Friday, 4-24 | 9:36 AM

Swine Flu Cases Without Swine Exposure

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On April 21, 2009, the Centers for Disease Control and Prevention (CDC) issued an *MMWR Dispatch* describing 2 cases of swine influenza A (H1N1) infection that occurred in Southern California in April. While both patients recovered uneventfully, the isolated viruses harbor novel genetic characteristics not seen in swine flu isolates in the U.S. prior to this event. The other striking feature of these cases is that there was no known contact with swine, raising the question of efficient human-to-human transmission of this virus.[1] Subsequent investigation has uncovered 5 additional cases, 2 of which occurred in Texas, with 1 requiring hospitalization. All individuals afflicted have recovered.[9]
[MMWR Dispatch: http://www.cdc.gov/mmwr/preview/mmwrhtml/mm58d0421a1.htm]

Cases Occurred in San Diego County and Imperial County Without Swine Exposure

The first case occurred in an unvaccinated 10 year-old boy from San Diego County who presented with standard flu symptoms to an outpatient clinic. The clinic, involved in a clinical study, utilized an investigational diagnostic device that identified the patient's isolate as influenza A, but was unable to ascertain whether it was H1N1, H3N2, or H5N1. Reference labs were unable to type the isolate further. More sophisticated testing done at the CDC determined that the isolate was swine influenza A (H1N1). The boy and his family reported no exposure to pigs. The boy recovered within 1 week; his brother and mother had similar symptoms during the month, but no respiratory specimens were collected from them.[1]

The second case occurred in an unvaccinated 9 year-old girl from Imperial County, which is adjacent to San Diego County. Like the first patient, this patient presented with standard influenza symptoms and sought care at an outpatient clinic. The patient had attended an agricultural fair where pigs were present, but she did not enter the area where the pigs were displayed. Her brother and cousin had similar symptoms, but they were not tested for infection. The diagnosis of swine influenza A (H1N1) was again made by CDC after receiving an influenza A isolate that could not be subtyped.[1]

Case and contact investigations are ongoing, but no epidemiologic link between the 2 patients has been found.[1]

Unique Genetic Makeup of Virus

The characterization of the viruses revealed them to be similar to each other. The viral hemagglutinin (HA) gene is similar to that of swine influenza viruses that have been circulating in the U.S. since 1999; however, its neuramindase (NA) and matrix (M) genes are similar to Eurasian viruses. This specific combination of HA, M, and NA genes has not been seen before anywhere in the world. The viruses were determined to be resistant to the adamantanes, but sensitive to the neuraminidase inhibitors, oseltamivir and zanamivir.[1]

Swine Flu 101

Influenza viruses circulate among waterfowl, swine, and humans, but other mammals may also be infected. Until 1997, avian viruses were thought to be unable to infect humans directly, as they were thought to require a "mixing-vessel" (e.g., swine) as an intermediary to allow the virus to adapt to humans. The experience with the H5N1 virus and other wholly avian viruses has proven that this step is unnecessary. However, swine do potentially play a major role in influenza epidemics given their ability to be infected efficiently with both avian and human strains, thus creating a potential platform for the recombination of viruses from different lineages. Swine are receptive to infection from avian and human viruses because they possess receptors for both. While avian influenza preferentially binds to receptors containing alpha-2,3 sialic acid-galactose linkages, human viruses bind to alpha-2,6 linkages. Humans contain only alpha 2,6 residues in the upper respiratory tract, while pigs have both types. Once an avian virus is in swine, it can develop tropism for human receptors.[2] A recent report from Indonesia indicates that H5N1 viruses have attenuated their virulence in swine, suggesting a degree of adaptation to mammalian hosts.[3] However, there is no evidence to date that a pandemic strain has originated from swine, and this hypothesis is being questioned.[2]

Swine Flu in Humans

The first isolation of a swine flu virus from a human occurred in 1974, confirming a long held suspicion that swine flu viruses could infect humans.[4] A 2007 review article on this topic presented data from 50 cases reported in the medical literature and offered several salient points regarding human cases:

- Case fatality rates were 14% (likely reflecting case ascertainment bias).
- 61% of civilian cases reported swine exposure.
- Person-to-person transmission did occur.[4]

CDC reports the receipt of approximately 1 human swine flu case report every 1 to 2 years (swine flu has been a nationally reportable condition since 2007). Since 2005, 12 cases have been reported in the U.S., most with exposure to pigs.[1]

Most swine influenza infections do not have a presentation distinct from human influenza infections. Seroprevalence studies have shown 23% positivity in those with occupational exposure to pigs.[2]

The Fort Dix Incident

The most widely known incident of swine flu in humans centers around an outbreak of a lethal influenza virus at Fort Dix in New Jersey in 1976. During that outbreak, 13 soldiers had severe respiratory illness, and 1 soldier died. A novel H1N1 swine influenza virus (Hsw1N1) was isolated, and approximately 230 other soldiers displayed evidence of infection.[5] The virus did not spread outside Fort Dix, no swine exposure was ever elucidated, and swine were never definitively established as the source.[2,5] The incident prompted a massive vaccination campaign that was plagued with problems.[2,8]

1918 and the Swine Flu

The current swine influenza strains circulating in pigs worldwide include H1N1, H3N2, and H1N2. In the U.S., one of the sub-types of the H1N1 virus has been circulating since the early 20th century. [2] Recent research has shown that this virus was likely seeded into the swine population from humans during the 1918 influenza pandemic and is a derivative of the 1918 pandemic strain—illustrating that interspecies transmission of the 1918 virus was from humans to pigs, not pigs to human. [6]

Is Swine Flu a Threat?

The current reports of 7 cases of swine flu in individuals with no epidemiologic link to swine is concerning—especially given the similar illnesses in family members—because it may indicate intrusion of a novel influenza virus into the human species with potential for human-to-human spread. Enhanced influenza surveillance may be responsible for the discovery and could be indicative of more widespread swine influenza prevalence; however, if these strains were circulating, the widespread pandemic surveillance would have been expected to detect them prior to the current cases. One recent paper on the topic states that "laboratory confirmed swine influenza in humans may be the 'tip of the iceberg.'"[7]

While both of the recent cases occurred in unvaccinated children, it is not clear that vaccination with the seasonal vaccine provides substantial protection against swine strains. Specific vaccines targeted to swine viruses may be needed for optimal protection.

Given that swine flu viruses must at some point originate from swine, the transmission belt of the virus requires the initial infection of individuals with exposure to swine. Seroprevalence studies have shown that this species jump occurs during occupational exposures, providing an impetus for the development of a swine influenza vaccine for use in individuals who are exposed to swine on a regular basis. Vaccination of these high-risk individuals may serve as a barrier to dissemination of the virus to members of the general public, of whom the current cases are representative.

References

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