CRONOLOGIA H1N1

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MMWR

Weekly

April 24, 2009 / 58(15);400-402

Swine Influenza A (H1N1) Infection in Two Children --- Southern California, March--April 2009

On April 21, this report was posted as an MMWR Early Release *on the* MMWR *website* (http://www.cdc.gov/mmwr).

On April 17, 2009, CDC determined that two cases of febrile respiratory illness occurring in children who resided in adjacent counties in southern California were caused by infection with a swine influenza A (H1N1) virus. The viruses from the two cases are closely related genetically, resistant to amantadine and rimantadine, and contain a unique combination of gene segments that previously has not been reported among swine or human influenza viruses in the United States or elsewhere. Neither child had contact with pigs; the source of the infection is unknown. Investigations to identify the source of infection and to determine whether additional persons have been ill from infection with similar swine influenza viruses are ongoing. This report briefly describes the two cases and the investigations currently under way. Although this is not a new subtype of influenza A in humans, concern exists that this new strain of swine influenza A (H1N1) is substantially different from human influenza A (H1N1) viruses, that a large proportion of the population might be susceptible to infection, and that the seasonal influenza vaccine H1N1 strain might not provide protection. The lack of known exposure to pigs in the two cases increases the possibility that human-to-human transmission of this new influenza virus has occurred. Clinicians should consider animal as well as seasonal influenza virus infections in their differential diagnosis of patients who have febrile respiratory illness and who 1) live in San Diego and Imperial counties or 2) traveled to these counties or were in contact with ill persons from these counties in the 7 days preceding their illness onset, or 3) had recent exposure to pigs. Clinicians who suspect swine influenza virus infections in a patient should obtain a respiratory specimen and contact their state or local health department to facilitate testing at a state public health laboratory.

Case Reports

Patient A. On April 13, 2009, CDC was notified of a case of respiratory illness in a boy aged 10 years who lives in San Diego County, California. The patient had onset of fever, cough, and vomiting on March 30, 2009. He was taken to an outpatient clinic, and a nasopharyngeal swab was collected for testing as part of a clinical study. The boy received symptomatic treatment, and all his symptoms resolved uneventfully within approximately 1 week. The child had not received influenza vaccine during this influenza season. Initial testing at the clinic using an investigational diagnostic device identified an influenza A virus, but the test was negative for human influenza subtypes H1N1, H3N2, and H5N1. The San Diego County Health Department was notified, and per protocol, the specimen was sent for further confirmatory testing to reference laboratories, where the sample was verified to be an unsubtypable influenza A strain. On April 14, 2009, CDC received clinical specimens and determined that the virus was swine influenza A (H1N1). The boy and his family reported that the child had had no exposure to pigs. Investigation of potential animal

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Emergence of a Novel Swine-Origin Influenza A (H1N1) Virus in Humans

Novel Swine-Origin Influenza A (H1N1) Virus Investigation Team*

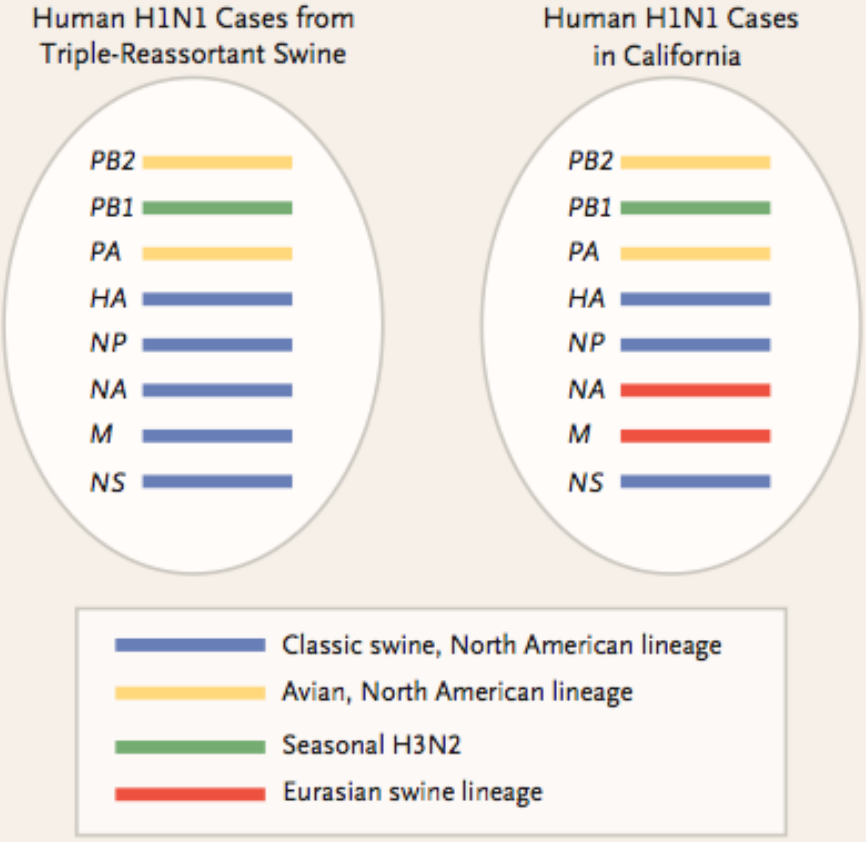
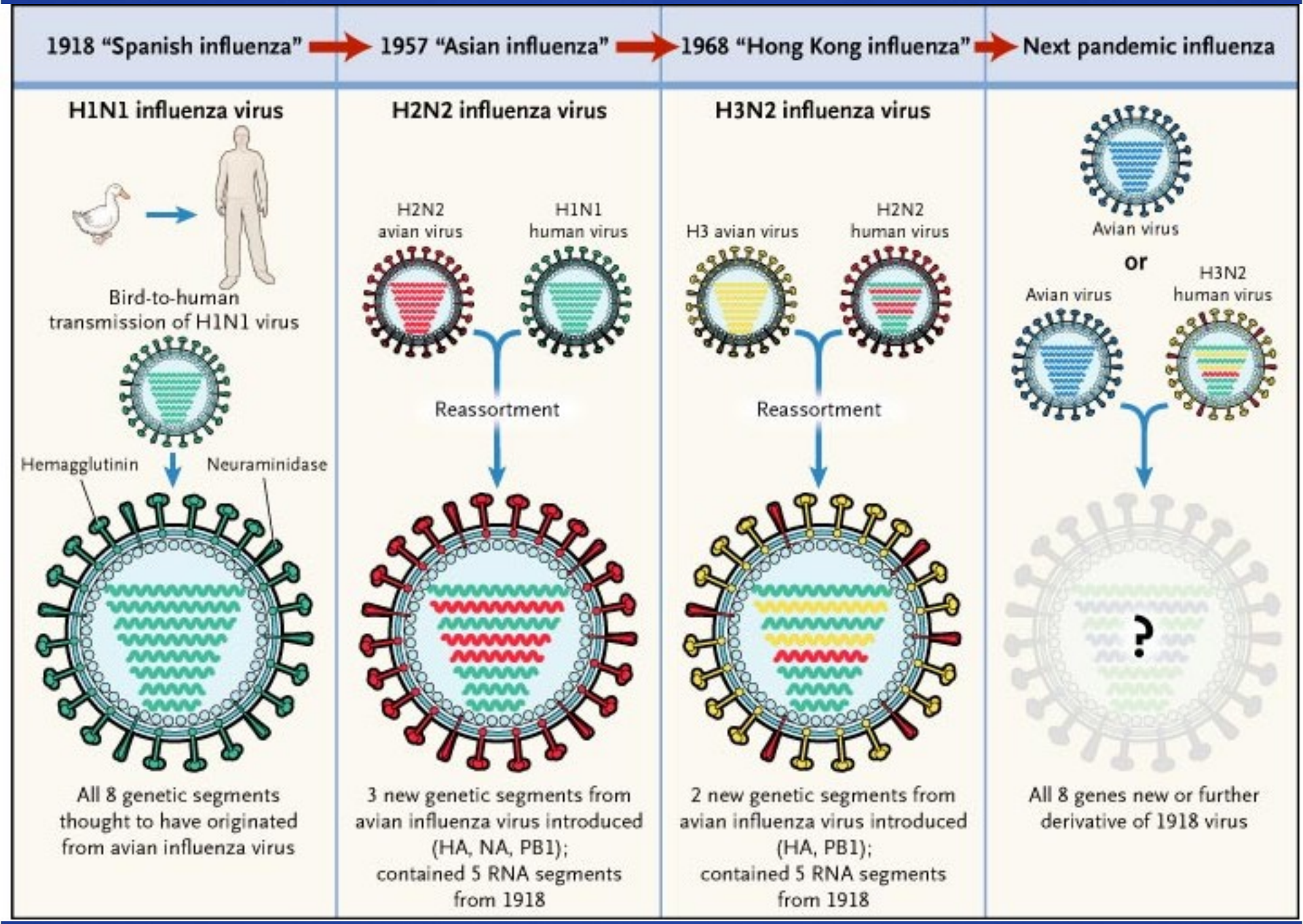
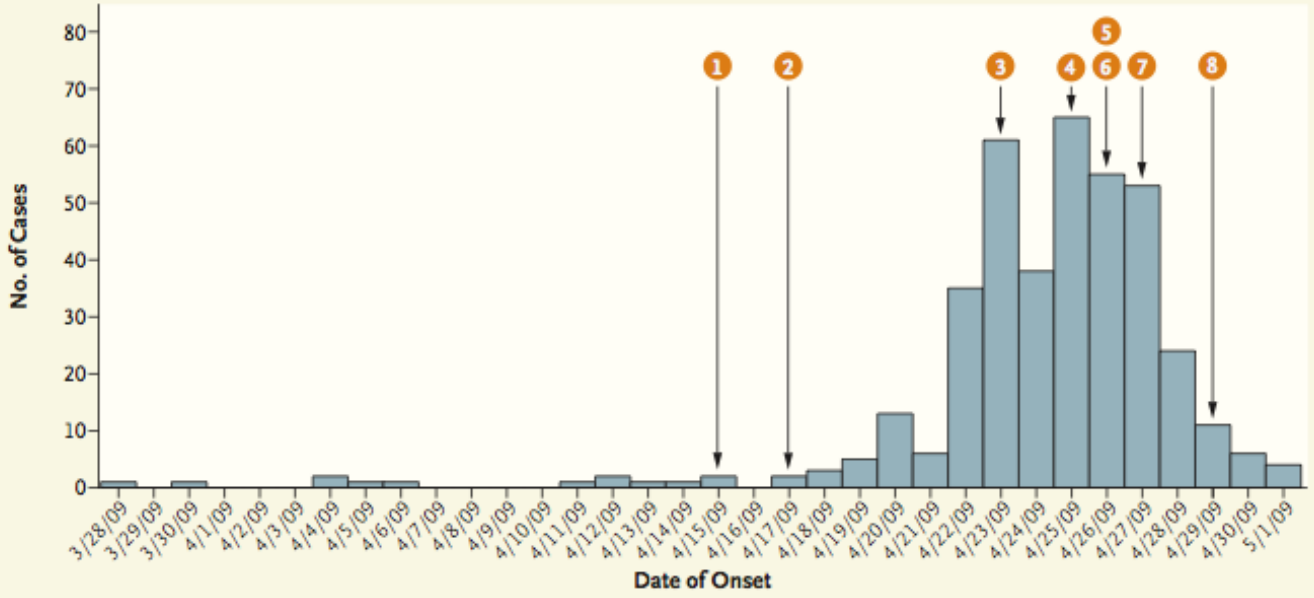


Figure 3. Comparison of H1N1 Swine Genotypes in Recent Cases in the United States.

The triple-reassortant strain was identified in specimens from patients with infection with triple-reassortant swine influenza viruses before the current epidemic of human infection with S-OIV. *HA* denotes the hemagglutinin gene, *M* the M protein gene, *NA* the neuraminidase gene, *NP* the nucleoprotein gene, *NS* the nonstructural protein gene, *PA* the polymerase PA gene, *PB1* the polymerase PB1 gene, and *PB2* the polymerase PB2 gene.


1918 "Spanish influenza"
1957 "Asian influenza"
1968 "Hong Kong influenza"
Next pandemic influenza
H1N1 influenza virus
Bird-to-human transmission of H1N1 virus
Hemagglutinin
Neuraminidase
All 8 genetic segments thought to have originated from avian influenza virus
H2N2 influenza virus
H2N2 avian virus
H1N1 human virus
Reassortment
3 new genetic segments from avian influenza virus introduced (HA, NA, PB1); contained 5 RNA segments from 1918
H3N2 influenza virus
H3 avian virus
H2N2 human virus
Reassortment
2 new genetic segments from avian influenza virus introduced (HA, PB1); contained 5 RNA segments from 1918
Avian virus
or
Avian virus
H3N2 human virus
?
All 8 genes new or further derivative of 1918 virus



1. April 15, 2009 — CDC identifies S-OIV from specimen taken from Patient 1.
2. April 17, 2009 — CDC identifies S-OIV from specimen taken from Patient 2 and the U.S. government notifies World Health Organization (WHO) of Patients 1 and 2 per International Health Regulations.
3. April 23, 2009 — CDC conducts first press briefing related to outbreak.
4. April 25, 2009 — WHO declares public health emergency of international concern.
5. April 26, 2009 — WHO raises global pandemic alert to phase 3, characterized by sporadic cases or small clusters of disease caused by human–animal transmission of an influenza reassortant virus.
6. April 26, 2009 — United States declares public health emergency.
7. April 27, 2009 — WHO raises global pandemic alert to phase 4, characterized by human-to-human transmission of an animal or human–animal influenza reassortant virus able to cause "community-level outbreaks."
8. April 29, 2009 — WHO raises global pandemic alert to phase 5, characterized by human-to-human transmission of the virus in at least two countries in one WHO region.

Figure 1. Epidemiologic Curve of Confirmed Cases of Human Infection with Swine-Origin Influenza A (H1N1) Virus with Known Date of Illness Onset in the United States (March 28–May 5, 2009).

Data regarding the date of onset of illness were available for 394 patients. This epidemiologic curve does not reflect all cases of infection with S-OIV from March 28 through May 5, 2009, because of the lag in case reporting and laboratory confirmation.

WHO PHASE

The current WHO phase of pandemic alert is 6.

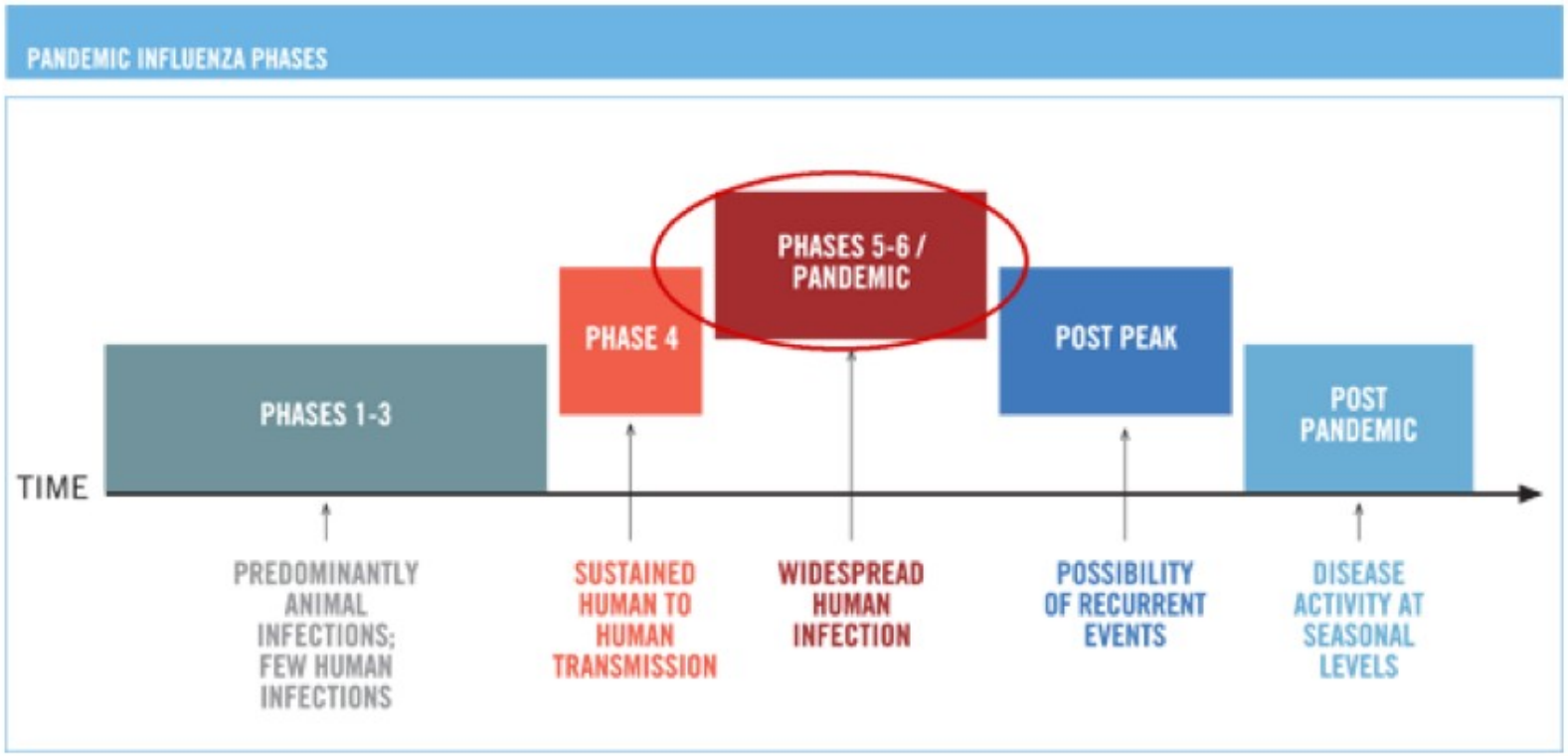


Table 1. Characteristics and Symptoms of the 642 Patients with Confirmed Swine-Origin Influenza A (H1N1).

Characteristic	Value
Male sex — no./total no. (%)	302/592 (51)
Age	
Median — yr	20
Range — yr	3 mo to 81 yr
Age group — no./total no. (%)	
0–23 mo	14/532 (3)
2–4 yr	27/532 (5)
5–9 yr	65/532 (12)
10–18 yr	212/532 (40)
19–50 yr	187/532 (35)
≥51 yr	27/532 (5)
Student in school outbreak — no./total no. (%)	104/642 (16)
Recent history of travel to Mexico — no./total no. (%)*	68/381 (18)
Clinical symptoms — no./total no. (%)	
Fever	371/394 (94)
Cough	365/397 (92)
Sore throat	242/367 (66)
Diarrhea	82/323 (25)
Vomiting	74/295 (25)
Hospitalization — no./total no. (%)	
Total	36/399 (9)
Had infiltrate on chest radiograph	11/22 (50)
Admitted to intensive care unit	8/22 (36)
Had respiratory failure requiring mechanical ventilation	4/22 (18)
Treated with oseltamivir	14/19 (74)
Had full recovery	18/22 (82)
Vaccinated with influenza vaccine during 2008–2009 season	3/19 (16)
Died	2/36 (6)

* A recent history was defined as travel to Mexico no more than 7 days before the onset of illness.

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ORIGINAL ARTICLE

Pneumonia and Respiratory Failure from Swine-Origin Influenza A (H1N1) in Mexico

Rogelio Perez-Padilla, M.D., Daniela de la Rosa-Zamboni, M.D., Samuel Ponce de Leon, M.D., Mauricio Hernandez, M.D., Francisco Quiñones-Falconi, M.D., Edgar Bautista, M.D., Alejandra Ramirez-Venegas, M.D., Jorge Rojas-Serrano, M.D., Christopher E. Ormsby, M.Sc., Ariel Corrales, M.D., Anjarath Higuera, M.D., Edgar Mondragon, M.D., and Jose Angel Cordova-Villalobos, M.D., for the INER Working Group on Influenza*

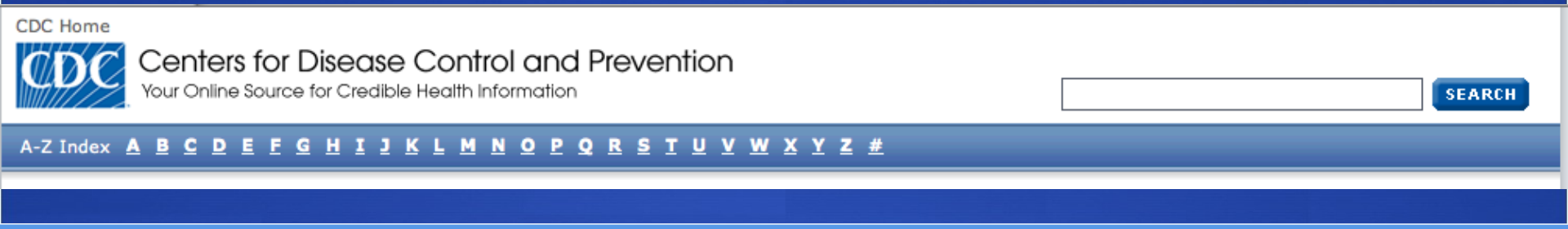
offered any protection against S-OIV infection, however. We did not find a factor that, before the onset of illness, predicted a worse outcome or death among our patients.

Since 2000, the WHO has prompted countries to prepare for a potential influenza pandemic. In Mexico, pandemic influenza planning began in 2001. Activities included the introduction of yearly influenza vaccination and a program to develop the country's national vaccine production. In 2006, a strategic reserve of oseltamivir, antibiotics, and protective items for health care personnel was established. This reserve is the source of the oseltamivir prescribed to our patients and to most hospitalized patients in Mexico. The experience in our institution highlights the need to reinforce precautions and use of personal protective equipment to prevent the infection of health care workers.

In conclusion, S-OIV infection can cause serious illness and death in young, previously healthy persons. Future studies should identify predictive factors for severe disease and, especially, the effectiveness of early oseltamivir treatment and protection offered by having undergone seasonal influenza vaccination.

No potential conflict of interest relevant to this article was reported.

We thank Celia Alpuche, M.D., from the Mexican national reference laboratory (Instituto Nacional de Referencia Epidemiologica); the CDC for providing training and primers for the real-time RT-PCR assay for the swine influenza; the Canadian National Microbiology Laboratory; Michelle Weinberg for careful review of a draft of the manuscript; and all the patients and the personnel of INER who cared for them.



- Novel H1N1 Flu: Background on the Situation A Pandemic Is Declared On June 11, 2009, the World Health Organization (WHO) signaled that a global pandemic of novel influenza A (H1N1) was underway by raising the worldwide pandemic alert level to Phase 6. This action was a reflection of the spread of the new H1N1 virus, not the severity of illness caused by the virus. At the time, more than 70 countries had reported cases of novel influenza A (H1N1) infection and there were ongoing community level outbreaks of novel H1N1 in multiple parts of the world.Since the WHO declaration of a pandemic, the new H1N1 virus has continued to spread, with the number of countries reporting cases of novel H1N1 nearly doubling……..

Managing and Reducing Uncertainty in an Emerging Influenza Pandemic

Marc Lipsitch, D.Phil., Steven Riley, D.Phil., Simon Cauchemez, Ph.D., Azra C. Ghani, Ph.D., and Neil M. Ferguson, D.Phil.

The early phases of an epidemic present decision makers with predictable challenges[1] that have been evident as the current novel influenza A (H1N1) virus has spread. The scale of the problem is uncertain when a disease first appears but may increase rapidly. Early action is required, but decisions about action must be made when the threat is only modest — and consequently, they involve a trade-off between the comparatively small, but nearly certain, harm that an intervention may cause (such as rare adverse events from large-scale vaccination or economic and social costs from school dismissals) and the uncertain probability of much greater harm from a widespread outbreak. This combination of urgency, uncertainty, and the costs of interventions makes the effort to control infectious diseases especially difficult.

Plans for addressing influenza pandemics define a graded series of responses to emerging pandemic viruses, ranging from very limited interventions to stringent measures such as closing schools and other public venues, encouraging people to work at home, and using antiviral drugs for treatment and prophylaxis. Such grading of responses is based on the pandemic's severity; for example, the United States' Pandemic Severity Index is calibrated to the case fatality ratio (www.pandemicflu.gov/plan/community/community_mitigation.pdf). Mild responses are prescribed for a strain resembling seasonal influenza, which kills perhaps 0.1% of those infected, with higher rates in the very young and elderly, whereas stringent measures are envisioned for a very severe pandemic with a case fatality ratio of 2% or more and deaths concentrated in the middle age groups.

This approach makes sense in theory, but in practice, decisions have had to be made before definitive information was available on the severity, transmissibility, or natural history of the new H1N1 virus. The United States, for example, passed the 1000-case mark on May 4, and the second death was reported on May 5. Crudely speaking, the case fatality ratio thus appeared to be 0.2%, near the upper end of the range for seasonal influenza, and superficially, this statistically uncertain estimate seems remarkably accurate given the data available on May 27, by which point there were 11 deaths and 7927 confirmed cases (a case fatality ratio of 0.14%).

However, two principal sourc-

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Vaccination is the most effective means of preventing influenza-associated morbidity and mortality. Because previous seasonal vaccinations do not appear to confer protection against 2009 H1N1, new vaccines have been licensed and are available.

The manufacturing and licensure process for this vaccine was based on the same standards as the seasonal influenza vaccines.

The vaccine is based on the A/California/07/2009 (H1N1) strain and is available in both live-attenuated and inactivated formulations.

Given the prior broad H1N1 infection experience in the population, a single dose is adequate for those older than 9 years.

With a single administration of the 2009 H1N1 vaccine, a robust immune response was seen in 80% to 96% of adults aged 18 to 64 years and in 56% to 80% of adults aged 65 years or older.

Children younger than 10 years will require 2 administrations of the vaccine separated by at least 21 days. Although clinicians are advised to start providing the 2009-2010 seasonal vaccine as soon as it becomes available, some patients will likely present for vaccination for both seasonal and 2009 H1N1 influenza.

Mayo Clin Proc.•January 2010;85(1):64-76
•doi:10.4065/mcp.2009.0588• www.mayoclinicproceedings.com

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FUTURE CONSIDERATIONS

Influenza activity in the southern hemisphere can be informative regarding the impact of 2009 H1N1 in the months ahead. Reports from Peru indicate that 8381 cases were confirmed between May 9, 2009, and September 27, 2009, with 137 confirmed influenza-related deaths. This translated to an estimated case fatality rate of 1.71% based on confirmed cases. Because the number of confirmed cases is undoubtedly lower than actual, this estimated case fatality rate is likely higher than actual. By comparison, the crude case fatality rate of the 1918 influenza pandemic is estimated to have been greater than 2.5%.

The basic reproduction number (R0), used to define the average number of secondary cases generated in a susceptible population from 1 primary case, was estimated to be between 1.2 and 1.7, consistent with other reports. If the R0 is greater than 1, a pandemic can occur; however, when R0 is less than 1, a pandemic will not occur. By comparison, the R0 of the 1918 virus was estimated to have exceeded 1.3 and may have approached 3.1

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•doi:10.4065/mcp.2009.0588• www.mayoclinicproceedings.com

TABLE 5. **Initial Target Groups for 2009 H1N1 Vaccine**

Children and young adults aged 6 mo through 24 y
Adults aged 25 through 64 y at risk of influenza-related complications because of underlying chronic medical conditions
Pregnant women
Persons who live with or provide care for infants <6 mo
Health care and emergency medical services personnel[a]

[a] Includes all persons working in health care facilities with potential exposure to influenza-infected patients or infectious material.

Mayo Clin Proc. • *January 2010;85(1):64-76*

Sindrome Guillain Barré e vaccino H1N1

In early studies, the immunogenicity and safety of the 2009 H1N1 vaccine have been similar to the seasonal influenza vaccine. **Concerns regarding the risk of Guillain- Barré syndrome (GBS)** after influenza vaccination have been raised. These concerns stem from the suspension of the 1976 H1N1 National Influenza Immunization Program because of reports of vaccine-related GBS. Subsequent analysis estimated an attributable risk of developing vaccine-related GBS from the 1976 H1N1 vaccine at just less than 1 per 100,000 persons in the adult population. ***Studies have been unable to show a consistent association between GBS and influenza vaccination, and studies suggest a higher risk of GBS from influenza itself rather than from the vaccine.*** Patients should be advised that adverse effects from the 2009 H1N1 vaccine are expected to be similar to those of the seasonal vaccine and notably involve the possibility of self-limited tenderness at the injection site of the inactivated vaccine and nasal congestion, rhinorrhea, or cough with the live-attenuated vaccine.

Mayo Clin Proc. • *January 2010;85(1):64-76*

The NEW ENGLAND JOURNAL of MEDICINE

EDITORIAL

Pandemic Influenza Vaccine Policy — Considering the Early Evidence

Kathleen M. Neuzil, M.D., M.P.H.

"Policy decisions regarding influenza rest on judgments about the behavior of the virus, the impact of the disease and our ability to interdict its course. But the virus is capricious, the disease elusive, and our remedies imperfect," said a report on the 1976 swine-flu epidemic at Fort Dix.[1]

Two peer-reviewed articles now publicly available at NEJM.org, by Greenberg et al. (ClinicalTrials.gov number, NCT00938639)[2] and Clark et al. (NCT00943358),[3] describe preliminary data on the immunogenicity of the influenza A (H1N1) 2009 monovalent vaccine. These data have been eagerly anticipated, as governments, public health officials, and other stakeholders respond to the first influenza pandemic in over 40 years. The authors and their collaborators are to be commended for their prompt execution of the trials and rapid sharing of the results.

In the study by Clark et al., one or two doses of an adjuvanted influenza vaccine containing 7.5 μg of HA (50% of the standard dose), administered on various schedules, elicited robust antibody titers.[3] Although two doses (for a total of 15 μg of HA) yielded higher antibody levels than one dose, the seroprotective titer was attained in at least 80% of subjects in every group. Without a nonadjuvanted control group, it is impossible to determine the contribution of the adjuvant to these responses. Two previous studies comparing half-dose to full-dose seasonal vaccines support the finding that nonadjuvanted influenza vaccine may be immunogenic at a dose of 7.5 μg.[4,5] Pending data from the nonadjuvanted group studied by Clark et al. are vital to understanding the contribution of adjuvant to the immunogenicity of this vaccine.

with one dose, rather than later on a two-dose schedule, is advantageous. From a logistic standpoint, administering one dose will greatly simplify vaccination programs and should reduce costs.

These immunogenicity data are difficult to extrapolate to children or to adults who have underlying immune suppression or high-risk conditions, for whom influenza vaccine is recommended. Experience with traditional seasonal vaccines tells us that the immune responses in older children, pregnant women, and immunocompetent adults with chronic conditions are roughly similar to those of healthy nonpregnant adults.[6,7] On this basis, the new data suggest that the standard 15-μg HA dose of the 2009 H1N1 vaccine should be immunogenic in those groups. The immune responses in children are unknown. Owing to the recognized morbidity associated with the 2009 H1N1 virus in children, this population is recommended to be among the first to receive vaccine in the United States.[8,9] Younger children generally have inferior responses to inactivated vaccines, as compared with healthy adults, and children under 9 years of age are recommended to receive two doses the first year that they receive influenza vaccine.[9] Immunogenicity data in young children are critical to guide policy decisions.

In our current global situation, in which decisions are pending, but positive results would allow supplies to be stretched even further.

Both vaccines tested have generally acceptable side-effect and adverse-event profiles, with pain or tenderness at the injection site being the most common adverse event observed. The local reactions seen with the adjuvanted vaccines were moderately higher than those generally seen with nonadjuvanted vaccines. Any association of uncommon adverse events with the vaccine cannot be ascertained in studies of this size. It is reassuring that the manufacturing process for these vaccines is identical to that used for seasonal vaccines, which have a strong record of safety. Although concerns linger about the association of the 1976 swine influenza vaccine with the Guillain–Barré syndrome, the syndrome was rare, with approximately 1 case for every 100,000 persons vaccinated. The rate was even lower among persons under 25 years of age.[11] One notable difference is that in 1976, we did not have a pandemic influenza virus that was spreading quickly throughout the world, and causing illness and death, as we do today. A plan for robust and comprehensive safety surveillance should be in place to detect uncommon events rapidly during the upcoming vaccination campaigns, so that risk–benefit ratios can be reassessed.

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No Further Guillain-Barré Syndrome Reports in Europe

By Jennie Smith
Elsevier Global Medical News
February 04, 2010

The European Medicines Agency has issued its ninth weekly report on adverse reactions to Europe's three major pandemic flu vaccines. It found a decline in reported reactions corresponding with a decline in the number of new vaccinations, as pandemic influenza A(H1N1) infections wane across Europe, according to the report released Feb. 3.

The agency has logged no new reports of Guillain-Barré syndrome following vaccinations since mid-January, leaving its total number of reported GBS cases at 38. The EMeA emphasized that the total represents a rate lower than the background rate of 2 cases annually per 100,000 people. Through Feb. 1 an estimated 35.7 million Europeans have been vaccinated with three centrally authorized pandemic vaccines. "What we are seeing is in line with what would normally be associated with any nonvaccinated population," said agency spokeswoman Monika Benstetter. The adverse reactions were recorded through the week ending Jan. 24. "Every new case will be carefully evaluated and closely followed," she said.

Guillain-Barré syndrome has nonetheless been among the most closely watched-for reactions to pandemic vaccines both in Europe and North America, in part because a slightly increased risk of GBS was associated with one 1976 pandemic influenza A vaccine. No consistent GBS risk has been established in relation to seasonal influenza vaccines.

In September 2009, the U.S. Centers for Disease Control and Prevention asked neurologists to prepare to report GBS cases to its own vaccine-safety monitoring program, and so far the CDC has received 61 reports of GBS following pandemic flu vaccinations. In Ontario, health officials are reportedly probing 17 cases of GBS following pandemic flu vaccinations. Cases of postvaccination GBS in teenage patients have been reported in both the United States and Europe.

Defining the safety profile of pandemic influenza vaccines

Although the current pandemic is considered moderate in terms of overall severity, the influenza A H1N1 2009 virus causes an average **6–14 deaths per 1 000 000** Population. Moreover, certain severe disease patterns of the influenza A H1N1 2009 virus are distinct from seasonal influenza viruses. **The ongoing worldwide safety evaluation of pandemic H1N1 vaccines is unprecedented and will provide the most documented safety profile of any vaccine in history**. The available data show that pandemic H1N1 vaccines are immunogenic and have an acceptable safety profile. They provide an important public health tool to minimise further harm from the virus.

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We declare that we have no conflicts of interest.

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BMJ

RESEARCH

Mortality from pandemic A/H1N1 2009 influenza in England: public health surveillance study

Liam J Donaldson, chief medical officer for England,[1] Paul D Rutter, clinical adviser,[1] Benjamin M Ellis, clinical adviser,[1] Felix E C Greaves, clinical adviser,[1] Oliver T Mytton, clinical adviser,[1] Richard G Pebody, consultant medical epidemiologist,[2] Iain E Yardley, clinical adviser[1]

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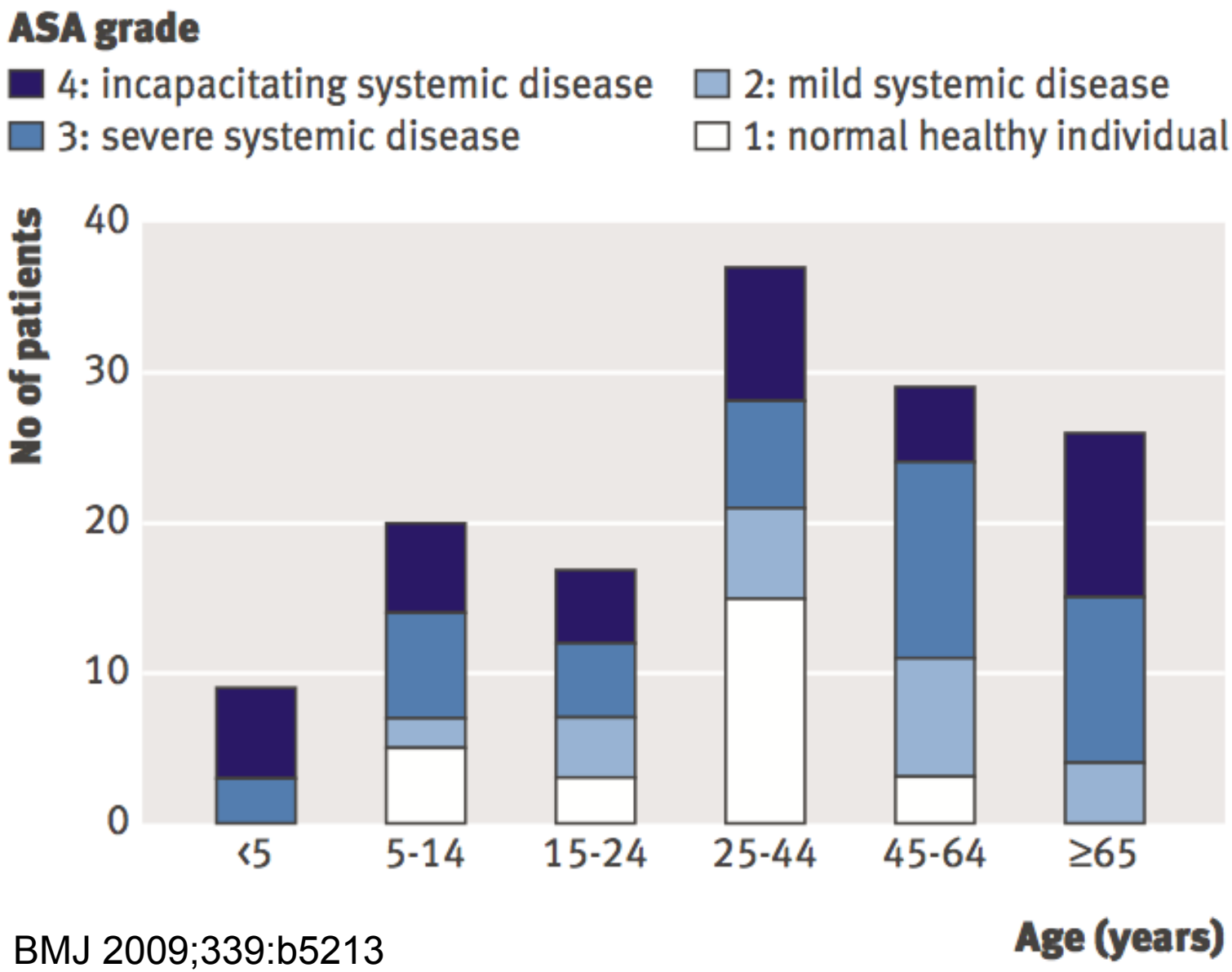

BMJ 2009;339:b5213

Fig 2 | Age and pre-morbid health of patients who died from causes related to pandemic A/H1N1

BMJ 2009;339:b5213

WHAT IS ALREADY KNOWN ON THIS TOPIC

Past pandemics of influenza have produced assessments of mortality based on calculations of "excess death"; these estimates depend on death certification, which is known to be unreliable

Early reports of case fatality rates for the present A/H1N1 pandemic have used laboratory confirmed cases as the denominator, likely to be a gross underestimate of incidence

WHAT THIS PAPER ADDS

The current estimated case fatality rate, using an estimate of symptomatic cases in the community as the denominator, is lower than previous estimates

In the current pandemic children have experienced the highest attack rate and the lowest case fatality rates, while older people are much less susceptible but are more likely to die when affected

BMJ

RESEARCH

Mortality from pandemic A/H1N1 2009 influenza in England: public health surveillance study

Liam J Donaldson, chief medical officer for England,[1] Paul D Rutter, clinical adviser,[1] Benjamin M Ellis, clinical adviser,[1] Felix E C Greaves, clinical adviser,[1] Oliver T Mytton, clinical adviser,[1] Richard G Pebody, consultant medical epidemiologist,[2] Iain E Yardley, clinical adviser[1]

Conclusions: Viewed statistically, mortality in this pandemic compares favourably with 20th century influenza pandemics. A lower population impact than previous pandemics, however, is not a justification for public health inaction. Our data support the priority vaccination of high risk groups. We observed delayed antiviral use in most fatal cases, which suggests an opportunity to reduce deaths by making timely antiviral treatment available, although the lack of a control group limits the ability to extrapolate from this observation. ***Given that a substantial minority of deaths occur in previously healthy people, there is a case for extending the vaccination programme and for continuing to make early antiviral treatment widely available.***

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Perspective

SEPTEMBER 17, 2009

Poverty, Wealth, and Access to Pandemic Influenza Vaccines

Tadataka Yamada, M.D.

On June 11, 2009, Margaret Chan, director general of the World Health Organization (WHO), declared that the status of the influenza A (H1N1) pandemic had reached phase 6 — active transmission on a global scale. Until now, the

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Poverty, Wealth, and Access to Pandemic Influenza Vaccines

Tadataka Yamada, M.D.

On June 11, 2009, Margaret Chan, director general of the World Health Organization (WHO), declared that the status of the influenza A (H1N1) pandemic had reached phase 6 — active transmission on a global scale. Until now, the case fatality rate of this influenza has been quite low, but history teaches us that the situation could take a turn for the worse during the next wave of the pandemic. If a 1918-like pandemic were to occur today, tens of millions of people could die, the vast majority of them in the world's poorest countries.

Fortunately, the prospects for developing an effective vaccine to prevent infection with the current H1N1 virus are excellent, and the world's pharmaceutical companies are working diligently at this task. In contemplating equal access to such a vaccine, it is important to consider three key issues: manufacturing capacity, cost, and delivery.

Only a few countries in the world have plants for manufacturing influenza vaccine, and three companies — GlaxoSmithKline, Sanofi-Aventis, and Novartis — account for most of the world's manufacturing capacity. The number of doses of vaccine against H1N1 influenza that could be produced with the existing capacity is very large, but the sobering truth is that even if production were switched over completely from seasonal influenza vaccine to pandemic influenza vaccine, there would not be nearly enough for everyone in the world. The size of the gap in potential supply depends greatly on the dose that is required, and it may be possible to reduce the necessary dose by as much as 75% with the use of an adjuvant. The challenging problem is that much, if not most, of the manufacturing capacity is already spoken for through purchasing contracts held by many of the world's wealthy countries.

The second issue is cost. Despite the enormous technological investment required to create a vaccine, the traditional cost of seasonal influenza vaccines even in wealthy countries is quite low. For the pandemic H1N1 influenza vaccine, the major manufacturers have indicated a willingness to offer tiered pricing, with affordable prices for poor countries. Going even further, Sanofi-Aventis has committed to donating 100 million doses of its vaccine to a stockpile for poor countries, and GlaxoSmithKline has committed to donating 50 million doses. Nevertheless, financial commitments from wealthy

Fabrizio Pregliasco epidemiologo Università di Milano

- Fabrizio Pregliasco, epidemiologo dell'Università di Milano, ha descritto l'impotenza umana nella capacità di predire l'esordio di una PANDEMIA con una metafora: «Siamo come le galline che ogni mattina aspettano il mangime e non capiscono perché, all'improvviso, un brutto giorno, l'allevatore invece di portare da mangiare tira loro il collo»