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Learning Objectives

After studying the literature presented in this Pediatric Respiratory Care series, participants will be able to

- Assess the relationship between breastfeeding and hospitalization for diarrhea and lower respiratory tract infection during the first 8 months after birth
- Outline the interactive effects of genetic and environmental factors, such as a family history of asthma, postnatal exposure to parental smoking, house-dust mite allergens, and breastfeeding, on the occurrence of respiratory morbidity in infancy

Target Audience

This educational activity is designed for pediatricians, primary care physicians, pediatric and family nurse practitioners, neonatologists, infectious disease specialists, allergists, pulmonologists, immunologists, and other healthcare professionals involved in the care and management of pediatric respiratory patients.

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Breastfeeding Lowers Infant Hospitalization for Diarrheal and Respiratory Infection

Breastfeeding all infants, exclusively, for at least 6 months was recommended by the World Health Organization (WHO). In developing countries, it has been shown that exclusive breastfeeding has a large protective effect on infant mortality and severe morbidity. Yet, the importance of breastfeeding healthy, full-term infants from developed countries has not been well established. The objective of the current study is to assess the effect of breastfeeding on hospitalizations for diarrhea and lower respiratory-tract infection (LRTI) in the first 8 months after birth in the contemporary United Kingdom.

The Millennium Cohort Study conducted by Quigley and associates is a national population-based survey of 18,819 infants born in the United Kingdom. The main outcome measure was the parental report of hospitalization for diarrhea and LRTI during the first 8 months after birth. Parents were interviewed for the first time (sweep 1) when most infants were aged 9 months (6 to 12 months of age). Data were analyzed by the month of age with adjustments for confounders. Infant feeding was categorized per month into the following three groups: not breastfed, partially breastfed, and exclusively breastfed.

Detailed information about infant feeding, infant health, and a range of confounding factors was collected from 15,890 healthy, singleton, full-term infants who were born between the years 2000 and 2002. Seventy-one percent of infants were ever breastfed; with 34.2% and 24.8% receiving breast milk for 4 and 6 months, respectively, and only 1.2% of infants were exclusively breastfed for at least 6 months. In the first 8 months after

birth, 12% of infants experienced at least one hospital admission. The most common causes of hospitalization were LRTI (3.2%), diarrhea (1.1%), and asthma/wheezing (0.9%).

The impact of current breastfeeding on hospitalizations as a result of both diarrhea and LRTI in the same month was assessed with adjustments for confounders. Compared with those not breastfed, infants exclusively breastfeeding had a large and statistically significant reduction in their risk of hospitalization for diarrhea (adjusted odds ratio [OR], 0.37; 95% confidence interval [CI], 0.18-0.78) and LRTI (adjusted OR, 0.66; 95% CI, 0.47-0.92). The effect of partial breastfeeding was weaker. Population-attributable fractions suggest that 53% of hospitalizations for diarrhea could have been prevented each month by exclusive breastfeeding and 31% of those could have been prevented by partial breastfeeding. Similarly, 27% of hospitalizations for LRTI could have been prevented each month by exclusive breastfeeding and 25% of those by partial breastfeeding.

The effect of past breastfeeding was evaluated by assessing the association between the months since breastfeeding cessation and hospitalization. The protective effect of breastfeeding regarding hospitalization for diarrhea and LRTI wears off after breastfeeding cessation. A statistically significant increase in the risk of hospitalization was noted for both outcomes. For diarrhea, the protective effect did not persist beyond the first month after breastfeeding cessation. There appeared a doubling of risk for hospitalization for every month after breastfeeding cessation in infants aged 1 to 4 months (adjusted OR, 1.98;

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Disclosures:

- * Dr Piedra is professor of pediatrics and molecular virology and microbiology at Baylor College of Medicine. He has indicated relevant financial relationships as noted: he receives grant/research support from MedImmune, Inc. and Sanofi Pasteur; he is a member of the speakers bureau for MedImmune, Inc.; he is an expert witness for Sanofi Pasteur; he is an ad hoc consultant for MedImmune, Inc., Sanofi Pasteur, GlaxoSmithKline, Novartis, and Roche; and he is part of a collaborative research agreement with NIH and Baylor.
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Breastfeeding *(Continued)*

95% CI, 1.32-2.96) and a 28% increase in risk in those aged 5 to 7 months (adjusted OR, 1.28; 95% CI, 1.01-1.61). For LRTI, the protective effect of breastfeeding weakened as soon as breastfeeding ceased.

Quigley and colleagues were able to conclude from their study that breastfeeding, particularly when exclusive and prolonged, protects against severe morbidity, including diarrhea and LRTI for infants in the contemporary United Kingdom. They also recommend that a population-level increase in

exclusive, prolonged breastfeeding would greatly benefit public health. The information obtained from this study may be used as a reference for the estimation of cost-effectiveness regarding breastfeeding interventions.

Quigley MA, Kelly YJ, Sacker A. Breastfeeding and hospitalization for diarrheal and respiratory infection in the United Kingdom Millennium Cohort Study. *Pediatrics*. 2007;119:e837-e842.

COMMENTARY

JAIME FERGIE, MD, Director, Pediatric Infectious Disease, Driscoll Children's Hospital, Corpus Christi, Texas.

With the current emphasis on cost-effective medicine, I find it difficult to come up with a more cost-saving intervention than breastfeeding. This study is of particular interest because of the following factors: The size of the cohort; the fact that it was conducted in a developed nation with good sanitation; and the clear endpoint of hospitalization. Therefore, the benefit of breastfeeding is not limited to the infection/prevention point of view in countries or communities with poor sanitary conditions. Even though the study did not consider wheezing or asthma a lower respiratory-tract infection (LRTI), and therefore could have excluded many cases of bronchiolitis, the authors tell us that the positive effects of breastfeeding were similar to the reported results when they included wheezing or asthma in the definition of LRTI. Although the findings were not as strong, partial breastfeeding also appears to be beneficial. Unfortunately, the study excluded premature infants and babies who were sick during the neonatal period, a population which is both at a higher risk for hospitalization and is the target of immunoprophylaxis for the prevention of RSV. A discussion on the large number of hospitalizations that could have been prevented, if breastfeeding had been initiated, should be of interest to third-party payers who will be able to see that the time spent counseling mothers may have a direct monetary benefit.

Effects of Family History of Asthma and Environmental Factors on Respiratory Morbidity in Infancy

Asthma is one of the most important chronic diseases occurring in childhood and is the main cause of school absences. A steady increase in the prevalence of asthma has been observed worldwide. High incidences of asthma-related contacts and hospitalizations result in the substantially high healthcare costs of treating this disease in children. It is known that the development of asthma-related respiratory morbidity is determined by genetic and environmental factors. However, the interaction of these factors is not clear. Kuiper and colleagues conducted a study to assess the interactive effect of a family history of asthma and certain environmental factors on the occurrence of respiratory morbidity in infancy.

Two hundred twenty-one infants with a positive family history of asthma and 308 with a negative family history of asthma were prenatally selected and followed until the age of 2 years. Exposure to environmental factors and the occurrence of respiratory symptoms were reported by parents at 6, 12, and 24 months. Respiratory illness diagnoses were captured prospectively during consultations with the general practitioners (GP) during the children's first 2 years of life. Environmental factors included in the study were passive smoking and house dust

mite (Der p 1), cat (Fel d 1), and dog (Can f 1) allergens, as well as breastfeeding. By using a multiple logistic regression analysis, the increased risk from a family history of asthma and/or environmental factors was expressed in odds ratios (ORs) adjusted for relevant covariables.

Infants with a positive family history of asthma, defined as the presence of at least one first-degree family member with a history of asthma (biological mother, biological father, or a sibling), had more respiratory tract- and asthma-related morbidity during the first 2 years of life when compared with infants who had a negative family history of asthma. Adjusted ORs ranged from 1.7 (95% CI, 1.0-2.8) for physician-diagnosed expiratory wheezing to 4.9 (95% CI, 1.7-13.6) for physician-diagnosed croup.

Statistically significant interactions between having family history of asthma and the postnatal exposure to parental smoking, as well as between having a family history of asthma and the postnatal exposure to house-dust mites (Der p 1), were observed for wheezing ever ($P=0.023$ and $P=0.015$ respectively) and for attacks of wheezing ($P=0.033$ and $P=0.046$, respectively). Parental smoking increased the effect of a positive family history of asthma on wheezing ever with an adjusted OR of

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Family History of Asthma *(Continued)*

5.8 (95% CI, 2.5-13.8) and attacks of wheezing (OR, 6.8; 95% CI, 2.7-16.9). Similarly, exposure to Der p 1 also potentiated the effect of a positive family history of asthma on wheezing ever (OR, 10.2; 95% CI, 2.8-36.3) and attacks of wheezing (OR, 7.1; 95% CI, 7.1-21.0). Moreover, when the infants were exposed to both parental smoking and Der p 1, the increase in the positive family history of asthma effect was even more pronounced; the adjusted ORs for wheezing ever and attacks for wheezing were elevated to 30.8 (95% CI, 6.9-137.2) and 26.2 (95% CI, 5.9-115.6), respectively.

Significant interaction between a positive family history of asthma and breastfeeding was also observed for parentally reported tonsillitis and otitis media, as well as for GP-diagnosed acute otitis media. The risks for tonsillitis and acute otitis media were significantly higher in formula-fed infants with a positive family history of asthma than they were in those with a negative family history of asthma (OR, 9.2; 95% CI, 2.1-39.7 and OR, 2.9; 95% CI, 1.1-7.2, respectively). Breast feeding attenuated

the risk for these diagnoses (tonsillitis: OR, 1.8; 95% CI, 0.8-3.8; and acute otitis media: OR, 0.7; 95% CI, 0.4-1.3).

Kuiper and associates concluded from their observations that a family history of asthma was a significant risk factor for the occurrence of respiratory tract- and asthma-related morbidity during the first 2 years of life. The relation between a positive family history of asthma and respiratory morbidity was modified by postnatal exposure to environmental factors; parental smoking and house dust-mite exposure increased the risk, while breastfeeding reduced the risk for respiratory morbidity. The investigators suggested the clinical implications from this study indicate mothers should be encouraged to breastfeed their children when they cannot stop smoking or improve household sanitation.

Kuiper S, Muris JWM, Dompeling E, et al. Interactive effect of family history and environmental factors on respiratory tract-related morbidity in infancy. *J Allergy Clin Immunol.* 2007;120(2):338-395.

Clinical Insights® in Pediatric Respiratory Care Post-Test

1. Regarding the association between breastfeeding and hospitalization in the first 8 months after birth, which of the following statements is false?
 - a. Exclusive breastfeeding markedly reduces the risk of hospitalization for lower respiratory tract infection (LRTI).
 - b. 53% of diarrhea hospitalizations could have been prevented each month by exclusive breastfeeding.
 - c. Cessation of breastfeeding has no impact on the risk of LRTI hospitalization.
 - d. In the first 8 months after birth, the most common cause of hospitalization is LRTI.
2. The adjusted odds ratios (ORs) for parental smoking and house-dust mite Der p 1 allergen on the increase in the effect of family history of asthma on wheezing ever were shown to be 5.8 and 10.2, respectively. Which of the ORs is expected to be seen if these infants are exposed to both parental smoking and Der p 1?
 - a. 5.8
 - b. 10.2
 - c. 1.7
 - d. 30.8

1. c. The protective effect of breastfeeding on LRTI hospitalization weakens as soon as breastfeeding stops.
 2. d. When infants were exposed to both postnatal parental smoking and Der p 1, the increase in the positive family history of asthma effect was even more pronounced. The adjusted OR was elevated to 30.8 (95% CI: 6.9-137.2) for wheezing ever.

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