

Behind the 2009 A H1N1 Flu Vaccine

“Pandemics happen. They happened before and they’ll happen again. If it isn’t the H5N1 (bird flu) virus, it’ll be another virus.” Mike Leavitt, U.S. Health and Human Services Secretary, ABC News teleconference,

November 2, 2005

Each of us should consult with our physician in making decisions regarding the risks and benefits of any vaccination for either ourselves or family members.

Whether you or any family member decides to be vaccinated for the current influenzas (either seasonal flu or the so-called swine flu) is a personal decision. However, whether you receive a "swine flu" vaccination or not, it is important to have accurate information about the flu, the vaccine, and also other preventive steps that you can take.

The Swine Flu Pandemic

Every day, the news media bombards us with new “information” about the “swine flu pandemic” and recently we learned that four vaccines had been “approved” by the Food and Drug Administration (FDA). The official name for the so-called flu swine, which is currently circulating the globe, is **2009 A H191**. The government states that this vaccine is safe and effective.

Rising Anxiety

Anxiety over a potential H1N1 epidemic or pandemic is increasing. Surveys show that a majority (approximately 58 percent) of Americans believe this influenza virus may put them at risk for serious illness.

Nevertheless, according to a September survey of 1502 adults, **only 31 percent of Americans plan on getting the H1N1 flu vaccine** this year. **Primary barriers appear to be doubts about the safety and efficacy of the vaccine.**

✓ *A “flu pandemic” occurs when a new influenza virus emerges for which people have little or no immunity. The influenza virus, therefore, spreads easily from person to person and can cause serious illness and many deaths.*

✓ *A flu epidemic is the term that describes a national or local outbreak.*

Whispers from the Past

The 1918 Influenza Pandemic

A vaccine has been developed to combat the pandemic virus, relatively few are eager to be vaccinated. This should not be surprising.

Although the government states every year that the seasonal flu is safe and effective, approximately 40 percent of eligible Americans receive seasonal influenza vaccines; this includes health care workers. Although a vaccine is available, thirty six thousand individuals die from the seasonal flu each year.

If this has pandemic potential, why aren't Americans eager to get the new vaccine?

Americans offer many reasons for not getting the seasonal flu, including the belief that they are not at risk. Some express fear that the vaccine is neither safe nor effective.

And many Americans remember the 1976 Swine Flu debacle or fiasco as it is often called.

In 1976, a young military recruit developed influenza and died quickly. Several hundred additional individuals also developed influenza (although no one else died). All victims were

confined to a small geographical area (Fort Dix, New Jersey).

Fearing a pandemic, public health officials, rushed to judgment and a mass vaccination program vaccinated twenty four percent of Americans.

The feared swine flu pandemic or epidemic of 1976 never materialized. However, soon after the vaccination program began, the media and the medical community started reporting cases of serious complications (Guillain-Barré syndrome or "French polio") in individuals who received the vaccine. Guillain-Barré is a rare neurological condition that causes muscle weakness or paralysis. In individuals, who received the vaccine.

Was this flu vaccine responsible for the sufferings and deaths of these Guillain-Barré victims? To this day, we do not know for certain how many, if any, of the more than one thousand 1976-1977 identified Guillain-Barré cases were due to the swine flu vaccine or to other causes.

Many questions remain about the 1976 swine flu epidemic. However, public officials also learned many important lessons from their experiences with the 1976 influenza vaccine. The most important may be *"expect the unexpected."*

- ✓ On the positive side, surveillance for influenza disease worked well -- despite the fact that surveillance did not involve computers. And, best of all, there was no pandemic.
- ✓ On the cautionary side, surveillance for "untoward events" showed that only when large numbers of people are exposed to a vaccine or drug are adverse reactions identified (e.g., Guillain-Barr syndrome with influenza vaccines; paralysis with the Cutter polio virus vaccine in 1955).

- ✓ *The World Health Organization (WHO) considers swine flu a global emergency and declared it "pandemic" (June 12, 2009).*
- ✓ *The U.S. government (Secretary of Health and Human Services (HHS)) declared swine flu to be a public health emergency (April 25, 2009).*
- ✓ *The Federal Drug Administration licensed four vaccines in mid September 2009. The Emergency Use Law (enacted in 2007) allowed the FDA to approve these vaccines although they have not undergone normal testing for safety and effectiveness.*

Vaccine Testing

The latter suggests that the two month time compressed US clinical trials with 2400 volunteers may not provide many people with the reassurance they need to agree to be vaccinated. These trials began in August 2009

Unfortunately, the 2009 A H1N1 flu vaccine has not gone through normal testing procedures

- ✓ *The 1918 influenza pandemic caused at least 675,000 U.S. deaths and up to fifty million deaths worldwide.*
- ✓ *The 1957 influenza pandemic caused at least 70,000 U.S. deaths and one to two million deaths worldwide. The responsible strain (H2N2) was first identified in China This strain has not circulated in people since 1968 and so people younger than thirty do not have immunity.*
- ✓ *The 1968 influenza pandemic caused about 34,000 U.S. deaths and 700,000 deaths worldwide. Labeled the Hong Kong flu virus, H3N2 viruses still circulate today.*

(government funded clinical trials are in process and will complete in 2010). It is understandable, therefore, why many people

question whether this vaccine will effectively protect them against the flu. And, more importantly, many wonder if the government can accurately assess the potential for complications, given the initial compressed time period allowed for testing.

Public health officials currently state that they do not think this new flu vaccine will raise the risk for neurological (e.g., Guillain-Barré) or other illness.

A Different Influenza Virus

Influenza is caused by viruses. A virus is a biological agent that reproduces inside the cells of living hosts (e.g., people, birds, pigs, monkeys, etc.).

There are three types of influenza viruses: A, B, and C. Type C viruses rarely cause disease in people. Although Type B viruses cause disease, they do not result in epidemics or pandemics. Only Type A influenza viruses cause epidemics or pandemics. (2009 H1N1 is a Type A virus.)

Influenza A viruses have eight segments. This segmented structure (genome) allows influenza A viruses from different species to mix and create **new** influenza A viruses.

The 2009 A H1N1 influenza virus was originally referred to as “swine flu.” Further research showed that the term "Swine flu" was somewhat misleading. The 2009 A H1N1 is a different virus: it comprises a **quadruple assortment of virus segments from pigs, birds, and humans**. The 2009 A H1N1 virus has two genes from flu viruses that circulate in European and Asian swine; it also has bird (avian) genes; and human genes.

This type of virus can change rapidly as it uses the host (humans, pigs, birds) to make copies of itself. Like Human Immunodeficiency Viruses (HIV), influenza A viruses reproduce so rapidly that copying mistakes are rampant. These copying mistakes can rapidly change the "character" of the virus, including ability to infect a host, overwhelm host defenses, cause serious illness or no illness, or increase or decrease the viruses' abilities to move between species.

Authority for Vaccine Approval

If the 2009 A H1N1 vaccine has not gone through normal clinical testing processes (despite its apparent uniqueness from seasonal influenza viruses), how did it get approved for manufacture and delivery?

The new vaccines for the 2009 A H1N1 flu virus were approved under the **Emergency Use Authorization law**, which allows the Federal Drug Administration (FDA) to license medical products that have not undergone normal safety and effectiveness testing. For the **Emergency Use Authorization** law to go into effect, the Secretary of Health and Human Services (HHS) must declare an emergency. (*FDA Guidance: Emergency Use Authorization of Medical Products, July 2007*)

In the last week of August 2009, the President’s Council of Advisers on Science and Technology released projections of the potential severity of the 2009 A H1N1 influenza pandemic:

- ✓ 120 million people would be coughing, sneezing, feverish and otherwise sick with the symptoms of flu;

- ✓ 90,000 people will be dead from the illness; and
- ✓ 50 to 100 percent of intensive care unit hospital beds (in hard-hit regions) will be filled with flu patients.

At the time these projections were made, the Director of the Centers for Disease Control, confirmed that the government had given vaccine manufacturers permission to begin bottling the still investigational (untested) influenza vaccines and get them ready for shipment. (There are four varieties of vaccine; one is a "mist".)

Although results from trials on the vaccine's safety and effectiveness were not complete, public officials asserted these urgent actions were necessary and the President's Council of Advisers on Science and Technology also recommended that manufacturers "... *proceed with filling and finishing even before dosage information is available...*"

Framework for Projections

So what is the basis for these dire predictions from governmental representatives and the somewhat unprecedented response, i.e., preparing and manufacturing a vaccine before safety, effectiveness or dosage have been established?

According to a member of the President's Advisory panel, these pandemic projections are based on data from previous flu epidemics (1918, 1957, 1968) together with recent data from last spring's outbreaks of this influenza around the globe.

These past pandemic data were then analyzed using models developed for the government's 2005 avian flu pandemic preparedness initiative.

Most people cannot analyze whether these methods are appropriate for predicting what

<p>Pandemic Projections =</p> <p>Data from previous flu epidemics (1918, 1957, 1968) + Spring outbreaks of H1N1</p> <p style="text-align: center;">+</p> <p>Analytical models developed for the 2005 avian flu pandemic preparedness initiative</p>
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might happen in a flu pandemic. Many have questions as to what factors and people were most important in making the decision to announce a pandemic; manufacture and bottle a vaccine before testing was complete; and start a vaccination program well before the risks and benefits of the vaccine could be confidently assessed.

Financial Implications in a Weak Economy

A pandemic in which thousands of people sickened and died across the globe also raises the spectre of economic consequence: Pandemic disease will be risky for an all ready shaky global economy.

Important potential risk factors include:

- ✓ An overloaded health care system, which may be unable to care for patients because workers stay home or there are insufficient numbers of available hospital beds. (One survey found that 57 percent of health care workers would stay home to protect their own health or that of their family.)
- ✓ Decreases in worker productivity as they stay home with the flu or are hospitalized.
- ✓ Impact on tourism as travelers avoid affected areas or don't travel at all.
- ✓ Businesses in industries affected by a pandemic (or fear of a pandemic) could

fail, leaving their debts unpaid, e.g., the powerful economic retail engine might be affected as shoppers avoid crowded malls and stores.

- ✓ Debtors may die, leaving their debts unpaid.

“The good faith of the public is a precious commodity. When one day a pandemic is trumpeted, and the next day the outbreak is called no more than normal flu and under control, and then a call goes out for a multibillion dollar vaccine program to defend against a major pandemic, one risks the public feeling whiplash and the credibility of public officials being damaged.” (Virology Journal 2009, 6:51, 7 May 2009)

- ✓ As workers lose jobs and other sources of income, families will need help, possibly adding to the burdens of governmental and other agencies.

Experience in the US

In the US, the 2009 A H1N1 is reported to affect people very differently. Many individuals have mild infections while others have been hospitalized. There also have been deaths.

No one understands why the flu is more severe in specific demographic groups, e.g.,

- ✓ Healthy young people from birth through age 24;
- ✓ Pregnant women; and
- ✓ Adults 25 to 64 who have underlying medical conditions.

Although most U.S. cases have been mild to-date, there have been a number of deaths and hundreds of hospitalizations — mostly in young people, aged 5 to 24.

Optimism and Concerns

A Stable RNA Virus?

Currently no information is available that suggests this “pandemic influenza virus” has become more deadly, more resistant to new flu drugs or resistant to the vaccine, which is currently being tested.

The virus is reported to be remarkably stable. This status, however, may change, particularly given the ability of RNA viruses to mutate or change.

Additional Reasons for Optimism

There are, however, additional reasons for optimism in considering the potential of this virus to wreak havoc on our country and globally.

- ✓ We live in an age of antibiotics and antivirals that can prevent the onset of pneumonia and other illnesses -- which have been major causes of death in previous influenza epidemics and pandemics.
- ✓ Antiviral drugs are available that can prevent illness in vulnerable individuals or reduce severity in stricken patients -- if administered quickly. (When used for prevention, these drugs are about seventy to ninety percent effective in preventing illness in healthy adults. The CDC is urging doctors not to prescribe these antiviral drugs for healthy adults to forestall a shortage.)
- ✓ A vaccine is now available for the seasonal flu and a vaccine for 2009 A

H1N1 should be available in October. **Seasonal** influenza vaccines are highly effective in preventing influenza disease. The CDC and FDA predict that the vaccine, which has been developed to work against 2009 A H1N1, will be similarly effective. The United States has ordered enough vaccine for 195 million doses, meaning that “we will have enough vaccine available for everyone,” according to the Health and Human Services secretary.

children younger than 2, adults older than 49 or pregnant women.

The intranasal vaccine is a "live" vaccine. It was initially thought that this type of vaccine would more effectively prevent the flu. Recently, however, studies of seasonal flu (not 2009 A H1N1) have shown that the live vaccine is less effective in adults.

The seasonal flu mist is not new. Are these changes in recommendations due to a change in the flu virus or a failure to conduct adequate clinical trials?

Causes for Concern

“Medicine sometimes snatches away health, sometimes gives it.” ~Ovid,
Tristia

Vaccines and Other Treatments

Five companies to-date are manufacturing vaccines. Four vaccines have been approved although clinical trials to test effectiveness and safety began in mid August. These trials were sponsored by manufacturers. In addition, the government is sponsoring five large clinical trials; these are expected to be completed in 2010.

Although some manufacturers' versions of vaccine are currently in clinical trials; others may not be required to undergo clinical testing. Assumptions of safety and effectiveness will be based on experience with vaccines that began testing in August.

Flu Mist Intranasal Vaccine

The first vaccine available to the public will be MedImmune's FluMist intranasal vaccine. The intranasal vaccine has not been approved for

Licensing and Dosage

Officials from the National Institute of Allergy and Infectious Diseases recently pronounced that the "approved" vaccines were safe and produced adequate immunity with only one dose. Previously, researchers had thought that two doses would be required.

The vaccines approved on September 16, 2009 are made by Australia's CSL, Switzerland's Novartis, France's Sanofi Pasteur and Maryland's MedImmune, which makes an inhalable vaccine.

Distribution in Multi-dose Vials

The Influenza 2009 A H1N1 vaccine will be distributed in multi-dose vials (MDV). The purpose of using multi-dose vials was to ensure "efficient manufacture; earlier vaccine availability; and ease of vaccine distribution."

Unfortunately, multi-dose vials are prone to bacterial contamination. Their use has been reported to be a potential source of infection in a number of studies. Studies have shown that *Pseudomonas*, *Enterobacter*) and *Serratia*

species,. *Streptococcus* species have all been transmitted in association with multi dose vials. Fatal toxic shock syndrome. has also been reported. Transmission of hepatitis B, hepatitis C and HIV have been associated with improper handling of multi dose vials.

Preservatives (such as thiomersal) reduce the survival of bacteria and are added to multidose vials to reduce the risks of infection.

While one approved version of the inactivated vaccine will contain thiomersal, another will not. Thiomersal, of course, has been accused of causing autism and other alleged vaccine associated diseases.

Some 2009 A H1N1 influenza vaccines will be available in single-dose units, which will not require the use of thimerosal as a preservative.

In addition, the live-attenuated version of the vaccine, which is administered intranasally (through the nose), is produced in single-units and will not contain thimerosal.

Vaccine Administrators

Individuals, who administer the 2009 A H1N1 Influenza vaccine, should have specific training regarding the safe storage, transport and delivery of this specific vaccine.

It is unlikely that many vaccines will be administered under these circumstances in the US.

Preventing the Flu

As noted above, each of us should consult with our physician in making decisions regarding the appropriateness of any vaccination for ourselves and family members.

However, whether you receive a vaccination or not, every one should follow common sense measures to prevent infecting others. These measures include the following:

- ✓ Covering the nose/mouth when coughing or sneezing;
- ✓ Using tissues to contain respiratory secretions and disposing of respiratory secretions in the nearest waste receptacle after use;
- ✓ Washing hands frequently with soap and water, alcohol-based hand rubs, or antiseptic handwash after any contact with your own or other people's respiratory secretions.
- ✓ Washing hands after touching potentially contaminated objects and materials or animals.
- ✓ Washing your hands before touching your nose, mouth or eyes.

The CDC also recommends that individuals, who are coughing, wear respiratory masks and maintain a distance of at least six feet away from others.

Influenza Viruses are Infectious

Influenza viruses are very infectious, i.e., they are easily transmitted between people and from inanimate surfaces to people.

An influenza virus, for example, can be transmitted by touching a non porous surface (e.e., a grocery cart handle or a faucet handle) up to 48 hours after someone harboring a flu virus has accidentally deposited the virus there. Porous surfaces, such as clothing and furniture, can be infectious for up to eight hours.

In addition, influenza viruses can be found on objects such pens, books, elevator buttons, table tops and coffee cups. (First floor elevator buttons are usually a literal cafeteria for the bugs that cause both influenza and colds.) Using a pen or turning on a water faucet, which have been contaminated with viruses, and then

accidentally touching your nose or eyes, can also transmit the virus to you. Beware of door knobs, locks, toilet flushers, or even toilet paper rolls.

Kitchen Sponges

Many people are surprised to learn that kitchen sponges are the number one source of germs in the house. Running a sponge through the dishwasher may not kill the viruses and bacteria and may, actually, deposit these germs on the dishes with which they are washed. Despite one study to the contrary, putting a sponge in the microwave is not sufficient to kill bacteria and viruses.

Influenza Medications

Pandemic H1N1 swine flu virus is sensitive to the antiviral drugs Tamiflu and Relenza. The FDA has also given "emergency use" status for these drugs to be given for 2009 A influenza - either as a preventive or to lessen the effects of the flu.

These antiviral drugs are most effective when taken within 48 hours of the start of flu symptoms. Not everyone needs those drugs. Most people who come down with swine flu recover fully — without antiviral treatment.

But the CDC strongly recommends antiviral treatment for people at risk of severe flu complications, who come down with flu-like symptoms. Since it's very important to start these drugs soon after symptoms appear, doctors should offer treatment to at-risk patients if they suspect they have the flu.

Doctors are urged not to rely on rapid flu tests, which have received "emergency use" approval; also (they are too unreliable for definitive diagnosis). Lab-based tests take too long.

Influenza Lingers

Patients with flu-like symptoms — fever plus at least cough or sore throat or other flu symptoms — should stay home for seven days after symptoms began or until all symptoms have been gone for 24 hours — whichever is longer.

N95 Respirators

It is important to wear a face mask (preferably a N95 respirator) if you must come into close contact with a sick person. "Close contact" means within 6 feet. Note: There is no definitive proof that a face mask prevents flu transmission. Do not rely on a face mask to prevent infection. (The N95 should be used only once and not reused.)

Also, people who have or are suspected of having this flu should wear a face mask, if available and tolerable, when sharing common spaces with other household members, when outside the home, or when near children or infants.

There's a difference between a face mask and a respirator. A face mask does not seal tightly to the face. Face masks include masks labeled as surgical, dental, medical procedure, isolation, or laser masks.

Respirators are N95- or higher-rated filtering face pieces that fit snugly to the face. Respirators filter out virus particles when correctly adjusted — which is not as simple as it sounds. But it's hard to breathe through them for extended periods, and they cannot be worn by children or by people with facial hair.

Summary

In summary, decisions whether to receive vaccinations are personal.

So far, the 2009 A H1N1 influenza appears to be more severe among healthy young people from birth through age 24; pregnant women;

and adults (age 25 to 64), who have underlying medical conditions. There is some speculation that older adults may have some immunity based on previous exposures to viruses from past pandemics. CDC laboratory studies have shown that about one third of these individuals have some antibody response. (This does not necessarily mean, however, that these people have sufficient protection.)

The government believes that the risk of potentially unnecessary costs in a mass vaccination campaign are minimal. They believe that the potential cost of a pandemic is astronomical.

According to the CDC, between five and twenty percent of Americans develop influenza each year. More than 200,000 are hospitalized from complications and about 36,000 people die. Older people, young children, and people with chronic medical conditions are at higher risk for influenza related complications.

So, whether you receive the 2009 A H1N1 flu or the seasonal flu, you should still continue to practice all possible preventive steps.

