

Protecting young babies from influenza

N MacDonald, R Bortolussi; Canadian Paediatric Society, Infectious Diseases and Immunization Committee



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Unknown to many physicians and parents, infants younger than six months of age are at significant risk for serious illness with influenza, leading to higher rates of hospitalization, more prolonged intensive care unit (ICU) stays and higher fatality rates (0.88 per 100,000 children) than almost any other age group (1-5). The purpose of the present Paediatric Infectious Disease Note is to provide a brief overview of the epidemiology and clinical features of influenza in infants younger than six months of age and to outline prevention options for decreasing influenza in this high-risk age group.

EPIDEMIOLOGY OF SEASONAL INFLUENZA

In the United States, prospective surveys and national estimates have shown influenza hospital admission rates for infants younger than six months of age to range between 1.8 and 7.2 per 1000 young infants; many-fold higher than the rates of influenza hospitalization for older infants and children, and for those 65 to 80 years of age (6-8). These may well be underestimates of hospitalization rates because many infants and children with laboratory-confirmed influenza are not accurately diagnosed by physicians as influenza cases (7). In one survey (7), 28% of hospitalized laboratory-confirmed cases of influenza were not given this discharge diagnosis. A prospective cross-Canada study (1) in 2003/2004 by the Canadian Immunization Monitoring Program, ACTive noted that more than one in five (23%) of the 505 children admitted to nine tertiary care hospitals with influenza were younger than six months of age, while 34% were between six and 23 months of age. More importantly, of those infants younger than six months of age hospitalized with influenza, 84% were previously healthy with no underlying comorbidity compared with only 62% previously healthy in the six- to 23-month age group and much less than one-half in those older than 23 months.

HOW DO YOUNG INFANTS PRESENT CLINICALLY?

In the prospective cross-Canada study (1), while most children admitted with influenza had fever, cough, rhinorrhea and some respiratory distress, those younger than six months of age were less likely to have cough and pneumonia than older infants and children, but more likely to have rhinorrhea and dehydration. As well, if these young babies needed ICU admission, the duration was significantly longer than

for older children requiring ICU admission (4.75 days versus 2.76 days; $P=0.04$). An American study (7) also showed differences in the clinical findings by age group. For those younger than six months of age, admission for fever and to rule out sepsis was a common scenario.

HOW CAN INFLUENZA BE PREVENTED IN INFANTS YOUNGER THAN SIX MONTHS OF AGE?

Although infants younger than six months of age are known to be at high risk for serious influenza illness, prevention is problematic. In contrast to infants older than six months of age, the influenza vaccine has limited immunogenicity in these very young infants (9-11). While improved influenza vaccines may eventually be developed for this very young age group, until then, alternative strategies are the best options.

There are now two recommended strategies for decreasing seasonal influenza risk in this vulnerable young infant age group:

- immunization of the caregivers and family of the young infant, and
- influenza immunization of the pregnant woman.

Both the National Advisory Committee on Immunization in Canada and the Advisory Committee on Immunization Practices in the United States recommend influenza immunization for household contacts of infants younger than six months of age and influenza immunization of all pregnant women for the benefit of the mother (12,13). Unfortunately, the seasonal influenza vaccine rates of uptake among parents of young infants (14) or among pregnant women (15,16) in Canada or the United States have not been stellar.

INFLUENZA IMMUNIZATION OF PREGNANT WOMEN – THE ADDED BENEFIT FOR BABIES

Influenza immunization in pregnancy is important for protecting pregnant women against serious influenza illness (12). Two large cohort studies, one in Nova Scotia and one in Tennessee, United States, (15,17), compared hospitalization rates in defined influenza seasons of pregnant women predominately not immunized against influenza, stratified by trimester and adjusted for comorbidities. The studies found elevated rates of hospitalization during the influenza season compared with the noninfluenza season. In the Nova Scotia study (15), third trimester healthy

pregnant women with no comorbidities had a fivefold higher relative risk of hospitalization for respiratory illness during influenza season compared with their hospitalization risk in the influenza season in the year before pregnancy.

Not only is influenza immunization important for the health of the pregnant woman, but the concept raised two decades ago that maternal influenza antibodies passed to the infant before birth or via breast milk could offer young infants protection against serious illness from influenza (18,19), was recently proven correct in a randomized controlled trial. A study (20) in Bangladesh has shown that seasonal influenza immunization of pregnant women can significantly decrease respiratory illness with fever in both the women and in their young infants. The relative risk reduction in influenza-proven cases in the young infants was 64%. The number of pregnant women needed to treat to see benefit in the infants was only 17. This impressive effectiveness for young infants of influenza immunization of pregnant women substantively builds on the earlier American observations from two decades before where natural maternal infection was found to offer protection to the infant (18,19)

An American cost-effectiveness analysis of influenza immunization in pregnant women, that did not even take into account this additional benefit for the young infant, determined that influenza vaccine in pregnancy is cost-effective compared with supportive treatment of influenza illnesses in pregnancy, resulting in an estimated savings of approximately US\$50 per immunized woman (21). This saving will be increased when the added protection benefits for young infants are factored in.

HOW SAFE IS INFLUENZA VACCINE IN PREGNANCY? IS THERE A RISK FOR THE UNBORN CHILD?

While some have questioned the safety of seasonal influenza immunization of pregnant women for the unborn child, there is strong evidence that this vaccine is safe. The influenza vaccine is a killed vaccine and cannot replicate or cause influenza in the pregnant woman. There is no evidence of any associated teratogenic effects. In a review of American data for 2000 to 2003 (approximately two million pregnant women receiving influenza vaccine) by the Vaccine Adverse Event Reporting System in the United States, no unexpected vaccine adverse events were detected (22). The miscarriage rates in early pregnancy were the same for immunized and nonimmunized women. Moreover, pooled data from 10 published studies of influenza vaccine in pregnancy (six cohorts, three retrospective trials and one randomized controlled trial; more than 10,000 women and more than 50,000 controls) do not suggest any added risk of influenza vaccine in pregnancy for the unborn child (16,20,23-31).

CONTROVERSY OF SEASONAL INFLUENZA VACCINE AND H1N1 INFECTION

A key issue for many provincial influenza immunization programs is how to administer both the seasonal and the

H1N1 influenza vaccines when information necessary to make decisions is evolving rapidly. A very preliminary unpublished study from Canada has suggested that getting a seasonal influenza vaccine may increase the chance of getting H1N1. Further investigation into this possible association by the Centers for Disease Control and Prevention in the United States and the World Health Organization has been negative. Nevertheless, the Canadian study is being taken very seriously by health officials in Canada. Although the influenza season is still early, several provinces have already identified people with H1N1 illness. Therefore, many provinces and territories have decided to launch the influenza seasonal immunization programs as soon as possible for the elderly and to concentrate the H1N1 influenza immunization efforts on the younger population based on the observations that those older than 65 years of age appear to be at low risk of getting H1N1 but remain at high risk of becoming seriously ill with seasonal influenza. For the rest of the population, particularly children, youth and pregnant women, who are among those at greater risk for serious H1N1, the focus is to distribute the H1N1 vaccine as quickly and efficiently as possible. These are interim plans based on available information at this time.

HOW CAN PAEDIATRICIANS AND FAMILY PHYSICIANS INCREASE INFLUENZA PROTECTION FOR YOUNG BABIES?

- Discuss with pregnant women, or women planning to become pregnant, the personal benefit of influenza immunization in pregnancy and the added benefit of maternal immunization for infants younger than six months of age.
- Encourage all pregnant women to receive the influenza vaccine as soon as the vaccine is available before the influenza season.
- Update medical colleagues who deal with pregnant women and advocate for influenza immunization because of the benefits of immunization to both the pregnant woman and the baby on board.
- Encourage hand hygiene as a means to limit the spread of viral infection.
- Encourage and facilitate, wherever possible, influenza immunization of all household contacts of infants younger than six months of age including parents of infants being discharged from normal newborn care units and neonatal ICUs.

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COMMENTAIRE SUR LES MALADIES INFECTIEUSES EN PÉDIATRIE

Protéger les jeunes bébés contre la grippe

N MacDonald, R Bortolussi; Société canadienne de pédiatrie, comité des maladies infectieuses et d'immunisation



**Société
canadienne
de pédiatrie**

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De nombreux médecins et de nombreux parents ne le savent pas, mais les nourrissons de moins de six mois sont très vulnérables à une grave maladie causée par la grippe, qui entraîne des taux plus élevés d'hospitalisation, des séjours plus longs à l'unité de soins intensifs (USI) et un taux de mortalité plus élevé (0,88 cas pour 100 000 enfants) que

presque tous les autres groupes d'âge (1-5). Le présent commentaire sur les maladies infectieuses en pédiatrie vise à donner un bref aperçu de l'épidémiologie et des caractéristiques cliniques de la grippe chez les nourrissons de moins de six mois et à exposer les possibilités de prévention afin de réduire les cas de grippe au sein de ce groupe d'âge à haut risque.

Correspondance : Société canadienne de pédiatrie, 2305, boulevard St Laurent, Ottawa (Ontario) K1G 4J8, téléphone : 613-526-9397, télécopieur : 613-526-3332, Internet : www.cps.ca, www.soinsdenosenfants.cps.ca