American Academy of Pediatrics

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Prevention and Control of Influenza: Special Considerations for Newborns and Very Young Infants

Children younger than 5 years of age, especially very young infants (those younger than 12 weeks of age), are at increased risk of influenza-related complications and, therefore, should be observed carefully for any signs and symptoms of influenza.

When very young infants younger than 12 weeks of age present with fever *and* irritability, cough, tachypnea, or vomiting, their condition warrants comprehensive medical evaluation. See the **Triage Algorithm for Children [≤18 years] with Influenza-Like Illness** [although originally created during the 2009-2010 influenza season, this algorithm is appropriate for use during the 2011-2012 influenza season].

Pediatricians who have questions about treating older infants and children with suspected influenza can refer to the information in this document, the policy statement from the American Academy of Pediatrics (AAP), **"Recommendations for Prevention and Control of Influenza in Children, 2011-2012"** and the recommendations of the **Centers for Disease Control and Prevention (CDC)**.[1,2] These recommendations highlight the importance of clinical judgment in the treatment of children with suspected influenza, emphasizing that prompt, thoughtful action is critical.

In general, treatment should be considered:

- For any child younger than 2 years of age with confirmed or suspected influenza virus infection.[3]
- When a decrease in duration of clinical symptoms is felt to be warranted by the physician. Early treatment provides the most benefit, particularly if initiated within 48 hours of illness onset.

Although influenza testing can be a particularly important tool to prevent the spread of illness, the use of antiviral treatment should not be delayed, whether or not a physician decides to test for influenza.

Answers to common questions for newborns and infants younger than 12 months of age are provided below.

1. What is the appropriate dosing for antiviral medications in term and preterm infants with suspected or confirmed influenza?

No prospective, controlled studies have been completed in this age group, and no antiviral medications are licensed by the Food and Drug Administration (FDA) for these very young

infants. Nevertheless, recommendations for use of oseltamivir in this very young age group (as outlined in the now-expired 2009 H1N1 pandemic Emergency Use Authorization [EUA] that authorized use of oseltamivir in infants as young as newborns) still should be followed.

Earlier treatment provides more optimal clinical responses, but treatment after 48 hours of symptoms in the child with moderate-to-severe disease or with progressive disease might still provide some benefit. Dosages for both oseltamivir treatment and chemoprophylaxis in children of all ages can be found in the **Table** below.

Details for term and preterm infants younger than 12 months of age are provided below.[4,5,6]

- **Term infants, 3 through 11 months of age,** can receive oseltamivir *treatment*[*] for 5 days using 3 mg/kg/dose, twice daily. When *chemoprophylaxis*[**] is recommended, the regimen for this age group lasts 10 days at 3 mg/kg/dose, once daily.
- **Term infants younger than 3 months of age** can receive oseltamivir *treatment* for 5 days using 3 mg/kg/dose, twice daily. *Chemoprophylaxis* for infants younger than 3 months of age is not recommended unless the exposure situation is judged critical (ie a family member is hospitalized or critically ill), because of the lack of data on use of oseltamivir in this age group.
- **Preterm infants.** Current dosing recommendations are not intended for preterm infants, who may have slower clearance of oseltamivir because of immature renal function, and the dose recommended for term infants can lead to variable or very high drug concentrations in this age group. Very limited data from a cohort of preterm infants suggest that a dose of 1 mg/kg/dose, twice daily, produces comparable drug exposure as does a dose of 3 mg/kg/dose in term infants. No data on recommended duration of oseltamivir treatment in preterm infants are available. These infants should be followed clinically and by serial reverse-transcription polymerase chain reaction (RT-PCR) tests of respiratory tract swab specimens to determine clearing of influenza virus.

2. Are there any efficacy, effectiveness, and adverse effects data on antiviral medication use in term and preterm infants with suspected or confirmed influenza?

No safety concerns have been identified in studies conducted to date in this high-risk population. Studies of oseltamivir in term and preterm infants have provided pharmacokinetic, pharmacodynamic, and safety data but have not been designed to yield clinical efficacy results. However, because children younger than 12 months of age are at increased risk of death from influenza, the AAP and CDC recommend that children in this age group receive antiviral treatment for suspected or confirmed influenza virus infection.

[*] Definition: Treatment is the use of medicine to try to cure or make better.
[**] Definition: Chemoprophylaxis is the administration of a drug to prevent a disease when the disease has not yet occurred.

3. Are there any efficacy or adverse effects data on newborns whose mothers receive influenza vaccines prior to delivery?

Studies have found that infants born to immunized women have better influenza-related health outcomes.[7,8,9,10,11,12] In addition, there is evidence that influenza vaccination in pregnancy decreases the risk of preterm birth.[9,13] There is no contraindication to injectable trivalent inactivated influenza vaccine (TIV) during pregnancy.

More needs to be done to encourage annual vaccination, because both pregnant women and their infants are at higher risk of complications from influenza. Data suggest that fewer than half of pregnant women receive the seasonal influenza vaccine. Any woman who is pregnant, considering pregnancy, or breastfeeding during the influenza season should receive TIV only. Data reviewed by the CDC during the 2009 H1N1 pandemic emphasize the importance of influenza vaccination for pregnant women, regardless of pregnancy trimester, and of prompt, empiric treatment with appropriate antiviral medications for pregnant women with suspected or confirmed influenza.[2]

4. If a newborn (either term or preterm) appears sick (temperature instability, not feeding well, etc), should he/she be tested for influenza? If yes, when should this be performed and what test should be used?

Because hospitalized newborns may be in a group setting with a high potential for widespread infection, such as a newborn nursery or a neonatal intensive care unit (NICU), influenza testing can be a particularly important tool to prevent the spread of illness. However, oseltamivir treatment should be started as soon as possible after illness onset during periods of high local influenza activity and should not be delayed while waiting for a definitive influenza test result. Note that newborns and preterm infants may not always manifest fever with influenza virus infection.

RT-PCR and viral culture testing are preferred for neonates. The reliability of rapid influenza diagnostic testing can vary significantly. Compared with RT-PCR and viral culture testing, rapid influenza diagnostic testing has a sensitivity of 50% to 70% and a specificity of 90% to 95%. False-positive results are more likely when disease prevalence is low, and false-negative results are more likely when disease prevalence is high. Strategic use of rapid influenza diagnostic testing includes accounting for the weakness of this method (ie, influenza should not be ruled out on the basis of a negative rapid influenza diagnostic test result for a child with influenza-like illness, especially during peak influenza activity).

5. If there is an influenza outbreak in a NICU or newborn nursery, should exposed infants receive antiviral chemoprophylaxis?

There is no routine antiviral treatment or chemoprophylaxis recommended for neonates who are at risk of influenza virus infection in a NICU or newborn nursery. Therefore, the decision to use chemoprophylaxis should be made at the local level with the input of the appropriate specialists (ie, pediatric infectious disease subspecialists, hospital epidemiologists, and neonatologists).

The antiviral safety profile when used in these very young term infants is likely good, albeit quite limited by the number of patients evaluated prospectively in clinical trials.

- For chemoprophylaxis, the CDC "Interim Guidance on the Use of Influenza Antiviral Agents" for this season echoes the AAP policy statement: antiviral chemoprophylaxis of influenza for children younger than 12 weeks should *not* be used unless the physician feels that preventive care is critical.
- As detailed above, for treatment, oseltamivir should still be used when appropriate following the dosing in the **Table** below.

Resources:

- **AAP Online Influenza Resource Page**
- **CDC Guidance on the Use of Influenza Antiviral Agents**
- **CDC Rapid Influenza Diagnostic Testing for Influenza**
- **PediaLink® Continued Medical Education (CME) Influenza Course Series**
- **Food and Drug Administration – Tamiflu and Relenza Emergency Use Authorization Disposition Letters and Question and Answer Attachments**
- **Food and Drug Administration - Drug Safety Communication: Important Safety Changes for Tamiflu® (oral suspension)**

Note: The CDC convened a meeting in August 2010 called "Pandemic Influenza Revisited: Special Considerations for Pregnant Women and Newborns" to gain input from experts on 4 main topics: antiviral prophylaxis and therapy, vaccine use, intrapartum/newborn issues, and nonpharmaceutical interventions and health care planning. Select AAP members participated, and meeting proceedings were published in an article included in the June 2011 supplement to the *American Journal of Obstetrics and Gynecology* titled: **"Preparing for Influenza After 2009 H1N1: Special Considerations for Pregnant Women and Newborns."**

Some topics were determined to be outside of the purview of the meeting. Select pediatric-focused questions were shared with the AAP. The responses to these questions are based on recommendations provided by both the CDC Advisory Committee on Immunization Practices (ACIP) policy document **"Prevention and Control of Influenza with Vaccines: Recommendations of the Advisory Committee on Immunization Practices (ACIP), 2011"** and the AAP policy statement **"Recommendations for Prevention and Control of Influenza in Children, 2011–2012."**

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Table: Recommended Dosage and Schedule of Influenza Antiviral Medications for Treatment and Chemoprophylaxis for the 2011-2012 Influenza Season: United States*

Medication	Treatment (5 days)	Chemoprophylaxis (10 days)
Oseltamivir[a]		
Adults	75 mg, twice daily	75 mg, once daily
Children >12 mo		
Body weight		
≤15 kg (≤33 lb)	30 mg, twice daily	30 mg, once daily
>15 to 23 kg (33 to 51 lb)	45 mg, twice daily	45 mg, once daily
>23 to 40 kg (>51 to 88 lb)	60 mg, twice daily	60 mg, once daily
>40 kg (>88 lb)	75 mg, twice daily	75 mg, once daily
Children 3 to <12 mo[b]	3 mg/kg per dose, twice daily	3 mg/kg per dose, once daily
Children 0 to <3months[c]	3 mg/kg per dose, twice daily	Not recommended unless situation judged critical because of limited data on use in this age group
Zanamivir[d]		
Adults	10 mg (two 5-mg inhalations), twice daily	10 mg (two 5-mg inhalations), once daily
Children (≥7 y for treatment, 5 y for chemoprophylaxis)	10 mg (two 5-mg inhalations), twice daily	10 mg (two 5-mg inhalations), once daily

*The table is excerpted and adapted from American Academy of Pediatrics, Committee on Infectious Diseases. Recommendations for prevention and control of influenza in children, 2011-2012, Committee on Infectious Diseases. *Pediatrics*. 2011;128(4): 2011-2295. *Note: The table provides dosages for both oseltamivir treatment and chemoprophylaxis in children of all ages. Current dosing recommendations are not intended for preterm infants (see footnote c).*

[a] Oseltamivir is manufactured by Roche Laboratories (Nutley, NJ) and is administered orally without regard to meals, although administration with meals may improve gastrointestinal tolerability. Oseltamivir is available as Tamiflu in 30-, 45-, and 75-mg capsules and as a powder for oral suspension that is reconstituted to provide a final concentration of 6 mg/mL. The volume of oral suspension is being changed from 12 mg/mL to 6 mg/mL this year to reduce frothing when shaken. **Oral suspensions in 12-mg/mL concentrations will remain available until supplies run out. For the 6-mg/mL suspension, a 30-mg dose is given with 5 mL of oral suspension, 45-mg dose is given with 7.5 mL oral suspension, 60-mg dose is given with 10 mL oral suspension, and 75-mg dose is given with 12.5 mL oral suspension.** If the commercially manufactured oral suspension is not available, the capsules may be opened and the contents mixed with a sweetened liquid to mask the bitter taste, or a suspension can be compounded by retail pharmacies (final concentration: 15 mg/mL). For patients with renal insufficiency, the dose should be adjusted on the basis of creatinine-clearance rate. For treatment of patients with a creatinine-clearance rate of 10 to 30 mL/min: 75 mg, once daily, for 5 days. For chemoprophylaxis of patients with creatinine-clearance rate of 10 to 30 mL/min: 30 mg, once daily, for 10 days after exposure or 75 mg, once every other day, for 10 days after exposure (5 doses) [see **www.cdc.gov/flu/professionals/antivirals/antiviral-drug-resistance.htm**.])

[b] Weight-based dosing is preferred; however, if weight is not known, dosing according to age for treatment (give 2 doses per day) or prophylaxis (give 1 dose per day) of influenza in term infants younger than 1 year of age may be necessary: 0 to 3 months (treatment only), 12 mg (2 mL of 6-mg/mL commercial suspension); 4 to 5 months, 17 mg (2.8 mL of 6-mg/mL commercial suspension); 6 to 11 months, 24 mg (4 mL of 6-mg/mL commercial suspension). Although the Emergency Use Authorization recommendations for use of oseltamivir in children younger than 1 year of age expired on June 23, 2010, this drug remains appropriate for use when indicated.

[c] Current weight-based dosing recommendations are not intended for preterm infants. Preterm infants may have slower clearance of oseltamivir because of immature renal function, and doses recommended for term infants may lead to very high drug concentrations in this age group. Limited data from a cohort of preterm infants who received an average dose of 1.7 mg/kg, twice daily, revealed drug concentrations higher than those observed with the recommended treatment dose in term infants (3 mg/kg, twice daily). Observed drug concentrations were highly variable among preterm infants. These data are insufficient to recommend a specific dose of oseltamivir for preterm infants.

[d] Zanamivir is manufactured by GlaxoSmithKline (King of Prussia, PA) and is administered by inhalation using a proprietary "Diskhaler" device distributed together with the medication. Zanamivir is a dry powder (not an aerosol) and should not be administered using nebulizers, ventilators, or other devices typically used for administering medications in aerosolized solutions. Zanamivir is not recommended for persons with chronic respiratory diseases such as asthma or chronic obstructive pulmonary disease that increase the risk of bronchospasm.

Data source: Fiore AE, Fry A, Shay D, Gubareva L, Bresee JS, Uyeki TM; Centers for Disease Control and Prevention. *MMWR Recomm Rep*. 2011;60(RR-1):1-24.

[1] American Academy of Pediatrics, Committee on Infectious Diseases. Recommendations for prevention and control of influenza in children, 2011—2012. *Pediatrics*. 2011;128(4):2011-2295

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