Kathryn Beardsall, M.R.C.P.
University of Cambridge
Cambridge CB2 0QQ, United Kingdom

Francis de Zegher, Ph.D.
University of Leuven
B3000 Leuven, Belgium

David B. Dunger, M.D.
University of Cambridge
Cambridge CB2 0QQ, United Kingdom
dbd25@cam.ac.uk

for the NIRTURE Investigators

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THE EDITORIALISTS REPLY: The normal glucose concentration in healthy newborn infants who are less than 4 weeks of age, as suggested by Van den Berghe et al., is lower than that which would be acceptable after the first few hours of life. Though the definition of hypoglycemia remains controversial in healthy term infants and routine monitoring is discouraged, maintaining glucose concentrations above 2.5 mmol per liter (45 mg per deciliter) is recommended for symptomatic infants.[1] It is unclear what constitutes normoglycemia in very-low-birth-weight infants; however, glucose concentrations of 4.3 to 7.6 mmol per liter (77 to 137 mg per deciliter) are used as norms for euglycemia[2,3] and hyperglycemia is defined as concentrations greater than 8.3 mmol per liter (150 mg per deciliter). Therefore, in our opinion, the very-low-birth-weight infants in the study by Beardsall et al., with mean glucose concentrations of 6.2 mmol per liter in the intervention group and 6.7 mmol per liter in the control group, did not have pronounced hyperglycemia.

Sudha Kashyap, M.D.
Richard A. Polin, M.D.
Columbia University College of Physicians and Surgeons
New York, NY 10032

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Effectiveness of Maternal Influenza Immunization

TO THE EDITOR: In their article on maternal influenza vaccination, Zaman et al. (Oct. 9 issue)[1] address a very important preventive health intervention that had substantial benefits to both mothers and infants. However, the potential effect of breast-feeding on the outcome remains unclear. Was there an association between breast-feeding and apparent immunity to respiratory illness in the two study groups? Though the authors mention that the mean numbers of weeks of exclusive breast-feeding were similar in the two groups, the range varied from 1 to 25 weeks. Was any subgroup analysis done to investigate for an association between the duration of breast-feeding and the development of infection? This is an important factor to consider, since previous studies have shown that breast-feeding may decrease susceptibility to influenza as a result of passive antibody transfer.[2] It would be interesting to note whether breast-feeding provided an additional protective factor to the infants in this study, as has been observed in epidemiologic data previously.[3]

Saira S. Tandon, M.D.
Lutheran Medical Center
Brooklyn, NY 11220
dr_saira_ahmad@hotmail.com

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THE AUTHORS REPLY: Although breast-feeding is known to have an effect on the infant immune response,[1] its effect should be equal in the two study groups in a randomized trial. In Table 1 of our article, we report similar mean numbers of weeks of exclusive breast-feeding in the two study groups (P=0.18).

We have now explored in detail the distribution of the duration of exclusive breast-feeding in each study group (Fig. 1). Both groups showed a left-skewed distribution, with a peak around the 20th week. However, the distribution in the influenza-vaccine group appears bimodal, with an additional peak around the fifth week. The comparison of means and distribution does not suggest that breast-feeding is a significant confounder. If anything, the slightly shorter duration of breast-feeding in the influenza-vaccine group would tend to reduce the observed effect of influenza immunization.

Effect modification by breast-feeding cannot be ruled out. We plan to conduct a detailed secondary analysis to explore differential vaccine effectiveness according to breast-feeding status in a variety of infant age groups and to assess the concentration of IgA antibodies in breast milk.

Saad B. Omer, M.B., B.S., Ph.D.
Emory University
Atlanta, GA 30322

K. Zaman, M.B., B.S., Ph.D.
International Centre for Diarrheal Disease Research
Dhaka 1212, Bangladesh

Mark C. Steinhoff, M.D.
Cincinnati Children's Hospital
Cincinnati, OH 45229
m.steinhoff@gmail.com

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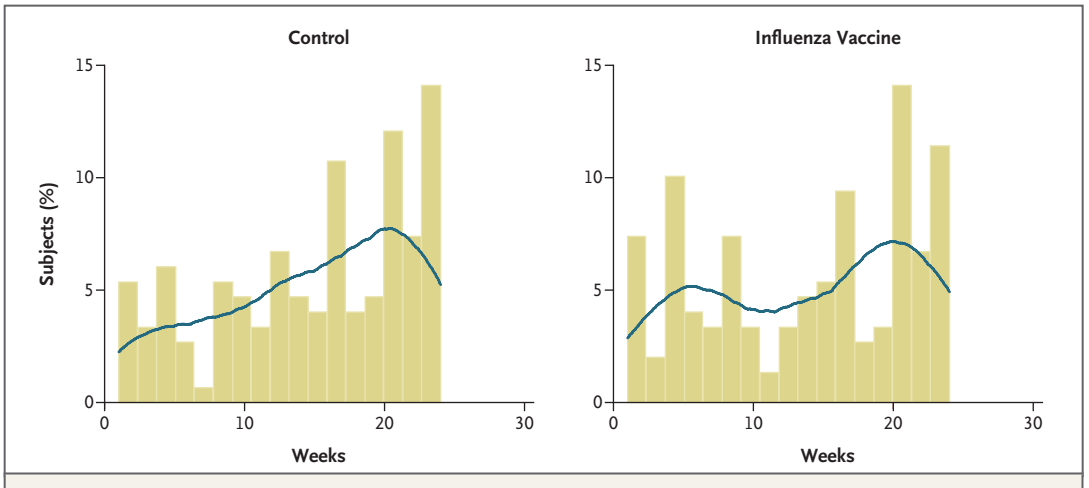

Figure 1. Distribution of the Mean Number of Weeks of Exclusive Breast-feeding.
The solid line represents the kernel-density estimation.

Uric Acid and Cardiovascular Risk

TO THE EDITOR: In their review of uric acid and cardiovascular disease, Feig and colleagues (Oct. 23 issue)[1] state that "it is worth noting that humans and apes have higher uric acid levels than most other mammals, since they lack the hepatic enzyme uricase, which degrades uric acid to allantoin." That is not entirely accurate. The uricase gene underwent mutational silencing during hominoid evolution in the Miocene epoch some 8 million to 24 million years ago, an event that was