

**SUMMARY**  
**Centers for Disease Control and Prevention**  
**Clinician Briefing**  
**Influenza**  
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## **INFLUENZA**

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*\*\*Please note: Data and analysis discussed in these presentations were current when presented. Data collection and analysis are ongoing in many cases, therefore updates may be forthcoming elsewhere on this website, through publications such as [CDC's Morbidity and Mortality Weekly Report](#) or other venues. Presentations themselves will not be updated. Please bear this in mind when citing data from these presentations*

### **Background**

- Influenza is a viral respiratory infection that can be prevented by vaccination.
- Recent analyses show the health impact of flu on US mortality has increased in 1990s.
  - Deaths from influenza have increased from an average of ~20,000 per year in the 1970s and 1980s to an average of about 36,000 per year in the 1990s.
  - US population is aging, and rates of death from influenza are particularly high in the elderly.
  - Influenza A-H3N2 viruses were predominant during the 1990s.
- A key characteristic of the epidemiology of influenza is its tremendous variability from year to year
  - Types/subtypes of viruses
  - Timing (start, peak, end) of influenza season
  - Impact
- In recent years, recommendations for use of influenza vaccine have broadened.
  - Vaccination recommended for all persons age 50 to 64 years
  - Vaccination encouraged, when feasible, for children age 6-23 months (Advisory Committee on Immunization Practices [ACIP] has voted to upgrade this to a recommendation for 2004 influenza season)
- In addition to the inactivated influenza vaccine, other tools have become available.
  - LAIV (live attenuated influenza vaccine) is available for the first time this year.

- Approved for healthy patients aged 5 to 49 years
- Efficacy is comparable to inactivated influenza vaccine
- For healthy persons 5-49, inactivated influenza vaccine and LAIV can be considered equivalent in terms of protection
- However, important to note that inactivated influenza vaccine is preferred for health care workers, because the potential risk of transmission to patients is not clear at this time
- Supplies of LAIV plentiful at this time
- New antivirals, the neuraminidase inhibitors, are available.
  - Antivirals can play a very useful role, particularly in controlling outbreaks where they can be used both for treatment and prophylaxis.
- Several rapid-detection tests suitable for diagnosing influenza in clinical settings are commercially available.
  - Less sensitive than virus culture or PCR
  - However, can provide preliminary information very quickly while other confirmatory tests are being done
  - Very useful for rapidly detecting and starting outbreak control methods in places such as hospitals, nursing homes, etc.
- Concerns about another influenza pandemic continue to increase.

## **Current Season**

### **2003-04 SEASON IN US**

- Started early with first community outbreaks reported from Texas
- West Central states (Texas, Colorado) reporting highest levels of activity but ~ 28 states reporting some influenza with sharp increases in past few weeks
- Earliest start to influenza season since 1976-77 season
- National percentages of visits for influenza-like illnesses are 3.3%, which is above the national baseline of 2.5%
- Pneumonia and influenza deaths are below the epidemic threshold, but deaths typically lag by a few weeks
- No hard statistical data, but anecdotal reports suggest that highest rates of illness are occurring in children in Texas
- Case reports of deaths and severe illnesses in children also have been received
- Early H3N2 influenza activity also being reported from Canada and European countries such as the UK
- Last few seasons in US have been mild
- This year may turn out to be quite severe based on
  - predominance of A-H3 viruses in the US this season,
  - historic association between H3 viruses and higher levels of illness and death
  - reports of relatively severe season in Australia during summer
- For more detailed surveillance information, go to  
<<http://www.cdc.gov/ncidod/diseases/flu/fluvirus.htm>>

## **2003-04 VIRUSES**

- All three viruses (A-H1, A-H3, and B) have been reported this year in the US; however, most have been A viruses, and most A viruses have been subtyped as H3N2.
- >80% of the H3s characterized at CDC have been Fujian-like viruses, which differ somewhat from the Panama strain in this season's vaccine.
- A major virological characteristic of influenza viruses is that they continuously change, or drift, because of mutations.
- Drift results in new strain variants, one of which usually becomes predominant worldwide for a few years before another variant emerges and replaces the older virus.
- Emergence of new strains is expected, but the exact timing cannot be predicted. Therefore WHO maintains a global surveillance system to monitor the emergence of new strains.
- Although Fujian viruses are predominant right now, it is quite possible that other viruses such as A-H1 or B could become more common or predominate later in this year's influenza season.

## **INFLUENZA VACCINE AND SARS**

- Influenza vaccination for purposes of SARS is not recommended,
- Depending on the relative incidence of influenza viruses and other respiratory pathogens during a time period, influenza vaccination will not necessarily reduce the number of people presenting with flu-like symptoms since many of these illnesses can be caused by other respiratory pathogens unaffected by influenza vaccine. This means influenza vaccination may not necessarily and predictably reduce the number of cases of respiratory illnesses that need to be distinguished from SARS.
- Physicians and patients may erroneously assume that someone who has received vaccine and who has a febrile respiratory illness automatically has a higher chance of having SARS leading to unnecessary anxiety. Since vaccine is not 100% effective, vaccinated persons still can develop a febrile respiratory illness from influenza and can also become sick from another agent.

## **VACCINE MATCH**

- The current vaccine's A-H3 component is the Panama virus.
- The newly emerging Fujian strain is an evolution or variant of the older Panama strain.
- Laboratory tests show that the two viruses can be distinguished on the basis of their antigenicity but that there also is cross-reactivity between the two viruses.
  - Antibody to Panama will react to Fujian viruses but at lower levels than if the strains were antigenically identical.
- This means that vaccination with the current vaccine is expected to provide some level of protection against the Fujian viruses but less than if the match between the two viruses were optimal.

- In the past when mismatches have occurred, vaccine effectiveness has ranged from 30% - 80%.
- Since vaccine effectiveness cannot be measured in the lab, the precise level of effectiveness against the Fujian virus is not known at this time, but it is expected to be significant.
- The reason why the Fujian virus is not contained in this season's vaccine is that it began to emerge in late January, just before the strain selection meeting in February. In essence, the Fujian virus emerged too late to be included in this year's vaccine. (Strains need to be selected in February to allow time to produce and distribute a vaccine.)
- Each year's vaccine contains inactivated type A-H1, type A-H3, and type B viruses.

### **TAKE HOME MESSAGES**

- Over time, influenza is expected to have an increasingly serious impact in the US due to the aging population.
- Influenza activity has started early in the US this year.
- Although we cannot predict, all signs suggest it will be a severe season.
- It is critical for healthcare providers to push with vaccination activities now and to continue them through the season or until vaccine supplies run out.
- Critical target groups include
  - All persons  $\geq 50$
  - All persons  $\geq 6$  months with certain chronic conditions including heart disease, lung disease, diabetes, or immune-deficiency diseases
  - Pregnant women in 2<sup>nd</sup> or 3<sup>rd</sup> trimester
  - Persons in close contact with high risk groups
    - Especially healthcare workers
    - Household members of people in high-risk groups
  - Vaccine also encouraged for children 6-23 months and their caregivers. In 2004, this will become a full ACIP recommendation.
- Despite current drift among H3 viruses, it is essential for vaccination activities to go ahead.
  - It is expected that the current 2003 influenza vaccine will provide a significant degree of protection against drifted virus.
  - Influenza vaccine provides protection against other influenza viruses, and later in the season, viruses other than the Fujian strain could predominate
- Vaccine is by far the best way to prevent influenza.

### **INFLUENZA VACCINATION PROGRAM**

**Walter A. Orenstein, MD**  
**Assistant Surgeon General and**  
**Director, National Immunization Program**

## **Vaccine Supply**

- CDC estimates approximately 83.9 million doses of influenza vaccine have been produced for use this season.
- This exceeds the estimated 79 million doses that were actually sold to providers in 2002.
- All of the manufacturers still have vaccine available for purchase.
- As of November 19<sup>th</sup>, a total of approximately 6,827,540 doses were still available. Of this number approximately 3 million doses are inactivated vaccine, and 3.8 million doses are live attenuated influenza vaccine (LAIV).

## **Medicare Reimbursement Increases**

- The catalog price for Aventis vaccine has been \$8.50; Evans vaccine has been \$7.25-\$7.50; and Chiron (FluMist™) has been \$46.00, although there may be some rebates
- The Medicare reimbursement rate is \$9.95
- Effective March 3, 2003, Medicare's administration and vaccine rate allowances for both influenza and pneumococcal vaccines increased.
- Actual administration rate allowances increased approximately 94% over last year from an average of \$3.98 to \$7.72
- Administration rates for this season range from \$5.34 to \$10.98 depending on geographic location.
- For specific location rates visit [www.cms.hhs.gov/preventiveservices/2.asp](http://www.cms.hhs.gov/preventiveservices/2.asp)

## **Vaccine Safety**

### **INACTIVATED INFLUENZA VACCINE**

#### ***Misperceptions about the Vaccine***

- Some people are not getting vaccinated because of concerns about vaccine effectiveness. People can still get a respiratory illness if vaccinated. The vaccine only protects against influenza, which actually accounts for 1/4 to 1/3 of febrile illness during the season.
- There is the misconception s that you can get the flu from the flu shot. The virus in the influenza vaccine is inactivated and split. It cannot cause influenza.

#### ***Side Effects of Vaccination with Inactivated Influenza Vaccine***

- In randomized trials, the most common side effects of vaccination with inactivated influenza vaccine are sore arm and redness at the injection site. Symptoms are generally mild and last <2 days.
- Systemic reactions (body aches, fevers, chills) are much less common now with use of only split-virus vaccines and not whole-virus vaccines but may be more common after the first dose of influenza vaccine.
- In randomized clinical trial studies in adults, fever was not associated with vaccination.

- Severe allergic reactions are rare. Risk of anaphylaxis was estimated to be 1 in 4 million in the swine influenza vaccine surveillance. I am aware of no other rate estimates.
- Other uncommon complications
  - Institute of Medicine report on immunization safety found:
    - Guillain Barré syndrome was likely associated with influenza vaccine in 1976, but that information is inadequate to accept or reject a causal relationship in other years.
    - Evidence supported rejecting a causal relationship between influenza vaccination and relapse of multiple sclerosis (MS).
    - Evidence is inadequate to accept or reject a causal relationship between influenza vaccination and
      - Incident MS
      - Other demyelinating neurologic disorders
      - Optic neuritis

## **LIVE ATTENUATED INFLUENZA VACCINE (LAIV)**

### ***Side Effects***

- Symptoms are reported more often in healthy recipients of LAIV than in healthy recipients of placebo. These include:
  - Nasal congestion/runny nose
  - Sore throat
  - Cough
  - Chills
  - Tiredness/weakness

### ***Side effects in children***

- Nasal congestion/runny nose
- Headache
- Fever
- Vomiting
- Abdominal pain
- Myalgias
- One unpublished study in 12- to 59- month-olds suggested an association of influenza vaccination with asthma or reactive airways disease. Further analyses and studies are pending on this issue.

## **Best Practices For Increasing Influenza Vaccination Coverage Rates**

### **WHAT PROVIDERS CAN DO TO INCREASE THE VACCINATION RATES OF THEIR PATIENTS**

- Encourage patients to get vaccinated against influenza; CDC formative research with seniors shows that patients heavily rely on the advice of healthcare providers.
- Provide bilingual patient education materials.

- Tell patients their vaccination helps protect others, for instance, parents and grandchildren
- Tell them that influenza is a serious disease
- Tell them that influenza-related deaths average 36,000 per year, and hospitalizations average 114,000 per year

### **HOW TO INCREASE VACCINATION RATES IN THE GENERAL POPULATION**

These are the strategies recommended by the Community Preventive Services Task Force for persons 65 and older:

- Standing orders
- Patient reminder/recall systems
- Provider reminder
- Assessment/feedback
- Reduced out-of-pocket cost
- Expanded access

### **KEY MESSAGES FOR PATIENTS**

- Getting an influenza vaccination every year is your best protection against this serious disease
- Your flu vaccination helps protect others
- Right now is the BEST time to get vaccinated, but December is not too late

### **WHY HEALTHCARE PROVIDERS SHOULD GET VACCINATED**

- To protect themselves, their patients, and their families
- In 1991 the vaccination coverage rate of healthcare workers was reported to be 36% (National Health Interview Survey 2001)
- Healthcare workers take care of ill patients; they get sick; and they work while sick.
- Healthcare workers transmit influenza to their patients.
- Healthcare workers have introduced influenza into long-term care facilities (*MMWR* 1999;48: 177-181).
- Studies have shown an inverse correlation between influenza vaccine coverage and patient mortality (*Lancet* 2000;355 93-97)

### **WHAT WORKS TO INCREASE THE VACCINATION RATES OF HEALTHCARE WORKERS**

- Systems and administrative changes are key for vaccination in general.
- Studies show that convenience is a key factor--vaccination clinics, and vaccination at conferences.
- Other approaches that have been effective include mobile vaccination immunization units, vaccination fairs (some offered incentives at fairs), vaccination at no cost, a reminder letter from an influential staff person, and offering vaccinations during both day and night shifts.

## **CDC's Influenza Campaign**

### **WHAT CDC IS DOING TO EDUCATE THE PUBLIC AND PROVIDERS**

#### ***Public***

- CDC has created a portfolio of educational materials targeting people of a variety of ages and backgrounds. There are Spanish versions of most materials.
- The materials include flyers, brochures, posters, and a three-sided stand-up table tent.
- Samples of the materials have been direct-mailed to approximately 4500 people, including all members of the Association of State and Territorial Health Officials and the National Association of County and City Health Officials, immunization program managers, and members of the National Public Health Information Coalition.
- All materials are available for download from the National Immunization Program (NIP) web site at [www.cdc.gov/nip/flu](http://www.cdc.gov/nip/flu)
  - The site was launched September 2, 2003, and to date the “Flu Gallery,” <http://www.cdc.gov/nip/flu/gallery.htm>, has received over 400,500 hits.
  - During the month of October, the influenza home page was the most accessed page on the NIP web site.
- We have produced a public service announcement in English and Spanish and have produced English and Spanish video news releases and audio news releases.

#### ***Providers***

- Additionally, this season we have created a provider kit called “Immunize Now,” which is aimed at encouraging doctors and nurses to vaccinate their patients and to get vaccinated themselves.
  - The kit has been distributed to 20,000 providers.
  - The kit contains information on
    - What’s new this season, (such as the Medicare reimbursement increase, the increase in estimated influenza-related deaths and hospitalizations, and the most recent information on racial and ethnic disparities in influenza immunization)
    - Recommendations for use of the vaccine
    - An influenza pocket guide
    - Bilingual flyers and posters targeting patients
  - The kit is available for download from the NIP web sit, and CDC has also collaborated with the American Medical Association to have it posted on their web site.

### **RESOURCES FOR CLINICIANS**

English-language influenza hotline for clinicians (800) 232-2522

NIP web site [www.cdc.gov/nip](http://www.cdc.gov/nip)

NIP Flu Gallery <http://www.cdc.gov/nip/flu/gallery.htm>



## QUESTIONS AND ANSWERS

Kate Traynor

American Society of Health-System Pharmacists

I understand from the FDA Advisory Committee meeting that met at the beginning of the year to decide on the strains for the flu vaccine that there was a great deal of concern that the Panama strain would not protect against the Fujian, and listening to what's coming out of CDC now, it seems that there is less concern about this. Can you comment on this? Have there been new tests performed that make you feel more confident that you're going to get protection from the Panama strain?

Dr. Orenstein

At this year's VRBPAC (Vaccine and Related Biologic Products Advisory Committee) meeting, which is the advisory group to FDA, there was discussion about the newer viruses. But what was not available at that time were any candidate viruses to actually go into the vaccine, and so I think that at that time we knew that there was beginning to emerge a drifted variant and we still know that now. What we know is that the antibodies to the current vaccine do react with the viruses that are circulating now, the Fujian viruses.

Again, as I mentioned, when you look at past years in which there's been a mismatch, you see that there has been a fair amount of effectiveness against the drifted variant, using the older vaccines. But we still really don't know what the effectiveness estimates will be for this year. We don't have specific numbers, but we do feel that there will be some effective coverage against the older viruses. I think that's all we can say right now. We certainly hope to have more specific estimates later in the year, but we don't have them right now.

Kate Traynor

Okay, that includes - I know you're getting a lot of cases in Texas and California. Do you have any data on whether the people who have gotten the flu have been immunized?

Dr. Orenstein

Right now we don't. We simply don't have vaccination data on people who are getting sick, even in those locations. We are in pretty close contact with the Texas and Colorado health authorities and so on, but we don't have that information.

Kevin Teale

State of Iowa Health Department

You touched on it briefly, about the issue of children apparently being hit hard. Would you like us to get that message out and, if so, I guess what sort of talking point would you like us to get out in that particular issue, about the importance of having children vaccinated this year?

Dr. Fukuda

I think a couple of things. One is that frequently kids are the first group of people who get affected during an influenza virus sweep into a community, and that seems to be what

we're seeing right now. There is some concern about severe cases of influenza among children, and it would be important for you to get the word out that physicians, clinicians and hospitals should be on the watch for particularly severe cases. These include things such as encephalopathy associated with influenza viruses. This is a finding that has been reported in Japan now for the last few years and it's something that hasn't really been picked up on in the United States. But this is the year in which we may see that occur more often.

I think it still means that we shouldn't concentrate just on kids, however. I do expect to see that activity will begin picking up in older age groups and, as always, the elderly probably remain the most vulnerable group of all. So it is good to get the word out to people, to be looking at kids, but also to be cognizant of the other groups.

Then finally, since there is language to encourage vaccination of children six to twenty-three months of age, I think this is a good time to remind physicians about that and also to get the word out that next year this will be a full recommendation.

Dr. Orenstein

If I could just add to that, Keiji. We need to remember also that for children under age nine two doses are recommended. So it's particularly important in getting the word out that they need to come in as soon as possible, because we want a second dose a month later.

Dr. Fukuda

Yes, that's a really important point. Children under nine who have not been vaccinated before do need a priming dose, and you need to wait a month or a little bit longer before the second dose is given. So getting vaccine into them early is important.

Kevin Teale

One of the issues we've heard out in the field is that doctors' offices, of course, will do the influenza vaccine for children, but your secondary level, your Wal-Marts, your K-Marts, your grocery stores, tend to shy away from giving it to children.

Dr. Orenstein

We have been working with some of the mass vaccinators that run those clinics and, yes, they are more concerned about giving vaccine to children. So some of the options for children are more limited, I agree.

Dr. Baden

While we're waiting for additional questions, let me say that, as always, if you have follow-up questions, you can contact the influenza hotline that Keiji gave out earlier.

Dr. Orenstein

The other issue (source for information on influenza) is the web site, [www.cdc.gov/nip/flu](http://www.cdc.gov/nip/flu), and we will be sending out some information to you all, at least in terms of which

distributors and which companies told us they had flu (vaccine) before. In terms of e-mail addresses, (if you have questions, contact) ksapsis@cdc.gov.

Dr. Baden

If you have any difficulty with that, you can also send questions to our regular e-mail address. That's COCA@cdc.gov.

Dr. Fukuda

Actually, while we're waiting for other questions, I do want to put one request out there. We are concerned that there may be more children who are developing serious influenza-related illnesses. If you could get the word out that if any of your constituents or the physicians in your hospitals do see cases of severe influenza, particularly neurologic complications and particularly encephalitis or what appears to be sudden death, something like that related to influenza, that if you would, contact us at CDC and we would be interested in following up on those cases. The telephone number that clinicians can call is 404-639-3747. They can ask for either Dr. Tim Uyeki or Dr. Niranjana Bhat, and we will follow up on those telephone calls.

Lisa Miller

Colorado Department of Public Health

I was just wondering what, if anything, we could learn from the season, and maybe especially the end of the season, in the Southern Hemisphere, where the Fujian strain was circulating.

Dr. Fukuda

In the Southern Hemisphere, the reports from Australia were that the season was moderately severe to severe and really comparable to what they had seen during the Sydney era. Sydney is one of the earlier H3N2 viruses and really one of the more severe viruses in the 1990s.

In talking with the authorities in New Zealand, they also saw the same kind of viruses, although they do feel that their season was somewhat milder than what was seen in Australia. In Australia, also, they did notice that it appeared that there was more sickness among children than in other seasons. So that's basically what we have learned from the Southern Hemisphere.

LJ Tan

American Medical Association

Thank you. Actually part of my question has already been answered. Keiji, LJ here. Is there any way you all can craft some language as to what you want us to tell our docs to look out for, in terms of severe influenza indications in children?

Dr. Fukuda

LJ, sure. In fact I think that Tim, Dr. Uyeki, is working with *MMWR* to craft a notice to readers. That, I believe, is going to be going out in the December 12<sup>th</sup> *MMWR*.

LJ Tan

Okay, so we should just look out for that then?

Dr. Fukuda

Yes, I think that will probably contain the contact information and really what is being looked for.

Cornelia Massolo

Genesys Regional Medical Center

There was an article in the paper on Saturday of three occurrences of Coumadin reactions after receiving the flu shot. Coumadin levels were ten times or higher above normal, and, in investigating -- this occurred at a different hospital, so I'm going off of the article -- in investigating, nothing had changed among these patients. There were no new medications, no illnesses in the previous weeks prior to the flu or after the flu, but within a couple of days these people were very ill, requiring hospitalization. One was admitted to ICU as a precaution.

Have you heard about this at all, (about this) occurring anywhere else? It's kind of scary, because the people who are on Coumadin are really, often, the people who also need the flu vaccine.

Dr. Orenstein

I am not aware of information where there have been significant problems with bleeding from this, but certainly we will look into it. I think, certainly, we do recommend it for these people, but we will have to look into that. I've not seen the article that you're referring to.

Cornelia Massolo

I can fax the article, if you'd like. This is in Michigan.

Dr. Orenstein

Okay, if you could fax it to 404-639-8626, attention Walt Orenstein, I'd appreciate it.

Susan East

Yes, I missed the first three digits of the clinician (influenza) hotline number. Could someone repeat that number for me?

Dr. Orenstein

It's 1-800-232-2522.

Dr. Baden

I just want to clarify that this is a separate line than the clinician information line, which is dealing with other topics. But this line that Dr. Orenstein gave you is specifically for flu immunizations. Any other questions, Wendy?