Mumps Outbreak Among a Highly Vaccinated University Community—New York City, January–April 2014

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Background. On 14 January 2014, a vaccinated student presented with parotitis. Mumps immunoglobulin M (IgM) testing was negative and reverse-transcription polymerase chain reaction (RT-PCR) testing was not performed, resulting in a missed diagnosis and the start of an outbreak at a New York City (NYC) university.

Methods. Mumps case investigations included patient interviews, medical records review, and laboratory testing including mumps serology and RT-PCR. Case patients were considered linked to the outbreak if they attended or had epidemiologic linkage to the university. Epidemiologic, clinical, and laboratory data for outbreak cases residing in NYC were analyzed.

Results. Fifty-six NYC residents with mumps were identified with onset between 12 January and 30 April 2014. Fifty-three cases (95%) were university students, 1 (2%) was a staff member, and 2 (4%) had epidemiologic links to the university. The median age was 20 years (range 18–37 years). All cases had parotitis. Three cases were hospitalized, including 1 of 2 cases with orchitis. Fifty-four (96%) cases had received ≥1 mumps-containing vaccine, 1 (2%) was unvaccinated due to religious exemption, and 1 (2%) had unknown vaccination status. Two of the 44 (5%) cases tested by serology were mumps IgM positive, and 27 of the 40 (68%) tested by RT-PCR were positive.

Conclusions. Mumps outbreaks can occur in highly vaccinated populations. Mumps should be considered in patients with parotitis regardless of vaccination status. RT-PCR is the preferred testing method; providers should not rely on IgM testing alone. High vaccination coverage and control measures likely limited the extent of the outbreak.

Keywords. mumps; outbreak; parotitis; university; vaccination.
of State and Territorial Epidemiologists definition as a confirmed case if they had positive laboratory confirmation either with mumps reverse-transcription polymerase chain reaction (RT-PCR) testing or viral culture, or as a probable case if they had a positive serologic test for mumps immunoglobulin M (IgM) or an epidemiologic link to the outbreak [16].

Medical records were reviewed, and patients were interviewed regarding their symptoms, vaccination status, and settings attended during their infectious and incubation periods. Student cases were asked to provide information about housing, course schedules, and participation in any campus clubs or organizations.

Immunization records from providers, the university health center, and NYC’s population-based immunization information system, the Citywide Immunization Registry (CIR), were reviewed. The CIR was established in 1996 after the NYC health code required all providers in NYC to report immunizations given to all children aged <8 years, and in 2005, the requirement was expanded to include immunizations administered to all children aged <19 years [17, 18]. In accordance with New York State Public Health Law and NYS Sanitary Code, the university requires documentation of 2 doses of measles-containing vaccine and 1 dose of mumps-containing vaccine or other evidence of immunity [19]. This university recorded immunization dates for each antigen separately, and only recorded the required number of doses. For example, students with 2 doses of MMR vaccine were documented as having 2 doses of measles-containing vaccine and 1 dose of mumps-containing vaccine.

**Laboratory Investigations**

Serologic testing was performed at various commercial laboratories and the NYC DOHMH Public Health Laboratory (PHL). At the PHL, serum specimens were tested for mumps-specific IgM antibodies using enzyme-linked immunosorbent assay (Serion, catalogue number ESR103M). Specimens with indeterminate IgM results were considered IgM negative for the purpose of the analysis. RT-PCR was performed at the PHL. RNA was extracted from buccal swab specimens using the NucliSens easyMAG automated extraction system (bioMérieux, Durham, North Carolina). Mumps virus RNA was detected using a real-time RT-PCR assay targeting the nucleoprotein (N) gene [20].

**Statistical Analysis**

Outbreak-associated cases residing in NYC were included in the analyses. Fisher exact test was used to compare the proportion of cases testing positive by RT-PCR, stratified by timing of specimen collection. The analysis was conducted using SAS software, version 9.2 (Cary, North Carolina).

**RESULTS**

**Case Identification and Investigation**

A total of 56 cases were identified during the outbreak investigation with onset from 12 January 2014 and 30 April 2014 (Figure 1). Three additional cases linked to the outbreak resided outside of NYC and were excluded from our analyses.

The index case was a university student who developed unilateral parotid swelling on 12 January 2014. The student was seen at the university health center, and mumps serologic testing was performed; however, the provider ruled out a mumps diagnosis given the negative IgM result. RT-PCR testing was not performed. The index case exposed another student who subsequently presented to the student health center with symptoms consistent with mumps on 31 January 2014; the student was diagnosed with sialoadenitis, and diagnostic testing for mumps was not performed. On 19 February 2014, the student health center reported 5 students with parotitis to the DOHMH, including the index case and 4 students who presented to student health for evaluation on 18 February.

Of the 56 total cases, 28 (50%) cases were classified as confirmed and 28 (50%) were classified as probable cases (Figure 1). Among all cases, 53 (95%) were university students, 1 (2%) case was a university staff member, and 2 (4%) cases had other epidemiologic links to the university. The median age of cases was 20 years (range 18–37 years). Twenty-six (46%) cases were female. All cases had parotitis and 2 male cases (7%) had orchitis. Three (5%) cases were hospitalized.

No single source of transmission was identified. Multiple common settings where exposure may have occurred were identified; 28 (50%) cases shared a classroom with at least 1 other case and 24 (43%) cases resided in a dormitory where at least 1 other case resided (n = 8 dormitories).

Student cases identified while infectious were excluded from classes and, when feasible, dormitories for the remainder of their infectious period. Non-case students who did not have documentation of mumps vaccination or other presumptive evidence of immunity to mumps were excluded from school during the outbreak. The university sent 4 notifications to the campus community, and the DOHMH alerted providers citywide and health departments nationally through Epi-X, the Centers for Disease Control and Prevention’s communication system for public health professionals to share and access information, as students were expected to travel during spring break [21].

Fifty-four (96%) cases had documentation of at least 1 mumps-containing vaccine including 32 (57%) cases with 2 documented doses. One (2%) case was unvaccinated due to religious exemption, and the vaccination status of 1 (2%) non-student case was unknown.

**Laboratory Investigations**

Of the 56 cases, 52 (93%) had laboratory testing performed. Of the 40 cases who had RT-PCR testing performed, 27 (68%) tested positive (Figure 2A); of the 44 cases who had mumps IgM serologic testing performed, 2 (5%) tested positive (Figure 2B). Mumps virus was isolated from 2 of 11 (18%) cases tested by
viral culture. When comparing specimens collected <2 days vs ≥2 days after parotitis onset, 83% vs 44%, respectively, of specimens tested for RT-PCR were positive (P = .015).

DISCUSSION

This outbreak investigation highlighted several challenges with mumps diagnosis in the post-vaccination era and the consequences for disease transmission. The investigation demonstrated the role of mumps transmission among vaccinated persons, limited sensitivity of diagnostic tests, and lack of provider suspicion for mumps and awareness of appropriate diagnostic testing. Although the national mumps vaccination program has been highly effective in significantly reducing the incidence of mumps in the United States [1, 7, 9], sporadic mumps outbreaks still occur, particularly in congregate settings [10–12]. In the prevaccine era, mumps was common in primary school-aged children, with most children infected by age 14 [1, 22]. In the postvaccination era, there has been a shift in the epidemiology of mumps to adolescents and young adults, as seen in several recent outbreaks in college and university settings [11, 12, 23–25]. The results of this outbreak investigation highlight the importance of maintaining a high index of clinical suspicion in patients presenting with parotitis, regardless of age, vaccination status, or laboratory test results.

Laboratory confirmation of mumps is challenging, particularly in vaccinated populations [10, 12, 20]. Mumps IgM serologic testing had low sensitivity (5%) in this investigation, consistent with prior outbreaks among vaccinated populations [10, 12, 20]. In this outbreak, only serologic testing was performed on the index case, and negative results likely contributed to the missed diagnosis. Reliance on serologic testing alone may have also contributed to delayed recognition of other outbreaks [26–28]. The timing of IgM serologic testing is also important; the sensitivity of IgM testing may improve as specimens are collected further from symptom onset [20, 29]. In unvaccinated persons, mumps IgM antibody is usually detectable within 5 days after illness onset and peaks at about 7 days post-onset [30, 31]. However, patients often present for medical care soon after symptoms appear. Furthermore, vaccinated persons may not mount an IgM response or the IgM response may be transient [30, 31]. The sensitivity also varies between different assays [20, 29]. In a study by Rota et al, the IgM sensitivity in unvaccinated persons ranged from 80% to 90% by assay, compared with 9%–51% among recipients of 2 doses of MMR [20]. Although the sensitivity of mumps IgM is impacted by assay type and timing of collection, the overall sensitivity in vaccinated persons still remains low, and a negative mumps IgM result should not exclude a mumps diagnosis [10, 12, 20, 26].

The overall sensitivity of RT-PCR testing in this outbreak (68%) was much higher than that of serologic IgM testing, consistent with findings from other investigations [10, 12, 20, 26, 32, 33]. The sensitivity of RT-PCR may be impacted by the assay and genes targeted. In this investigation, RT-PCR sensitivity was similar to that seen in a prior mumps outbreak in NYC using the RT-PCR assay targeting the same nucleoprotein (N) gene, but higher than that using the short hydrophobic (SH) gene (57%) [20]. The timing of specimen collection also impacts the sensitivity of RT-PCR testing, with higher positivity rates for specimens collected closer to the time of symptom onset [10,
In our investigation, virus detection by RT-PCR was significantly higher for swabs collected <2 days after onset relative to those collected ≥2 days (83% vs 44%; \(P < 0.05\)). Despite RT-PCR testing being more sensitive than IgM testing in a vaccinated population, not all providers were aware that RT-PCR is a recommended diagnostic test for mumps. The initial cases in this outbreak had serologic testing only; if RT-PCR testing had been performed, these diagnoses might not have been missed.

The mumps virus is primarily transmitted through respiratory droplets. Extended person-to-person contact in congregate, high-density settings, such as university campuses, may facilitate mumps transmission [10, 26, 27, 34, 35]. In our investigation, no single source of transmission was identified, but there were multiple settings of overlap, including dormitories and classrooms, which may have facilitated this outbreak.

It is possible that the herd immunity threshold level, estimated to be 88%–92%, exceeded the population immunity level in this congregate setting with a high population density [36]. The median mumps vaccine effectiveness is estimated to be 78% (range 49%–92%) for 1 dose and 88% (range 66%–95%) for 2 doses [1]. As part of a New York State–mandated survey, the school self-reported that >99% of all students had at least 1 dose of mumps-containing vaccine or positive mumps serology demonstrating immunity. Ninety-six percent of cases in this outbreak had at least 1 dose of mumps-containing vaccine, and 57% of cases had 2 doses of mumps-containing vaccine; it is likely that most had received 2 doses of mumps-containing vaccine as the school self-reported that >99% of students received 2 doses of measles-containing vaccine (most commonly given together as MMR vaccine), as required for school entry. However, we were not able to obtain documentation of a second dose of mumps-containing vaccine for all cases with 1 documented dose because the university did not maintain records for nonrequired doses. Also, mumps IgG avidity testing was not performed, so we were unable to evaluate for evidence of waning immunity.

Our evaluation has several limitations. The university only maintained documentation of the 1 required dose of mumps-containing vaccine, so we were unable to confirm receipt of a second dose for all cases. We were unable to identify the immunizing providers for these cases to obtain their complete vaccination records, and many students were from other states and therefore their records were not in the CIR. Although single-antigen mumps-containing vaccine was available in the United States at the time these cases were likely to have been vaccinated, it is probable that these cases received 2 doses of mumps-containing vaccine because they would have been vaccinated after the 2-dose measles vaccination schedule was recommended with the use of MMR vaccine in 1989 [37]. Because there was only 1 unvaccinated case, we were unable to determine how vaccination status impacted serologic testing for mumps.

Despite laboratory confirmation for 52% of cases, 48% of the cases only had an epidemiologic link to the outbreak. There are various other causes of parotitis, and misclassification of cases without laboratory confirmation was possible [38–40]. However, mumps is the only documented cause of epidemic parotitis; persons with parotitis and epidemiologic link to the university during the outbreak period likely had mumps infection [4, 30].

**CONCLUSIONS**

Despite the decline in the incidence of mumps, it is important for providers to maintain a high index of suspicion, report suspected cases to local health departments, and collect buccal swabs for RT-PCR testing in addition to serologic specimens. When feasible, buccal swab specimens should be collected as soon as possible after parotitis onset for higher likelihood of mumps virus detection by RT-PCR. It is important to recognize that negative test results do not preclude a mumps diagnosis, especially among vaccinated patients. Earlier recognition and reporting and appropriate diagnostic testing during this
outbreak would have allowed for earlier implementation of control measures and might have prevented or limited the scope of the outbreak. Maintaining high vaccination rates remains one of the most important ways to prevent cases and outbreaks of mumps. Very high vaccination coverage at this large university likely prevented a much larger outbreak.

Notes

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