COCA Conference Call – Seasonal Influenza Vaccination: Now is the time!
Dr. Andrew Kroger
October 23, 2007

Coordinator: Welcome and thank you for standing by. At this time all participants are in a listen only mode. During the question and answer session, please press Star 1 on your touch tone phone.

Today's conference is being recorded. If you have any objections you may disconnect at this time.

Now I will turn the meeting over to Miss Alycia Downs, you may begin.

Alycia Downs: Good afternoon and thank you for joining us for today's COCA conference call entitled Seasonal Influenza Vaccination, Now is the Time.

We are very pleased to have Dr. Andrew Kroger present. Andrew Kroger graduated from Yale University in 1998 with a joint MD MPH. He is a medical officer in the national center for immunization and respiratory diseases, the immunization services division.

As one of the traveling trainers in the education, information and partnership branch, Dr. Kroger has given over 100 presentations that include immunization updates and pandemic influenza preparedness.

He is also the author of the newest addition of the CDC's general recommendations on immunization.

As for today's objectives, after the presentation, the participants should be able to recommend seasonal influenza vaccinations to those groups at high risk for complications from influenza.

Recommend seasonal influenza vaccinations to those groups at risk of transmitting influenza to high risk persons, and to schedule vaccinations as the first season influenza vaccine in line with CDC's recommendations.

I will now turn the call over to Dr. Kroger, you may begin.

Andrew Kroger: Thank you Alycia and thanks everyone for joining today. It's a real pleasure to be able to share with you this presentation on influenza and influenza vaccines for the 2007-2008 season based on the most recent recommendations of the Advisory Committee on Immunization Practices.

You should currently be on the title slide and I'm going to ask you to now switch to slide two, and I'll begin just with a brief discussion of influenza disease. Influenza is a highly infectious respiratory viral illness that we've known about for four centuries.

The first epidemic of what we think was influenza was reported in 1510, although true influenza disease could not be definitively confirmed until 1933 when the virus was first isolated.

And of course our first vaccine to prevent disease was licensed 12 years later. I want you to hit page down now and go to slide three.

Influenza virus strains can be subdivided into primarily two genetic types. Type A causes moderate to severe illness in all age groups. The reservoir for

disease is actually migratory water fowl but disease can occur in humans as well as other animals. This type frequently undergoes mutation.

Type B changes less rapidly than Type A and causes milder epidemics. It affects humans only and primarily affects children.

Why don't you go now to slide four. This is a graphic representation of Type A influenza. Influenza types are further subdivided into subtypes that are characterized by two proteins on the surface of the virion. These proteins are responsible for the pathogenesis of the influenza virus.

One is called hemagglutinen labeled H on this graphic and is responsible for viral attachments to the epithelium and entry into the respiratory tract.

Neuraminidase, labeled N on this diagram is responsible for lysing an infected cell after replication and release of daughter virions to spread infection.

Why don't you go to the next slide, and this slide has a number of builds, so I'm going to ask you to click "page down" three more times until all the bullets are opened. You should still be on the same slide.

These two types of proteins, hemagglutinen and the neuraminidase are also surface antigens responsible for generating the human immune response to infection.

Immunity to influenza virus reduces both the likelihood of infection and severity of disease. This is why most people can remember a severe respiratory illness in their past that was probably the first episode of influenza infection.

And future infections were frequent but probably less severe. Now antibodies are part of this immune response, and they're generated against the H and N antigens. And they are specific to these antigens.

Now influenza virus is a challenge because it has the ability to change its H and N antigens and in this way avoid or weaken the previously developed immune responses.

There are two types of antigenic change and they are known as drift and shift. Go to the next slide and hit page down one additional time, there are two builds on this slide, this is antigenic drift, this is a type of mutation that is relatively minor, results in little to no change in the H and N antigens.

The mutations that occur are called point mutations, they usually result from spontaneous changes in only one or a few base pairs.

Even though there aren't changes to these primary pathogenic antigens, there are usually enough mild infections plus new infections that are transmissible to sustain an epidemic which occurs pretty much yearly.

But we have a different strain as a result of the drift. Now, an example of antigenic drift was the mutation that occurred in 2004 following the 2003-2004 season in which the H3N2 Fujian strain was dominant.

By 2004 a drifted strain, H3N2 California began to circulate and this became the dominant virus in 2005, so this is one example of something that happens pretty frequently. Why don't you go to the next slide and hit it one additional time, hit page down because there's another build on this slide.

We're now on slide seven, "Influenza Antigenic Changes" and this slide talks about antigenic shift. Antigenic drift is a challenge, but antigenic shift is far, far worse.

This occurs less frequently, but is a major genetic change that results in substantive alteration of the hemagglutinen antigen such that we give our shifted strain a new subtype label.

And this occurs when gene segments actually exchange between two strains of influenza virus that are infecting the same species. If this shift occurs and the new virus remains transmissible among humans, a pandemic can occur.

Now one such example of an antigenic shift which has lead to a pandemic was the Hong Kong pandemic. In the years 1957 through 1967, the H2N2 subtype circulated but was replaced by H3N2 when reassortant virus immerged from co-infection that occurred in what's known as a mixing vessel, a species besides birds or humans.

This was first detected in Hong Kong and became a global pandemic when it spread to the west coast of the U.S. as well as spread to other nations. And 40,000 deaths resulted from this pandemic.

This was considered a mild pandemic with 40,000 deaths, of course the Spanish influenza pandemic of 1917-1918 was much more severe with 20 to 50 million deaths worldwide.

That's pretty much all that I'm going to say about pandemic influenza since the focus of this talk is seasonal influenza. So I'm going to ask you to now turn to slide eight and now we're going to focus on seasonal influenza solely,

and talk about the significant disease burden of this microbe. First of all infection is very common, 10 to 20% of the population is infected every year. Hit page down two more times, there's a couple builds on this slide, three bullets.

Because of the communicability of this virus and because of antigenic drift which keeps a certain percentage of the population susceptible, more than 200,000 hospitalizations occur every year.

Now these hospitalizations primarily occur in persons 65 years old and older or in children 2 years old and younger.

Although there is wide variability, there are an average of 36,000 deaths that occur every year, and 90% of these deaths occur in persons 65 years old and older.

So a very significant public health disease due to the commonality of infection and the fact that it can lead to severe disease in certain persons.

The next slide, slide nine emphasizes this point further that the elderly are at highest risk of morbidity and mortality from influenza. What you see here are cause-specific mortality data, or deaths due to pulmonary and circulatory complications from influenza infection.

These data comes from the year 1998, and you can see the data are stratified by age where the cause-specific mortality rate is only 0.4 to 0.6 per 100,000 for persons 49 years of age and younger.

But the mortality rate for those 65 years old and older is 98.3 per 100,000. A pretty stunning figure and testament to the fact that influenza as a cause of death is actually frequent but goes unrecognized.

The cardiopulmonary complications, exacerbation of existing chronic heart disease or chronic lung disease, is what typically occurs in persons 65 years old and older and sometimes influenza as a cause can be disguised if not reported accurately.

Why don't we go to the next slide, these data are hospitalization rates for influenza by age and risk group. The data come from several studies between 1972 and 2004. Now when we say risk group, we mean people that are at high risk for complications of influenza, and "not high-risk" means those that are not.

And I'm going to discuss later in the presentation exactly what those conditions are. It affects our recommendations, and that's to come later.

But what you can see from this slide is that the highest rates of hospitalization, which range from 500 to 900 per 100,000 in the high-risk groups like the elderly.

But however, also note that if you look in the right hand column at "not high-risk" persons and you look at children younger than 2 years of age, you can see that there are hospitalization rates that are higher than the high-risk adolescents and adults.

And this serves to strengthen our recommendation to really vaccinate the youngest children universally for they are universally at risk for hospitalization.

Why don’t we go to the next slide, slide eleven, then talk a little bit about influenza epidemiology. The reservoir as I’ve already mentioned for Type A influenza is wild birds, although of course disease circulates in both birds and humans during a season.

And of course there is some species-specificity between those subtypes that commonly circulate in humans.

Now transmission of influenza is via the respiratory route, generally through large droplet transmission which requires close contact.

There is anecdotal evidence of transmission at greater distances, this evidence comes from case reports in hospitals of longer transmission in poorly ventilated areas or from laboratory demonstrations of transmission through the mechanism of airborne transmission, that is, small droplet nuclei. So there probably is some component of airborne transmission as well.

The peak time of disease for season influenza is December through March in the Northern hemisphere, and that’s the temperate areas of the Northern hemisphere.

Of course it can occur earlier or later and keep in mind that in the tropics the disease occurs year round.

Communicability of influenza occurs one to two days before infection is clinically apparent, and that probably enhances the transmissibility and makes this a difficult disease to control.

And then communicability lasts until four to five days after disease onset.

Let me go now to the next slide. This is a graph of influenza seasonal trends, the CDC conducts and reports trends in influenza disease beginning in October.

Here you can see some data from a surveillance system known as the 122 cities surveillance system. These are data from death records from 122 U.S. cities with populations over 100,000 that identify influenza or pneumonia as a cause of death.

These data are represented over time on a sinusoidal curve that displays upper and lower bounds for the number of expected deaths from influenza. And then the red line depicts the actual number of deaths from influenza by week.

And you can see that for this week, data from the week ending October 6, 2007 at the right hand side of this curve, at the end, the number of actual deaths exceed the expected number.

So I mean one could argue that influenza has already become epidemic this season from this data. There are other surveillance systems as well that are used in combination to establish trends.

On the next slide, slide thirteen, here are some more surveillance data from the same week. And this map represents reports from state epidemiologists on the pattern of influenza outbreaks, positive laboratory results and influenza-like illness from each of the 50 states.

It allows CDC to kind of give a sense regionally what's happening with disease prevalence. As you can see on this map there are cross-hatched states that represent areas where either an outbreak has already occurred or where

there has already been a positive laboratory result; this activity is defined as sporadic.

And you can also see that there's really not much clustering; it's spread out pretty much and that's not really that unusual for this early in the season.

So what we know so far is that the season has begun of course and it already looks like it may be epidemic influenza which is really what happens every year with this disease.

Okay, so let's go to our next slide now and we will begin a discussion of the influenza vaccines.

This is the best tool we have for preventing the severe complications from influenza disease. There are two types of influenza vaccine, there's the inactivated subunit influenza vaccine and the live attenuated influenza vaccine.

The inactivated vaccine, abbreviated "TIV" is given as an intramuscular shot. It is trivalent, meaning it contains three strains of inactivated influenza virus, and they are the three strains that are expected to circulate during the season and that's determined several months prior to influenza disease season.

The vaccine must be given annually to those for whom the vaccine is recommended. The live attenuated vaccine or LAIV is administered intrnasally, it also is trivalent and contains the exact same three influenza virus strains.

And this vaccine also must be given annually. Let's go to the next slide. We're very pleased to announce that we do expect to have a large vaccine supply this year totalling 127 to 132 million doses.

And this consists of product from five manufacturers listed above. If you look at this list you can see the amounts available. MedImmune is the sole supplier of live attenuated influenza vaccine, and they have estimated 7 million doses available.

The other vaccines listed there, GSK, which is an abbreviation for Glaxo Smith Kline predicts 35 million doses. Novartis predicts 40 million doses, Sanofi Pasteur predicts 50 million doses, CSL, which stands for Commonwealth Serum Laboratories hasn't really provided an estimate, they were recently licensed as a producer of inactivated vaccine.

Now vaccination supply can be a complicated issue because there are so many formulations available. The next slide shows the inactivated vaccine formulations that are available this season.

This slide does exclude the new CSL product. Formulations can vary and they may be packaged differently, they may have different age indications and may or may not contain Thimerosal.

If you click page down there's a build, you'll see a red box appear. It is important to note that as children younger than five years are a group specifically recommended to receive vaccine, keep in mind that there is only one manufacturer that produces vaccine that can be given to children younger than 4 years of age: Sanofi Pasteur, which produces the vaccine Fluzone.

Also note in looking at the Thimerosal column that there are actually formulations of Thimerosal free product that are available for all age groups as several of the Fluzone formulations can be provided to children and adults.

So why don't we go to the next slide. On September 28th the FDA announced its approval of the newest inactivated influenza vaccine and its name is Afluria. If you go to the next slide I have some information on Afluria influenza vaccine.

Afluria is trivalent and produced in hen's eggs like the other influenza vaccines. It is approved for persons 18 years of age and older. It's available in two formulations, a preservative free pre-filled syringe as well as multi-dose vial.

This vaccine has a similar adverse reaction profile as the other inactivated influenza vaccines and what that means is predominately local reactions like soreness or swelling.

Go to the next slide and I want to just put this slide in here just to emphasize the point that influenza vaccine recommendations are unique in that annual vaccination is required to sustain protection in those persons that are at risk.

And there really are three reasons why this is. First, influenza vaccine expires June 30th of every year so that if future protection is needed a new vial must be entered the following season.

Now why is protection required with each new season? That's the real question. Well if you look at the second bullet it's known that by nine months following immunization antibodies can be detected in 70% of vaccinees. That sustains the vaccinees through the influenza season.

But by a year out this number has decreased further, and so we know the antibodies do wane and you know this is not a problem with other vaccines sometimes but with influenza because the incubation period for influenza virus is so short, two to four days, really protection in the form of an antibody response is required immediately following infection. So this is why we need to provide annual immunization as well.

And then lastly the surface antigen can drift or shift so that last year's vaccine might not provide protection the following year.

Go to the next slide and you can see a list of the vaccine strains that were chosen for the 2007-2008 season. These are chosen in the February preceding the start of the Northern hemisphere influenza season based on the current circulating strains and some predictions about circulation based on what's happening in the Southern hemisphere.

This season's influenza vaccines contain two Type A strains and that's typical of every year, an H3N2 strain which is the Wisconsin strain and the Solomon Islands strain the H1N1 strain.

There is also one Type B strain, the Malaysia strain which is part of the Victoria lineage of Type B influenza virus. There are two lineages.

This season only the Solomon Island strain was changed from last year's vaccination formulation. Go to the next slide.

The efficacy of inactivated influenza vaccine is based upon how well the strains are matched to the current circulating strains as well as other factors like the age and health status of the influenza vaccine recipient.

In general among healthy persons younger than 65 years the vaccine is 70 to 90% effective depending on how well matched the strains are to the circulating strains.

However for persons older than 65 years the vaccine is really only 30 to 40% effective and so we hear this a lot but the important message is even though the vaccine may not prevent infection outright, it is 50 to 60% effective in preventing hospitalization in this age group and 80% effective in preventing death in this age group.

So it is ideal for preventing the complications of influenza even though it may not prevent all influenza disease in persons 65 years of age and older.

Let’s go to the next slide. The inactivated influenza vaccines can cause local reactions such as soreness and swelling in 15 to 20% of vaccine recipients. Fever can occur at times with this vaccine but it is less common.

Allergic reactions are very rare and actually they can be minimized by screening, and in the case of influenza vaccine, one health condition you can screen for is an anaphylactic allergy to eggs since influenza vaccine is produced in embryonated chicken eggs. Someone that has an anaphylactic allergy to eggs would be contraindicated from receiving this vaccine.

So it’s worthwhile to screen for that. Neurologic reactions are very rare. One that has come to some attention of late is Guillain-Barré syndrome which occurs in one of every million vaccinees and thankfully this conditions is much much rarer than the likelihood of a complication from influenza disease in persons at high risk.

So this risk can also be minimized by screening for a history of Guillain-Barré syndrome that occurred within 6 weeks following a dose of influenza vaccine; this would be considered a precaution for further dosing.

Let me go to the next slide. One of the most common misconceptions that we hear is that the influenza vaccine gave me the flu, so I think it's important to point out that the inactivated influenza vaccine contains only non-infectious fragments of the influenza virus and therefore it's incapable of causing influenza disease.

I'll point out also that the live attenuated influenza vaccine is attenuated so while it can cause flu-like symptoms it also cannot really cause influenza disease.

What happens often is that many people who may feel symptomatic after receiving influenza vaccine are most likely either infected with a different virus or they became infected with influenza in the two weeks following vaccination, or previously. Because it does take this long for the vaccine to provide protection so someone may very well be vaccinated and then come down with disease because the vaccine hasn't taken effect yet.

And of course we target influenza vaccination season to occur alongside the influenza disease season, so this can happen more often than you might think. Let me go to the next slide.

Here is a schedule for the inactivated vaccine TIV, again it has to be given annually to sustain protection in those at risk. Children younger than 9 years of age actually require 2 doses of influenza vaccine separated by four weeks in their first year of being vaccinated.

Important to note, there's actually another group of children that require two doses and I will discuss this group later. Children between 6 and 35 months of age require a 0.25 milliliter dose.

Children 3 to 8 years of age require a 0.5 milliliter dose and I'll point out again that children 9 years old and older require only one dose per season regardless of the amount of doses received in previous seasons.

Let me go to the next slide titled LAIV efficacy. We'll now talk a little bit about the LAIV vaccine. From an efficacy standpoint, these two vaccines are identical for most groups.

In studies that independently looked at each vaccine, efficacy was 85% for LAIV and 71% for TIV following experimental challenge with influenza. There really wasn't a direct comparison between the two vaccines and this difference in efficacy between the two are not statistically significant.

There has been a recent publication in a 2007 New England Journal of Medicine that documented that LAIV was more effective than TIV in preventing culture confirmed influenza in children younger than 5 years old.

If you go to the next slide and I'll talk a bit about safety of LAIV. Safety studies in children did not identify an increase in upper respiratory tract symptoms, fever or other systemic symptoms after using LAIV.

However, early studies did demonstrate an increased risk of asthma or reactive airways disease in children between 12 and 59 months of age.

A more recent study has found that children 18 months through 4 years of age did not have an increase in asthma symptoms compared to previous seasons

but as I will mention later that there are some additional recommendations with the use of LAIV for children that do have a history of wheezing.

I'll talk about that a little bit later. In adults, LAIV was associated with an increased rate of cough, runny nose, nasal congestion, sore throat and chills, but there was no increase of the occurrence of fever.

And there were no serious adverse reactions that were detected when comparing the vaccine recipients to placebo recipients.

Go to the next slide. Now LAIV does have a restricted indication profile when compared to TIV as it is a live vaccine. It can be given to healthy persons or those that do not have a medical condition that increases their risk for complications of influenza.

So it is ironic that many people that have a strong recommendation to receive influenza vaccine are restricted to the inactivated vaccine.

However, LAIV is indicated for healthy persons specifically 5 through 49 years of age although I should mention that there is a new age approval for children 2 through the 5th birthday as well. And you can read about this on the CDC website as well. And I will note here that whereas asthma has traditionally been a contraindication for LAIV it does remain a contraindication for children 2 through 5 years of age as well. But there are actually more stringent or more specific contraindications for children 2 through 5 years of age, a history of wheezing alone is enough to cause us to preferentially recommend the inactivated vaccine.

But there are many groups outside of this of course that are recommended to receive LAIV, anyone that wishes to reduce their own risk of influenza who is healthy and not pregnant can receive this vaccine.

And this is an ideal vaccine for health care workers as well and this is a very important message to get across that health care workers may receive LAIV, they obviously see many patients that have chronic disease, patients that can't receive the live vaccine.

But the health care workers can. One exception to this are contacts of patients that are severely immunosuppressed. We're talking about patients that are in protected environments, bone marrow transplant patients and their contacts really should not receive LAIV, we prefer TIV in this case.

But for the majority of health care workers, LAIV is an excellent vaccine for them. Now I'm going to go through contraindications at a later point in this talk as well for LAIV and TIV.

Let's go to the next slide, "LAIV schedule". Children 2 years through 9 years of age again should receive two doses of LAIV separated by four weeks if it's their first vaccination season if they haven't received LAIV or TIV previously.

Otherwise they can receive one dose and persons 9 years through 49 years of age should receive one dose.

The volume of vaccine is 0.2 milliliters divided equally between the nostrils. Go to the next slide. There's been concern ever since LAIV was licensed about environmental contamination since this is a nasal spray vaccine.

While this time of contamination is probably unavoidable it really should not be a concern. The LAIV vaccine virus is genetically manufactured to replicate in the nasopharynx but not the lungs, it is cold adapted so it can only replicate in the cooler environment of the nose where it's administered.

In this way it can generate an immune response but cannot replicate in the lungs and cause influenza disease. Nevertheless it is possible that the virus can be shed, that means it's possible to recover virus in the nasopharynx of vaccinees and this has been noted after 7.6 days following vaccination in adults and longer in children.

There was one instance of transmission of vaccine virus, transmission as opposed to shedding is recovery of the virus, vaccine virus in someone that's not vaccinated.

This was in a daycare setting, important to note that the recovered vaccine virus retained its cold adapted temperature sensitive characteristics. So attenuated vaccine virus is really not thought to cause influenza symptoms and it is not thought to be a risk for persons administering the vaccine or anyone else that might come in contact in the environment with this vaccine virus.

Go to the next slide. Healthcare providers should be reassured that there have been no instances of transmission of LAIV reported in the U.S. among health care providers and I will repeat that ACIP does recommend LAIV be given to persons for whom it is not contraindicated and this will include many eligible health care providers except for those that care for the severely immunosuppressed persons in a protective environment.

And we've also recommended that health care providers are asked to restrict contact with bone marrow transplant patients, those in the protective

environments, for seven days after receiving LAIV otherwise there are no special precautions that are required.

Go to the next slide, LAIV like TIV has to be stored at refrigerator temperature, 35 to 46 degrees Fahrenheit. If the vaccine is frozen inadvertently it should be returned to the refrigerator and can be used thereafter.

Go to the next slide. The CDC publishes annual recommendations for the use of influenza vaccine. This year the following groups of persons are recommended to receive vaccine and this does not represent a change from previous seasons.

First of all, all children 6 through 59 months of age, all adults 50 years old and older, persons 5 through 49 years of age at high risk for complications (and I am going to go through what that means on the next slide), pregnant women, residents of nursing homes, household contacts of persons at high risk for complications, and health care workers.

So this is pretty much our traditional list of groups at risk of the severe complications from influenza.

This is now slide 33, conditions that place one at high risk for complications from influenza. And by the way I will mention that they include a bacterial pneumonia, viral pneumonia, exacerbation of heart and lung disease, myocarditis, otitis media, and Reye's syndrome.

So this slide shows persons at risk for these complications. The risk factors include age, so babies from the moment they are born until 59 months of age are considered at high risk.

Note that infants from birth to 6 months can't receive vaccine themselves but their contacts must receive vaccine, they are at high risk.

All adults 50 years old and older are considered high risk, persons with chronic lung disease which includes asthma, chronic heart disease, metabolic diseases like diabetes, that's considered high risk, chronic renal disease.

Anyone at high risk from aspiration, this would include spinal cord injury, seizure disorders, immunosuppression, and this is from either disease like HIV/AIDS or from drugs such as high dose steroids or cancer chemotherapy, pregnancy is a high risk condition as well.

And children 18 years old and younger who are on chronic aspirin therapy, they're at risk of complications of diseases like Reye's syndrome if they were to be infected with influenza and develop influenza disease.

So they are recommended to receive vaccine. That's a long list on this slide, I should note that finally that if you count all the individuals that meet these criteria and are eligible for vaccine plus their contacts which include health care workers, this equals 73% of the total population.

Let's talk a little more specifically about some of these risk factors on the next slide. Take a look at HIV infection, the risk of hospitalization for cardio pulmonary complications is very high in HIV infected patients, the risk of death is 100 fold higher.

TIV induces protective antibody titers in many HIV infected persons, the factors that can influence this include high CD4 T-cell count as well as minimal AIDS related symptoms.

So we do recommend the use of this vaccine in HIV infected persons. There have been reports of transient increases in HIV replication with the use of the influenza vaccine, but influenza vaccination has not been shown to negatively affect the long term course of HIV patients.

And so by preventing these complications of influenza TIV will benefit many HIV infected persons.

The next slide talks about pregnancy, it's another condition for which inactivated influenza vaccine is recommended. The risk of cardio-pulmonary complications from influenza is four times higher for pregnant women compared to non-pregnant women.

This makes sense, pregnancy brings physical changes that include reduced lung capacity as well as an increased workload on the heart because of increased stroke volume.

This risk of complications is comparable to non-pregnant adults that have other high risk medical conditions, so we recommend TIV for pregnant women regardless of gestational age.

Slide thirty six represents a new recommendation from this year's publication of the ACIP influenza recs. Basically we recommend that immunization providers should administer influenza vaccine to any person who wishes to reduce their likelihood of becoming ill with influenza or transmitting influenza to others.

This reflects both an abundant supply of vaccine this year and a large percentage of the total population that is at risk of acquiring or transmitting influenza.

Let me go to the next slide. The other new influenza vaccine recommendation this year involves the vaccination of children between 6 months and the 9th birthday through 8 years of age.

For some years now we've recommended that these children being vaccinated for the first time receive two doses. However sometimes children do not return for their second dose.

Beginning this year ACIP and AAP will recommend two doses of influenza vaccine for children in their second vaccination year that received only one dose in their first year.

Let me go to the next slide for the rationale behind this recommendation. It's complicated but with influenza vaccine, the first vaccine dose serves as a priming force for the immune system.

A second dose is necessary to generate the appropriate antibody response to fight influenza that season. We of course want the first and the second dose to ideally be given as early as possible in the fall.

Studies have been performed in children that do in fact receive one dose of vaccine in the spring and a second dose the following fall and what the data show are that children younger than 9 that receive vaccine in this pattern may be less protected than children that receive two doses the previous season and then receive one dose in the current season.

And this is especially seen if there is a drift in the B type circulating strain of influenza.

Because we want to vaccinate as early as possible in the influenza season and we're not going to really know how much drift occurs until probably the season begins, it was decided that this should be a general recommendation regardless of how early we find out whether drift occurs.

Why don't we go to the next slide. So in a child's second vaccination season, if they received only one dose in the first season for the first row, then in the second season they should receive two doses.

If they receive two doses in the first season, they only need one dose in their second season and one dose thereafter if they remain at risk.

Go to the next slide which discusses mixing and matching of TIV and LAIV for children recommended to receive two doses it's okay if one dose is TIV and the other is LAIV provided that neither vaccine is contraindicated.

You can mix and match therefore. The fourth bullet on this slide is a moot point actually because the interval between the two doses is the same for TIV and LAIV now, four weeks.

Note that on the recommendation to receive two doses only exists for children until their 9th birthday, at this point the cumulative effect of priming by either vaccination or natural infection is thought to be significant enough to require only one dose per season regardless of previous doses.

And this one dose recommendation applies to all age groups 9 years of age and older.

I’m going to conclude now with contraindications and precautions for inactivated influenza vaccine. Contraindications for the inactivated vaccine include a severe allergic reaction following a prior dose of vaccine or to a vaccine component, an allergic reaction following a vaccine component is a contraindication.

Again for screening purposes, the most common condition that might exist is a allergy, anaphylactic reaction to chicken eggs because the vaccine is grown, isolated and grown in chicken eggs.

A precaution for inactivated influenza vaccine includes moderate or severe acute illness, as with all vaccines you can always withhold the dose and give it later when a patient has recovered.

Another precaution is a history of Guillain-Barré syndrome within 6 weeks of a prior dose of inactivated influenza vaccine. So this is a precaution, note that if you have a patient that is at high risk of complications from influenza, the risk of these complications is much higher than the risk of Guillain-Barré even in those that have a prior history of Guillain-Barré.

For the last slide I’ll talk about live attenuated influenza vaccine, contraindications and precautions, it’s a live vaccine, there are contraindications that are age based.

It’s only approved for person 2 years through 49 years of age, so outside of that age group it’s contraindicated. Other contraindications include pregnancy, persons with an underlying medical condition including children and adolescents receiving chronic aspirin therapy, immunosuppression of course since it’s a live vaccine.

Like inactivated, a precaution for live vaccine is a history of Guillain-Barré syndrome within 6 weeks of a previous dose of influenza vaccine. And I should mention also, as with the inactivated influenza vaccine an allergy, an anaphylactic allergy to eggs is a contraindication as well, it's not on this slide.

My last few slides I'll talk about other interventions besides vaccination. Antivirals, the recommendations are the same as last year. We ask that you use neuraminidase inhibitors, you can use Oseltamavir and Zanamavir for chemoprophylaxis and treatment. .

You should avoid the adamantane class of antivirals because the resistance to the adamantanes remains high for the second season in a row running around 25%.

And then for my last slide, I want to emphasize healthy habits for the prevention of influenza. Always a good idea if you're healthy to avoid close contact with those that are sick. Wash your hands often and don't touch your eyes, nose and mouth to decrease the spread of germs.

When you're ill, cover your mouth and nose with your tissue or upper sleeve, when you sneeze or cough and stay home from work or school when you are sick.

Now obviously those of us on the front line in providing health care don't like removing ourselves from the equation so this last bit of guidance is sometimes the simplest yet the hardest to follow.

So let me take this opportunity to repeat and conclude with the important message that if you are a health care provider, probably the best thing you can do is get influenza vaccine.

If you can't do it for yourself, please do it for your patients, it is a patient safety issue.

And with that I will conclude and give it back to our moderator.

Alycia Downs: Well thank you very much that was a very informative presentation. We can now open up the lines for the question and answer session.

Coordinator: Thank you. If you would like to ask a question, please press Star 1. To withdraw your request press Star 2. Once again, if you'd like to ask a question please press Star 1.

Question: Yes, thank you Dr. Kroger for a very nice presentation.

As an infectious disease epidemiologist we find many health care workers in the public resistant to instance of vaccination on the claims that it gave them the flu, but upon further examination we find no evidence of further spread of any infectious disease.

And so we often explain to them that they feel bad after they have influenza vaccination or often their immune system reacting to these foreign proteins. Can you respond to this, are there any data on that particular point and is that a reasonable hypothesis to explain some of their symptoms?

Andrew Kroger: Well, that's a great question. The guidance on that issue is related to the type of vaccine in general that you're using. So if you're talking about the inactivated influenza vaccine, the reactions as with all inactivated vaccines that occur typically are local reactions, swelling, erythema can occur, soreness, pain in the arm.

And with of course the live attenuated influenza vaccine, there are reports of adverse reactions such as runny nose or congestion that occur with the use of this vaccine.

Beyond those generally recognized adverse reactions, I don't know how to explain any other type of symptoms other than you know in fact it may be influenza, that they became infected after getting vaccine before the vaccine took effect.

And then they practiced good health habits and did not transmit, and that could be explaining that finding.

Question cont'd: The absence of secondary infections in households, inactivated vaccine recipients though may generate the hypothesis that there's something other than an infectious disease going on.

And the immune reaction and indeed an exuberant over reaction, not necessarily a cytokine storm, but at least an exuberant reaction may help to explain that.

Andrew Kroger: Yeah, yeah, I guess what kind of symptoms are they?…

Question cont'd: Generally flu like symptoms, malaise, low grade fever, anorexia.

Andrew Kroger: Yeah, tough to know, I mean again it could be other infectious diseases as well that are circulating, RSV or you know rhinovirus, coronavirus, other cold viruses, it's really hard to know exactly you know whether these symptoms are due.

You know systemic symptoms are typically not seen with inactivated vaccines because they don't really contain you know the whole organism of interest and that organism is not alive.

So you know I wouldn't suspect a lot of systemic reactions from the shot, and again from the live vaccine you might have some systemic symptoms like that.

Question cont'd: All right. And this same hypothesis, I wish we had a method to check them out.

Andrew Kroger: Yeah, I mean as far as the whole cytokine storm theory that's being looked at with pandemic influenza You know what we've seen with H5N1 or looking at that kind of concept of persons not exposed, and young persons actually having a more profound response because of a robust immune response.

Question cont'd: Okay, thank you.

Andrew Kroger: You're welcome.

Coordinator: You may ask your question.

Question: Thank you. I just attended a state wide conference in Minnesota that was Dr. Schatz' immunization conference two weeks ago.

And at that conference they had stated that antibodies to not wane during the year. So I guess I'm confused, I'm getting two different messages, because on slide 19 you did address that antibodies do wane during the year.

Andrew Kroger: They begin to wane sometime after nine months we think. I mean studies show that 70% of vaccines still have an antibody response at nine months following vaccination.

So they will wane eventually, which is one of the reasons why immunization is recommended annually.

One of the three reasons that I mentioned, others being that the vaccine is manufactured to expire after June 30th and also that the viruses themselves may drift, and therefore you would need to have the more updated formulation.

Question cont'd: But if it were, if the were the same strains let's say two years in a row, Dr. Tan was explaining that technically it does not wane. But you would have enough antibodies to protect yourself for the following year, but because it would create mixed messages, that's why we vaccinate annually.

Andrew Kroger: I had not heard that to be honest that you would be protected that far out but that is, so that is news to me, I can kind of look into that.

Question cont'd: And then also what studies, where can I find these studies? You had mentioned that there are studies indicating waning after 9 months.

Andrew Kroger: Yes, the just a second, I can get that one for you. The citation is definitely in the seasonal influenza vaccine recommendation, that's where that comes

from, so I guess I'll have you start there. It should give you a citation for that nine months cut off there.

Question cont'd: So it's in the MMWR. Okay.

Andrew Kroger: And the 70%, the seasonal one, yeah, the one that comes out every year.

Question cont'd: Okay I will look there. Thank you.

Andrew Kroger: You're welcome. I'll take the next question.

Coordinator: You may ask your question.

Question: My question is I was interested in the last statement you made where the risk of influenza is greater than the risk of anything to do with Guillain Barre.

Since I'm chronic, is that different?

Andrew Kroger: If someone has a history of Guillain-Barré and in terms of chronic or having had a past acute episode, I don't, I can't address that distinction to be honest, I mean you would definitely be considered to have had a history of Guillain-Barré if you're suffering chronic symptoms from the disease.

If you are acutely ill at any time, you can always defer a vaccine dose. I mean it's a precaution for patients that are acutely ill, but for patients that have had a past history of Guillain Barre their symptoms resolved, then from the contribution of risk from a subsequent episode of Guillain-Barré we know that you are more likely to have a subsequent episode.

Hence our recommendation, that risk is lower than the risk of complications, it's one in a million is the risk of Guillain Barre happening following vaccination, is lower than your risk of a severe complication if you were to be infected with the influenza virus if you are high risk.

Now in a specific case where someone is suffering symptoms, I mean I guess you know I would have to defer probably to your treating clinician for, to gauge the level of acuteness of illness.

And so I would have to leave it there.

Question cont'd: Okay, thank you.

Andrew Kroger: You're welcome.

Coordinator: You may ask your question.

Question: I was interested in that the slide for influenza antivirals said Zanamavir for treatment only. The redbook had indicated that it could also be used for prophylaxis. Could you elaborate on that?

Andrew Kroger: In fact you know with, on our website it may say that for certain age groups you can use it for treatment as well.

Question cont'd: Because I mean we use it of course as backup, it's not used as user-friendly as say Oseltamavir. But we've been mentioning it as an alternative for both treatment and prophylaxis.

Andrew Kroger: That slide may have been a little misleading. [Slide was actually incorrect and has been corrected] It can be used for treatment in certain age groups, there's

an age group cutoff, and actually if you do look on our website, for persons 7 years and older, you can use it as a treatment as well.

And even for younger, many clinicians will use it anyway. But that distinction is sometimes hard to make.

Question cont'd: Again the redbook had said for prophylaxis that it would be 5 and above.

Andrew Kroger: Got it. Okay.

Coordinator: You may ask your question.

Question: I apologize, someone walked into my office right when you got to slide 42 and it was talking about the contraindications people with severe allergy reaction to eggs, is there any type of vaccine for influenza that they could take?

Andrew Kroger: Yeah, I mean the contraindication, which is a condition in a vaccine recipient that would cause you to withhold the dose, is a severe allergic reaction to a vaccine component and you know the one for which people will have common allergies is egg, residual egg proteins since the vaccine is isolated, the vaccine virus is isolated and grown in eggs.

Or an allergic reaction that follows a prior dose of the vaccine, so I mean most of your other common allergies that are out there are not considered, food allergies I'm talking about are not considered a contraindication for influenza vaccine.

Egg is the primary food allergy.

Question cont'd: So is there, you know I've heard discussion about the flu mist and you know versus getting an injection, and so is there something that people who do have the egg allergy could take?

Andrew Kroger: Oh I see what you're, I'm sorry, actually what we recommend in a situation for someone that has an anaphylactic allergy to eggs is the primary outlet would be consultation with an allergist.

You know I don't know what the status is of any type of any desensitization protocols, but no, if you have an anaphylactic allergy to egg, you're kind of restricted since both licensed vaccines are produced in eggs.

So vaccine is really not going to be an option, unless you really kind of explore further the nature of the allergy.

Question cont'd: Okay, thank you.

Coordinator: You may ask your question.

Andrew Kroger: Hello?

Question: I have an employee that works in a chemotherapy center and she has a latex allergy. Should I be administering the live attenuated influenza vaccine to her?

Andrew Kroger: I think I'm going to hand you over to COCA. There is a COCA website to send in that question because I don't know off hand that issue of latex allergy.

Alycia Downs: Yeah, if you can just send your question to us at COCA, C-O-C-A at cdc.gov, we will try to get that information to you.

Question cont'd: And am I correct in assuming she would not be able to receive the trivalent intramuscular vaccine because of her latex allergy?

Andrew Kroger: I want to give you the complete answer and I don't really have it right now. The important thing to keep in mind here though is you have to be talking about an anaphylactic allergy to latex and not a contact allergy.

You know if your hands get a little red from wearing latex gloves, that's primarily going to be a contact allergy, that would not be a contraindication for vaccines that contain latex.

But if you have hives, wheezing, you know shortness of breath, swelling of the lips and throat, that type of anaphylactic response to latex, then it very well might be.

But again I need to kind of, I need to get back to you on that in terms of the latex content of vaccines.

Question cont'd: Thank you very much.

Andrew Kroger: You're welcome.

Coordinator: You may ask your question.

Question: It was answered previously regarding the egg hypersensitivity that the studies are still mixed. Is there any hope for those who have true anaphylaxis to eggs receiving any of the inactivated vaccines currently?

Andrew Kroger: None of the currently licensed ones, but there are vaccines that are being researched right now in tissue culture and primarily in the context of pandemic influenza activities that may yield you know a solution in the future.

But currently no, I mean all the vaccines that are licensed are produced in eggs.

Question cont'd: Thank you.

Coordinator: At this time we have no further questions.

Alycia Downs: Dr. Kroger, thank you again for providing our listeners with this information. And I want to thank our participants for joining us today.

In case you didn't get a chance to ask your question or you think of one later, please send an email to coca@cdc.gov. That's C-O-C-A at cdc.gov. The recording of this call and transcript will be posted to the COCA website as they come to us.

And that is www.emergency.cdc.gov/coca. Please stay tuned for our next COCA conference call this Friday October 26th at 1:00 pm eastern on MRSA. We will be sending an announcement out to the listeners soon.

So I want to thank Dr. Kroger again, that was a wonderful presentation and I hope everyone has a wonderful day.

END