0031-3998/09/6606-0599
PEDIATRIC RESEARCH

Vol. 66, No. 6, 2009
Printed in U.S.A.

SCIENCE – IN THE NEWS

Pandemic Influenza A (H1N1)

Ever since its sudden and surprising appearance on the world stage in the spring of 2009, the pandemic influenza A (H1N1) virus has challenged the medical and scientific communities in ways we rarely encounter. Of the many unanswered questions that remain about this novel virus, perhaps the most intriguing is that of how it originated and, most importantly, that of how we can limit its dissemination in the human population. The exact geographic origin of the pandemic influenza A (H1N1) virus and the precise time and events that led to its emergence are still unknown and may never be resolved. The first isolate to be identified by the Centers for Disease Control and Prevention (CDC) on April 15 was obtained from a 10-y-old boy from San Diego County, CA. Within days, there was a successful characterization of the full genetic composition of the eight RNA segments of the viral genome. Six of the genes were similar to segments previously found in a swine influenza strain known to circulate in North America, causing sporadic infections in persons with exposure to pigs. Swine influenza viruses have previously only rarely been transmitted to humans and had not shown the ability to be transmitted from person-to-person. The current swine virus is an exception. This may be due to the fact that it represents a multiple reassortant, containing RNA segments from classical swine influenza, Eurasian swine influenza, avian influenza, and avian *via* human to pig. Although reassortment of swine lineages seems to have occurred years before its emergence in humans, the precise timing of the immediate origin of the epidemic remains unclear (1).

At this writing, it also remains unclear how much morbidity and mortality to expect from H1N1 influenza. Based on comparisons to the 1957 pandemic, the CDC estimates that H1N1 could strike up to 40% of US population in the next 2 y and that the death toll might rise to several hundred thousand. In the United States, as of September 10, the CDC was reporting 9079 hospitalizations and 593 deaths related to H1N1. Globally, the World Health Organization was reporting 254,206 cases and at least 2,837 deaths. In contrast to seasonal influenza, current evidence indicates that this virus causes more severe illness among young people, with the highest attack rate being in children aged younger than 5 y. In the United States, most deaths were in at least one of two groups: aged younger than 5 y, and/or those with high-risk chronic medical condition. Notably, among children with high-risk conditions, the majority had neurodevelopmental disabilities (*e.g.* developmental delay or cerebral palsy). Other high-risk conditions appearing to predispose to more severe disease include asthma, chronic obstructive airways disease, obesity, or pregnancy. The elderly may be relatively protected because of multiple previous exposures to H1N1 virus, through either repeated natural infections or immunization. Although the severity of disease does not seem to be much worse than seasonal influenza, the H1N1 strain does have a predilection to infect the lower respiratory tract and, interestingly, the gastrointestinal tract.

Vaccination is the primary strategy for prevention of H1N1-associated morbidity and mortality. Vaccination strategies were initially planned with the assumption that two doses would be required, given the immunologic naïveté of humans (particularly those younger than 24 y) with this strain of influenza. However, two recent reports (2,3)—one study using a traditional "split vaccine approach," and the other testing a surface antigen vaccine adjuvanted with the immunostimulant, MF59—indicate that a single dose of vaccine seems sufficient to confer a protective level of immunity with a favorable side-effect profile. Final recommendations regarding the administration of one *versus* two doses, as well as the target populations for vaccination, have not yet been formalized, but the likely recommendation will be a single dose of vaccine with the highest priority assigned to the high-risk groups of pregnant women, people younger than 24 y or caring for infants, people with high-risk medical conditions, and health-care workers.

Initial testing of the pandemic virus demonstrated susceptibility to neuraminidase inhibitors (oseltamivir and zanamivir) and resistance to adamantanes (amantadine and rimantadine). However, sporadic cases of oseltamivir resistance have quickly emerged, including two well-publicized cases in children at a summer camp where oseltamivir had been administered to 600 campers as prophylaxis. These reports prompted the CDC to recommend that the use of prophylaxis should be reserved only for people at highest risk and should not be used for healthy people after exposure in community settings.

Now that autumn is upon us and the H1N1 influenza pandemic continues, the role that reopening schools plays in amplifying transmission of the pandemic virus, both within schools and into the wider community, is an important consideration. The World Health Organization (WHO) recently issued advice on measures that can be undertaken in schools to reduce the impact of the H1N1 influenza pandemic, including, in some instances, school closure. As the WHO points out in its statement (4), "decisions about if and when schools should be closed during the pandemic are complex and highly context-specific." At this stage, it is difficult to predict whether such an intervention will be necessary. For now, the top priority for pediatricians should be to advocate for immunization, particularly in high-risk children, once a H1N1 vaccine becomes available. Continued research into the molecular virology, immunobiology, and epidemiology of this pandemic is a major priority. Although the intrinsic pathogenicity of this strain of H1N1 seem to be modest compared with the pandemic strain of 1918, no research on pandemic influenza is ever wasted, since history demonstrates that pandemics are inevitable in human experience. Thus, lessons learned from this pandemic are likely to be valuable when the next reassortant influenza virus makes its way into the human population. – *Bazak Sharon and Mark R. Schleiss*

REFERENCES

1. Smith GJ, Vijaykrishna D, Bahl J, Lycett SJ, Worobey M, Pybus OG, Ma SK, Cheung CL, Raghwani J, Bhatt S, Peiris JS, Guan Y, Rambaut A 2009 Origins and evolutionary genomics of the 2009 swine-origin H1N1 influenza A epidemic. Nature 459:1122–1125
2. Greenberg ME, Lai MH, Hartel GF, Wichems CH, Gittleson C, Bennet J, Dawson G, Hu W, Leggio C, Washington D, Basser RL 2009 Sep 10 Response after One Dose of a Monovalent Influenza A (H1N1) 2009 vaccine—preliminary report. N Engl J Med, [Epub ahead of print]
3. Clark TW, Pareek M, Hoschler K, Dillon H, Nicholson KG, Groth N, Stephenson I 2009 Sep 10 Trial of Influenza A (H1N1) 2009 Monovalent MF59-adjuvanted vaccine—preliminary report. N Engl J Med [Epub ahead of print]
4. Available at: http://www.who.int/csr/disease/swineflu/notes/h1n1_school_measures_20090911/en/index.html. Accessed September 14, 2009