touching the corpse, pose a substantial risk for Ebola transmission.

What is added by this report?

A single, traditional funeral of a prominent pharmacist was associated with a sharp increase in the number of reported Ebola cases in a previously low-incidence district of Sierra Leone. Twenty-eight laboratory-confirmed cases occurred in persons who reported attending the pharmacist's funeral. Sixteen (57%) patients had direct contact days or weeks before the funeral, 21 (75%) reported touching the corpse, and eight (29%) died. Rapid and effective outbreak control limited the second and third generations to four cases each, including one death.

What are the implications for public health practice?

Because of the potential for high levels of transmission from a single patient or event, vigilant Ebola surveillance and rapid response are essential, and immediate, safe, dignified burials by trained teams are critical to interrupting transmission and controlling Ebola. Enhanced community-based surveillance strategies, such as a community event-based surveillance system, will be critical to quickly identify high-risk events and prevent ongoing transmission.

Fear, stigma, and discrimination might lead to underreporting of Ebola cases (*8*), and there was likely underascertainment of Ebola cases, deaths, and exposures. During the time of the investigation, Moyamba DHMT and CDC witnessed and received anecdotal reports of persons who were fleeing the area and hiding from surveillance and contact tracing teams. Self-reported data are limited by patients' and proxies' ability to recall exposures and dates, and social desirability bias and fear might have led to underreporting of Ebola symptoms and contact with ill persons or corpses.

To achieve and maintain zero new infections, enhanced community-based surveillance strategies, such as the community event-based surveillance system, which employs community health monitors to detect and report Ebola trigger events (e.g., two or more ill or dead family or household members) (*9*), are critical to the rapid identification of high-risk events to prevent transmission. Safe, dignified burials by trained burial teams using appropriate protective equipment are critical to the interruption of transmission and control of Ebola in both low-incidence and high-incidence settings, as well as in rural and urban settings (*10*). Early identification of Ebola cases along with prompt isolation, testing, and care of patients can limit transmission, improve likelihood of survival, and ensure safe burials of persons who die, ultimately preventing deaths from occurring at home and unsafe burials in the community. Ebola response teams can strengthen community Ebola surveillance.

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Progress Toward Measles Elimination — Nepal, 2007–2014

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In 2013, the 66th session of the Regional Committee of the World Health Organization (WHO) South-East Asia Region (SEAR) established a goal to eliminate measles and to control rubella and congenital rubella syndrome (CRS)* in SEAR by 2020 (*1*,*2*). Current recommended measles elimination strategies in the region include 1) achieving and maintaining ≥95% coverage with 2 doses of measles-containing vaccine (MCV) in every district, delivered through the routine immunization program or through supplementary immunization activities (SIAs)†; 2) developing and sustaining a sensitive and timely measles case-based surveillance system that meets minimum recommended performance indicators§; 3) developing and maintaining an accredited measles laboratory network; and 4) achieving timely identification, investigation, and response to measles outbreaks. In 2013, Nepal, one of the 11 SEAR member states, adopted a goal for national measles elimination by 2019 (*3*). This report updates a previous report (*4*) and summarizes progress toward measles elimination in Nepal during 2007–2014. During 2007–2014, estimated coverage with the first MCV dose (MCV1) increased from 81% to 88%. Approximately 3.9 and 9.7 million children were vaccinated in SIAs conducted in 2008 and 2014, respectively (*1*). Reported suspected measles incidence declined by 13% during 2007–2014, from 54 to 47 cases per 1 million population. However, in 2014, 81% of districts did not meet the measles case-based surveillance performance indicator target of ≥2 discarded non-measles cases¶ per 100,000 population per year. To achieve and maintain measles elimination, additional measures are needed to strengthen routine immunization services to increase coverage with MCV1 and a recently introduced second dose of MCV (MCV2**) to ≥95% in all districts, and to enhance sensitivity of measles case-based surveillance by adopting a more sensitive case definition, expanding case-based surveillance sites nationwide, and ensuring timely transport of specimens to the accredited national laboratory.

Immunization Activities

In 1979, monovalent measles vaccine was introduced as MCV1 in three districts in Nepal for vaccination of infants at age 9 months; in 1989, the program was scaled up nationally (*5*). After a nationwide SIA conducted in 2012–2013, measles-rubella (MR) vaccine was introduced into the national routine immunization schedule in 2013 and replaced monovalent measles vaccine as MCV1 administered at age 9 months. MCV2, in the form of MR vaccine, was introduced into the routine immunization program in September 2015 and is recommended for vaccination at age 15 months.

Administrative vaccination coverage data (number of vaccine doses administered divided by the estimated target population) are reported each year from the 75 districts in Nepal to the National Immunization Programme, where they are aggregated and reported to WHO and the United Nations Children's Fund (UNICEF) through the Joint Reporting Form (JRF). WHO and UNICEF use reported administrative and immunization coverage survey data to estimate coverage through routine immunization services (*6*). In Nepal, estimated coverage with MCV1 increased from 81% in 2007 to 88% in 2014. In 2014, reported MCV1 coverage was <90% in 38 (51%) districts, 90%–94% in 15 (20%) districts, and ≥95% only in 22 (29%) districts.

To increase coverage, in 2011, Nepal initiated the "fully immunized village" concept, with the goal of achieving 100% coverage with all routinely recommended vaccines

* Measles elimination is defined as the absence of endemic measles cases for a period of ≥12 months, in the presence of adequate surveillance. One indicator of measles elimination is a sustained measles incidence of less than one case per million population. Rubella/CRS control is defined as 95% reduction in disease burden from 2013 levels.

† SIAs are immunization campaigns, typically carried out using two targeted age ranges. An initial, nationwide catch-up SIA targets all children aged 9 months–14 years, with the goal of eliminating measles susceptibility in the population. Periodic follow-up SIAs then target all children born since the last SIA. Follow-up SIAs generally are conducted every 2 to 4 years and target children aged 9–59 months; the goal of a follow-SIA is to eliminate any measles susceptibility that has accumulated in recent birth cohorts and to protect children who did not respond to the first dose of measles vaccine.

§ The SEAR measles surveillance indicators include 1) ≥2 discarded non-measles non-rubella cases per 100,000 population at the national level per year; 2) ≥2 discarded non-measles non-rubella cases per 100,000 per year in ≥80% of subnational administrative units; 3) ≥80% of suspected measles cases tested for measles immunoglobulin M antibodies; 4) ≥80% of suspected cases have an adequate investigation conducted within 48 hours of notification; 5) ≥80% of laboratory-confirmed chains of transmission have adequate samples collected for detecting measles or rubella virus and tested in an accredited laboratory; and 6) an annualized incidence rate of zero for confirmed endemic measles cases.

¶ A suspected case that has been investigated and identified as a non-measles case using testing in a proficient laboratory or epidemiologic linkage to a laboratory-confirmed outbreak of another communicable disease that is not measles.

** A second dose of MCV (MCV2) was introduced into the routine immunization program in September 2015 and is recommended at age 15 months.

within the administrative boundary of each village using a strength-focused strategy called "appreciative inquiry," a model that seeks to engage participants in self-determined change. In contrast to approaches for problem-solving that focus on deficiencies, appreciative inquiry offers processes and potential for the community to positively explore, collectively imagine, collaboratively design, and jointly commit to strengthening routine immunization and increasing MCV1 and MCV2 coverage. By 2014, a total of 823 (21%) of 3,915 villages and 10 (13%) districts were declared fully immunized, and a goal of having the entire country declared fully immunized through routine immunization services by 2017 was established (*7*).

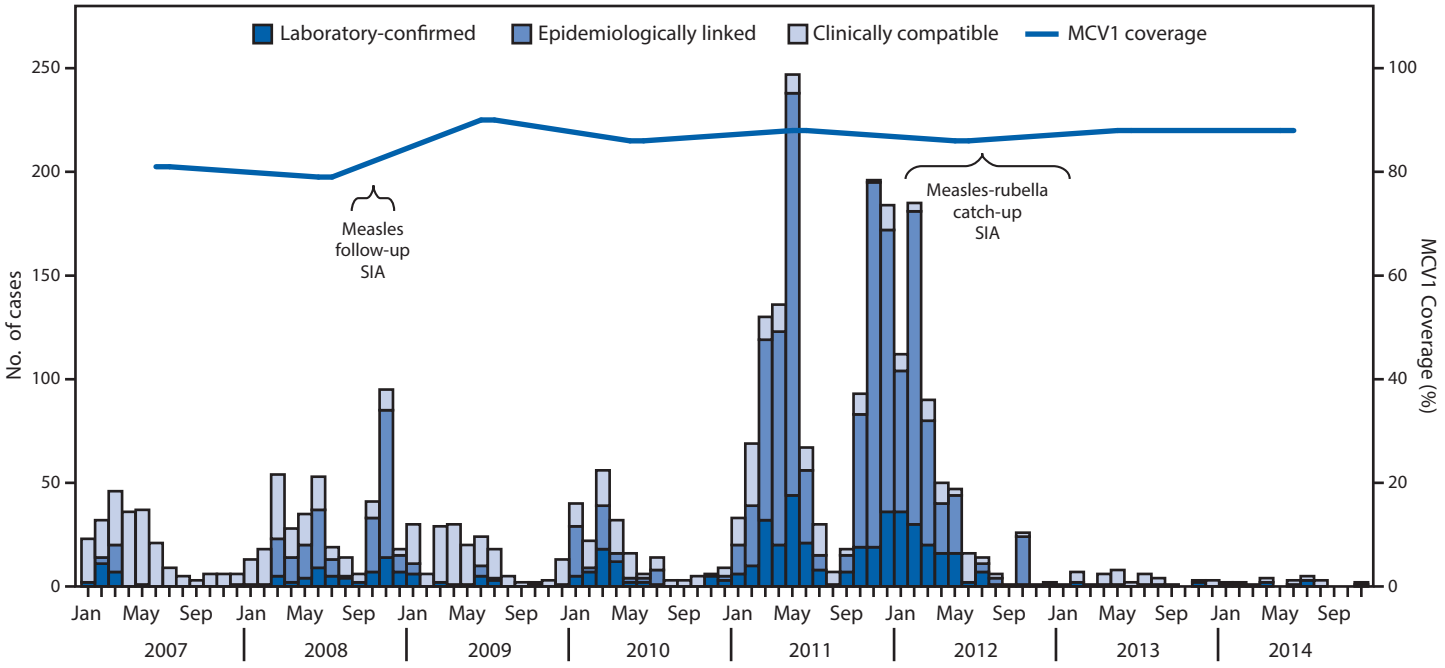
During 2007–2014, two nationwide SIAs were conducted in phases. The first SIA, in 2008, used monovalent measles vaccine, reached 3.9 million children aged 9 months–4 years (971,470 and 2,932,045 during the first and second phases, respectively), and achieved 93% administrative coverage (Figure). The second nationwide SIA, conducted during 2012–2013, used MR vaccine, reached 9.7 million children aged 9 months–14 years (1,843,087; 2,203,863; and 5,638,149 during the first, second, and third phases, respectively), and achieved 100% administrative coverage.

Surveillance Activities and Measles Incidence

Suspected measles cases[††] are reported from all health facilities through the national Health Management Information System (HMIS), and then compiled and reported to WHO and UNICEF through JRF (*2*). In 2003, measles case-based surveillance in Nepal was initiated as part of the Vaccine Preventable Disease (VPD) surveillance network on the existing acute flaccid paralysis surveillance system supported by WHO; data are provided from 735 reporting units, which include major health care centers and hospitals (approximately 10% of all government health facilities, including all inpatient facilities) throughout all 75 districts. During 2000–2006, case-based surveillance largely focused on investigation and

[††] A suspected measles case is defined as an illness in any person a clinician suspects of having measles infection, or in any person with fever and maculopapular rash, and cough, coryza, or conjunctivitis.

FIGURE. Confirmed measles cases,* estimated coverage with the first dose of measles-containing vaccine (MCV1), and supplementary immunization activities (SIAs)[†,§] — Nepal, 2007–2014



* Includes laboratory-confirmed, epidemologically linked, and clinically confirmed, as reported through the national case-based surveillance system. National measles case-based surveillance system data as reported to WHO South-East Asia Region as of December 2015.

† The national measles follow-up SIA targeted children aged 9 months–4 years, implemented in two phases: the first phase was conducted from September 10, 2008 in 29 districts targeting 971,470 children; the second phase was conducted from December 6, 2008 in 46 districts targeting 2,932,045 children. The implementation period for each phase lasted a minimum of 9 days; the overall administrative coverage was 93%.

§ The national measles-rubella catch-up SIA targeted children aged 9 months–14 years, implemented in three phases: the first phase was conducted during February 26–March 25, 2012 in 15 districts in Far and Midwest Development Region (DR) targeting 1,843,087 children; the second phase was conducted during September 17–October 16, 2012 in 25 districts in Midwest and Western DR targeting 2,203,863 children; and the third phase was conducted during December 14, 2012–January 13, 2013 in 35 districts in Central and Eastern DR targeting 5,638,149 children. The overall reported aministrative coverage was 100%.

reporting of suspected measles outbreaks. In 2007, enhanced measles case-based surveillance with individual case investigations and monitoring of performance indicators began; during 2007–2014, case-based surveillance expanded from 31 to 219 sites (*4*).

Cases are confirmed through the VPD surveillance network by outbreak investigations and case-based surveillance, with laboratory testing of specimens obtained from persons with suspected measles conducted by the National Public Health Laboratory in Kathmandu, the only WHO-accredited MR laboratory in the country. As a measure of surveillance sensitivity, the proportion of districts reporting ≥2 discarded non-measles cases per 100,000 population per year increased from 19% in 2007 to 52% in 2009. The increase could be attributed to an increase in detection and testing of non-measles cases through the VPD surveillance network that occurred during a large rubella outbreak that peaked in 2009. However, the proportion of districts reporting ≥2 discarded cases per 100,000 population declined to 19% again in 2014 (Table 1).

During 2007–2014, reported suspected measles incidence decreased 13%, from 54 to 47 cases per million population, based on aggregate data. During 2007–2014, a total of 10,047 suspected measles cases were reported through measles case-based surveillance, among which 2,849 (28%) were confirmed[§§] (Table 2). The majority of confirmed cases occurred in children aged 9 months–4 years (44%) and 5–9 years (29%). Among confirmed measles cases, 45% had received ≥1 dose of MCV. After the 2012–2013 nationwide MR SIA, the number of reported confirmed measles cases declined by 98%, from 1,035 in 2011 to 25 in 2014. In 2014, among 347 suspected measles cases reported through case-based surveillance, 314 (84%) had serum specimens tested, and nine (3%) were laboratory confirmed as measles (Table 2). During 2007–2012, the reported measles virus genotypes in Nepal were D4 and D8; genotyping for cases detected during 2013–2014 was not done (*8*).[¶¶]

Discussion

During 2007–2014, reported incidence of suspected measles in Nepal decreased 13% after implementation of recommended elimination strategies. However, based on laboratory-confirmed and epidemiologically linked cases, the decline is likely much greater: only nine laboratory-confirmed cases were reported in 2014. The number of reported measles cases decreased after each nationwide SIA; these campaigns were carefully planned to prevent an accumulation of a large number of measles-susceptible persons, a situation that can result in large measles outbreaks (*9*).

Although reported routine MCV1 coverage in Nepal was 88% in 2014, 71% of districts reported <95% MCV1 coverage (approximately half reported <90% coverage). In addition to routine challenges to program improvement, natural disasters can also hinder measles elimination measures, with unanticipated interruptions of routine services and reprioritization of resources. For example, in April 2015, a massive earthquake caused major devastation and disrupted routine immunization services in affected districts. To sustain the gains achieved by the nationwide SIAs, the fully immunized village concept is being expanded to increase routine immunization coverage, and measles risk assessments are being conducted to identify and prioritize activities in low-performing districts (*7*).

A second dose of MCV was introduced into the routine immunization program nationwide in 2015 for vaccination of children at age 15 months. Achieving and sustaining measles elimination will require high levels of population immunity that can be achieved by reaching ≥95% coverage with both MCV1 and MCV2. Because the second dose is unique among currently recommended vaccines in Nepal, in that it is administered during the second year of life, it will take time, education, and outreach to achieve high attendance at this immunization visit and reach ≥95% coverage. Despite these challenges, the MCV2 visit will provide an opportunity to catch up on missed doses of vaccines recommended during the first year of life (especially MCV1) and a platform for introduction of future vaccines recommended during the second year of life.

High quality measles surveillance remains a challenge in Nepal. The WHO/UNICEF JRF data included totals of suspected cases (i.e. "clinically compatible" cases) from all health facilities (HMIS with aggregate case reporting), and most of those reported cases were not confirmed by laboratory testing or epidemiologic linkage to another confirmed case. Because measles case-based surveillance has only been implemented in 11% of health facilities (the VPD surveillance network), suspected cases are underreported through case-based surveillance. Key district-level surveillance indicators, such as the non-measles discarded case reporting rate, reflect underreporting and low sensitivity of the measles-specific case definition used in Nepal. The large number of clinically compatible cases reported in the case-based surveillance system indicates a failure to collect specimens for laboratory confirmation, in part because of challenges associated with transporting specimens to the laboratory in Kathmandu. Case-based surveillance sensitivity could be increased by expanding case-based surveillance to all health facilities in the country; by using a more sensitive rash-fever case definition; by potentially using

[§§] Includes laboratory-confirmed, epidemiologically linked, and clinically compatible cases.

[¶¶] In Nepal, specimens for genotyping were collected from cases once a measles outbreak was confirmed. Genotype data received from the Measles Nucleotide Surveillance database.

TABLE 1. National measles case-based surveillance performance indicator targets and progress — Nepal, 2007–2014

Indicators	Target	Year							
		2007	2008	2009	2010	2011	2012	2013	2014
Reporting rate of discarded non-measles cases at the national level per year	≥2	1.6	4.0	6.5	3.0	4.6	4.2	1.0	1.2
Proportion of subnational administrative units (districts) reporting at least two discarded non-measles cases per 100 000 population per year	≥80	19	35	52	37	49	45	16	19
Percentage of suspected measles* cases adequately investigated† ≤48 hours of notification	≥80	69	51	58	61	75	53	92	95
Proportion of suspected cases with adequate specimens§ tested for measles in a proficient laboratory¶	≥80	48	44	52	60	41	46	85	84
Proportion of results reported by the laboratory within 7 days of specimen receipt**	≥80	69	94	88	84	84	62	88	97
Proportion of weekly surveillance units reporting to the national level on time	≥80	88	93	93	95	92	91	92	90

* A suspected measles case is defined as an illness in any person a clinician suspects of having measles infection, or in any person with fever and maculopapular rash and cough, coryza, or conjunctivitis.
† An adequate investigation includes collection of all the following data elements about each suspected case of measles or rubella: patient name or identifiers, place of residence, place of infection (at least to district level), age (or date of birth), sex, date of rash onset, date of specimen collection, measles-rubella vaccination status, date of last measles-rubella or measles-mumps-rubella vaccination, date of notification, date of investigation and travel history.
§ An adequate specimen is a blood specimen collected ≤28 days of the onset of rash.
¶ A proficient laboratory is one that is World Health Organization (WHO)-accredited and/or has an established quality assurance program with oversight by a WHO-accredited laboratory.
** Changed to 4 days in 2015.

TABLE 2. Measles incidence,* number of reported measles cases by case classification, age group, and vaccination status — Nepal, 2007–2014

Year	WHO/UNICEF JRF reporting†		Measles case-based surveillance§												
			Case classification					Age group of confirmed measles cases No. (%)					MCV doses received by confirmed measles case No. (%)		
	No. reported suspected measles cases	Incidence (cases/million population)	No. suspected measles cases¶	No. confirmed measles cases** (%)	No. laboratory-confirmed cases	No. epi linked cases	No. clinically compatible cases	<9 mos	9 mos–4 yrs	5–9 yrs	10–14 yrs	≥15 yrs	≥1	Zero	Unknown
2007	1,415	54	657	230 (35)	22	16	192	23 (10)	78 (34)	64 (28)	37 (16)	28 (12)	134 (58)	47 (20)	49 (21)
2008	2,089	78	1,494	394 (26)	61	188	145	32 (8)	241 (61)	80 (20)	21 (5)	20 (5)	191 (48)	165 (42)	38 (10)
2009	189	7	1,971	176 (9)	20	11	145	7 (4)	77 (44)	59 (34)	21 (12)	12 (7)	117 (66)	31 (18)	28 (16)
2010	190	7	1,026	216 (21)	53	62	101	28 (13)	98 (45)	53 (25)	26 (12)	11 (5)	118 (55)	76 (35)	22 (10)
2011	2,359	84	2,310	1,035 (45)	190	719	126	45 (4)	455 (44)	290 (28)	138 (13)	107 (10)	364 (35)	505 (49)	166 (16)
2012	3,362	118	1,919	732 (38)	166	497	69	21 (3)	279 (38)	257 (35)	113 (15)	62 (8)	331 (45)	321 (44)	80 (11)
2013	1,861	68	323	41 (13)	10	0	31	10 (24)	18 (44)	8 (20)	2 (5)	3 (7)	16 (39)	22 (54)	3 (7)
2014	1,279	47	347	25 (7)	9	0	16	5 (20)	11 (44)	5 (20)	2 (8)	2 (8)	14 (56)	8 (32)	3 (12)

Abbreviations: epi = epidemiologically; JRF = Joint Reporting Form; MCV = measles-containing vaccine; UNICEF = United Nations Children's Fund; WHO = World Health Organization.
* Measles incidence calculated on the basis of reported suspected measles cases and population by member states through WHO/UNICEF JRF.
† National measles case data as reported to WHO South-East Asia Region Office (SEARO) as of December 2015 through the WHO/UNICEF JRF. Nepal uses administrative data reported through the national Health Management Information system (HMIS) to report in the JRF. The HMIS receives data from all the health facilities in the country, including private and public clinics and hospitals.
§ Data from case-based measles surveillance through the Vaccine Preventable Diseases surveillance network reported to WHO SEARO as of December 2015.
¶ A suspected measles case is defined as an illness in any person a clinician suspects of having measles infection, or in any person with fever and maculopapular rash and cough, coryza, or conjunctivitis.
** Includes laboratory-confirmed, epidemiologically linked, and clinically compatible cases. An epidemiologically linked case is one that meets the clinical case definition and is linked epidemiologically to a laboratory-confirmed or another epidemiologically confirmed case.

alternative methods for specimen collection and transport, such as dried blood spots; and by increasing the collection and timely transport of specimens to the national laboratory. In addition, specimens for genotyping need to be collected on a proportion of measles and rubella cases to track transmission pathways, identify outbreak sources, and detect connections among cases.

The findings in this report are subject to at least two limitations. First, MCV1 coverage estimates can be affected by erroneous inclusion of SIA doses or doses administered to children outside the target group, inaccurate estimates of the target population size, and inaccurate reports of the number of doses delivered. Second, surveillance data might substantially underestimate disease incidence, because not all patients seek care, and not all patients who seek care are reported.

The endorsement in 2015 of the Nepal National Measles Elimination Strategy by the national government provides an opportunity to achieve and maintain measles elimination, by continuing to strengthen routine immunization services through innovative approaches, conducting high quality SIAs, enhancing case-based surveillance, increasing the number of specimens sent for laboratory confirmation, and identifying

Summary

What is already known about this topic?

Before 2007, estimated coverage with the routine first dose of measles-containing vaccine (MCV1) in Nepal was ≤85% nationally; no districts had ≥95% MCV1 coverage, and measles was one of the major causes of childhood death.

What is added by this report?

During 2007–2014, MCV1 coverage increased from 71% to 88%; approximately 3.9 and 9.7 million children were vaccinated during supplemental immunization activities (SIAs) in 2008 and 2014, respectively; and annual suspected measles incidence declined 13%, from 54 to 47 cases per 1 million population. In 2013, a goal was set for measles elimination in Nepal by 2019. Challenges to achieving elimination include suboptimal MCV1 coverage at national and subnational levels and a low-performing measles case-based surveillance system.

What are the implications for public health practice?

Achieving ≥95% 2-dose measles vaccination coverage in all districts will require strengthening routine immunization services through innovative approaches, such as the "fully immunized village" approach, and implementing periodic high-quality SIAs. Improved measles case-based surveillance performance and sensitivity are needed for rapid case detection and outbreak preparedness and response.

opportunities for synergies with other public health programs. In 2015, Nepal established the National Verification Committee for Measles Elimination, which is aligned with the global framework for the verification of progress toward measles elimination (*10*). As Nepal nears measles elimination, building capacity for epidemiologic investigations and outbreak preparedness and response to rapidly identify and contain outbreaks is needed. In addition to eliminating measles, these actions can enhance all aspects of the national public health system.

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Zika Virus Infection Among U.S. Pregnant Travelers — August 2015–February 2016

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On February 26, 2016, this report was posted as an MMWR Early Release on the MMWR website (http://www.cdc.gov/mmwr).

After reports of microcephaly and other adverse pregnancy outcomes in infants of mothers infected with Zika virus during pregnancy, CDC issued a travel alert on January 15, 2016, advising pregnant women to consider postponing travel to areas with active transmission of Zika virus. On January 19, CDC released interim guidelines for U.S. health care providers caring for pregnant women with travel to an affected area (*1*), and an update was released on February 5 (*2*). As of February 17, CDC had received reports of nine pregnant travelers with laboratory-confirmed Zika virus disease; 10 additional reports of Zika virus disease among pregnant women are currently under investigation. No Zika virus–related hospitalizations or deaths among pregnant women were reported. Pregnancy outcomes among the nine confirmed cases included two early pregnancy losses, two elective terminations, and three live births (two apparently healthy infants and one infant with severe microcephaly); two pregnancies (approximately 18 weeks' and 34 weeks' gestation) are continuing without known complications. Confirmed cases of Zika virus infection were reported among women who had traveled to one or more of the following nine areas with ongoing local transmission of Zika virus: American Samoa, Brazil, El Salvador, Guatemala, Haiti, Honduras, Mexico, Puerto Rico, and Samoa. This report summarizes findings from the nine women with confirmed Zika virus infection during pregnancy, including case reports for four women with various clinical outcomes. U.S. health care providers caring for pregnant women with possible Zika virus exposure during pregnancy should follow CDC guidelines for patient evaluation and management (*1*,*2*). Zika virus disease is a nationally notifiable condition. CDC has developed a voluntary registry to collect information about U.S. pregnant women with confirmed Zika virus infection and their infants. Information about the registry is in preparation and will be available on the CDC website.

Zika virus is a mosquito-borne flavivirus that was first isolated from a rhesus monkey in Uganda in 1947 (*3*). For several decades, only sporadic human disease cases were reported from Africa and Southeast Asia. In 2007, an outbreak was reported on Yap Island, Federated States of Micronesia (*3*), and outbreaks subsequently were reported from several Pacific Island countries (*4*). Local transmission of Zika virus was first identified in the Region of the Americas (Americas) in Brazil in May 2015 (*5*). Since that time, transmission of Zika virus has occurred throughout much of the Americas; as of February 18, a total of 32 countries and territories worldwide have active transmission of Zika virus (http://www.cdc.gov/zika/geo/active-countries.html). Interim guidelines for evaluation and management of pregnant women who have traveled to areas with ongoing local transmission of Zika virus include offering laboratory testing after return from travel (*2*).

During August 1, 2015–February 10, 2016, CDC received 257 requests for Zika virus testing for pregnant women. Among these requests, 151 (59%) included information indicating that the woman had a clinical illness consistent with Zika virus disease (i.e., two or more of the following signs or symptoms: acute onset of fever, rash, conjunctivitis, or arthralgia). The remaining requests did not document an illness compatible with Zika virus disease, but reporting of symptom information might have been incomplete.

Laboratory confirmation of recent Zika virus infection includes detection of 1) Zika virus, viral RNA, or viral antigen, or 2) Zika virus immunoglobulin M (IgM) antibodies with Zika virus neutralizing antibody titers ≥4-fold higher than neutralizing antibody titers against dengue or other flaviviruses endemic to the region where exposure occurred. Among the 257 pregnant women whose specimens were tested at CDC, 249 (97%) tested negative for recent Zika virus infection and eight (3%) had confirmed Zika virus infection. In addition to the eight patients with laboratory testing performed at CDC, one confirmed case was reported to CDC from a state health department with capacity to test for Zika virus infection.

Among nine pregnant women with confirmed Zika virus disease, no hospitalizations or deaths were reported. All nine women reported at least one of the four most commonly observed symptoms (fever, rash, conjunctivitis, or arthralgia), all women reported rash, and all but one woman had at least two symptoms. Among the six pregnant women with Zika virus disease who reported symptoms during the first trimester, outcomes included two early pregnancy losses, two elective pregnancy terminations, and delivery of a live

born infant with microcephaly; one pregnancy is continuing. Among two women with Zika virus infection who had symptoms during the second trimester of pregnancy, one apparently healthy infant has been born and one pregnancy is continuing. One pregnant woman reported symptoms of Zika virus infection in the third trimester of pregnancy, and she delivered a healthy infant.

Selected Case Reports

Patient A. In January 2016, a pregnant woman in her 30s reported symptoms of fever, rash, arthralgia, myalgia, and malaise at 6–7 weeks' gestation. She had traveled to a Zika-affected area at approximately 5 weeks' gestation. Serologic testing confirmed recent Zika virus infection. She experienced a spontaneous early pregnancy loss and underwent a dilation and curettage at approximately 8 weeks' gestation. Products of conception were sent to CDC for testing, and Zika virus RNA was detected by reverse transcription-polymerase chain reaction (RT-PCR) and immunohistochemical (IHC) staining (*6*).

Patient B. In January 2016, a pregnant woman in her 30s underwent laboratory testing for Zika virus infection. She reported a history of travel to a Zika-affected area at approximately 11–12 weeks' gestation. One day after returning from travel, she developed fever, eye pain, and myalgia. The next day, she developed a rash. Serologic testing confirmed recent Zika virus infection. At approximately 20 weeks' gestation, she underwent a fetal ultrasound that suggested absence of the corpus callosum, ventriculomegaly, and brain atrophy; subsequent fetal magnetic resonance imaging demonstrated severe brain atrophy. Amniocentesis was performed, and Zika virus RNA was detected by RT-PCR testing. After discussion with her health care providers, the patient elected to terminate her pregnancy.

Patient C. In late 2015, a woman in her 30s gave birth to an infant at 39 weeks' gestation. The infant's head circumference at birth was 27 cm (<3rd percentile), indicating severe microcephaly (http://www.cdc.gov/growthcharts/who_charts.htm). After delivery, an epidemiologic investigation revealed that the woman had resided in Brazil until 12 weeks' gestation. She reported that she had experienced fever, rash, arthralgia, and headache at 7–8 weeks' gestation. Evidence of Zika virus infection in the mother was confirmed by serologic testing. Molecular and pathologic evaluation of the placenta demonstrated Zika virus RNA by RT-PCR and IHC, respectively. The infant exhibited hypertonia, difficulty swallowing, and seizures, and computerized tomography scan demonstrated multiple scattered and periventricular brain calcifications. Funduscopic examination revealed a pale optic nerve and mild macular chorioretinitis. Newborn hearing screening was normal. The infant was discharged from the hospital with a gastrostomy feeding tube.

Patient D. A pregnant woman in her 30s traveled to a Zika-affected area at approximately 15 weeks' gestation. She reported symptoms of fever, rash, arthralgia, and headache beginning at the end of her travel (at approximately 17–18 weeks' gestation). Serologic testing confirmed evidence of Zika virus infection. At approximately 40 weeks' gestation, she delivered a full-term, apparently healthy infant with no reported abnormalities and a head circumference of 34.5 cm. Cranial ultrasound, newborn hearing screen, and ophthalmologic examination of the infant were all normal.

Discussion

On January 19, 2016, CDC released interim guidelines recommending that pregnant women who had traveled to areas with ongoing local transmission of Zika virus and who had symptoms consistent with Zika virus disease be tested for Zika virus infection (*1*). These guidelines were updated and expanded on February 5 to offer Zika virus testing to all pregnant women with Zika virus exposure, regardless of the presence of symptoms (*2*). Although Zika virus testing can be performed in some state, territorial, and local health departments, most testing before mid-February 2016 was performed at CDC. Based on tests performed at CDC as of February 17, 2016, only a small number of pregnant women who reported clinical illness consistent with Zika virus disease had laboratory evidence of a recent Zika virus infection. The combination of clinical signs and symptoms consistent with suspected Zika virus disease, including fever, rash, conjunctivitis, and arthralgia, is not specific to Zika virus disease; there are other causes of this clinical presentation (*7*). Among the nine pregnant women with Zika virus infection, all reported a clinical illness, including eight women with ≥2 signs and/or symptoms, and one with a generalized rash. The finding of reported clinical illness among all women who tested positive for Zika virus might be related to the initial testing criteria for pregnant women recommended by CDC, which required the presence of clinical illness consistent with Zika virus disease. Additional testing performed as of February 24, 2016 identified no confirmed cases among 162 pregnant women without reported symptoms.

Two women with confirmed Zika virus infection experienced spontaneous pregnancy losses in the first trimester of pregnancy. Although Zika virus RNA was detected in the specimens from both of these cases, it is not known whether Zika virus infection caused the pregnancy losses. First trimester pregnancy loss is common, occurring in approximately 9%–20% of all clinically recognized pregnancies (*8*), with higher rates in older women. Pregnancy loss has been observed in association

Summary

What is already known about this topic?

Because of the risk for Zika virus infection and its possible association with adverse pregnancy outcomes, CDC issued a travel alert on January 15, 2016, advising pregnant women to consider postponing travel to areas with ongoing local transmission of Zika virus. CDC also released guidelines for Zika virus testing for pregnant women with a history of travel while pregnant to areas with ongoing Zika virus transmission.

What is added by this report?

This report provides preliminary information on testing for Zika virus infection of U.S. pregnant women who had traveled to areas with Zika virus transmission. As of February 17, 2016, nine U.S. pregnant travelers with Zika virus infection had been identified. No Zika virus–related hospitalizations or deaths were reported among pregnant women. Pregnancy outcomes included two early pregnancy losses, two elective terminations, and three live births (two apparently healthy infants and one infant with severe microcephaly); two pregnancies (18 weeks' and 34 weeks' gestation) are continuing without known complications.

What are the implications for public health practice?

In this small case series, Zika virus infection during pregnancy was associated with a range of outcomes, including early pregnancy losses, congenital microcephaly, and apparently healthy infants. Additional information will be available in the future from a newly established CDC registry for U.S. pregnant women with confirmed Zika virus infection and their infants.

with Zika virus infection (*6*) and after infections with other flaviviruses (e.g., dengue, West Nile, Japanese encephalitis) (*9*–*11*); however, a causal relationship has not been established. Additional histopathologic evaluation and RT-PCR testing of tissues from pregnancy losses might provide additional insight into maternal-fetal transmission of Zika virus and the link between maternal-fetal transmission and pregnancy losses.

Seven pregnant women with confirmed Zika virus infection reported fever during pregnancy. Fever has been determined to increase the risk for adverse pregnancy outcomes, including neural tube defects (*12*). It is not known whether fever might have affected pregnancy outcomes among these pregnant women with Zika virus infection. Because of the potential risks for poor outcomes associated with fever during pregnancy, acetaminophen should be used to treat fever during pregnancy (*12*).

Approximately half a million pregnant women are estimated to travel to the United States annually from the 32 (as of February 18, 2016) Zika-affected countries and U.S. territories with active transmission of Zika virus (personal communication, Bradley Nelson, February 23, 2016). These numbers might decrease if pregnant women follow CDC recommendations (*1*) and postpone travel to areas with ongoing local Zika virus transmission. Pregnant women and their partners should also be aware of the risk for Zika virus infection through unprotected sex with an infected male partner, and carefully follow CDC interim guidelines for preventing sexual transmission of Zika virus infection (*13*). Health care providers should notify their state, local, or territorial health department about women with possible exposure to Zika virus during pregnancy for assistance in arranging testing and interpreting results. CDC has developed a registry to collect information on U.S. pregnant women with confirmed Zika virus infection and their infants. Information gathered from public health officials or health care providers will include clinical information about the pregnancy and the infant at birth and through the first year of life. This voluntary registry has been determined to be a nonresearch public health surveillance activity, and as such, it is not subject to institutional review board requirements. Health care providers are encouraged to discuss participation in the U.S. registry* with pregnant women with Zika virus infection.

*For inquiries about the U.S. Pregnancy Registry, please contact the corresponding author.

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Transmission of Zika Virus Through Sexual Contact with Travelers to Areas of Ongoing Transmission — Continental United States, 2016

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On February 26, 2016, this report was posted as an MMWR Early Release on the MMWR website (http://www.cdc.gov/mmwr).

Zika virus is a flavivirus closely related to dengue, West Nile, and yellow fever viruses. Although spread is primarily by *Aedes* species mosquitoes, two instances of sexual transmission of Zika virus have been reported (*1*,*2*), and replicative virus has been isolated from semen of one man with hematospermia (*3*). On February 5, 2016, CDC published recommendations for preventing sexual transmission of Zika virus (*4*). Updated prevention guidelines were published on February 23.* During February 6–22, 2016, CDC received reports of 14 instances of suspected sexual transmission of Zika virus. Among these, two laboratory-confirmed cases and four probable cases of Zika virus disease have been identified among women whose only known risk factor was sexual contact with a symptomatic male partner with recent travel to an area with ongoing Zika virus transmission. Two instances have been excluded based on additional information, and six others are still under investigation. State, territorial, and local public health departments, clinicians, and the public should be aware of current recommendations for preventing sexual transmission of Zika virus, particularly to pregnant women (*4*). Men who reside in or have traveled to an area of ongoing Zika virus transmission and have a pregnant partner should abstain from sexual activity or consistently and correctly use condoms during sex with their pregnant partner for the duration of the pregnancy (*4*).

Zika virus disease is an arboviral disease and a nationally notifiable condition in the United States (*5*). For the purposes of this report, a confirmed or probable case of sexually transmitted Zika virus disease was defined as an illness meeting the confirmed or probable arbovirus surveillance case definition in a person whose only known risk factor was sexual contact with a partner who recently traveled to an area with ongoing Zika virus transmission (*6*).

During February 6–22, 2016, two confirmed and four probable cases of Zika virus sexual transmission were reported to CDC by health officials from multiple states. Median patient age was 22.5 years (range = 19–55 years), and several women were pregnant. In all cases where type of sexual contact was documented, the contact included condomless vaginal intercourse and occurred when the male partner was symptomatic or shortly after symptoms resolved. Three illustrative cases are presented.

Case 1. In mid-January, immediately after returning to the United States from a 10-day trip to the Caribbean, a man developed illness with fever, arthralgia, bilateral conjunctivitis, and a maculopapular, pruritic rash. The illness lasted 6 days. No hematospermia or prostatitis was noted. On the 1st or 2nd second day of illness, he had condomless vaginal intercourse with his female partner. The woman developed a febrile illness 13–14 days after sexual contact, with rash, conjunctivitis, and myalgia. Zika virus RNA was detected in the woman's serum by reverse transcription-polymerase chain reaction (RT-PCR) assay. Test results for the man are pending. The woman had no recent history of travel outside of the continental United States, and local mosquito-borne transmission of Zika virus was not considered possible; the vectors that transmit the virus are not present or active where she lives, based on the location and current temperatures.

Case 2. In late January, a man returned to the United States after a 4-week trip to Central America. The same day, he developed fever, arthralgia, generalized pruritus, myalgia, and eye discomfort. He had condomless vaginal intercourse with his female partner several times during the following 8 days. Ten days after the man's return, his female partner developed fever, pruritic rash, arthralgia, eye pain, photophobia, headache, vomiting, and myalgia. Zika virus infection in the woman was confirmed by RT-PCR testing of serum. Serum collected from the man tested positive for Zika virus immunoglobulin M (IgM) antibodies; confirmation is pending. The woman had no recent history of travel outside the continental United States, and current local mosquito-borne transmission of Zika virus was not considered possible where she lives.

Case 3. In mid-January, a man returned from Central America with fever, rash, arthralgia, conjunctivitis, headache, and myalgia. His symptoms began 3 days earlier and persisted until approximately 3 days after his return. On the day of his return, he had sexual contact with his female partner. Ten days later, the woman developed rash, arthralgia, conjunctivitis, and myalgia. Serum collected from the woman tested positive for Zika virus IgM; confirmation is pending. Test results for the man are pending. The woman had no recent history of travel outside of the continental United States, and current local mosquito-borne transmission of Zika virus was not considered possible where she lives.

* http://emergency.cdc.gov/han/han00388.asp.

Summary

What is already known about this topic?

Zika virus is spread primarily by *Aedes* species mosquitoes, though recent reports have described two instances of sexual transmission of Zika virus, and replicative virus has been isolated from semen of one man with hematospermia. CDC released interim guidance for prevention of sexual transmission of Zika virus on February 5, 2016.

What is added by this report?

This report provides information on six confirmed and probable cases of sexual transmission of Zika virus from male travelers to female nontravelers. This suggests that sexual transmission of Zika virus might be more common than previously reported.

What are the implications for public health practice?

Men who reside in or have traveled to an area of ongoing Zika virus transmission who have a pregnant partner should abstain from sexual activity or consistently and correctly use condoms during sex (i.e., vaginal intercourse, anal intercourse, or fellatio) with their pregnant partner for the duration of the pregnancy.

Discussion

The cases described here suggest that sexual transmission of Zika virus is more common than previously reported. To date, all reported cases of sexual transmission of Zika virus have been from symptomatic male partners. Sexual transmission of Zika virus from infected women to their sex partners and from persons who are asymptomatically infected has not been reported. Prevention of infection during pregnancy is particularly important because of the growing evidence linking maternal Zika virus infection with congenital microcephaly, fetal loss, and other adverse reproductive health outcomes (*7*). Whether sexual transmission of Zika virus poses a different risk for congenital infection than that of mosquito-borne transmission is unknown.

Zika virus testing is currently recommended to establish a diagnosis in exposed persons with signs or symptoms consistent with Zika virus disease, and can be offered to asymptomatic pregnant women who have been exposed to Zika virus (*8*). In these recommendations, exposure has been defined as living in or having traveled to an area with ongoing Zika virus transmission (*8*). Health care providers should now consider any person who has had condomless sex (i.e., vaginal intercourse, anal intercourse, or fellatio) with a male partner who has traveled to an area of ongoing Zika virus transmission and who has had symptoms of Zika virus disease during travel or within 2 weeks of return as potentially exposed. Routine testing of men who have traveled for the purpose of assessing risk for sexual transmission is not recommended (*4*).

Men who reside in or have traveled to an area of ongoing Zika virus transmission who have a pregnant partner should abstain from sexual activity or consistently and correctly use condoms during sex with their pregnant partner for the duration of the pregnancy (*4*). Pregnant women should discuss their male partner's recent travel history and any illness consistent with Zika virus disease (http://www.cdc.gov/zika/symptoms) with their health care provider; providers can consult CDC's guidelines for evaluation and testing of pregnant women (*4*). At this time, the length of time that virus might persist in semen is unknown. A recent report described detection of Zika virus RNA in semen by RT-PCR as long as 62 days after illness onset; however, infectious virus was not cultured from semen (*9*). Recommendations for prevention of sexual transmission of Zika virus will be updated as new information regarding the risks for transmission becomes available.

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Announcement

National Kidney Month—March 2016

March is designated National Kidney Month to raise awareness about the prevention and early detection of kidney disease. Approximately 10% (20 million) of U.S. adults aged ≥20 years have chronic kidney disease (CKD), and most of them are unaware of their condition (*1*,*2*). If left untreated, CKD can lead to kidney failure, requiring dialysis or transplantation for survival.

Major risk factors for CKD include diabetes, high blood pressure, and aging (*1*). Furthermore, youth are being increasingly affected by diabetes (*3*), placing them at risk for becoming part of the adult population with CKD over time. Onset of diabetes at a young age means longer duration of diabetes in early adulthood, a powerful factor in CKD progression regardless of age, sex, or type of diabetes (*4*). Currently, a method of preventing type 1 diabetes is unknown. Therefore, prevention of type 2 diabetes might offer the greatest benefit for stemming the onset of CKD at any age. Among persons at risk for developing type 2 diabetes, lifestyle changes to increase physical activity, improve nutrition, and lose weight have been shown to prevent or delay its onset (*5*).

In collaboration with partners, CDC supports and maintains the CKD Surveillance System website (http://www.cdc.gov/ckd/surveillance) to document and monitor over time the burden of CKD and its risk factors in the U.S. population, including children and adolescents, and to track progress in CKD prevention, detection, and management. Information is available about kidney disease prevention and control (http://www.nkdep.nih.gov) and about diabetes prevention and control (http://www.cdc.gov/diabetes).

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Sleep Awareness Week — March 6–12, 2016

Sleep Awareness Week, the National Sleep Foundation's annual campaign to educate the public about the importance of sleep in health and safety, will be observed March 6–12, 2016. The American Academy of Sleep Medicine and the Sleep Research Society recommend that adults aged 18–60 years sleep ≥7 hours each night to promote optimal health and well-being (*1*). However, 35% of U.S. adults report typically sleeping <7 hours (*2*). Adults who do not get enough sleep on a regular basis are more likely to suffer from chronic conditions, such as obesity, high blood pressure, diabetes, and poor mental health (*1*).

Developing good sleep habits, such as going to bed at the same time each night and rising at the same time each morning; ensuring that the bedroom environment is quiet, dark, relaxing, and neither too warm nor too cool; turning off or removing distracting or light-emitting electronic devices from the bedroom; and avoiding large meals, nicotine, alcohol, and caffeine before bedtime, is an important first step toward improving one's sleep. Persons who have trouble sleeping in spite of good sleep habits, are excessively sleepy during the day, or who have symptoms of sleep disorders, such as snoring, should discuss these issues with their physician. General information about sleep and sleep disorders is available from CDC (http://www.cdc.gov/sleep).

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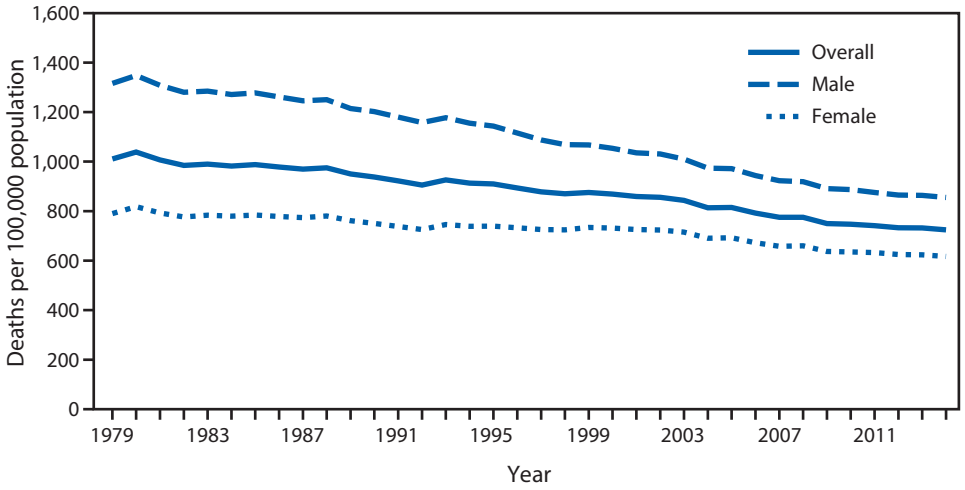
QuickStats

FROM THE NATIONAL CENTER FOR HEALTH STATISTICS

Age-Adjusted Death Rates,* by Sex — United States, 1979–2014



* Deaths per 100,000 standard population (year 2000).

The age-adjusted death rate for the United States declined from 1,010.6 deaths per 100,000 population in 1979 to 724.6 per 100,000 population in 2014, the lowest rate ever recorded. Over the same period, rates for females declined 21.9% from 789.9 to 616.7, while rates for males declined 35.0% from 1,316.2 to 855.1, thus narrowing the mortality gap between males and females.

Source: CDC. Underlying cause of death 1979–2014. CDC WONDER. Atlanta, GA: US Department of Health and Human Services, CDC; 2015. http://wonder.cdc.gov/.

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