

# Helping Mothers Prevent Influenza Illness in Their Infants

Although pediatricians are well aware that influenza can be a problem for infants younger than 6 months, they may be less familiar with the high rates of influenza disease and complications among pregnant women. We provide here a summary of recent data on increased risk of influenza in pregnancy and in very young infants and on vaccine protection of these 2 groups at high-risk. Pediatricians should be aware of their central role in assisting in the vaccine prevention of influenza in pregnancy and in the young infant.

## INFLUENZA PANDEMICS IN PREGNANT WOMEN AND NEWBORNS

Healthy pregnant women are at increased risk of morbidity and mortality from pandemic influenza infection. During the 1918–1919 influenza pandemic, the case-fatality rate of pregnant women with influenza was reported to be 30% to 50% in the United States.<sup>1–3</sup> Similarly, the 2009 H1N1 influenza pandemic disproportionately affected pregnant women.<sup>4–6</sup> By August 2009, 788 H1N1-infected pregnant women had been reported to the Centers for Disease Control and Prevention (CDC), and 30 of these women died (5% of all reported 2009 H1N1 influenza deaths in this period).<sup>7</sup>

The increased risk of influenza during pregnancy is related to the physiologic changes of decreased pulmonary tidal volume and increased cardiac output. In addition, suppressed type 1 T-helper cell-mediated immunity impairs maternal response to infection with several viruses including influenza and smallpox.<sup>8,9</sup> Seasonal influenza-related hospitalization in healthy pregnant women occurs at a rate of 1 to 2 per 1000,<sup>10–12</sup> a risk that is 18-fold greater than that for healthy nonpregnant women.<sup>10</sup>

Historically, young infants have had high rates of illness during pandemics. Between August 30, 2009, and May 22, 2010, the CDC reported 225 laboratory-confirmed influenza-associated pediatric deaths, of which 49 were in children younger than 2 years old.<sup>13</sup>

## INFLUENZA RISK TO THE FETUS

Although recent and past pandemics have clearly demonstrated influenza risk for pregnant women, there are limited data on seasonal influenza-related risk to the fetus. Influenza virus can cross the placenta, but there is no direct evidence that the virus invades the bloodstream of the fetus.<sup>14</sup> Many studies have reported adverse fetal outcomes associated with influenza, but these associations have been inconsistent.<sup>11,15–22</sup>

## EPIDEMIC SEASONAL INFLUENZA RISK FOR INFANTS 0 TO 6 MONTHS OLD

Newborns and young infants experience increased rates of influenza infection, outpatient visits, and hospitalization.<sup>23,24</sup> Data from the Ten-

**AUTHORS:** Elizabeth P. Schlaudecker, MD,<sup>a</sup> and Mark C. Steinhoff, MD<sup>b</sup>

<sup>a</sup>Division of Infectious Diseases and <sup>b</sup>Global Health Center, Cincinnati Children's Hospital Medical Center, Cincinnati, Ohio

### ABBREVIATION

CDC—Centers for Disease Control and Prevention

Opinions expressed in this commentary are those of the author and not necessarily those of the American Academy of Pediatrics or its Committees.

[www.pediatrics.org/cgi/doi/10.1542/peds.2010-2041](http://www.pediatrics.org/cgi/doi/10.1542/peds.2010-2041)

doi:10.1542/peds.2010-2041

Accepted for publication Aug 23, 2010

Address correspondence to Mark C. Steinhoff, MD, Cincinnati Children's Hospital Medical Center, 3333 Burnet Ave, ML-2048, Cincinnati, OH 45229-3039. E-mail: [mark.steinhoff@cchmc.org](mailto:mark.steinhoff@cchmc.org)

PEDIATRICS (ISSN Numbers: Print, 0031-4005; Online, 1098-4275).

Copyright © 2010 by the American Academy of Pediatrics

**FINANCIAL DISCLOSURE:** Dr Steinhoff has been a consultant for Novartis/Grants-BMGF, US Agency for International Development, Thrasher Research Fund, GlaxoSmithKline, Wyeth, Merck, and Sanofi-Aventis; Dr Schlaudecker has indicated she has no financial relationships relevant to this article to disclose.

FREE

nessee Medicaid database showed high hospitalization rates of ~1% for infants younger than 6 months: 104 in 10 000 compared with 4 in 10 000 in older children.<sup>24</sup> A recent prospective 5-year surveillance study in 3 states revealed that the average annual rates of hospitalization associated with influenza were 45 per 1000 infants younger than 6 months compared with 3 to 9 per 1000 for older children; overall, 0- to 6-month-olds were 48% of all 0- to 5-year-old hospitalized children.<sup>25</sup> In some winters as many as 9% of all infants younger than 6 months were hospitalized or seen in a clinic or emergency department<sup>25</sup> (Fig 1).

### INFLUENZA IMMUNIZATION FOR YOUNG INFANTS

Currently, influenza vaccine is not approved or licensed for infants younger than 6 months. Recent studies in <6-month-old infants revealed that 2 doses of trivalent inactivated influenza vaccine (TIV) are safe and moderately immunogenic against some influenza strains.<sup>26,27</sup>

### SAFETY, IMMUNOGENICITY, AND EFFICACY OF INFLUENZA VACCINE IN PREGNANCY

Influenza vaccines are safe for pregnant women,<sup>10</sup> as indicated by data from >10 000 immunized women described in a recent review<sup>28</sup> and from policy documents.<sup>29,30</sup> The CDC has recommended influenza immunization for pregnant women since 1997,<sup>31</sup> and the recommendation was expanded in 2004 to include first-trimester vaccination. Even without accounting for the reduction of infant disease, influenza immunization in pregnancy is cost-saving.<sup>32</sup>

### PROTECTING INFANTS WITH MATERNAL IMMUNIZATION

Results of a novel randomized trial in Bangladesh demonstrated a significant 63% reduction of laboratory-confirmed influenza among infants of mothers who received influenza vaccine, and there was a 36% reduction of flu-like illnesses in the mothers.<sup>33,34</sup> Results of a similar case-control study in the United States confirmed these findings by revealing 85% effectiveness of maternal immu-

nization in preventing influenza-associated hospitalization in infants.<sup>35</sup>

### VACCINE COVERAGE IN PREGNANT WOMEN IN THE UNITED STATES

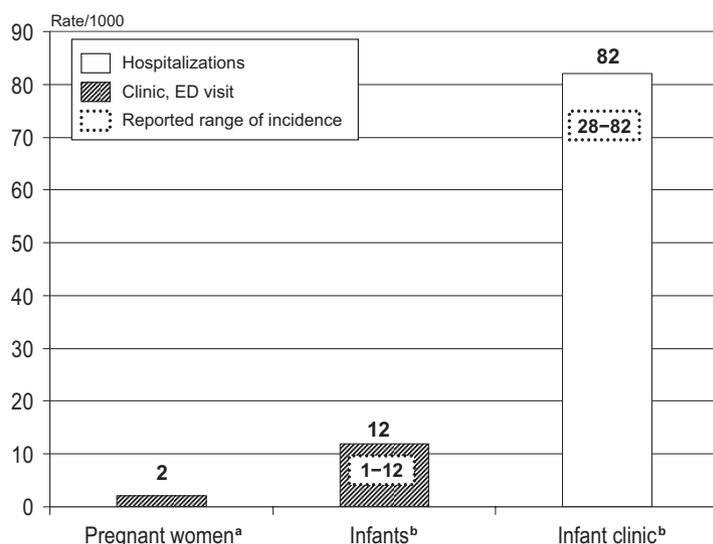
It is unfortunate that pregnant women continue to have the lowest vaccine-coverage rates of all adults recommended to receive seasonal influenza vaccination<sup>32,36</sup>; only 13% of pregnant women were immunized in 2003.<sup>37</sup> Immunization with monovalent pandemic 2009 H1N1 vaccine for pregnant women reached 38% in December 2009,<sup>38</sup> which perhaps reflects pandemic concerns.

### WHAT IS THE ROLE OF PEDIATRICIANS?

Results of a 2004 survey revealed that 30% of obstetric clinicians did not stock influenza vaccine in their offices.<sup>39</sup> Although this statistic may have changed, pediatricians are well placed to provide prenatal, antenatal, and postnatal counseling about the benefits for mothers and their infants from maternal influenza vaccination. Prenatal visits to the pediatrician's office provide an excellent opportunity to encourage pregnant mothers to receive influenza immunization to protect themselves and their infant. During postpartum neonatal visits to the delivery hospital or well-child checks within the first week, mothers should be offered influenza vaccination, especially if they are breastfeeding. Postpartum maternal vaccine will likely prevent influenza in the infant.

### CONCLUSIONS

Pregnant women and their infants are at increased risk for complications of influenza infection. New data show that vaccination of pregnant women is safe and effective and also provides excellent protection for the infants. Pediatricians should use all contacts with pregnant and postpartum mothers to promote maternal immunization to protect them and their young infants.



**FIGURE 1**

Influenza hospitalization and clinic visits by pregnant women and 0- to 6-month-old infants; shown is the range of incidence per 1000 persons per influenza season. <sup>a</sup> Seasonal analysis, influenza-associated hospitalization (1974–1992, Tennessee) (range: 1–2 per 100).<sup>24</sup> <sup>b</sup> Laboratory-proven influenza (2000–2004, Tennessee, New York, and Ohio).<sup>25</sup>

Even if pediatricians are unable to provide influenza vaccines to pregnant women within their practice settings, they should use available medical con-

tacts to ensure immunization of this high-risk population.

Immunizing pregnant women means that 1 influenza shot will protect the

mother, the fetus, and the 0- to 6-month-old infant—a 3-for-1 bargain. Similarly, postpartum maternal immunization is a 2-for-1 bargain.

## REFERENCES

1. Nuzum JW, Pilot I, Stange FH, Bunar BE. 1918 pandemic influenza and pneumonia in a large civil hospital. *JAMA*. 1918;71(19):1562–1565
2. Woolston WJ, Conley DO. Epidemic pneumonia (Spanish influenza) in pregnancy: effect in one hundred and one cases. *JAMA*. 1918; 71(23):1898–1899
3. Bland PB. Influenza in its relation to pregnancy and labor. *Am J Obstet*. 1919;79: 184–197
4. Jamieson DJ, Honein MA, Rasmussen SA, et al; Novel Influenza A (H1N1) Pregnancy Working Group. H1N1 2009 influenza virus infection during pregnancy in the USA. *Lancet*. 2009;374(9688):451–458
5. Louie JK, Acosta M, Jamieson DJ, Honein MA. Severe 2009 H1N1 influenza in pregnant and postpartum women in California. *N Engl J Med*. 2010;362(1):27–35
6. Creanga AA, Johnson TF, Graitcer SB, et al. Severity of 2009 pandemic influenza A (H1N1) virus infection in pregnant women. *Obstet Gynecol*. 2010;115(4):717–726
7. Siston AM, Rasmussen SA, Honein MA, et al; Pandemic H1N1 Influenza in Pregnancy Working Group. Pandemic 2009 influenza A (H1N1) virus illness among pregnant women in the United States. *JAMA*. 2010; 303(15):1517–1525
8. Lederman MM. Cell-mediated immunity and pregnancy. *Chest*. 1984;86(3 suppl):6S–9S
9. Sridama V, Pacini F, Yang SL, Moawad A, Reilly M, DeGroot LJ. Decreased levels of helper T cells: a possible cause of immunodeficiency in pregnancy. *N Engl J Med*. 1982; 307(6):352–356
10. Mak TK, Mangtani P, Leese J, Watson JM, Pfeifer D. Influenza vaccination in pregnancy: current evidence and selected national policies. *Lancet Infect Dis*. 2008; 8(1):44–52
11. Hartert TV, Neuzil KM, Shintani AK, et al. Maternal morbidity and perinatal outcomes among pregnant women with respiratory hospitalizations during influenza season. *Am J Obstet Gynecol*. 2003;189(6): 1705–1712
12. MacDonald NE, Riley LE, Steinhoff MC. Influenza immunization in pregnancy. *Obstet Gynecol*. 2009;114(2 pt 1):365–368
13. Centers for Disease Control and Prevention. 2009–2010 influenza season week 20 ending May 22, 2010. Available at: [www.cdc.gov/flu/weekly](http://www.cdc.gov/flu/weekly). Accessed July 2, 2010
14. McGregor JA, Burns JC, Levin MJ, Burlington B, Meiklejohn G. Transplacental passage of influenza A/Bangkok (H3N2) mimicking amniotic fluid infection syndrome. *Am J Obstet Gynecol*. 1984;149(8):856–859
15. Acs N, Banhid F, Puho E, Czeizel AE. Maternal influenza during pregnancy and risk of congenital abnormalities in offspring. *Birth Defects Res A Clin Mol Teratol*. 2005;73(12): 989–996
16. Acs N, Banhid F, Puho E, Czeizel AE. Pregnancy complications and delivery outcomes of pregnant women with influenza. *J Matern Fetal Neonatal Med*. 2006;19(3):135–140
17. Austin DF, Karp S, Dworsky R, Henderson BE. Excess leukemia in cohorts of children born following influenza epidemics. *Am J Epidemiol*. 1975;101(1):77–83
18. Fedrick J, Alberman ED. Reported influenza in pregnancy and subsequent cancer in the child. *Br Med J*. 1972;2(5812):485–488
19. Hakulinen T, Hovi L, Karkinen-Jääskeläinen M, Penttinen K, Saxén L. Association between influenza during pregnancy and childhood leukaemia. *Br Med J*. 1973; 4(5887):265–267
20. Harris JW. Influenza occurring in pregnant women. *JAMA*. 1919;72(14):978–980
21. Nishiura H. Excess risk of stillbirth during the 1918–1920 influenza pandemic in Japan. *Eur J Obstet Gynecol Reprod Biol*. 2009; 147(1):115
22. Brown AS, Derkits EJ. Prenatal infection and schizophrenia: a review of epidemiologic and translational studies. *Am J Psychiatry*. 2010;167(3):261–280
23. Glezen WP, Paredes A, Taber LH. Influenza in children: relationship to other respiratory agents. *JAMA*. 1980;243(13):1345–1349
24. Neuzil KM, Mellen BG, Wright PF, Mitchel EF, Jr, Griffin MR. The effect of influenza on hospitalizations, outpatient visits, and courses of antibiotics in children. *N Engl J Med*. 2000; 342:225–231
25. Poehling KA, Edwards KM, Weinberg GA, et al; New Vaccine Surveillance Network. The underrecognized burden of influenza in young children. *N Engl J Med*. 2006;355(1): 31–40
26. Halasa NB, Gerber MA, Chen Q, Wright PF, Edwards KM. Safety and immunogenicity of trivalent inactivated influenza vaccine in infants. *J Infect Dis*. 2008;197(10):1448–1454
27. Walter EB, Englund JA, Blatter M, Nyberg J, Ruben FL, Decker MD. Trivalent inactivated influenza virus vaccine given to two-month-old children: an off-season pilot study. *Pediatr Infect Dis J*. 2009;28(12):1099–1104
28. Tamma PD, Ault KA, del Rio C, Steinhoff MC, Halsey NA, Omer SB. Safety of influenza vaccination during pregnancy. *Am J Obstet Gynecol*. 2009;201(6):547–552
29. Bozzo P, Djokanovic N, Koren G. H1N1 influenza in pregnancy: risks, vaccines, and antivirals. *J Obstet Gynaecol Can*. 2009;31(12): 1172–1175
30. Pickering LK, Baker CJ, Freed GL, et al; Infectious Diseases Society of America. Immunization programs for infants, children, adolescents, and adults: clinical practice guidelines by the Infectious Diseases Society of America. *Clin Infect Dis*. 2009;49(6): 817–840
31. Fiore AE, Shay DK, Broder K, et al; Centers for Disease Control and Prevention. Prevention and control of seasonal influenza with vaccines: recommendations of the Advisory Committee on Immunization Practices (ACIP), 2009 [published correction appears in *MMWR Recomm Rep*. 2009;58(32): 896–897]. *MMWR Recomm Rep*. 2009; 58(RR-8):1–52
32. Beigi RH, Waring AE, Bailey RR, Assi TM, Lee BY. Economic value of seasonal and pandemic influenza vaccination during pregnancy. *Clin Infect Dis*. 2009;49(12): 1784–1792
33. Zaman K, Roy E, Arifeen SE, et al. Effectiveness of maternal influenza immunization in mothers and infants. *N Engl J Med*. 2008; 359(15):1555–1564
34. Steinhoff MC, Omer SB, Roy E, et al. Influenza immunization in pregnancy: antibody responses in mothers and infants. *N Engl J Med*. 2010;362(17):1644–1646
35. Benowitz I, Esposito D, Gracey K, Martinello R, Shapiro E, Vázquez M. Influenza vaccine given to pregnant women reduces hospitalization due to influenza in their infants. *Clin Infect Dis*. 2010; In press
36. Lu P, Bridges CB, Euler GL, Singleton JA. Influenza vaccination of recommended adult populations, U.S., 1989–2005. *Vaccine*. 2008; 26(14):1786–1793

37. Centers for Disease Control and Prevention. National Health Interview Survey—2003. Table: self-reported influenza vaccination coverage trends, 1989–2003 among adults by age group, risk group, race/ethnicity, health-care worker status and pregnancy status, United States. Available at: <http://cdc.gov/flu/professionals/vaccination/pdf/vaccinetrend.pdf>. Accessed May 30, 2010
38. Centers for Disease Control and Prevention. Interim results: influenza A (H1N1) 2009 monovalent vaccination coverage—United States, October–December 2009. *MMWR Morb Mortal Wkly Rep.* 2010;59(2):44–48
39. Influenza vaccination in pregnancy: practices among obstetrician-gynecologists—United States, 2003–04 influenza season. *MMWR Morb Mortal Wkly Rep.* 2005;54(41):1050–1052

**Do Parents Worry About the Right Things?:** *Standing in a long checkout line, I casually remarked to the woman standing in front of me that her young daughter had lovely ringlets of hair. The mother immediately replied that both she and the girl hated the hair. So many strangers touched her daughter's hair she was sure someone was bound to snatch her. Upon hearing that, a pert 8-year-old standing behind me, chimed in that her father had told her that she was the most likely person in the family to be stolen.*

*According to an article in The New York Times (Belkin L, September 18, 2010) the 5 things that parents are most worried about are kidnapping, school snipers, terrorists, dangerous strangers and drugs. The Centers for Disease Control, however, reports that the 5 most common causes of injury to children under the age of 19 are car accidents, homicide, child abuse, suicide and drowning. It would seem that parents are poor judges of childhood risk. Reasons for this include the national attention given to horrifying and rare events, immediate access to information from around the world, and complacency about the dangers of normal activities such as driving. We also have difficulty balancing short with long-term risks. To protect children from abduction, children are driven to play dates and supervised by parents. However, what is the risk of childhood obesity in a child routinely driven to all functions? So while the mothers in front and back of me discussed strategies to prevent childhood abduction, I simply whispered to myself, I hope the girls are wearing a seatbelt on the drive home.*

Noted by WVR, MD

## Helping Mothers Prevent Influenza Illness in Their Infants

Elizabeth P. Schlaudecker and Mark C. Steinhoff

*Pediatrics* 2010;126;1008

DOI: 10.1542/peds.2010-2041 originally published online October 18, 2010;

### Updated Information & Services

including high resolution figures, can be found at:  
<http://pediatrics.aappublications.org/content/126/5/1008>

### References

This article cites 36 articles, 2 of which you can access for free at:  
<http://pediatrics.aappublications.org/content/126/5/1008#BIBL>

### Subspecialty Collections

This article, along with others on similar topics, appears in the following collection(s):  
**Infectious Disease**  
[http://www.aappublications.org/cgi/collection/infectious\\_diseases\\_sub](http://www.aappublications.org/cgi/collection/infectious_diseases_sub)

### Permissions & Licensing

Information about reproducing this article in parts (figures, tables) or in its entirety can be found online at:  
<http://www.aappublications.org/site/misc/Permissions.xhtml>

### Reprints

Information about ordering reprints can be found online:  
<http://www.aappublications.org/site/misc/reprints.xhtml>

American Academy of Pediatrics

DEDICATED TO THE HEALTH OF ALL CHILDREN™



# PEDIATRICS®

OFFICIAL JOURNAL OF THE AMERICAN ACADEMY OF PEDIATRICS

## Helping Mothers Prevent Influenza Illness in Their Infants

Elizabeth P. Schlaudecker and Mark C. Steinhoff

*Pediatrics* 2010;126;1008

DOI: 10.1542/peds.2010-2041 originally published online October 18, 2010;

The online version of this article, along with updated information and services, is located on the World Wide Web at:

<http://pediatrics.aappublications.org/content/126/5/1008>

Pediatrics is the official journal of the American Academy of Pediatrics. A monthly publication, it has been published continuously since 1948. Pediatrics is owned, published, and trademarked by the American Academy of Pediatrics, 141 Northwest Point Boulevard, Elk Grove Village, Illinois, 60007. Copyright © 2010 by the American Academy of Pediatrics. All rights reserved. Print ISSN: 1073-0397.

American Academy of Pediatrics

DEDICATED TO THE HEALTH OF ALL CHILDREN™

