

Pediatric Issues related to 2009 H1N1 Influenza

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Coordinator: Good afternoon and thank you all parties for standing by. At this time, your lines will be on a listen-only until the question-and-answer session. At that time, you may press star 1 if you would like to ask a question.

Today's conference is being recorded. If you have any objections, you may disconnect at this time. I would now like to turn today's conference over to Ms. Alycia Downs. Thank you, ma'am. You may begin.

Alycia Downs: Good afternoon and welcome to today's COCA conference call on pediatric issues related to 2009 H1N1 influenza, including an update on the recent study of pediatric deaths associated with H1N1, children with special healthcare needs, and antiviral guidance.

We are very excited to have CDC subject matter experts present on this call. We have with us today Dr. Tim Uyeki, Dr. Deborah Christiansen and Dr. Georgina Peacock. We are using a PowerPoint presentation for part of this call that you should be able to access from our Website.

If you have not already downloaded the presentation, please go to emergency.cdc.gov/coca, click on conference call information summaries and slidesets.

The PowerPoint can be found under the call-in number and passcode. There will be no continuing education credits or contact hours available for this call. I will now turn it over to Dr. Peacock.

Georgina Peacock: Hello and thank you for joining us today. As Alycia said, I'm Georgina Peacock. I'm the co-lead on the children's health team relating to the H1N1 response here at the CDC and our function is to work on internal and external communication and coordination around children and the 2009 H1N1 influenza situation.

We are delighted to have a few people talking today on this call. We'll first have Dr. Christensen talk about the morbidity and mortality weekly report article that was released week entitled "Surveillance for Pediatrics as Associated with 2009 Pandemic Influenza A H1N1 Virus Infection, United States, April through August of 2009."

As a background, I wanted to share with you that during the past five years, CDC has tracked deaths among children under the age of 18 with influenza infections.

The number of deaths reported to CDC each year has ranged from 46 to 153 deaths and this is a very - deaths in children from influenza or influenza-related pediatric deaths - are a somber reminder of the importance of protecting children from the flu.

We know with seasonal flu that the children that are at highest risk are children younger than five years of age and among children younger than five years of age, the risk for severe complications from seasonal influenza is highest among children less than two years old.

In addition, children of any age with chronic medical conditions like asthma, diabetes, neurologic or neuromuscular conditions or heart disease are also at a higher risk. In addition to this, even children who are otherwise healthy can rarely have severe or fatal outcomes after influenza infection.

So at this point I'd like to turn the call over to Dr. Christensen to talk to us about some of the details of this morbidity and mortality weekly report article.

Deborah Christensen: Thank you, Dr. Peacock. This is Dr. Deborah Christensen. I'm an epidemic intelligence service officer in the Division of Birth Defects and Developmental Disabilities at CDC.

And as Dr. Peacock said, we - there was a morbidity and mortality weekly report that was issued last Friday on surveillance for pediatric deaths associated with 2009 pandemic influenza A virus infection.

As of August 8, 2009, there were 477 deaths associated with laboratory-confirmed 2009 H1N1 flu in the United States, including 36 deaths among children less than 18 years of age that were reported to CDC.

They were reported from 15 state and local health authorities. They were all reported through the influenza-associated pediatric mortality case notification system since pediatric influenza-associated mortality is a reportable condition in children and has been for several years.

So I'm going to give a quick summary of the findings. One of the prominent findings is that two-thirds of children who died with 2009 H1N1 influenza had at least one high-risk medical condition and that can include pulmonary disease, cardiac disease, and strikingly neurologic and neuromuscular conditions.

And among these children with high-risk medical conditions, almost all of them - 22 out of 24 - had neurodevelopmental conditions. For example, moderate to severe developmental delay, cerebral palsy, epilepsy, muscular dystrophy, hydrocephalus, and some other conditions.

And among the children who had neurodevelopmental conditions, a majority of them had more than one neurodevelopmental diagnosis so they had cerebral palsy and seizure disorder or they had developmental delay in cerebral palsy and additionally a number of them also had a pulmonary condition that was listed under their past medical history.

This is consistent with a study of seasonal influenza-associated child deaths from the 2003-2004 season that also found that a considerable portion of children had a neurodevelopmental condition.

And it was the result of those studies that led to the ACIP including neurologic and neurodevelopmental and neuromuscular conditions in their recommendations for children who should be prioritized for influenza treatment and that was added to the ACIP recommendations in 2005.

In addition, there were some children in this case series who did not have any past medical history. They didn't have any chronic conditions that were noted.

A number of children were tested for bacterial infections meaning that they had blood cultures done or cultures from other sterile sites done or they had pathologic examination of lung tissue obtained from autopsy. And of 23 children who had any culture or pathology results reported, 10 of them had a bacterial co-infection.

And strikingly this included all six children who had pathology or culture results reported who were at least five years old and didn't have a recognized high-risk medical condition so these are kids that we don't normally think of being at high risk for complications from influenza.

This finding reinforces other data from seasonal influenza pediatric death surveillance indicating that bacterial co-infection along with influenza can cause very severe disease in children who may have been previously healthy.

So in summary, even children who are otherwise healthy can have severe or fatal outcomes after influenza infection although these are rare.

Children with certain chronic medical conditions including neurologic and neurodevelopmental conditions can have severe or fatal outcomes and it's important that parents recognize the signs of 2009 H1N1 early so that they can consult with their child healthcare provider.

This is especially important for those children who are known to be at higher risk for influenza-related complications including children who are less than five - particularly children less than two - and those with high-risk medical conditions, and now I think Dr. Peacock is going to talk about the signs and symptoms that parents can be looking for.

Georgina Peacock: So as a reminder, the symptoms of 2009 H1N1 flu virus infection in people include fever, cough, sore throat, runny or stuffy nose, body aches, headache, children fatigue, and then a significant number of people have also talked about diarrhea and vomiting associated with this infection.

As for warning signs indicating the need for urgent medical attention, these would include fast breathing or trouble breathing, bluish or gray skin color, not drinking enough fluids, severe persistent vomiting, not waking up or interacting, being so irritable that the child does not want to be held, or flu-like symptoms that improve and then return with fever and worse cough.

So in summary, children with certain high-risk medical conditions should seek the advice of their healthcare provider if they're having signs and symptoms of influenza. Clinicians are reminded that bacterial co-infections can occur and should be considered particularly in cases of severe or worsening illness.

As a reminder, flu-related deaths in children less than 18 years old should be reported through the state health department to the influenza-associated pediatric mortality surveillance system and the number of flu-associated deaths among children will be updated each week and can be found at www.cdc.gov/flu/weekly.

As a reminder, all children less than six months and caregivers of children less than six - sorry, all children greater than six months of age and caregivers of children less than six months of age should receive the seasonal influenza vaccine and the 2009 H1N1 vaccine when available.

In addition, all children should be current on recommended vaccinations including the 7-valent pneumococcal conjugant vaccine and children aged greater than two years with certain high-risk medical conditions are

recommended to receive the 23-valent pneumococcal polysaccharide vaccine in accordance with current guidance.

At this point, I would like to turn the call over to Dr. Tim Uyeki who represents our influenza division and is going to talk in more detail about testing and also current treatment guidance. Thank you, and thank you, Tim.

Tim Uyeki: Thank you, Georgina. So what I'd like to do is talk a little bit about diagnosis and then testing and treatment issues. In terms of diagnosis, you've heard from the previous speakers about the range of signs and symptoms of influenza and particularly uncomplicated disease.

It's important to note that some patients have presented without fever among children and in terms of diagnostic testing, so I think at this time and as we move into the fall/winter, it will be more challenging.

But at this time, influenza-like illness in a child is most likely to be consistent with influenza virus infection. At this time in the U.S., the vast majority of influenza viruses - nearly all are in fact - pandemic in novel 2009 H1N1 virus infection.

But as we move into the fall/winter, clinical diagnosis will be more challenging as the prevalence of other respiratory viruses increases among the pediatric population. For children who present with uncomplicated disease and who are stable, it's really a clinical diagnosis. There's no need for testing.

We would like to prioritize testing for influenza among patients who are hospitalized and by definition, a hospitalized patient is therefore complications of influenza. In the outpatient and ER setting, we believe that

laboratory testing is not necessary, particularly in patients with uncomplicated disease.

In patients who are tested, however, one should be aware of a variety of limitations of tests. In particular, there are tests in which a result is fairly rapidly available that may be able to influence clinical management such as rapid influenza diagnostic tests that are antigen detection tests.

However, these tests have suboptimal sensitivity and sensitivities with a range of anywhere from about 10% up to 70%. The majority of these tests that have been studied showing a sensitivity of less than 50% ability to detect influenza virus infection in upper respiratory tract specimens compared to real-time RTPCR.

And therefore you will get a fair amount of false negative results in a patient who actually has influenza but tests - rapid tests - negative. And therefore it's important for clinicians to realize that a negative rapid test and in fact a negative result on immuno-fluorescence testing - for example, direct fluorescent antibody staining - that might be available for a patient who comes to an emergency room or a patient even in a hospital -- the sensitivities of both immuno-fluorescence and rapid diagnostic tests are less than optimal, and a negative result does not exclude influenza virus infection.

Therefore we think that any outpatient or ER setting in which a patient does not require hospitalization, a clinical diagnosis is okay. However, if you get a positive result by rapid influenza diagnostic test or by immuno-fluorescence, that may be helpful to guide clinical management.

However, again, a negative test result does not rule out influenza virus infection and if treatment is warranted, treatment should be initiated (irregardless) of the result of a rapid diagnostic test.

Now in the inpatient hospitalized setting, the kind of testing should be really geared towards specific diagnosis of novel H1N1 virus infection with reverse transcriptase polymerase chain reaction.

Viral culture could also be done, will not have timely results for clinical management but it is important for public health issues including monitoring antigenic changes, genetic changes, and monitoring of anti-viral resistance.

In terms of treatment, at this time circulating strains of a novel H1N1 virus are susceptible to the antiviral, the neuraminidase inhibitors, also tamivir and zanamivir.

However, they are resistant to the (adamantine) drugs which are amantadine and rimantadine. Therefore, amantadine and rimantadine continue not to be recommended for treatment of novel H1N1 virus infection.

We do recommend and we do emphasize that antiviral treatment with a neuraminidase inhibitor drug - and that is also tamivir or zanamivir - should be initiated as soon as possible in any hospitalized patient.

So one, clinicians need to suspect a diagnosis of influenza in a patient being admitted and initiate empiric antiviral treatment with also tamivir or zanamivir as soon as possible if the drug had not been started prior to hospital admission. Now we believe that treatment should be initiated without - before waiting for the results of any diagnostic testing.

It is really early treatment that is going to be much more effective than a later treatment and there have been patients who have been admitted in which treatment was delayed until a few days later when results of PCR were available and it's a missed opportunity for earlier antiviral treatment.

The other - so besides hospitalized patients who are really prioritized to receive also tamivir or zanamivir treatment, we also recommend early treatment as soon as possible for pediatric patients who are in high-risk groups even if they do not require hospital admission.

So if they present in an outpatient clinic or an emergency room setting and they have - they are in a high-risk group, and those high-risk groups I think were just described, but again they include children less than five and in particular children less than two years of age and then children of any age who have certain chronic medical conditions.

And that would also include children who are on aspirin therapy for medical reasons - who are on chronic aspirin therapy - so examples of chronic conditions which were I believe described previously in this presentation include children with certain metabolic hematologic cardiac pulmonary complications and so forth and some neurological complications.

And so the most important thing is to initiate antiviral treatment as soon as possible. Now, there are also - our new guidance which has just been posted today also touches on some steps that might actually facilitate early antiviral treatment in patients who are at higher risk for complications of influenza.

And those include having providers discuss with the parents of these patients - inpatients - prior to early in the season to discuss signs and symptoms of influenza as well as considering in some patients some way to facilitate earlier

access, earlier treatment to also tamivir or zanamivir because these are prescription antiviral drugs.

And so some of these ways to potentially facilitate this include ensuring rapid access to telephone consultation and then clinically evaluating patients particularly those who are at - any patient who is reporting severe illness but especially as well persons who have high-risk conditions or fit into high-risk groups who are initiated on treatment.

In other words, don't just initiate treatment in high-risk persons but also evaluate them as well. So I'm not going to go through all the recommendations but you're welcome to see the guidance that's been posted in terms of some of our suggestions on ways to actually facilitate early empiric treatment of patients with underlying high-risk conditions at higher risk for complications of influenza.

And I think Dr. Peacock mentioned some of the signs and symptoms - some of the warning signs. I would just like to take this time just to reiterate some - just a few comments based upon pediatric cases, particularly critically ill pediatric cases that I've been aware of over the past several months and actually as recent as this weekend.

What we are seeing is we're seeing groups of patients so you heard from Dr. Christensen about some of the fatal pediatric cases and underlying conditions and some - although many did have underlying co-morbidity - some clearly had no previous - had been previously well.

And in some of these patients who are previously well including older children - 10 and older - some of them have presented very, very rapidly after illness onset within 24 to 48 hours of illness onset of influenza illness to

critical illness and in those patients, they should be strongly suspected to have invasive bacterial co-infection and be evaluated right away.

In an older children, a complaint of chest pain and in particular when a child is evaluated, particularly an older child who has (tachypnea), I think that is a patient who ought to be - and they present within the first few days of illness onset - that patient needs to be evaluated at an emergency room setting immediately, and the invasive bacterial co-infection needs to be considered.

As well as patients who present later than two days from illness onset, we have to always think about the possibility of invasive bacterial co-infection.

Now patients who have pure influenza without complications of invasive bacterial infection may present a bit later. Patients who have underlying co-morbidities may present anywhere from early to several days later in the clinical course.

And so I think that - I just want to make the point - that it's not just children who have chronic underlying co-morbidities but we especially should be concerned about a previously healthy child who presents with severe illness in the first few days after illness onset.

And I think what I'm going to do is just stop there other than to just mention that there have been some sporadic cases of oseltamivir-resistant novel H1N1 virus infection detected in the U.S.

These have generally occurred in patients who have either been on chemoprophylaxis for prevention of infection and illness who had exposure to confirmed cases.

It's also been detected in some patients who have - who are severely immuno-suppressed or immuno-compromised and these patients are at risk for prolonged viral shedding for weeks and months and development or emergence of oseltamivir resistance so I think that those are special populations in which we need to be concerned about and monitor.

And overall, this is one reason why it's important for judicious use of antivirals but on the other hand, we do want to emphasize treatment as soon as possible - as early as possible - in patients who are suspected to have influenza. I'll stop there. Thanks.

Alycia Downs: Okay, we can open up the lines for question and answers.

Coordinator: Thank you. At this time, if you would like to ask a question, please press star 1 on your touch-tone phone. Please unmute your phone and record your name clearly when prompted. Once again, that's star 1 if you would like to ask a question. One moment, please, for the first question.

One moment, please, and I have a question from Victor. Your line is open.

Question: Yeah, I have a question. What is going to be the recommendation for patients over the age of 65? Because based on the CDC recommendations, Medicare will - some Medicare advantage plans - will not recommend - or what is going to be the recommendation for Medicare patients to get payment - to receive payment - for the H1N1 flu vaccine?

Tim Uyeki: So thanks for that question. I cannot comment about reimbursement but I will comment that patients who are ill aged 65 years and older as you know, we do consider them as a high-risk population for complications of seasonal influenza.

We also would consider them to be at high risk for complications of novel H1N1 virus infection although the numbers of persons 65 years and older that have been ill or have been hospitalized have not been high.

This may change as activity picks up later this fall/winter and in addition, there are issues about the inability to distinguish between what is novel H1 versus what is seasonal influenza and treatment needs to be started on persons 65 years and older if they're suspected because they're essentially a high-risk group for complications of seasonal influenza.

So we would encourage early treatment of persons 65 years and older. There are limited data that do suggest that even people 65 years and older are at higher risk for complications of this pandemic influenza virus infection.

So our antiviral treatment recommendations would be very similar - I mean, for a person 65 years and older - similar to what we would recommend for seasonal influenza in that age group, but I can't comment about reimbursement.

Question cont'd: What about just the vaccination recommendation for healthy 65 and older - or after 70, everybody's got something, but...

Tim Uyeki: Yeah. So, in terms of recommendations, so as you know that population is definitely a high-risk group and is recommended as a priority group for seasonal influenza vaccination which there should be seasonal influenza vaccine either available now or very soon in your area.

However, with the pandemic H1N1 vaccine, that population is not within the priority group for vaccination and that has to do with the epidemiology and

the data so far on both fatal outcomes and hospitalizations with novel H1N1 virus infection to date.

That's not saying that they won't be vaccine - you know, won't be recommended - but the priority group does not include that now.

Question cont'd: Thank you.

Alycia Downs: And this is a reminder just to keep questions to the pediatric-focused area.
Thank you.

Coordinator: The next question. Your line is open.

Question: Hi. Given the data in terms of these high-risk kids, the ACIP recommendations don't cover household contacts, you know, outside daily caregivers for these high-risk kids.

Does that need to be re-evaluated in terms of immunization for the H1N1 vaccine, given that they seem to be bearing - these kids with neurodevelopmental issues - seem to be bearing significant burden of the severe disease?

Tim Uyeki: So, thanks for that. I mean, the ACIP target groups initially are persons who in terms of contacts as you're mentioning are persons who live or care for the youngest, you know, less than six months, but you're asking about household contacts of persons who are older than six months?

Question cont'd: Yeah, I guess, you know, that fall into this category of let's say, you know, CP, Down's Syndrome, some of the muscular dystrophy, those kinds of ones

where the description is that we're seeing a higher - significantly higher- rate of pediatric deaths in this 2009 H1N1.

Does it make sense then that since they're at significant risk, do we need to relook at caregivers for those children as well?

Tim Uyeki: Yeah, so I think you make important points. I think this is an issue of sort of prioritizing and certainly the very youngest, you know, the less than six months group, and then the next highest would be less than two years and so forth, it's simply a manner of prioritizing who are at the highest risk particularly for severe complications.

That is not to say that the group that you're mentioning again it should not be but it's just how the prioritization as voted by the ACIP was, and so yeah, I think as a general comment, there is a need for and there will be efforts to continually reevaluate and look at data as time goes on.

And all recommendations really should be looked as interim guidance, interim recommendations that will be revised depending upon new information as we go.

But in terms of the initial vaccine recommendations for this pandemic monovalent H1N1 vaccine, I'm not - I can't speak for the ACIP but you're aware of the sort of what was voted upon and the guidance that was issued.

Whether or not that will be changed later, I think that's up to the ACIP and I think it would be driven by new data.

Question cont'd: Could you also - I'm sorry. Can I ask one more question? It's regarding resistance to Tamiflu. There's some reports that this is appearing, the concern being last year we experienced influenza A which was not sensitive to it at all.

What other patterns is CDC seeing in terms of resistance to Tamiflu for novel H1N1 and is there anything that we can, you know, any predictions based on where that is?

Tim Uyeki: Okay, well thanks for that question. Yeah, I tried to mention that briefly but we have detected some sporadic cases of oseltamivir-resistant novel influenza A H1N1 virus infection and that is actually been - sporadic cases - have been detected in other countries.

But when you look at community-based surveillance and you look at broader global surveillance, there's no evidence that oseltamivir-resistant novel H1N1 virus is being transmitted in a sustained manner.

So that is the sort of the key question for public health so as you know, over the last couple of years there's been an increasing prevalence and in fact last season, '08-'09 influenza season in the U.S., 99.5% of seasonal influenza H1N1 viruses - not novel but seasonal H1N1 viruses - were resistant to oseltamivir.

So that is something that CDC will be monitoring very closely in the U.S. as we're monitoring it - we've been monitoring ever since - you know, we monitor it all the time. And certainly for the typical influenza season, we monitor it - certainly as this pandemic virus emerged and we have been doing that since April - and we'll continue to monitor that.

And particularly to detect if there is an increasing prevalence of oseltamivir resistance being detected in these novel H1N1 viruses and in particular if it looks like there's evidence of community-wide transmission. So far there's not. It's important that we need to monitor that and it's monitored globally.

Now the situations in which it's been detected as I mentioned have been again sporadic cases in which someone was on chemoprophylaxis for exposure to someone who was confirmed with novel H1N1 virus infection and in a number of these situations had ongoing exposure to this individual or individuals.

And then resistance - illness developed in the person on chemoprophylaxis as well as and detection of resistant virus was found. The other is in the severely immuno-suppressed and in a severely immuno-compromised patient as I mentioned and these kind of patients can have prolonged viral shedding.

It doesn't mean that this will develop, but they're at greater risk for this. And it has been detected in some patients and in those kind of patients, strict very, very good infection control needs to be adhered to in the healthcare setting so that we don't have transmission from those kind of patients - severely immuno-suppressed, immuno-compromised - to healthcare workers or visitors and then out to the community.

But at this point globally and in the U.S., there's no evidence that oseltamivir-resistant novel H1N1 viruses are being transmitted in a sustained manner. It's something we definitely need to monitor for and again, it's another reason to be somewhat judicious about the use of oseltamivir.

We can't predict if this is going to happen in sort of - if the prevalence of oseltamivir resistance - will increase. It's very, very, you know, again it's just been uncommon.

It's been sporadic and we do not, we have not and the World Health Organization has not changed any antiviral treatment recommendations. We continue to recommend oseltamivir or zanamivir for treatment.

Question cont'd: Thank you.

Coordinator: And I have a question from Yvonne. Your line is open.

Question: Hi, thank you. I have just more of a generic question about children so as I understand it, the recommendation is to treat before you have results back from any diagnostic testing and you're recommending treatment of high-risk groups and you're saying that children under five are in a high-risk group.

So is the recommendation then to treat every child under five who has respiratory symptoms because I'm getting a lot of calls from community physicians about how overwhelming that's going to be.

I mean again, we're talking about a large number of children who are going to be coming in with symptoms even if you get a confirmatory test back within a day or two, you're still going to be starting lots of medication on lots and lots of children.

It would seem to me that that would be actually increase the risk of resistance if in fact you were going to be treating also kids who ultimately were going to wind up having mild disease. Thank you.

Tim Uyeki:

Yeah, hi, Yvonne. I think this is a very good point and so you know, in terms of the pediatric population less than five years, it's really the less than two that are at highest risk and here we're talking about previously healthy kids and so focusing on the less than two is actually most important.

I think you bring up a good point. And it is true that we're trying to balance both early treatment of high-risk patients and that does include young children who are previously healthy, it does include children of any age with certain chronic conditions, and it is true that by empiric treatment you will treat some patients who do not have influenza virus infection.

And I think it's a balance and so part of this is the fact that rapid diagnostic tests are insensitive, certainly suboptimal sensitivity. If you get a positive test, I think that can be useful.

A negative test may not be but I think you bring up a really good point and we're trying to balance sort of targeted treatment to get early treatment administered and I think the flip side of that is as you mentioned probably initiate treatment for patients who may not have influenza.

And so again, I think among the less than five, prioritizing of less than two years is certainly important and then whether patients are treated or not, it's important for parents to be aware of the need to really evaluate the child and that there are clinical complications that can develop.

A child could deteriorate and they could deteriorate rather rapidly whether due to bacterial complications or to influenza virus infection itself so I think the need for continuous monitoring and reassessment if there's clinical deterioration is an important concept whether you're treated or not.

But I think you bring up a good point. Again, we're trying to balance earlier treatment with treatment that probably will not be for influenza. It's just a big challenge.

I think for children with underlying chronic co-morbidities, I think it's not an issue but - or it's less of an issue - but I think in the less than five, you bring up an important point.

Coordinator: And our next question will be from Lynette. Your line is open.

Question: Hi, yes. I just had a quick question. I needed to get the Website again in order to get the talk for today because some of the things I missed I really do want to get.

Alycia Downs: If you're looking for the PowerPoint for this presentation, you can go to emergency.cdc.gov/coca. There's a link for conference call information, summaries and slidesets and if you click on that, you can find the PowerPoint there.

Question cont'd: Thank you.

Georgina Peacock: And if you're looking for the CDC Website, then - that's related to H1N1 guidance - go to www.cdc.gov/h1n1 and you can find all the relevant guidance there.

Question cont'd: Thank you.

Alycia Downs: And again the transcript of this call and the audio file will both be posted to our Website within the next week.

Tim Uyeki: The updated interim recommendations for antivirals have been posted - are up as of this afternoon - and we will be also revising some of our clinical guidance that will be posted in the near future.

There's also guidance that's available about rapid diagnostic tests and other pieces of information that may be useful for clinicians.

Coordinator: And the next question. Your line is open. Do we have an Otis Chan online?

Question: Hello. This is (Curtis Chan) from San Francisco. Thank you so much for providing this guidance, particularly in the information related to children with higher co-morbidities and I think my question was really already addressed by Dr. Maldonado a couple of questions ago.

But I have a further question regarding if the CDC plans to really differentiate further on this two to five-year-old children who are healthy with mild illness. It seems that Dr. Uyeki had commented on it but he didn't think that the two to five-year-old children are really at significantly higher risk.

Tim Uyeki: Hi, (Curtis). Yeah, thanks. I think both to your point and to Dr. Maldonado's point, I think it's - these are very valid points. I think that we clearly do consider the less than two to be really where the - I mean, both for seasonal influenza and for novel H1N1 - to be higher risk of complications than the two to five-year group but we are considering all less than five lumped together here.

But in terms of further breakdown, I think that as I kind of alluded to as we get more clinical data - epidemiologic data - I think that we'll revise guidance as better information comes in.

Coordinator: And the next question. Your line is open.

Question: Hi, Tim. Thanks for your call today. I have a question about treatment beyond antivirals and if there's been any analysis of what elements of care such as antipyretics, hydration, etc. What are the most important elements that we can recommend parents follow?

I think there's going to be an awful lot of demand for advice and particularly for antivirals and if we're going to be discouraging that in the majority of situations, it'd be good to have some good information to provide parents.

Tim Uyeki: Well, thank you. I think that's really an important point. I think we'll have to look at that. I would just want to emphasize one point which I think most pediatricians are aware. And that is aspirin in a child who is not on chronic aspirin therapy for medical reasons, aspirin should not be administered with suspected novel H1N1. So that's an important message that pediatricians and family practitioners can get out and emergency room docs can get out.

And the other is I've always suggested that aspirin containing products such as bismuth subsalicylate should also be avoided and as was noted by my colleagues earlier, there have been a fair amount of patients who have experience gastrointestinal symptoms including diarrhea.

And so it is conceivable that bismuth subsalicylate might be utilized by parents or given by parents to kids, so in terms of fever reduction, I don't think we've explicitly put this in any guidance but I think acetaminophen and other antipyretics would be useful.

In general, I think non-steroidals are thought to be okay. I think that with young children in particular, dosing is really important as pediatricians know

to make sure parents are aware of the correct dosing both for acetaminophen and non-steroidal anti-inflammatory agents.

In terms of fluids, certainly with febrile illness, you know, fluid - insensitive fluid losses - and patients who are having vomiting or diarrhea, dehydration in these patients may be a concern and so encouraging fluid intake is important and if there's any concern the patient should be medically evaluated.

I think that we want to also say some very - I always like to talk about good news and bad news. The good news is that the vast, vast majority of children who will become ill with novel H1N1 virus infection will have self-limited mild to moderate illness.

Much of that will be typical influenza-like illness. Some of it may be slightly atypical including very mild upper respiratory tract illness without fever. Some of it may be high fever with influenza-like illness.

Some of it may also include vomiting or diarrhea but the vast majority of all children who become ill with novel H1N1 virus infection will have self-limited illness. They will recover without any antiviral treatment and they will never be hospitalized.

The bad news is that with high attack rates that can be expected as activity picks up, there will be a very small proportion of children who will experience complications of novel H1N1 virus infection including bacterial co-infection, exacerbation of chronic underlying conditions, and other conditions including just viral pneumonitis alone which will require urgent medical evaluation, hospitalization, and intensive care unit admission and possibly fatal outcomes.

And so the good news is most kids will be well after a short acute illness but there will be a small proportion who will require hospitalization.

Georgina Peacock: And one other additional thing that we do recommend to parents which is consistent with FDA recommendations is in children less than five years of age, they should be consulting a healthcare provider before using any over-the-counter cold or cough medication.

Coordinator: And our next question. Your line is open.

Question: Hi, this is (Dottie Verowise).

Coordinator: Yes. Your line is open.

Question cont'd: Oh, okay. Yeah, this is (Dottie Verowise) at San Mateo County Health Department in California. I have a comment and then a question.

The comment is regarding the recommendation for immunizing contacts with high-risk children or of children under six months being due to the fact that they can't receive the vaccine themselves where as the other children that are high-risk could receive vaccine themselves. So that the area contacts would be higher priority for immunization if those were children that had empiric immune responses.

Tim Uyeki: So, thank you very much for that very important point and I'm sorry I did not actually make that comment earlier and you're absolutely correct and that is that children aged less than six months are ineligible for pandemic influenza vaccine when it becomes available.

They're also ineligible for seasonal influenza vaccine and as you know, this year we're recommending universal pediatric vaccination six months through 18 years of age, so that's a really important point.

And so that for unvaccinated young infants less than six months of age, we want to try to protect the individuals around those young infants and so vaccination of those household members and caregivers can be done. Thanks for that point.

Question cont'd: You're welcome and then my question is regarding the children who develop severe H1N1 that were not febrile at presentation, can you give any more information about how they did present and whether those were the children that ended-up hospitalized because of the viral pneumonia or superinfection - co-infection?

Tim Uyeki: Yeah, so thanks. I'll basically sort of respond sort of in general. I think with seasonal influenza virus infection as well as with novel H1N1 virus infection, one can expect a very wide range of - wide clinical spectrum - ranging from asymptomatic virus infection in which you have absolutely no symptoms; you're fine but you are infected to very mild illness in which you might actually have no fever.

You may have upper respiratory tract, very mild symptoms, to your classic influenza-like illness in which you have fever and maybe high fever, headache, cough, sore throat, muscle aches and so forth and there may be some gastrointestinal symptoms with mild or influenza-like illness.

And then there's also a range of particularly more severe illness which may occur early in the clinical course, it may occur later in the clinical course. And so it's very difficult to say much more other than when there clearly are -

there are some data that have been published looking at patients who are not hospitalized, children who are not hospitalized, and a fair amount in some series have not had fever.

When we look at children who have been hospitalized and adults who have been hospitalized, more than 90% of them have had fever, so I think we also have to realize there have been a variety of complications that have been described but the clinical picture is evolving.

I think we will learn more as we go week to week globally and I think as more children become infected and ill as time goes, there will be some atypical complications that may be recognized.

And so with seasonal influenza as well as we have seen some cases with pandemic influenza, there are some complications of different organ systems that may not reflect virus infection of those organ systems but in fact virus infection of the respiratory tract, but with other complications including cardiac such as myocarditis although we have not heard about much myocarditis so far.

I think it can be expected as a severe complication. It certainly occurs with seasonal influenza. Certainly myositis, which is a well-recognized complication particularly in children leading to potentially rhabdomyolysis.

There have been neurologic complications such as encephalopathy or in forms associated encephalitis. So you know there are many, many different - there's basically very wide clinical spectrum that has been either documented or should be expected.

And I think we need to be open to a wide range of complications. So it's a little hard to quite answer your question other than to say that clearly children - some children have not have fever with this illness including some hospitalized patients.

But the majority of hospitalized patients have had fever at presentation.

Alycia Downs: We can take one more question.

Coordinator: Thank you, and the next question, your line is open.

Question: Hi, this is a little bit different question and it may not be something you can answer right off the bat but I had a question about in terms of prevention messaging.

Is there any specific message or recommendation from the CDC, especially for children with special needs regarding the impact of nutritional status and the need for attention to diet and nutritional supplementation perhaps especially with (sink) in regard to impact on bolstering the immune status to prevent or lessen severity of illness.

Is there anything that - in terms of messaging that might take advantage of getting some message out to that regard?

Tim Uyeki: Georgina, do you want to comment on that?

Georgina Peacock: Sure, well so our most important messaging that we're really focusing on is vaccination, so vaccination with seasonal flu now while it's available in offices.

Also making sure that children are - have their recommended vaccinations for pneumococcal vaccines and then we don't really have any messaging focusing on nutritional status. However obviously children who are struggling with nutrition or are malnourished are at higher risk for developing a number of different medical complications.

So certainly I think that's important but we don't have any messaging focusing on that.

Question cont'd: Okay, is there a way to talk further on that perhaps, or...?

Georgina Peacock: Sure, and actually I'd like to offer you an email where you can send things where we can delve into the answers a little bit more or find out other people that are working on things right here at the CDC.

And you can email other questions or inquiries like this to coca - C-O-C-A at cdc.gov. And I'm going to turn the call over now to Alycia and she will give you some more information.

But we look forward to getting your inquiries and we will make sure that we answer those in a timely manner. Thank you for joining us today.

Alycia Downs: I'd like to thank our presenters for providing our listeners with this information, as well as I'd like to thank our participants for joining us today.

If you have any additional questions or comments please send an email to coca@cdc.gov, C-O-C-A at cdc.gov. We will do our best to get you a timely response.

The recording of this call and the transcript will be posted to the COCA Website, emergency.cdc.gov/coca as soon as we get them, so please remember to keep an eye out for future COCA conference calls on this topic as well as previous calls that are archived to our Website. Thank you again for participating and have a wonderful day.

We're also going to have a COCA conference call on September 16 that is probably going to focus on the pediatric issues again. So we'll be having another pediatric COCA call on September 16th. If there are particular things that would be helpful to you to be provided in a call - in this venue, please also send those to the coca@cdc.gov.

And we thank you for joining us today and thank you very much to Dr. Christiansen and Dr. Uyeki for presenting today on this call.

Tim Uyeki: And thanks to California colleagues for questions.

Alycia Downs: Have a great evening, thank you.

Georgina Peacock: Thank you everyone.

Tim Uyeki: Bye.

Coordinator: And this concludes today's conference, you may disconnect at this time. Thank you.

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