

The Magic of Mother's Milk

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With the exception of the transmission of HIV and hepatitis viruses via breast milk, the myriad of benefits of breastfeeding are compelling. In a systematic review by Heinig and Dewey (1), breastfeeding for 6–12 months in developed countries is associated with a decrease in the incidence and/or severity of diarrhea, respiratory infections, otitis media, bacteremia, bacterial meningitis, botulism, urinary tract infection, and necrotizing enterocolitis in infants. Other possible beneficial effects of human milk are reported in such broad areas as sudden infant death syndrome, insulin-dependent diabetes mellitus, inflammatory bowel disease, other digestive diseases, lymphoma, allergic disease, cognitive development, and visual acuity (1). The SEARCH for Diabetes in Youth study reported that breastfeeding was protective in the development of childhood type 2 diabetes mellitus (T2DM) (2). For the infant, these beneficial effects may, in part, be derived from milk constituents that impact passive and innate immunity and protect the gastrointestinal tract through the action of the multiple and complex glycans, hormones including insulin (3,4), and mammary mRNAs (5,6) and microRNAs (7,8). The precise mechanism(s) by which these factors protect the health of the neonate are only now being slowly elucidated.

Breastfeeding is not only beneficial to the child but increasing evidence suggests that it is beneficial to the mother as well. Successful lactation improves maternal glucose tolerance (9), plasma lipid, and C-reactive protein values (10). Since a lactating woman transfers between 400 to 600 kcal per day to her infant, the obvious benefit is that lactating mothers lose more weight in the postpartum period than those who are not breastfeeding (11). However, a significant number of women fail to lose the weight they acquired during pregnancy and gain further weight with each successive pregnancy, increasing their risk of gestational diabetes mellitus (GDM) and subsequently impaired glucose tolerance and T2DM.

Lactation may have more far-reaching effects on maternal health than once thought. The Women's Health Initiative (139,681 postmenopausal women) reported a lower prevalence of hypertension, diabetes, hyperlipidemia, and cardiovascular disease with increasing duration of lactation,

and that women with a single live birth who breastfed for 7–12 months had a lower risk of cardiovascular disease (hazard ratio 0.72) than women who never breastfed (12). Breastfeeding for 3 or more months reduced the risk of T2DM, but breastfeeding for less than 1 month or not at all had no protective effects (13). McClure et al. reported that breastfeeding for more than 3 months was associated with a decrease in visceral fat 7-years postpartum in premenopausal women (14) and in a decreased carotid lumen diameter and adventitial diameter (15). From the U.S. Nurses' Health Study II (55,636 parous women), women who never breastfed their infants or curtailed lactation had an increased risk of hypertension compared with women who breastfed over 6 to 12 months per child (16). Finally, in the Nord-Trøndelag Health Study (HUNT2) in 1995–1997 (21,368 parous women aged 20–85 years), parous women aged 50 years or younger who had never lactated, compared with women who had lactated for 24 months or more over the course of their lives, had an increased risk for hypertension, obesity, and diabetes (17). Therefore, it would appear that breastfeeding is protective for the long-term health of the woman (Fig. 1).

In this issue of *Diabetes*, Ziegler et al. (18) report yet another association between breastfeeding and maternal health. Despite the retrospective nature of this study (and the others listed above), the investigators provide a number of intriguing observations that imply further support for the health benefit of lactation for mothers with GDM. It is not surprising that breastfeeding provided no protection from diabetes for those who were antibody-positive; this is most likely because of the ongoing autoimmune destruction of the β -cells. However, lactation for 3 or more months in those women with GDM who were antibody-negative afforded 10 additional years of protection from permanent diabetes. In addition, the effect again appeared to be dose dependent. We, as well as the authors, can only speculate on what aspect of breastfeeding might provide such a robust effect.

Several factors should be considered. First is the increased failure of women with GDM to lactate successfully that could not be controlled by diet alone. Based on the BMI of the women with GDM, one might assume similar degrees of insulin resistance, and thus women requiring exogenous insulin had less insulin secretory capacity. One might anticipate that exogenous insulin would improve metabolic control and facilitate lactation; however, we are unaware of clinical data suggesting that insulin treatment per se promotes successful lactation. The second issue is that of obesity alone. One might have anticipated that the decreased risk of developing diabetes would be linked to lactation-induced weight loss, but this is not the case. It is unlikely (although possible) that some factor(s) generated by the lactating mammary epithelial cells provides, in a dose-dependent fashion, a long-term beneficial effect on the development of diabetes and its associated metabolic complications.

However, it is likely that the Ockham's razor might be evoked here. In a meta-analysis of prepregnancy BMI and

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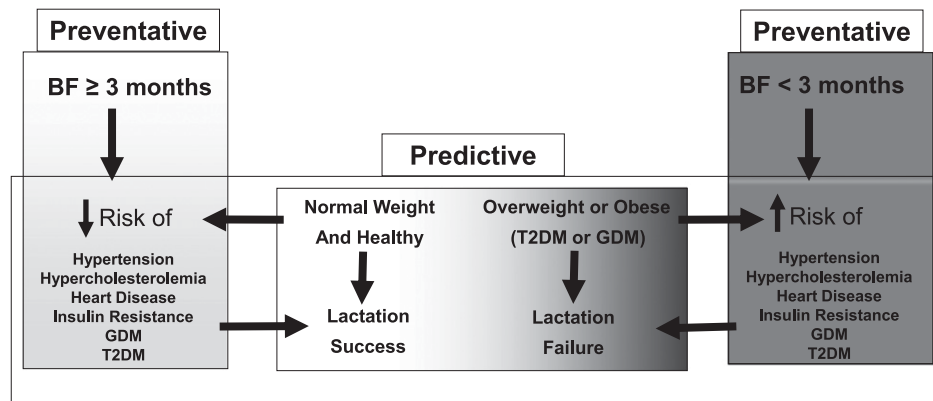


FIG. 1. Breastfeeding (BF) and women's health. This figure illustrates two potentially divergent models. In the preventative model (left panel), some factor(s) associated with breastfeeding ≥ 3 months lead to systemic effects resulting in reduction of long-term risks for obesity, cardiovascular disease, hypertension, and diabetes, whereas breastfeeding for < 3 months does not (right panel). An alternative model is the predictive model (horizontal panel), in which the mammary development and the hormonal, molecular, and metabolic events that permit initiation and/or sustenance of lactation are compromised by pre-existing conditions such as adiposity, inflammation, and insulin resistance. These pre-existing factors may place these women at higher risk for cardiovascular disease, hypercholesterolemia, hypertension, and diabetes, as well as lactation failure.

initiation and duration of lactation, Wojcicki (19) reported data from 13 studies (some excluding GDM and others including it) from which she concluded that overweight women have more difficulty in the initiation and persistence of lactation, and obese women have even greater difficulty. Thus, an alternative conclusion of the publication of Ziegler et al. (18) could be that successful breastfeeding, rather than being preventative, is predictive of a lower risk of future diabetes. We do not fully understand the effects of obesity (often associated with GDM) and the metabolic conditions associated with it—including GDM—on mammary development in girls, mammary epithelium development during pregnancy, and the initiation and maintenance of milk production. Therefore, the magic of mothers' milk will continue to be a focus of serious scientific investigation. Such studies should provide important clues as to the risk factors for diabetes in women and men as well as the factors that impact the initiation and maintenance of lactation in all women.

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