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2009 H1N1 / Swine Flu – Anatomy of an Outbreak

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As this article goes to print in the first week of May, we are ending the second full week of the 2009 H1N1 swine flu outbreak. It appears the World Health Organization (WHO) may raise its Pandemic Alert level to Phase 6, indicating a full-scale pandemic with sustained human-to-human infection. Despite this, there are signs that this outbreak will turn out to be relatively mild and may even fade altogether.

Why, then, the high level of concern from both WHO and the Centers for Disease Control and Prevention (CDC)? What is the significance of this outbreak? Are there any further actions we as individual clinicians should take? These questions and others will be examined in this article.

Background

A frequent question from the audience in flu pandemic presentations is "How much time will we have to prepare once a pandemic starts?" The 2009 swine flu outbreak provides an excellent example to illustrate just how little time we will have. This is of critical importance in planning for a pandemic at the national, state, and local level.

To understand the events of the past two weeks, it is helpful first to understand how flu activity is monitored at the state and national level.

More than 1,000 clinicians from around the United States voluntarily collect data on patients in their practice setting who present with influenza-like illness (ILI) and relay that information to the CDC on a weekly basis. ILI is defined by the CDC as temperature of ≥ 100° F PLUS either cough or sore throat in the absence of an alternative diagnosis such as pharyngitis due to group A *streptococcus*.[1] The CDC has found that ILI correlates well with influenza activity and is an excellent way to monitor the progress of a typical flu season. These "sentinel providers" also are asked to send occasional throat or nasopharyngeal swabs to the CDC for influenza culture so that the circulating strains can be monitored.

A graph of ILI found on the CDC web site shows that the season was winding down by week 14, the week ending April 11, 2009.[2] The number of people seen in clinics and emergency departments with ILI was actually below the baseline of approximately 2%, indicating that the rate of ILI was no higher than the background rate for the year.

As of week 14, CDC reported that the majority of the isolates tested during the influenza season that started October 1, 2008, were influenza A/ H1N1. About one-third of the isolates tested were influenza B, and there was a small number of A/H3N2 isolates.[1] Subtypes H1N1 and H3N2 have accounted for all the human influenza A strains that have circulated in the world since 1977.[3] Overall flu activity that week was down substantially on the national level, and only 15 states were still reporting regional or widespread activity.

Swine Flu Appears, then Events Unfold Rapidly

On April 22, 2009, CDC announced that it had detected two unusual cases of influenza in children in California.[4] The isolates were type A influenza, subtype H1N1, but they were clearly distinct from the A/H1N1 human influenza virus that had circulated earlier in the winter. They appeared to be of swine origin. The earliest of the two cases was a child with onset of symptoms on March 28, and both patients had already recovered at the time of the report.

That report was met with interest by some in the infectious diseases world but hardly raised an eyebrow elsewhere. In general, influenza viruses do not cross the species barrier, although isolated cases of swine or avian flu have been reported in humans before and are not necessarily cause for alarm.[5,6] The largest recent outbreak was caused by avian influenza type A, subtype H5N1, also known as "bird flu." This virus was first reported in 1997 in Hong Kong and has since infected more than 300 people, with a mortality rate over 60%.[7]

A/H5N1 is still circulating in the Eastern Hemisphere but has not yet been found in the Western Hemisphere. It has shown limited person-to-person spread. It has caused public health authorities throughout the world to advise their nations to prepare for a new pandemic, possibly coming from a mutated strain of A/H5N1 or from a currently unknown source. The last influenza pandemic to strike the world was Hong Kong flu in 1968, a type A, subtype H3N2 that caused the deaths of 1 million to 2 million people worldwide. At least 50 million people worldwide perished from the 1918 "Spanish Flu."

Everything changed on Thursday, April 23, when CDC reported human cases of swine influenza A/H1N1 in seven patients in California and Texas, with evidence of human-to-human spread. Anne Schuchat, Interim Deputy Director for Science at the CDC, indicated in a news conference that day that the virus has components from swine, human, and possibly avian sources. According to Dr. Schuchat, "That particular genetic combination of swine influenza virus segments has not been recognized before in the U.S. or elsewhere."[8] This news was particularly relevant because of the fact that swine can serve as intermediate hosts for both avian and human viruses. This allows for genetic reassortment and the production of novel viruses with human and avian components that can theoretically produce pandemic influenza.[5]

Suddenly there was cause for concern, and the CDC decided to send a team of seven epidemiologists to California to aid in the investigation. Part of the reason for the increased urgency was that three ingredients are required for a new flu pandemic: the emergence of a novel virus; a population with no existing immunity against the subtype; and rapid transmission from person to person. It appeared that the first two criteria had already been met. It was not yet clear if the third criterion had been.

After April 23, events unfolded with breathtaking speed best illustrated with a timeline. *(See Table.)*[9,10]

Discussion

As of May 5, it is still unclear if we are heading for a full-scale influenza pandemic with the impact of the pandemics we encountered in 1918, 1957, or 1968. The very high death rate initially reported from Mexico has been revised downward with each passing day. At this point the mortality rate in Mexico is about 4%, but the mortality rate in the United States and the rest of the world combined is not appreciably different from the mortality rate from routine seasonal flu. It is possible that

Table. H1N1 Timeline

Friday April 24: Mexico's Minister of Health confirms seven cases of swine flu in Mexico. There are 854 cases of pneumonia reported from Mexico City, with 59 deaths; further investigations are in progress. Data provided by the Mexican government to the WHO indicate an upturn in ILI cases in Mexico starting March 18. CDC confirms that the Mexican strains match those found in the U.S. The CDC begins to refer people to its web site for information on preparation for a pandemic. There are now 18 confirmed cases of H1N1 in the United States.

Saturday April 25: CDC sends a team to Mexico.

Sunday, April 26: There are now 20 cases confirmed in five U.S. states. A cluster of students is identified in New York; most have traveled recently to Mexico. The Department of Health and Human Services declares a public health emergency in the United States. Homeland Security Secretary Janet Napolitano announces the release of 25% of the 50 million treatment courses of Oseltamivir (Tamiflu) in the Strategic National Stockpile.

Monday April 27: There are 40 confirmed cases in five U.S. states. The median age of infected patients is 16 years, with a range of 7 to 54 years. All have recovered uneventfully. The new strain is susceptible to Oseltamivir and Zanamivir (Relenza). It is resistant to the older adamantane class of antiviral medications (Amantadine, Rimantidine). CDC reports that there is no cross-reacting antibody from the seasonal vaccine H1N1 against the H1N1 swine virus. This means that the new virus is so completely different from the human H1N1 subtype that there is no protection to be offered against the new strain by the influenza vaccine that was in use this season. CDC now confirms 26 cases in Mexico and advises that "non-essential" travel to Mexico should be avoided but does not recommend that the border to Mexico be closed.

Tuesday April 28: Sixty-four cases are confirmed in five U.S. states. WHO reports seven countries with confirmed swine flu H1N1 infection in humans: New Zealand, Canada, United Kingdom, Israel, and Spain. The WHO raises the worldwide pandemic alert level from Phase 3 on its 6-point scale, where it has been since the emergence of H5N1 avian flu, to Phase 4. This indicates confirmed person-to-person spread. The CDC directs clinicians to its Web site for guidance on detection and treatment of swine flu. President Obama requests $1.5 billion in emergency supplemental funding for swine flu.

Wednesday, April 29: There are now 91 confirmed cases in 10 U.S. states. CDC issues guidance on antiviral recommendations for patients with confirmed, probable, or suspected H1N1. Definitions of those terms in persons with acute febrile respiratory illness are as follows:[11]

- Confirmed: by RT-PCR or culture (available only at CDC but soon to be available in all state laboratories).
- Probable: positive for flu A, negative for human H1 and H3. Further testing at CDC required.
- Suspected: contact with confirmed patient within seven days of symptom onset or travel within seven days to an area with known swine flu activity or in a community with confirmed H1N1.

There is no recommendation to treat patients with ILI who are not in those categories. CDC and the Food and Drug Administration (FDA) issued recommendations in favor of using Oseltamivir in children younger than 1 year of age, a group for which the drug has not yet been approved.[12] The WHO raises its Pandemic Alert Level to Phase 5, indicating significant person-to-person transmission.

Thursday April 30: 109 cases are confirmed in 12 U.S. states. One death is reported in Texas, a 23-month-old child from Mexico City who had crossed into Texas shortly before her death. WHO reports 257 confirmed cases in 11 countries other than the United States and Mexico, with no deaths.

Sunday May 3: CDC completes the deployment of 25% of the supplies in the Strategic National Stockpile to all states in the continental United States.

Monday May 4: There are now 286 confirmed cases in 36 U.S. states with one confirmed death. WHO reports that 21 countries have a total of 1,085 confirmed cases of swine flu, with 25 deaths in Mexico (590 laboratory confirmed cases) and no deaths outside the United States and Mexico (209 laboratory confirmed cases).[13]

Mexico has undercounted the number of infected persons, driving the mortality numbers artificially high. More data are urgently needed to better understand the widely divergent mortality figures between Mexico and the rest of the world.

While the spread of the disease around the world has been quite rapid, the total number of infected patients has been relatively modest in the 4–6 weeks since the first case was identified. Even in Mexico, approximately two thirds of the patients who had ILI and were in a known endemic region tested negative for swine flu. It is not clear yet how easily the virus is spread, or how many additional cases result from each infected individual. If that number is small, as it was with the SARS virus, then this outbreak may fade.

We will probably know by the middle of May how severe this outbreak will be. Until we have more information, we should maintain our vigilance and continue to make preparations for a possible pandemic. It is also important to be aware that an aborted outbreak now may reappear next flu season as a more widespread pandemic.

(On May 1, the Medical College of Georgia Department of Emergency Medicine and the MCG Center for Operational Medicine broadcast a one-hour lecture on pandemic flu and H1N1. A videotape of that lecture can be viewed by going to www.mcg.edu/about/h1n1 and clicking on "Pandemic Influenza: What We Should Know" in the corner box.)

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