Antibodies Cross-Reactive to Influenza A (H3N2) Variant Virus and Impact of 2010–11 Seasonal Influenza Vaccine on Cross-Reactive Antibodies — United States

Since August 2011, a total of 12 human infections with influenza A (H3N2) variant viruses with genes from avian, swine, and human viruses (i.e., A [H3N2]v) that had acquired the M gene from influenza A (H1N1)pdm09 virus have been reported to CDC. Eleven of the cases occurred in children aged <10 years. In six cases, no history of recent exposure to swine was noted, suggesting that human-to-human transmission had occurred (*1–3*). This new gene constellation for A (H3N2)v viruses and its temporal association with an increase in human cases of A (H3N2)v highlight the need to better understand the risk for human infection with these viruses and the extent to which current seasonal vaccines might elicit cross-reactive antibodies to them. CDC conducted a preliminary analysis to evaluate the age-specific presence of serum cross-reactive antibody in U.S. populations vaccinated or not vaccinated with the 2010–11 seasonal trivalent influenza vaccine (TIV). The results indicated that 1) little or no cross-reactive antibody to A (H3N2)v exists among children aged <10 years, 2) immunization with the 2010–11 TIV had no impact on cross-reactive antibody levels in those aged <3 years, 3) cross-reactive antibody was detected in 20%–30% of those aged ≥10 years, and 4) among adults, vaccination with TIV provided a modest boost to the level of cross-reactive A (H3N2)v antibodies. Receipt of seasonal influenza vaccine continues to be recommended to protect against circulating human influenza viruses for all age groups and might provide limited protection against A (H3N2)v infection in the adult population. A vaccine virus specific for A (H3N2)v has been developed and could be used to produce an H3N2v vaccine, if needed.

Serum samples tested in this study were from two sources, a 2010–11 TIV study and the 2007–2008 National Health and Nutrition Examination Survey (NHANES). The TIV study sera included serum samples from children aged 6–35 months, adults aged 18–49 years, and older adults aged ≥65 years, all collected in the fall of 2010 before vaccination and again 3–4 weeks after vaccination. The children had no history of influenza vaccination and received 2 doses of vaccine, 4 weeks apart, with the postvaccination serum sample collected 3–4 weeks after the second dose. The TIV study serum samples were acquired through a contract and received as anonymous samples and thus were exempt from CDC institutional review board review. NHANES was the source of samples from children aged 4–17 years, which were part of a larger set received by CDC labeled only with age and date of sample collection. The protocol was reviewed and approved by the institutional review board of CDC's National Center for Immunization and Respiratory Diseases and the Research Ethics Review Board of CDC's National Center for Health Statistics.

Hemagglutination inhibition (HI) and microneutralization (MN) assays were performed following standard procedures* using A/Minnesota/11/2010 (H3N2)v and seasonal influenza viruses, A/Wisconsin/67/2005 (H3N2), and A/Perth/16/2009 (H3N2). A/Minnesota/11/2010 (H3N2)v is antigenically and genetically closely related to A (H3N2)v isolated from humans in 2011 (*3,4*). MN assays quantify antibodies that neutralize and prevent infection, whereas HI assays detect antibodies

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* Additional information available at http://www.who.int/influenza/resources/documents/manual_diagnosis_surveillance_influenza/en/index.html.

that inhibit the binding of virus to receptors on red blood cells. Serum HI titers of ≥40 are associated with reduction in the risk for influenza infection in adult populations. Although the 50% protective titer for the MN assay is not known, a previous study of antibody responses to persons infected with influenza A (H1N1)pdm09 virus showed that the MN titer was generally twofold higher than the HI titer when the HI titer was ≤160 (5). For this reason, titer achievements of ≥80 for the MN assay are presented.

Among 20 children aged 6–35 months, no evidence was found of antibodies to A (H3N2)v either before or after vaccination with the 2010–11 TIV, whereas 40% or 45% of children demonstrated seroconversion (i.e., a fourfold or greater increase in antibody titer) to the seasonal A (H3N2) virus contained in the vaccine by HI or MN assays, respectively, and 40% of children achieved HI titers of ≥40 and MN titers of ≥80 (Table 1). In contrast, among 30 adults aged 18–49 years, somewhat higher levels of prevaccination antibody to A (H3N2)v were detected, with 33% of this age group achieving HI titers of ≥40 and 43% achieving MN titers of ≥80. The proportion of adults aged 18–49 years with cross-reactive HI and MN antibody to A (H3N2)v increased to 50% and 63%, respectively, after immunization with TIV. As expected, after vaccination, 80% of these adults achieved HI titers of ≥40, and 70% achieved MN titers of ≥80 to the seasonal A (H3N2) vaccine component. Adults aged ≥65 years also exhibited prevaccination antibody to A (H3N2)v, with 17% of 30 achieving HI titers of ≥40 and 30% achieving MN titers ≥80. This increased

to 40% postvaccination by either assay. By comparison, 67% and 90% of adults aged ≥65 years exhibited postvaccination HI titers ≥40 or MN titers ≥80, respectively, to the seasonal A (H3N2) vaccine component. Therefore, in these two adult populations, receipt of TIV boosted the levels of antibodies to A (H3N2)v, but to a lesser extent than the antibody response to the A (H3N2) vaccine component.

Because the TIV study did not include persons aged 4–17 years, single serum samples collected during 2007–2008 as part of NHANES were used to assess the level of cross-reactive antibody to A (H3N2)v in this age group. The NHANES samples were stratified into two age groups (4–9 years and 10–17 years) based on analyses of HI and MN titers with A (H3N2)v viruses that showed a statistical difference between them by either assay (Table 2). Among 38 children aged 4–9 years, cross-reactive geometric mean HI and MN antibody titers to A (H3N2)v essentially were at baseline, with only 5% or 8% of children exhibiting HI titers ≥40 or MN titers ≥80 to H3N2v, respectively. Among 34 youths aged 10–17 years, a higher level of cross-reactive antibody to A (H3N2)v was detected. Among these older children, 26% and 29% had HI titers ≥40 or MN titers ≥80 to A (H3N2)v, respectively. For both age groups, HI titers ≥40 to a seasonal A (H3N2) virus that circulated in the years just before sample collection were detected in approximately two thirds of children.

Approximately one third of persons tested aged 10–49 years had cross-reactive antibodies that might provide some

TABLE 1. Cross-reactive hemagglutination inhibition and microneutralization antibodies to influenza A (H3N2) variant virus* among healthy persons before and after receipt of 2010–11 trivalent inactivated seasonal influenza vaccine, by age group — United States

Age group	No. of persons	Antigen	Hemagglutination inhibition[†]					Microneutralization[§]				
			Geometric mean titer[¶]		% with fourfold or greater increase in antibody titer[††]	% with titer ≥40		Geometric mean titer[¶]		% with fourfold or greater increase in antibody titer[††]	% with titer ≥80	
			Pre-vaccination (95% CI[**])	Post-vaccination (95% CI)		Pre-vaccination	Post-vaccination	Pre-vaccination (95% CI)	Post-vaccination (95% CI)		Pre-vaccination	Post-vaccination
6–35 mos	20	H3N2v	5*** (—)	5 (—)	0	0	0	5 (5–6)	5 (—)	0	0[†††]	0
		H3N2[§§§]	6 (5–7)	21 (9–49)	40	0	40	6 (5–9)	42 (15–115)	45	5	40
18–49 yrs	30	H3N2v	18*** (11–28)	32 (19–53)	17	33	50	55[¶¶¶] (31–98)	95 (51–177)	13	43[†††]	63
		H3N2[§§§]	17 (10–28)	85 (52–138)	47	30	80	31 (16–61)	172 (94–316)	50	27	70
≥65 yrs	30	H3N2v	13*** (9–20)	22 (13–37)	13	17	40	26[¶¶¶] (15–42)	51 (28–93)	17	30[†††]	40
		H3N2[§§§]	13 (8–21)	62 (37–107)	43	27	67	47 (26–84)	351 (205–601)	63	40	90

* A/Minnesota/11/2010.

[†] Assays conducted using 0.5% turkey red blood cells, 4 hemagglutinating units of virus, and sera treated with receptor-destroying enzyme, followed by adsorption with red blood cells if the serum sample contained nonspecific agglutinins.

[§] Assays conducted using 100 tissue-culture infectious doses of virus and heat inactivated sera.

[¶] A titer of 5 was used for all samples with a titer of <10. The dilution of serum in the first well is based on the combination of a 1:10 serum dilution with an equal volume of diluted virus for a final serum dilution referred to as 1:10.

[**] Confidence interval.

[††] A fourfold or greater increase in antibody titer, achieving a minimum titer of 40, indicates seroconversion (i.e., a response to the vaccine).

[***] Statistically different as determined by Wilcoxon test: 5 versus 18 (p<0.0001) and 5 versus 13 (p<0.001).

[†††] Statistically different as determined by Fisher's exact test: 0% versus 43% (p=0.0006) and 0% versus 30% (p=0.007).

[§§§] A/Perth/16/2009.

[¶¶¶] Statistically different as determined by a t-test (p=0.05).

TABLE 2. Cross-reactive hemagglutination inhibition and microneutralization antibodies to influenza A (H3N2) variant virus* in healthy persons aged 4–17 years, by age group — United States

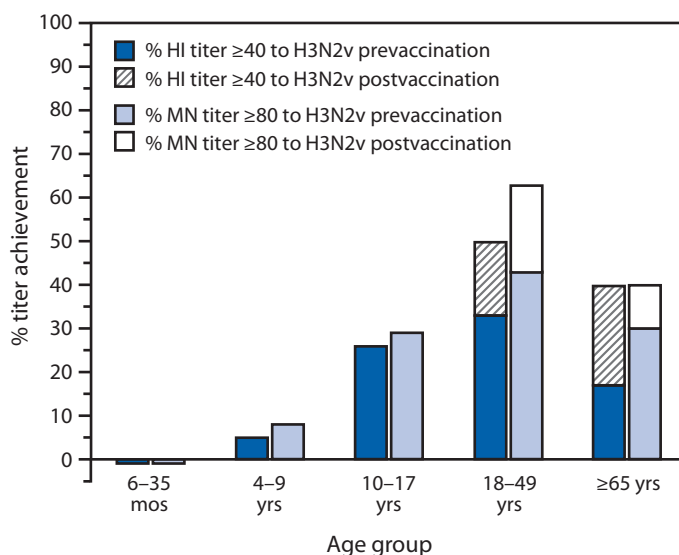| Age group	No. of persons	Antigen	Hemagglutination inhibition[†]		Microneutralization[§]	
			Geometric mean titer[¶] (95% CI[**])	% with titer ≥40	Geometric mean titer[¶] (95% CI)	% with titer ≥80
4–9 yrs[††]	38	H3N2v	7[§§] (5–9)	5[¶¶]	9*** (6–12)	8[†††]
		H3N2[§§§]	58 (38–87)	79	—[¶¶¶]	—[¶¶¶]
10–17 yrs[††]	34	H3N2v	13[§§] (8–21)	26[¶¶]	29*** (16–52)	29[†††]
		H3N2[§§§]	43 (26–71)	68	—[¶¶¶]	—[¶¶¶]

* A/Minnesota/11/2010.

[†] Assays conducted using 0.5% turkey red blood cells, 4 hemagglutinating units of virus, and sera treated with receptor-destroying enzyme, followed by adsorption with red blood cells if the serum sample contained nonspecific agglutinins.

[§] Assays conducted using 100 tissue-culture infectious doses of virus and heat inactivated sera.

[¶] A titer of 5 was used for all samples with a titer of <10. The dilution of serum in the first well is based on the combination of a 1:10 serum dilution with an equal volume of diluted virus for a final serum dilution referred to as 1:10.

[**] Confidence interval.

[††] Age at time of serum collection during 2007–2008.

[§§] Statistically different as determined by Wilcoxon test (p=0.001).

[¶¶] Statistically different as determined by Fisher's exact test (p=0.02).

[***] Statistically different as determined by Wilcoxon test (p<0.001).

[†††] Statistically different as determined by Fisher's exact test (p=0.03).

[§§§] A/Wisconsin/67/2005.

[¶¶¶] Not tested.

protection from infection with contemporary A (H3N2)v viruses (Figure). A slight drop in the cross-reactive antibody rates in persons aged ≥65 years was observed, but only the decrease in MN geometric mean titer was statistically significant (p=0.05). Children aged <10 years had minimal cross-reactive antibodies, suggesting that they are at higher risk for infection with A (H3N2)v viruses.

Reported by

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FIGURE. Percentage titer achievement for cross-reactive hemagglutination inhibition (HI) and microneutralization (MN) antibodies to influenza A (H3N2) variant virus* before and after receipt of 2010–11 trivalent inactivated seasonal influenza vaccine, by age group — United States

Legend:
- % HI titer ≥40 to H3N2v prevaccination
- % HI titer ≥40 to H3N2v postvaccination
- % MN titer ≥80 to H3N2v prevaccination
- % MN titer ≥80 to H3N2v postvaccination

Y-axis: % titer achievement
X-axis: Age group (6–35 mos, 4–9 yrs, 10–17 yrs, 18–49 yrs, ≥65 yrs)

* A/Minnesota/11/2010.

Editorial Note

Human infections with influenza A (H3N2)v were reported with increased frequency in 2011 compared with previous years; enhanced surveillance might be a contributing factor. The results in this report suggest that children aged <10 years have very low or undetectable levels of HI and neutralizing antibodies that react with A (H3N2)v and are likely to be the population most susceptible to infection with A (H3N2)v viruses among groups studied. These data are consistent with the findings that 11 of the 12 influenza A (H3N2)v cases reported in 2011 were in children aged <10 years (2).

This study also found that some persons aged ≥10 years had antibodies that are cross-reactive with A (H3N2)v. Twenty-six percent of those aged 10–17 years, 33% of those aged 18–49 years, and 17% of those aged ≥65 years had an HI titer ≥40 to A (H3N2)v, which is generally accepted to represent a 50% protective titer for seasonal influenza viruses in adult populations (6). These antibody levels suggest that persons aged ≥10 years might be less susceptible to infection with A (H3N2)v viruses, although the relationship between cross-reactive antibodies and cross-protective antibodies in A (H3N2)v infections has not been determined. Furthermore, a recent study suggests that the titer that is 50% protective might be higher for children (7). These levels of cross-reactive antibodies in unexposed populations are higher than those that were observed in older children and adults to influenza A (H1N1)pdm09 before the 2009 pandemic and are more similar to those detected in older adults at that time (8,9).

What is already known on this topic?

Twelve human infections with influenza A (H3N2)v virus were detected in the United States in 2011, compared with eight cases in the preceding 2 years. Most of these cases were in children aged <10 years.

What is added by this report?

Children aged <10 years have few or no cross-reactive antibodies to A (H3N2)v virus, but some older children and adults do have cross-reactive antibodies to the virus. Vaccination with the 2010–11 seasonal influenza vaccine had no impact on cross-reactive antibody levels in children aged <3 years but did boost cross-reactive antibodies in adults aged 18–49 years and ≥65 years, but only to levels that were lower than to seasonal A (H3N2) virus.

What are the implications for public health practice?

In the event of sustained human-to-human transmission of A (H3N2)v virus, children aged <10 years are likely to be the most susceptible to infection among groups studied. Although unlikely to protect against A (H3N2)v in this susceptible age group, receipt of seasonal influenza vaccine continues to be recommended to protect against circulating human influenza viruses for all age groups and might provide some protection against A (H3N2)v infection in the adult population. A vaccine virus specific for A (H3N2)v has been developed and could be used to produce an H3N2v vaccine, if needed.

Vaccination of adults (aged 18–49 years) and older adults (aged ≥65 years) boosted the levels of cross-reactive antibodies to A (H3N2)v, but to a lesser extent than the response to the A (H3N2) component of the vaccine. In children aged <3 years, receipt of TIV did not result in an antibody response to A (H3N2)v. A serologic study in Canada also showed no evidence of cross-reactive antibodies in children aged <10 years, and receipt of influenza vaccine did not induce a cross-reactive antibody response in those aged ≤4 years (10).

The findings in this report are subject to at least four limitations. First, the number of subjects in each age group was small, and the serum samples collected during 2007–2008 might underestimate or overestimate the current levels of cross-reactive antibodies in persons aged 4–17 years. Testing of a larger number of serum samples collected more recently is under way. Second, because of the participant selection criteria for the pediatric population, this population might not be representative of all children aged 6–35 months. Third, the populations aged 4–9 years and 10–17 years described in this report were not part of a vaccine study, so the impact of immunization with TIV in these age groups was not determined. Finally, antibody responses to viral antigens other than hemagglutinin and T-cell responses were not assessed but also might contribute to immunity to A (H3N2)v.

The composition of the 2011–12 seasonal TIV is identical to the 2010–11 vaccine evaluated in this report and is expected to provide limited cross-protection from A (H3N2)v in adults and no cross-protection in young children. In the event of sustained human-to-human transmission of (H3N2)v, an A (H3N2)v–specific vaccine would provide optimal protection for all ages. An A (H3N2)v reassortant vaccine strain based on the A/Minnesota/11/2010 virus has been developed and could be used to produce an H3N2v vaccine, if needed (*3*). Updated information and guidance documents related to A (H3N2)v viruses are available online from CDC at http://www.cdc.gov/flu/swineflu/influenza-variant-viruses.htm.

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Rabies Risk Assessment of Exposures to a Bat on a Commercial Airliner — United States, August 2011

On August 5, 2011, a bat flew through the cabin of a commercial airliner minutes after takeoff during an early morning flight from Wisconsin to Georgia, potentially exposing the passengers and flight crew to rabies virus. Three days later, the Wisconsin Division of Public Health (WDPH) requested assistance from CDC to conduct a rabies risk assessment for the passengers, flight crew, and ground crew members associated with the flight. No one was determined to have been exposed to rabies virus based on Advisory Committee on Immunization Practices guidelines for rabies prevention (1). An environmental assessment of the Wisconsin airport found a rigorous animal control and incident documentation program and no evidence of bat infestation. Although none of the persons assessed required postexposure rabies prophylaxis in this incident, bats active in daylight or found in areas where they are not normally found (e.g., aboard an aircraft) can pose risks for rabies transmission, and public health officials should be prepared to respond to such occurrences.

At 6:45 a.m. on August 5, 2011, a commercial airliner carrying 50 passengers, two pilots, and one flight attendant departed Madison, Wisconsin, bound for Atlanta, Georgia. Shortly after takeoff, a bat flew from the rear of the aircraft through the cabin several times before being trapped in the lavatory (2). The pilots were notified, and the aircraft returned to the airport. All passengers disembarked to allow maintenance crew members to remove the bat from the aircraft. The bat avoided capture and flew out the cabin door, through the airport terminal, and was seen exiting the building through automatic doors. After a search of the aircraft cabin for additional bats, 15 passengers reboarded the aircraft; 35 remaining passengers made alternative arrangements. Because the bat was not captured, the rabies status of the animal was unknown.

Assessment of Potential Exposures

On August 8, WDPH was notified of a news report describing the aircraft incident involving the bat. WDPH requested assistance from CDC to conduct a multistate investigation, assessing the potential risk for rabies and the need for rabies postexposure prophylaxis among passengers, the flight crew, and ground crew members associated with the flight.

A risk assessment tool was created to evaluate potential contact with the bat or its saliva, rabies vaccination history, and any circumstances during the flight that might have reduced the alertness of passengers and prevented an accurate description of events. Because of difficulties obtaining an accurate passenger manifest, the risk assessment tool also inquired about passenger knowledge of other passengers' identities and potential bat contact on board the flight. A separate risk assessment tool was developed for crew members and ground crew members to assess potential exposure and any history of bat infestation on the airport grounds. Additionally, an evaluation was conducted of any environmental circumstances that might have contributed to the bat's ability to enter the airliner.

During this investigation, the airline's initial departure manifest could not be provided to public health officials because it was voided when the flight was rescheduled with 15 passengers. Consequently, reservation manifests and airline weight calculations were needed to determine the possible number of persons exposed. Airline officials provided CDC with the names of the 15 confirmed passengers who reboarded the flight and the 33 persons who had made prior reservations. However, weight and flight records confirmed that 50 passengers were on board when the aircraft initially departed from Madison, and, on questioning, four of the 33 persons with reservations reported not boarding the flight. Telephone numbers were available for 36 of the 50 passengers; two passengers were contacted using e-mail, and one was contacted using a social network. Travel agencies were contacted to facilitate telephone contact of the remaining identified passengers, and a press release was issued to seek contact with the remaining unidentified passengers. Information for one unidentified passenger not listed on the flight manifest was obtained from a family member aboard the flight. Five passengers remained unidentified.

In all, CDC interviewed 45 (90%) of the 50 passengers on board the initial flight and confirmed that none had physical contact with the bat or exposure to its saliva, and all were alert during the flight. The 45 passengers were residents of 11 states. They ranged in age from 2 to 63 years (mean: 41.2 years), and 24 (53%) were male. Two passengers reported having been vaccinated previously against rabies.

The airline conducted the risk assessment of the two pilots, one flight attendant, and 16 ground crew members associated with the flight. None of the airline personnel reported contact with the bat, bat saliva, or altered alertness during the incident.

Airport Environmental Assessment

Because 10 ground crew members reported previous bat sightings at the airport, on August 22, WDPH, the Wisconsin Department of Natural Resources, Public Health Madison & Dane County, and airport authorities conducted an

environmental assessment of the airport to ascertain circumstances leading to the incident. The airport jetways, gates, and baggage handling areas were inspected. No bat droppings or other evidence of bats were seen. A review of airport animal incident records confirmed that few bats had been seen at the airport in previous years. Several measures were recommended to minimize the potential for exposure of passengers and airline personnel to bats, including using netting to cover crevices where bats might roost, extending and retracting the jetways at each gate before the first flight of the morning, and training airport employees on correct procedures for bat capture and submission for testing. No more bat sightings have been reported at the airport.

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Editorial Note

Since 2001, 15 (71%) of the 21 human rabies infections acquired in the United States were caused by rabies virus variants associated with bats (*3*). The major reservoirs of rabies in the United States are bats and wild mesocarnivores (e.g., raccoons, skunks, foxes, and coyotes). Approximately 6% of bats captured for testing in 2010 were infected with rabies virus (*3,4*). Although the prevalence in healthy bats that are not easily captured likely is much lower (*4*), a bat seen active during daylight hours or in an area where bats are not normally found, such as an aircraft cabin, should be tested for rabies as a public health precaution.

Worldwide, commercial air carriers transported approximately 2.5 billion passengers in 2009 and are expected to transport 3.3 billion by 2014 (*5*). As the number of airline passengers increases, transmission of infectious diseases before, during, and after a flight is an increasingly important public health concern. Transportation of animals, including exotic species, on aircraft has the theoretic potential for transmission of zoonotic pathogens. However, no air travel–associated zoonotic outbreaks resulting from direct animal-to-human transmission have been reported (*6*).

Among 42 reported cases of human rabies during 1995–2010 in the United States not associated with transplanted

What is already known on this topic?

Fifteen (71%) of the 21 human rabies infections acquired in the United States since 2001 were caused by rabies virus variants associated with bats.

What is added by this report?

In August 2011, 50 passengers and three flight crew members on a commercial airline flight departing from Madison, Wisconsin, potentially were exposed to a bat that flew back and forth in the aircraft cabin shortly after takeoff. The plane returned to the airport, and the bat escaped outdoors. None of 45 risk-assessed passengers, three flight crew members, or 16 ground crew members met Advisory Committee on Immunization Practices criteria for exposure to rabies; five passengers could not be located for risk assessment.

What are the implications for public health practice?

Although a bat, or any wildlife, aboard a commercial airliner is unlikely, public health practitioners should be prepared to respond to potential exposures to rabies and other infectious agents, including during air travel.

organs or tissues, 11 (26%) infections were among travelers to rabies-endemic countries and were related to direct contact with wildlife or a dog bite. None of the human rabies cases were attributed to exposure to rabies virus during travel on a public conveyance (*7*). Although human-to-human transmission of rabies virus can occur, only two documented cases of this type of transmission have been reported, other than cases associated with organ or tissue transplantation (*8*).

This investigation illustrates the unique challenges public health officials face when possible exposures to zoonotic pathogens occur in mass transit settings, particularly during air travel. Passenger reservation manifests can be inconsistent and provide limited contact information, necessitating other methods of communication to contact known and unknown travelers, including social networks, e-mail, press releases, and travel agencies. To date, five passengers on this flight remain unidentified.

Prevention strategies against rabies include public education regarding the risk for rabies virus transmission from bats and recommendations for overall avoidance of bats; however, aircraft present a unique environment in which avoidance might not be possible. Any potential human exposure to a bat should be investigated thoroughly and rapidly. A standard risk assessment in accordance with Advisory Committee on Immunization Practices recommendations (*1*) should be conducted, and the need for postexposure prophylaxis should be determined. Whenever possible, bats associated with potential exposure to humans or domestic animals should be collected and submitted for rabies diagnostic testing.

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Human Orf Virus Infection from Household Exposures — United States, 2009–2011

Orf, also known as contagious ecthyma, is a zoonotic infection caused by a dermatotropic parapoxvirus that commonly infects sheep and goats; it is transmitted to humans through contact with an infected animal or fomites. In humans, orf manifests as an ulcerative skin lesion sometimes resembling bacterial infection or neoplasm. Human infection typically is associated with occupational animal contact and has been reported in children after visiting petting zoos and livestock fairs (1). Cases lacking these exposure histories might be misdiagnosed, leading to unnecessary treatment of orf lesions, which do not usually require any specific treatment (2). This report describes four cases of human orf associated with household meat processing or animal slaughter, highlighting the importance of nontraditional risk factors. Orf should be included in the differential diagnosis of patients with clinically compatible skin lesions and a history of household meat processing or animal slaughter. Persons and communities with these exposure risks also should receive counseling regarding the use of nonpermeable gloves and hand hygiene to prevent infection.

Case Reports

Patient A. In April 2009, a woman aged 63 years punctured her right hand on a bone of a recently slaughtered goat near her home in Greece. She subsequently noted a small, pink and white papule at the site of injury that enlarged over the following week. The papule became tender and developed an erythematous border.

Two weeks later, the woman traveled to Pennsylvania to visit her son. By that time, a large bulla had developed at the wound site. On May 14, she went to an emergency department (ED) where a 3 cm bulla with a necrotic core was noted on her right palm (Figure 1). She had no fever, lymphedema, pain, or tenderness. Cultures were negative for bacteria and fungae. Histopathologic examination of the bulla roof revealed areas of necrosis and reticular degeneration of the epidermis with eosinophilic cytosolic inclusions typical of poxvirus infection. Bulla fluid and roof samples sent to CDC were positive by quantitative polymerase chain reaction (qPCR) for orf virus DNA. The outcome of patient A's infection is unknown.

Patient B. In October 2010, a man in Massachusetts aged 42 years assisted with a lamb sacrifice for the Muslim holiday Eid al-Adha, during which he held the lamb's head with his left hand. Approximately 5 days later, a small papular lesion developed on his left fifth finger, which gradually became swollen and painful.

Two weeks later, the man went to an ED at which the lesion was incised and drained; no pus was noted. He was prescribed cephalexin for presumed bacterial infection and discharged. After 1 week of treatment without improvement, a dermatologist was consulted. At that time, the lesion had become a 1.5 cm nodule with a violaceous border and a central crust; the back of the man's left hand and forearm were faintly erythematous with diffuse, nonpitting, tender edema (Figure 2). He had no lymphadenopathy or systemic symptoms.

On December 10, a biopsy of the lesion showed marked expansion and necrosis of the epidermis, focal reticular degeneration, diffuse lymphocytic infiltrate, papillary dermal edema, and telangiectasias. Bacterial culture showed rare, coagulase-negative staphylococci; fungal and mycobacterial cultures were negative. To prevent secondary infection, patient B was treated with mupirocin ointment and instructed to soak the hand in an astringent solution (aluminum acetate). Tissue sent to CDC for parapoxvirus testing was positive for orf virus DNA by qPCR. His lesion completely resolved within 4 weeks after the biopsy.

Patient C. In April 2011, a man of Ethiopian descent aged 35 years, residing in Massachusetts, cut his left thumb with a knife while slaughtering a lamb as part of Easter festivities. He washed the wound with water and applied lemon juice and alcohol. He did not seek medical attention.

One week later, the injury site had become swollen and tender without discoloration, drainage, or bleeding. A fluctuant lesion developed at the site, and the man sought care at a walk-in clinic 2 weeks after his injury. He was prescribed cephalexin for a presumed bacterial infection and advised to go to an ED for evaluation. At the ED, his thumb lesion was incised and drained. Cultures from the site grew *Staphylococcus aureus,* and antibiotics were continued. Incision and drainage were repeated 2 days later, but the lesion did not improve, and the patient was referred to hand surgery and infectious disease specialists.

At the infectious diseases clinic, the lesion was examined and noted to be 2 × 2 × 2 cm and firm, without discoloration, purulent discharge, fluctuance, or bleeding (Figure 3). The man had no systemic symptoms. Parapoxvirus infection was suspected, and the lesion was removed surgically. Histopathology showed hyperkeratosis, epidermal necrosis, and dermal infiltrate of mixed inflammatory cells consistent with orf infection; qPCR testing at CDC was positive for orf virus DNA. At follow-up 2 weeks after surgery, the man's thumb was healing and had no signs of infection.

FIGURE 1. Bulla caused by orf virus infection after puncture by a bone of a recently slaughtered goat — Pennsylvania, 2009

FIGURE 2. Nodule caused by orf virus infection after contact with a lamb being sacrificed for a holiday — Massachusetts, 2010

Patient D. In June 2011, a pregnant woman from Sudan, aged 28 years, cut her right hand on a bone while preparing a lamb's head at her at home in Virginia. The woman's family purchases a lamb's head from a local butcher or market twice yearly for a traditional Sudanese dish. Two weeks after the injury, she noted a lesion, but did not seek medical care because the lesion caused minimal discomfort.

On July 7, the woman was hospitalized for preeclampsia. While she was hospitalized, a dime-sized, crusted, vesicular lesion was incidentally noted on her right palm near the wrist. The lesion was opened, releasing a slight amount of serous

FIGURE 3. Lesion caused by orf virus infection after cutting thumb with a knife while slaughtering a lamb as part of festivities — Massachusetts, 2011

fluid, but no pus. A diagnosis of orf was suggested by an infectious disease consultant, and swabs of the crust were sent to CDC for parapoxvirus testing. Specimens were positive for orf virus DNA by qPCR. Several weeks after the initial evaluation, the woman was examined by a state public health officer who noted that the lesion was healing without signs of infection.

Reported by

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Editorial Note

Although human orf cases most commonly are reported as a result of occupational exposure to infected sheep and goats, household meat preparation and animal slaughter also pose risks for orf infection. Given the endemic state of orf among

sheep, goats, and certain other animals, and the largely decentralized nature of small ruminant markets for custom or home slaughter, feasible mechanisms to prevent infected sheep and goats from reaching consumers are limited.

Clinicians should be knowledgeable about household risks and should be able to recognize signs of orf infection. Human orf lesions generally appear on fingers, hands, or forearms after a 3–7 day incubation period. A typical lesion slowly progresses from a small, erythematous macule or papule (Figure 3) to a large nodule with a red center, white halo, and peripheral erythema (Figure 2). The nodule weeps, ulcerates, and crusts over (Figure 1). Papillomas might form before the lesion regresses. Most infections are self-limited, resolving in 4–8 weeks without scarring. Potential complications include erythema multiforme, deforming scars, and secondary bacterial infections (2–4); severe disease has occurred in immunocompromised hosts (5). Treatment consists of basic wound care, but case reports suggest that topical imiquimod might facilitate healing, especially in immunocompromised patients (5,6). Nonpermeable gloves should be used during direct contact with lesions; however, human-to-human transmission has not been reported. Protective immunity to orf is incomplete; persons can be infected multiple times (4).

Independent markets and local butchers offering live or freshly slaughtered animals are common in metropolitan areas and often cater to immigrants who prepare traditional meat dishes (e.g., patients A and D) or practice animal slaughter in association with religious observances (e.g., patients B and C). Clusters of orf infection have been reported in Turkey (2), Jordan (7), and Belgium (8) after Eid al-Adha because of increased animal slaughter for this event; a similar case previously was reported in the United States (9). Lamb sacrifice also plays a role in Passover and Easter observances, and many Sephardic Jews and Christians consume lamb during these spring holidays. In ethnically diverse communities, health-care providers might be unaware of patients having this type of animal contact and of the seasonal increases in contact associated with religious events. The popularity of hobby farming and home butchering also increases opportunities for household orf exposures.

In nonoccupational settings, where safe practices cannot be enforced, injuries can occur while handling animals, thus providing sites for orf inoculation. Patients A and D incurred puncture wounds from animal bones, and patient C cut his hand with a knife during slaughter; orf subsequently developed from those wounds. Persons who handle sheep or goats at home should be counseled to wear nonpermeable gloves, especially when wounds or rash are present. Injuries that occur during animal slaughter or processing should be cleansed thoroughly with soap and water.

What is already known?

Orf is a zoonotic infection caused by a parapoxvirus that commonly infects sheep and goats. Infection in humans produces an ulcerative skin lesion and typically is associated with occupational animal contact.

What is added by this report?

This report describes four cases of human orf associated with household meat processing or with animal slaughter for religious observances. These nontraditional exposure histories have led to delayed diagnosis and unnecessary treatments.

What are the implications for public health practice?

Orf virus infection should be included in the differential diagnosis of patients with clinically compatible skin lesions and a history of household meat processing or animal slaughter. Persons and communities with these exposure risks also should receive counseling regarding the use of nonpermeable gloves and hand hygiene to prevent infection.

Orf infection is rare in the general community. Persons who contract the virus occupationally likely know of its benign nature and might not seek treatment. Most physicians, therefore, have not encountered patients with orf and might mistake orf lesions for life-threatening conditions such as cutaneous anthrax or neoplasm (2,10). Rapid diagnosis is critical for preventing unwarranted psychological stress, unnecessary surgeries, and inappropriate antibiotic use. Histopathology and microscopy can support a diagnosis of a parapoxvirus infection. PCR can definitively identify orf virus (4) and is available at CDC (telephone: 404-639-4129); clinicians should contact their state health department to request PCR testing. Informational materials for at-risk patients and communities are available at http://www.cdc.gov/ncidod/dvrd/orf_virus.

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QuickStats

FROM THE NATIONAL CENTER FOR HEALTH STATISTICS

Percentage of Adults with Activity Limitations, by Age Group and Type of Limitation — National Health Interview Survey, United States, 2010*
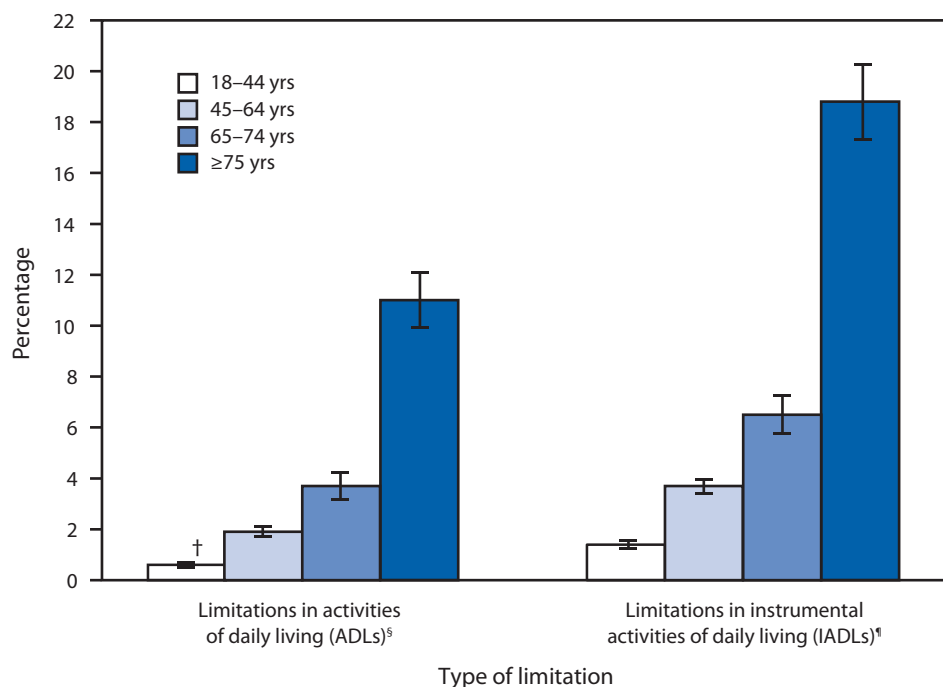
* Estimates are based on household interviews of a sample of the civilian noninstitutionalized U.S. population. Persons with unknown limitation status were excluded from the denominators.

† 95% confidence interval.

§ Limitations in ADLs are based on response to the question, "Because of a physical, mental, or emotional problem, does [person] need the help of other persons with personal care needs, such as eating, bathing, dressing, or getting around inside this home?"

¶ Limitations in IADLs are based on response to the question, "Because of a physical, mental, or emotional problem, does [person] need the help of other persons in handling routine needs, such as everyday household chores, doing necessary business, shopping, or getting around for other purposes?"

In 2010, the percentages of adults with limitations in activities of daily living (ADLs) and limitations in instrumental activities of daily living (IADLs) increased with age. Adults aged ≥75 years were almost three times as likely as adults aged 65–74 years (11.0% versus 3.7%) to require the help of another person with ADLs and with IADLs (18.8% versus 6.5%). Adults in each age group were more likely to require help with IADLs than with ADLs.

Source: Adams PF, Martinez ME, Vickerie JL, Kirzinger WK. Summary health statistics for the U.S. population: National Health Interview Survey, 2010. Vital Health Stat 2011;10(251).

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