SUPPLEMENT

Introduction to Current Knowledge on Micronutrients in Human Milk: Adequacy, Analysis, and Need for Research

Lindsay H Allen and Daphna K Dror

US Department of Agriculture, Agricultural Research Service, Western Human Nutrition Research Center, Davis, CA

The WHO (1) recommends breast milk as the sole source of nutrients for infants during the first 6 mo postpartum and as an important source for ages ≥2 y. This recommendation is supported by evidence that feeding breast milk, rather than formula or other liquids and foods, reduces the risk of infant morbidity and mortality, supports better child development (2), and influences the development and modulation of the infant's immune system. Moreover, although it has been known for several decades that, in addition to nutrients, human milk contains hundreds of important bioactive factors, we are beginning to understand the mechanisms by which human-milk oligosaccharides, proteins, peptides, and other factors interact with the intestinal microbiome to protect the infant against infections (3–5).

Because breast milk is essential for optimal infant health and development, we need to ensure that the nutritional status and nutrient intake of the lactating mother are adequate to replace the large amounts of her own nutrients that she secretes in her milk, and to ensure that the nutrient concentrations in her milk are adequate to meet the requirements of her infant and young child. The nutrition and public health communities have paid relatively little attention to this issue. Commonly, the health care system switches its focus after parturition to the health and development of the infant, whereas the diet and nutritional status of lactating women receive attention only in the form of advice to breastfeed and, in some cases, to eat a healthy diet. There are few nutritional recommendations for lactating women. For example, the WHO only has recommendations for iron and folic acid supplementation during lactation: "Oral iron supplementation, either alone or in combination with folic acid supplementation, may be provided to postpartum women for 6–12 wk following delivery for reducing the risk of anemia in settings where gestational anemia is of public health concern" (6). The quality of evidence for this recommendation was considered low, and importantly, maternal intakes or status of iron and folate do not affect the amounts of these nutrients in breast milk.

It is perhaps not surprising that little systematic research has been directed at understanding the effects of maternal nutritional status and intake on the secretion of nutrients in human milk. There is an understandable reluctance to question the nutrient content of breast milk in the many population groups who consume poor-quality diets, because although the mother may be inadequately nourished, exclusive breastfeeding is even more important for infants in high-risk environments. In addition, we know that maternal undernutrition has relatively little adverse effect on either the volume of milk produced or its macronutrient composition. This is not the case for most micronutrients. For example, it has been recognized for several decades that poor maternal status or intake of vitamin B-12, vitamin A, iodine, and riboflavin reduces the milk concentrations of these micronutrients. More than a decade ago, we categorized micronutrients during lactation as group I (those whose concentrations in milk are affected by maternal status or intake) or group II (those unaffected by maternal status or intake) (7). Another limitation was that, until recently, methods for micronutrient analysis in human milk were relatively poorly validated, as were methods of milk sampling due to uncertainty about the influence of time during a feeding, circadian variation, and recent maternal supplementation, for example. Most micronutrients were measured individually, which made complete analysis tedious and expensive—and

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Address correspondence to DKD (e-mail: daphnadror@gmail.com).

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therefore uncommon—but more recently, analytical platforms such as MS, have enabled the simultaneous analysis of most of the B vitamins, for example, which greatly increases the potential for obtaining better data. As a result, accumulating evidence suggests that the current data on human-milk composition, which are used to set recommended intakes for lactating women and infants, are inadequate due to limitations in the number of women sampled, methods of milk collection and analysis, and lack of information about the nutritional status of the mother.

The series of articles in this supplement, which was commissioned by the Bill & Melinda Gates Foundation, provides an update of knowledge on micronutrients in human milk and factors affecting micronutrient concentrations. An overview article reviews current knowledge on fat- and water-soluble vitamins and minerals as well as macronutrients in breast milk, including changes over the course of lactation, and the influence of maternal intake, status, supplementation, and other factors on breast milk concentrations of each nutrient (8). This is followed by an article that summarizes and critiques the values and assumptions currently used to set recommended nutrient intakes for infants and lactating women by committees in the United States and Canada, the WHO, the United Kingdom, and Europe. It reveals the paucity of data available for setting these recommendations and shows differences and similarities in the milk concentration values used to set recommended intakes across agencies and the resulting differences in estimated nutrient requirements for infants and lactating women (9). The next article in this series evaluates the analytical methods that have been used to quantify vitamins and minerals in breast milk. Strengths and limitations of the methods, effects of the timing of sample collection, and methods of sample preparation and analysis are discussed and their influence on validity of results is assessed. Recommendations are made for optimal measurement conditions and methods for each of the micronutrients considered (10).

Systematic reviews were conducted to provide an update of the available data on 3 nutrients of public health importance whose concentration in breast milk is known to be affected by maternal status. For vitamin A, we describe time trends during lactation, the influence of maternal vitamin A status, and habitual or supplementary intake and other factors that affect breast milk retinol. Retinol concentrations expressed directly and relative to milk fat are explored to shed light on the physiology and regulation of retinol in breast milk and its implications for maternal and infant health (11). Similarly, the systematic review on vitamin B-12 in human milk describes our knowledge about trends over the course of lactation, maternal influences, and caveats concerning sample preparation and analytical methods that have been used to derive results reported in the literature. The article highlights the inadequacy of longitudinal data upon which to base maternal and infant intake recommendations (12). The systematic review on iodine integrates recently published results with previously reviewed data. Attention is drawn to the lack of consensus on optimal breast milk iodine concentrations and infant iodine intake requirements. Factors influencing the widely variable breast milk iodine concentrations are discussed (13).

This body of work leads to the obvious question of what is the "normal" concentration of each micronutrient in breast milk. This information is essential for improving micronutrient requirement recommendations for infants and lactating women. In addition, some recommendations for infants are extrapolated upward to provide estimates for young children. Until there is systematically collected and analyzed information on the range of concentrations in the milk of adequately nourished mothers, it is not possible to evaluate how low values are in samples from undernourished women. The final article therefore describes a proposal to establish reference values for micronutrients in human milk on the basis of the range of concentrations in samples collected by using consistent methods, from well-defined populations (adequately nourished but not consuming micronutrient supplements or highly fortified foods), and analyzed efficiently and accurately with newly developed methods. Much in the same way that we use growth reference charts, these reference values will provide a way to evaluate where and when micronutrient interventions are needed to improve the status of infants and lactating mothers and the efficacy and effectiveness of such interventions. They will also enable better estimates of the nutrient requirements of infants, young children, and lactating women.

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