

2009 H1N1 Influenza and Pediatric Issues related to Antiviral Medications

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Coordinator: Good afternoon. And thank you all for holding. Your lines have been placed on a listen only mode until the question and answer portion of today's conference.

I would like to remind all parties the call is now being recorded; if you have any objections, to please disconnect at this time. I would now like to turn the call over to Georgina Peacock. Thank you. You may begin.

Georgina Peacock: Hi. And good afternoon and welcome to today's COCA conference call. I am the co-lead on the Children's Health Team and the H1N1 CDC Response in the Emergency Operations Center.

And what we are trying to do with these COCA calls is offer them about every two to three weeks to keep clinicians up-to-date on what's going on as far as the CDC response to the H1N1 influenza.

The purpose of the call today is to discuss pediatric issues related to the CDC updated Interim Recommendations for the Use of Antiviral Medications in Treatment and Prevention of Influenza for the 2009-2010 Season.

And this can be found at www.cdc.gov/h1n1flu/recommendations.htm.

We're very excited to have CDC subject matter experts Dr. Joe Bresee and Dr. Philip Peters present on this call.

We are using a PowerPoint presentation for this call that you should be able to access from our web site. If you haven't downloaded the presentation please go to emergency.cdc.gov/coca or C-O-C-A.

Click on conference call Information Summaries and Slide Sets and the PowerPoint can be found under the call-in number and pass code.

The objectives for this activities are to describe the current H1N1 situation, discuss interim recommendations for the use of antiviral medications to treat and prevent influenza and how these recommendations impact children, and finally identify potential issues as well as suggestions for additional resources that may be a benefit to healthcare providers.

Just now for a disclaimer, in compliance with continuing education requirements all presentations - all presenters must disclose any financial or other relationships with manufacturers of commercial products, suppliers of commercial services and commercial supporters as well as any use of unlabeled products or products under investigational use.

CDC, our planners and our presenters wish to disclose that they have no financial interest or other relationships with the manufacturers of commercial products, suppliers of commercial services or commercial supporters.

This presentation does not involve the unlabeled use of a product or products under investigational use. There is no commercial support.

And now I'm going to turn the call over to Dr. Bresee. Thank you.

Joe Bresee: Good afternoon everybody. This is Joe Bresee. I'm from the Influenza Division here at CDC.

I'm presenting remotely and can't see the slides so I'll rely on the folks back in Atlanta to right me if I'm on the wrong slide or to highlight the fact that I may be talking about a slide that's different than what you're looking at.

The first slide you should be looking at is a slide that's titled Novel Influenza H1N1 Detected with a little headline in a WR at the left side.

And I wanted to start here because I think as we think about what's happening now with influenza we're cognizant of the fact that we're having this call because of the emergence of what was called Swine Influenza, now called Novel Influenza H1, now called actually Pandemic Influenza H1.

And that's a context in which we're talking about, the emergence of this virus in two children detected first in mid-April.

Next slide, please.

You should be looking at a world map; the emergence of the virus in these two kids initially detected in California led to the realization of a slightly early emergence at least in Mexico and maybe earlier than that, spread rapidly around the country and around Mexico.

And as you see the world map as of a couple of weeks or maybe last week you see that the countries colored in indicate the countries where virus has been

detected and cases of illness have been detected. Just to say that more than 188 countries in the world have confirmed a case.

And those that have it clearly are those that probably do have cases that have just less test and capacity.

And this highlights the fact that the emergence of this new influenza virus has spread rapidly around the world via susceptible population and good transmission dynamics. And again the reason we're having a call about flu in early September.

If you look at the next slide let me get onto what's happening in the United States now. You should be looking at a slide with a blue background with a line graph that has the rates of influenza like illness in the country.

And these are the proportion of all patients who come to a bunch of clinics that we do surveillance in. And these are the proportion of all the people they see that have an influenza like illness.

And I want you to see three things about this slide. First, if you look at the red line that's this year. If you look at the red line you see the normal early (comp) with a regular flu season back in January, February, March, that's the normal influenza season.

The second red increase in the red line around May, June indicates the emergence of this virus and it spread through the U.S. population.

But as you see that slightly declining over the summer months, I want you to notice the fact that red line always stays well above the normal summer baseline, the last two years being an indication of this.

And so despite the fact that we've seen decreasing disease up until recently through the summer, I want people to realize that there has been as you know lots of influenza in many places in the country throughout the summer months when it's usually fairly quiet in terms of influenza.

And the third thing I want you to look at is the (far side) where we see an increasing rate of IOI represented by the slope of the red line on the far right side indicating that really in the last three weeks CDC has begun to get hints of increasing influenza activity in a variety of places in the country already and as you know is much earlier than we usually see increasing influenza activity.

The next three slides if you just flip through them every ten seconds or so, show the same curve by region. And the gestalt here and don't worry about the number so much, but the gestalt here is again the red lines represent this year, the other colored lines represent previous years, is that we're starting to see hints or increasing activity in almost every region of the country. And in some regions they're above baseline as you'll see.

And so you should flip through those three slides and just get the picture that we're seeing increasing influenza activity.

And the suspicion here is that increasing activity represents probably an early increasing activity for the season and not just a late summer blip but time will tell.

If we think about more severe disease, you look at the next slide which is a histogram of showing five peaks in disease over the last four years, these are

the pediatric deaths. As you know pediatric deaths are deaths among kids under 19 years old that have an influenza positive are reportable to CDC.

And this again if you look on the right side of the graph you see this current year with the - with pediatric deaths occurring in the normal seasonal year and then another hump of pediatric deaths occurring with the emergence of this virus.

So far since the emergence of the virus we have documented 44 deaths among children that are associated with this Pandemic AH1N1 virus. We'll watch that closely as we go through the season as it is a rough measure of the severity of the virus among the pediatric population.

The next slide shows the U.S. map. And this is an indication of geographic spread of influenza in the United States. And this week as you see the dark gray colors in this map, 13 states are reporting - I'm sorry, 11 states are reporting widespread activity and 13 states are reporting regional activity.

And again just to put this in context, this is far more influenza activity in terms of geographic spread than we normally see in mid-September.

The next slide shows the viral data and don't worry so much about the numbers here.

But just look at the right side of the curve and the far right side of the curve you see the orange and yellow parts of the histogram. This is only to show that while the rate of detection of influenza, the line here represents the proportion positive of all the tests done in participating labs. While the proportion has gone down, the lion share, almost all of that 97% of all the positive influenza

tests continue to be the Pandemic AH1 virus. And we're seeing almost none or very little of the H3 or H1 virus at this point in the season.

The next three slides get back to the epidemiology of the disease and what we know about it.

And as you'll see the slides are a bit dated but they still represent what we think is true about the epidemiology and the age distribution of the disease. The first slide represents just the rates of disease by age group.

And for this - for the purpose of this talk look at the big curves, the big bars which show that clearly kids and young adults are at the highest risk of acquiring this virus infection and (under the illness).

If you look at the next slide you see the clinical symptoms. Again which hasn't changed, highlight two things; first, that most of the symptoms that we see with this virus continue to be the classic respiratory symptoms, a cough and sore throat and respiratory issues.

But again you look at the right side where you see vomiting and diarrhea.

And consistently throughout the outbreak where it's been looked at both in the U.S. and in other countries about a quarter of the patients representing they're positive for this virus will have gastrointestinal symptoms. And we've certainly seen some patients present with those symptoms primarily and that's something to keep in mind.

The next slide, we turn our attention towards severe disease. And this is hospitalization rates by age group, by the same age groups I just showed you.

And again you see the pattern that the highest rates of hospitalizations occur in the youngest children with a sort of a reverse J-shaped curve with slightly higher rates than the elderly.

But again significantly lower than what you normally expect with an influenza virus.

If you look at the next slide with a blue background now, you'll see what we normally expect. The bars here represent rates in similar age groups of hospitalizations and the red line represents the rate by age group of mortality associated with influenza.

And really this is what we normally see so compare it with the curve you just looked at. You see a (girth) of illness in the elderly is what you'd expect.

The next slide again shows this with emerging infections program data. These are data from 12 or 10 sites in the United States that look at age distribution of hospitalizations attributable to flu.

And again the light blue represents what we normally see with the large - most of the hospitalizations occurring in elderly people. And again the dark blue represents this season where again you see high rates of hospitalizations in young people, young adults relative to the elderly people.

And the final data slide is the next one which again has a light and dark blue.

But just to remind everybody that there are identifiable risk factors that are risk factors for complications of influenza and so far the data for this virus shows that those complications that we see with normal flu are actually,

excuse me, the risk factors we see that - for normal flu are also holding true with this flu.

So (people) with no underlying conditions that are at high risk for severe flu should be protected from this flu as well.

And we'll talk about that in a minute.

Finally summary key points, I just wanted to point out that once the virus emerges, clearly spread quickly. And despite the summertime we continue to have circulation in the U.S. and we're seeing now signs that it's increasing. Some areas clearly were affected in the spring and we see that all the time with flu where we get spotty coverage of flu but we expect all areas of the country to be affected at some point this season.

Elderly seem to be relatively spared so far and we think that will persist. And the virus and while held in most people is capable of causing severe disease and death in many, especially those with underlying risk factors.

So far the virus remains sensitive to both tamivir and zanamivir and finally we're seeing increasing activity now and one could expect increasing activity in your community in the weeks and months to come.

Thanks very much.

Philip Peters: Well thanks Dr. Bresee. This is Philip Peters. I'm a Medical Officer on the 2009 H1N1 Influenza Task Force at CDC.

And if you could advance your slide to Interim Recommendations for the Use of Antiviral Medications for the 2009-2010 Influenza Season, I just wanted to state that this presentation will have two major parts.

First, we'll just briefly review the medications that are being recommended. And then we'll review - the second part we'll be reviewing the actual guidance in a little more detail trying to highlight some of the issues that are relevant for pediatric populations.

And then finally what's not in the slides but I thought we could mention briefly is that this guidance is a living guidance. It's not something that is set in stone and could evolve over time.

We have already gotten some feedback regarding this guidance from pediatric groups, pediatric clinicians.

And I can, you know, briefly mention what some feedback has been to date and how we might address that.

But if you advance the slide, the next slide is a schematic that shows influenza replication. This is just to show that we will only be discussing the neuraminidase inhibitors which work at the terminal phase of influenza replication and prevent the release of influenza virions from infected cells.

If you advance the slide to the slide that's titled Neuraminidase Inhibitors we will be discussing both oseltamivir marketed as tamiflu and zanamivir marketed as relenza.

The data for using these medications come from several sources. The initial randomized clinical trials show that they reduce the duration of an influenza

illness by one to one and a half days when administered within 48 hours of symptom onset.

Subsequent pools analysis of this randomized controlled trial data has shown evidence that these medications reduce the incidence of lower respiratory track complications, pneumonia and hospitalization from influenza.

And in addition many observational studies have been done and some in particular that are highlighted in the references have shown that oseltamivir use is associated with reduced mortality among hospitalized adults who have lab confirmed seasonal Influenza A viral infections.

So there are - there is a lot of good evidence for the efficacy of these medications.

If you advance the slide to the oseltamivir slide, this medication is available as a capsule or a suspension which is particularly relevant for pediatric patients. We'll discuss this a little further in the presentation.

But an important point to note is that the capsule formulation can actually be compounded by a pharmacist into an oral suspension and so that has implications. If a particular pharmacy doesn't happen to have the oral suspension, the capsule can actually be compounded by a general pharmacist into an oral suspension.

Again pediatric dosage is dependent on age and weight. It's FDA approved for ages greater than or equal to 1 year however there's also an emergency use authorization that's been approved for use of oseltamivir in persons who are less than 1 year.

The side effects include nausea and vomiting and there have been reports of neuropsychiatric events that have come almost completely from Japan among adolescents who have received oseltamivir.

Of note in the randomized controlled trials these medications were tolerated extremely well and there was very little difference between placebo and individuals that received the medication.

Regarding precautions, to note with kidney disease and reduced creatinine clearance the dose needs to be adjusted.

And there is not a lot of safety data for pregnant or nursing women. However treatment of pregnant women who are infected with influenza is recommended.

The next slide is zanamivir and in the top right corner there's a little picture of what the zanamivir device looks like. It's an orally inhaled powder. It's been FDA approved for treatment of people who are greater than or equal to 7 years old.

And there is also an emergency use authorization that expands the treatment indication for zanamivir to hospitalized patients. It was initially FDA approved for outpatients.

And also FDA - and also, excuse me, authorized the use for patients who are symptomatic for more than 48 hours or two days.

And this is an important point particularly among hospitalized patients even if they're presenting after 48 hours of their symptom onset. There is still - there

still seems to be use in treating with antiviral medications both for oseltamivir and zanamivir.

The side effects are a little more complicated for zanamivir. They can include wheezing and breathing problems. And there's a precaution with using this medication for individuals who have bronco spasm because it can precipitate or worsen bronco spasm. So particularly for individuals with asthma and COPD this is a precaution.

If you advance to the next slide there's a summary of antiviral resistance for data for 2008 and 2009 seasonal viruses and for the 2009 H1N1 influenza virus.

And as you can see 2009 H1N1 is resistant to the emancity and class of medications but susceptible in general to both oseltamivir and zanamivir.

There have been eight reported cases of resistance to oseltamivir out of 1,372 specimens that have been tested of the 2009 H1N1 virus. The majority of these cases have been individuals who had either received chemoprophylaxis or were severely immunosuppressed and were being treated for a prolonged period of time medication.

If you advance to the next slide the title is Treatment Recommendations. So I think we're now moving into the part of the talk that is talking about the actual antiviral recommendations.

And the first point we want to make is that above all obviously clinical judgment of yourselves and healthcare providers is the most important issue for treatment decisions.

And these guidelines are - sorry, these recommendations are supposed to help inform care and treatment decisions but should not obviously take the place of clinical judgment.

The predictors of hospitalization in children have been used to determine which children there should be more emphasis or prioritization for treatment. And predictors of hospitalization in children have included young age and general high risk medical conditions and particular cardiac disease and in particular neurologic and neuromuscular disease as well as evidence of lower respiratory-tract disease meaning pneumonia or radiographic evidence of pneumonia.

And there are some references to where those risk factors were defined.

If you advance to the next slide it is also titled Treatment Recommendations. The essential recommendations for treatment are that oseltamivir or zanamivir treatment is recommended for persons with suspected or confirmed influenza who have severe illness, for example patients that need to be hospitalized.

And it is also recommended for patients with suspected or confirmed influenza who have risk factors for severe illness.

If you advance to the next slide, Risk Factors for Severe Illness is the title. And so by this we mean in the guidance it says children younger than 5 years of age but we want to emphasize that it is the children who are younger than 2 years of age are the particular group that appears to be at higher risk for these complications. Persons who are greater than 75 years of age, pregnant women, persons with certain chronic medical or immunosuppressant conditions and in particular small risk factor group, persons younger than 19 years of age who are receiving long term asthma therapy because of Rhy's Syndrome concerns.

If you advance the slide the next is a distribution by age group of hospitalizations.

And Dr. Bresee already covered this so I won't cover it again. But it's just as many of you have seen, the difference with 2009 H1N1 virus has been the age distribution. And there are many more cases of influenza and hospitalization with influenza that have been seen among the younger age groups than with the typical seasonal influenza virus.

If you advance to the next slide, this is again EIP data from the laboratory confirmed hospitalizations. It's the cumulative rate of hospitalizations.

And this is again to show that just in the spring and summer of 2009 the hospitalization rates are already starting to approach what is seen from a winter season of influenza so as many of you have already seen there's a lot of influenza already within the community.

If you advance the slide to the medical conditions, this is a list of medical conditions that were considered high risk for influenza, complications, chronic pulmonary including asthma, cardiovascular conditions with the exception of hypertension by itself, renal disease, pathic disease, hematologic disease which includes sickle cell disease and metabolic disorders which includes diabetes.

The second bullet point there is proposed change in language to try to clarify what is meant by individuals with neurologic and neuromuscular conditions to state disorders that compromise respiratory function or the handling of respiratory secretions or that can increase the risk of aspiration such as

cognitive dysfunction, spinal cord injuries, seizure disorders and other neuromuscular disorders.

And this has been based on some of the experience with what has been seen with the pediatric deaths and what particular conditions were represented in - among the pediatric deaths.

And then a final bullet point, immunosuppression including immunosuppression caused by medications or caused by HIV.

If you advance to the next slide it begins with a bullet point that states approximately 70% of hospitalized patients with 2009 H1N1 influenza have had recognized high risk conditions.

One aspect to note however is that among children its been a slightly lower percent that have recognized high risk conditions so a slightly percent, 60% of children have had recognized high risk conditions and 40% of children who have been hospitalized have not had these conditions.

The influenza related pediatric deaths, MMWR that came out September 3rd and for which there was a COCA call about two weeks ago as well showed that 67% of children who died with 2009 H1N1 influenza had a high risk medical condition.

If you just look at children who are less than 5 years of age there were seven deaths in that case series, four of those children who were less than 5 years, four of the seven did not have a high risk medical condition.

So although children who have a high risk medical condition are obviously at the highest risk for complications. We are also seeing otherwise healthy children who are presenting with very severe disease.

Advance to the next slide. This is underlying conditions among hospitalized patients.

And Dr. Bresee also presented this so I won't dwell on this. And this is also a mix of adults and pediatric data.

But the same conditions that are high risk for seasonal influenza also appear to be high risk for 2009 H1N1 influenza.

Advancing to the next slide is the title of which is Clinical Considerations.

The first consideration is that healthy persons who develop an illness that is consistent with influenza so has suspected influenza and persons who appear to be recovering from an influenza illness generally do not need antiviral treatment.

And the caveat to that however is that patients who are presenting with a suspecting influenza illness but have evidence of a lower respiratory-tract illness such as signs of dypnea or tachypnea should receive empiric antiviral therapy.

So again this is a nuance to message that depends heavily obviously on clinician and healthcare provider clinical judgment.

But in general healthy persons who have a mild illness do not require treatment. But healthy individuals can also develop severe disease and

antivirals are very beneficial in that situation and should be given empirically and should not be delayed pending a diagnosis or a diagnostic test.

If you advance to the next slide it lists clinical warning signs. This is particularly relevant for younger children. As you know older children will present with more classic influenza illnesses.

But just to bring to everyone's attention that there can be quite atypical presentations particularly among younger children and/or - and immuno compromised children that have to be looked out for.

If you advance the slide next to influenza diagnosis, treatment when indicated for influenza should be initiated as early as possible.

And again the randomized controlled trials showed that the earlier treatment is begun the better the clinical benefit.

Therefore treatment should not wait for laboratory confirmation of influenza. If there's clinical suspicion that the patient has influenza and they are in a group or have a clinical syndrome that makes treatment appropriate treatment should be initiated and it should not be delayed for laboratory confirmation.

In addition a negative rapid influenza diagnostic test does not rule out a influenza as a cause of the illness.

And the sensitivity of rapid influenza diagnostic tests for detecting 2009 H1N1 influenza has been very low and has only ranged from 10 to 70%.

So a negative rapid test does not necessarily mean the individual does not have influenza and has been published recently, the rapid test has a relatively low sensitivity for 2009 H1N1 influenza.

If you advance to the next slide that's titled Actions to Improve Early Treatment, we're asking clinicians to consider actions that can be taken individually and by their practices and hospitals that can facilitate the early treatment of patients who need treatment the most, patients who are at the highest risk for influenza complications.

And several suggestions include informing patients who are in your practice or that you see who are at high risk for influenza complications of the signs and symptoms of influenza so that they know that they should seek early treatment if any of those signs or symptoms develop; also ensuring that these individuals also have rapid access to telephone consultation and clinical evaluation when needed so there's - to minimize overflow into emergency rooms.

And finally considering empiric treatment of patients who are at higher risk for influenza complications based on telephone contact if hospitalization is not indicated which is not to say that the patient would not be evaluated in outpatient setting shortly but if there's going to be a delay of one, two, three days before the patient can be seen in the outpatient setting, considering empiric treatment in the meantime because the earlier treatment has started the better the clinical benefit.

The next - if you advance to the next slide it states antiviral chemoprophylaxis. In general chemoprophylaxis should be reserved for persons who are at the highest risk for severe illness.

We are trying to emphasize early treatment as an alternative for chemoprophylaxis for individuals who are at high risk for severe illness and have had contact with someone likely to be infected with influenza.

So how this would work is that a patient who is at higher risk for severe disease, who has had contact with a suspected case of influenza could be consulted by their healthcare provider about the early signs and symptoms of influenza.

And then if any of those symptoms develop within the next week or so they would immediately contact their healthcare provider and the provider could make, you know, an immediate decision whether or not those symptoms justify treatment to try to facilitate treatment as quickly as possible but also to minimize the use of chemoprophylaxis within the community.

If you could advance to the next slide it is titled Outbreak of Antiviral Chemoprophylaxis.

In general outbreaks of influenza that occur in schools, camps or other group settings of otherwise healthy persons without risk factors for severe illness should not be managed with blanket general chemoprophylaxis.

Persons who are in settings should be educated about the signs and symptoms of influenza and then urge to consult their healthcare provider particularly if severe illness develops and severe symptoms develop.

And so advancing to the final slide, summary of interim recommendations for the use of antiviral medications, the take home points that we had from this presentation was one, that we want to emphasize a focus on treating severely

ill patients, for example hospitalized patients, and treating patients who have risk factors for severe illness.

Most treatment is going to be empiric because the widely available rapid tests have a very low sensitivity to diagnose 2009 H1N1 influenza. And treatment should be started early and should not wait for a confirmatory test that might take several days to get back.

Healthy patients in general with mild disease usually do not require treatment.

And then finally chemoprophylaxis use should be limited. And early treatment of high risk individuals is an alternative to chemoprophylaxis.

So that concludes the slides. And I think the one last thing I wanted to mention is that there were, you know, certain issues had been raised already about the recommendations and how they impact pediatric practice.

And obviously a difficulty of these recommendations is that they're for, you know, both children and adults. They apply to quite a lot of patients.

But one issue has been particularly among children who are in the 2 to 4 year-old age group. But this is a group that obviously develops a lot of illnesses that can be influenza like illnesses but not might necessarily be influenza and in general if they're having mild symptoms will recover quite well and may not always need treatment.

And we are working with clinicians and with the AAP and Pediatric IDSA to try to look at this issue particularly for children age two to four to see how the wording can be revised to emphasize more that it's really a clinical judgment that any children who are presenting with worrisome symptoms should be

treated but children with more mild illness do not necessarily need to be treated.

And the second issue that had been brought up was the use of the terms neurocognitive, neuromuscular can be interpreted differently by different groups.

And so we were using the terms as have been traditionally defined by ACIP but we're getting feedback that people were interpreting them more broadly than we intended and that needed some clarification.

So I think, you know, further issues - in the question and answer section further issues might be brought up and we want to be as responsive as possible to any of your concerns and we certainly welcome as much feedback as possible from the field about your experience.

So with that I think I just wanted to make one more point. The issue - as you might have recalled when I talked about oseltamivir I mentioned the pediatric formulation that is a suspension.

So you can write a prescription for pediatric formulation of oseltamivir that's a suspension.

And that in general has not been a medication that's been used very often prior to this year. At a particular pharmacy they might not have the suspension.

But an alternative is that the oseltamivir capsule can actually be compounded into a suspension.

So particularly for individuals who are less than one year of age where they're receiving in the dosages, the recommended dosages for that age group by weight or in the antiviral recommendations, this compounding may be an important source for getting the proper dosage to that group of patients.

And so that's something that we're trying - that we're working with distributors and pharmacies but also want to get the word out to clinicians and healthcare providers that compounding of a capsule is an alternative to using the pediatric suspension for these lower doses of oseltamivir.

So I think with that I'll stop and turn it back over to Georgina.

Georgina Peacock: Well thank you Dr. Bresee and Dr. Peters for those presentations. I think there's a lot of information in there.

And now we would like to give people an opportunity on the line to answer questions and so we'll just go from there. I'll turn it over to the Operator.

Coordinator: On the audio portion if you would like to ask a question please press star 1 on your touchtone phone. You will be prompted to record your name and please unmute your phone and record your name clearly when prompted. Once again to ask a question, please press star 1.

One moment please, for the first question. Our first question today.

Question: Hi. If a patient has been diagnosed to have H1N1 flu based on the nasopharyngeal swab is this patient - should this patient be receiving the H1N1 vaccine when it's available?

Philip Peters: Thank you for that question. That question has come up so that's not an area that I'm directly working on but that issue has come up on several conference calls that I've been privy to.

And I think, you know, one issue is can you - one issue with your patient is can you really be certain that the patient had a 2009 H1N1 infection and that there's a broad range of tests that might have been done to make that diagnosis.

And so I don't want to state a recommendation that's not an actual recommendation but Dr. Uyeki if you're on the phone or Dr. Bresee if you're on the phone do you - would you feel confident saying something particular about that group because this question does come up?

Joe Bresee: Yeah, so this is Joe. And it's a great question. Classically for seasonal flu we don't make that distinction and we recommend that people who meet the criteria or wish to get influenza vaccine get influenza vaccine without thinking about prior exposure to similar viruses.

And so I think we should approach this the same way. I think it's a fairly unlikely scenario to be honest that somebody has a PCR positive result for this virus.

So most cases (is the old saying) was our flu positive people or people with IOI and because the uncertainty about the actual exposure in those people those people should certainly get vaccine if they're in the recommended group to do so.

Of the small number of people that PCR confirmed to have influenza infection I think its reasonable still to have them vaccinated because of the uncertainty

of what immune response after natural infection will concur. But also again about the difficulties of diagnoses even in positive patients.

So I think that as a rule we would say if you're on the list to be vaccinated go ahead and get vaccinated without regard to prior illness history.

Question cont'd: Thank you.

Coordinator: Our next question.

Question: Yeah hi. I have two sort of unrelated questions. One, it's clear that in obese patients they seem to have a worse time with flu.

Are you recommending obese patients be either prophylaxed and if you treat them, are you doubling the dose?

The second question relates to immunosuppressed patients. We've had a number of cases in immunosuppressed, immuno deficient patients who have subsequently relapsed or apparently relapsed.

Are there any guidelines that you're collecting currently to indicate how long to treat a severely immuno deficient patient say relapsed (AOL) or bone marrow transplant patient or severely impaired rheumatology patient, longer with oseltamivir?

Philip Peters: I think that's a great question. And I think I'll take a crack at the first part of the question and Dr. Uyeki maybe you could address the second part about treating immuno compromised patients.

Yeah, thank you for pointing that out that there has been preliminary evidence that individuals who are - certainly individuals who are morbidly obese have a BMI greater than or equal to 40 and also perhaps people who are just obese with a BMI of 30 to 39 may be at increased risk for hospitalization and death with 2009 H1N1 infection.

In general the recommendation for treatment for an adult, it's not a higher dose for somebody who is obese.

But if you look at the guidance for pediatric patients the recommendation for the dosage is weight-based. So if you had somebody who was quite young but their weight was quite high they would be at the adult dose but would not be above that.

The caveat is that there has been consideration to use higher doses of oseltamivir for severely ill patients.

And so there have been case series reported of patients who are admitted to intensive care who have been treated with double the dose of oseltamivir.

But that's not something that's been studied. That's not something that's been studied very well. It's not something that we actually have a recommendation about.

But we do sort of mention that it has been used by certain groups particularly in severely ill patients.

Question cont'd: Thank you.

Philip Peters: Dr. Uyeki do you want to...?

Tim Uyeki: Sure.

Philip Peters: ...address the immuno compromised?

Tim Uyeki: So this is Tim Uyeki from the Influenza Division at CDC. Just a quick comment about the previous question, in patients who are critically ill including pediatric patients I think higher dosing can be considered and certainly longer duration of antiviral treatment should be considered.

In terms of patients who are severely immunosuppressed or severely immuno compromised, one of the challenges here is that these patients not only may be quite sick but they also have the propensity to shed virus for very prolonged periods of time for many weeks and months.

And so in terms of treatment of a symptomatic person certainly the standard treatment course of five days should be done.

But in longer course of treatment for a patient who continues to be critically ill should be considered including even a patient who is not critically ill but who is hospitalized.

So I think certainly longer dosing can be considered. These kind of patients present a huge challenge.

And we have not issued any formal guidance here.

But I think there are a number of considerations. One, given that these patients have high potential for a very prolonged viral shedding including even once

they have resolved some of their clinical illness. They may have asymptomatic viral shedding for a very, very prolonged period.

And because of this and there is the potential for the emergence of resistance to antiviral treatment, we have had some sporadic cases both in children as well as in adults that were severely immunosuppressed. One case a severely immuno compromised adult who have had very prolonged shedding and developed oseltamivir resistant novel H1N1 virus infection.

So once point is that they should be monitored and continue to be monitored at least on a weekly basis and infection control really needs to be maintained in the hospital setting because there is a risk, number one, of the emergence of oseltamivir resistance. And number two, because of the potential for prolonged shedding. This is a potential transmission risk to visitors as well as healthcare providers.

So the other thing that should be considered certainly if there is prolonged viral shedding and a patient is clinically deteriorated or certainly not improved, one should consider the potential for oseltamivir resistance to have been developed and respiratory specimen should be collected.

We would be happy to be contacted in those situations in which there is evidence of prolonged shedding and a potential suspected oseltamivir resistance.

In those kind of patients in which documented oseltamivir resistance is found those patients are certainly a candidate for and if patients are still symptomatic those patients are candidates for alternative antiviral treatment including with either orally inhaled zanamivir if tolerated or intravenous of zanamivir which

is available on a very, very limited compassionate use basis at this time which brings up the issue of this is not a CDC recommendation.

But initial treatment of these kind of patients one could consider combination antiviral treatment which may potentially be a strategy to reduce the emergence of antiviral drug resistance on monotherapy.

But again these are - there are pediatric infectious disease specialists with some expertise in this area that care for these kind of severely immunosuppressed patients.

So I'd be happy to refer clinicians for consultations with these experts, academic experts in the U.S. if and I'd be happy to be contacted at CDC to help you connect up them.

Thanks.

Question cont'd: Thank you.

Coordinator: Our next question is from Ann. Your line is open if you'd like to ask a question.

We can move onto the next question. Your next question.

Question: I just wondered if you could repeat the web site where the PowerPoint is.

Georgina Peacock: Sure. The PowerPoint is at emergency.cdc.gov/coca.

And the treatment guidelines are at
www.cdc.gov/h1n1flu/recommendations.htm.

Question cont'd: Thank you.

Alycia Downs: And if you send an email to coca@cdc.gov, that's C-O-C-A at cdc.gov we can also send those links to you.

Question cont'd: Thank you.

Tim Uyeki: I think one point that I'd like to make is that all of our guidance and information is really interim as, you know, we're all in this working with you guys. And, you know, kind of international basis as we learn more and more about the epidemiology and clinical characteristics of patients with this novel influenza AH1N1 virus infection. We will update our guidance recommendations information as warranted.

So everything should be construed as interim.

Georgina Peacock: So I think we have time for about one more question and then I wanted to let the listeners know that if you haven't had a chance to ask your question you can email coca@cdc.gov. It's C-O-C-A at cdc.gov with your questions and we will get those to the right people and get an answer back to you.

So if we could have one more question from the audience.

Coordinator: Our final question today.

Question: Yeah hi. We're trying to prepare for the need of extra pediatric beds.

And I was wondering from any of the graphs that you have if you have estimates of the percentage of children in each age group who acquire H1N1 who require hospitalization.

They only see the gross numbers of what percentage of all the hospitalizations are from each group.

I was wondering if you have any estimation of the percent of the kids who actually come down with H1N1 that end up in the hospital in each of those age groups.

Joe Bresee: This is Joe. It's a great question. And no, I don't. Off the top of my head I clearly don't.

And we are working on some models and some projections both from the spring and from other countries looking at the risk of outcomes given exposure and given infection by age group.

But I don't have those at this moment. When we do have this model together which is produced just for the purpose you're thinking of for projections of what the needs might be come fall, we'll make that public and maybe we'll tee that up for an upcoming COCA call but don't have them today, I'm sorry.

Georgina Peacock: So I wanted to thank Dr. Bresee, Dr. Peters and Dr. Uyeki for presenting on this call today.

And again if you have questions that you weren't able to get answers please email coca@cdc.gov, C-O-C-A at cdc.gov.

The recording of this call and transcript will be posted to the COCA web site at emergency.cdc.gov/coca within the next week. You will have a year to obtain continuing education for this call.

All continuing education credits and contact hours for COCA conference calls are issued online through the CDC Training and Continuing Education Online System, www.2A.cdc.gov/tceonline/.

Thanks again for participating and have a great day. And please let us know if you have any questions or if you have suggestions for future COCA calls. Again we are trying to have these every couple weeks to focus on issues that are interesting or needed for people who are taking care of children, for clinicians taking care of children.

So let us know and we look forward to presenting again in a couple weeks.
Thank you.

Coordinator: Thank you. And this concludes today's conference.

You may disconnect at this time.

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