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EDITORIAL

Breastfeeding and asthma: Where are we?☆

Asthma and atopic diseases are major public health problems worldwide.¹ Identifying modifiable factors associated with the pathogenesis of asthma, allergies, and eczema is important for developing targeted interventions for the prevention of these conditions, particularly among children at highest risk. The relation between breastfeeding and atopy has long been a subject of both interest² and debate.³ In describing a “golden jubilee of controversy” in 1988, Kramer proposed 12 methodological and biological criteria to evaluate studies of breastfeeding and allergy or asthma, including (but not limited to): non-reliance on late maternal recall of breastfeeding, duration and exclusivity of breastfeeding, strict diagnostic criteria of the outcome, ascertainment of severity, age of onset, and risk of the outcome; and assessment of dose-response effects.⁴

In the current issue of *Allergologia et immunopathologia*, Bjorksten et al. report a lack of association between breastfeeding and current wheeze, current rhinoconjunctivitis or current eczema among children of school age in Phase III of ISAAC (the International Study of Asthma and Allergy in Childhood).⁵ The authors noted an inverse association between breastfeeding and symptoms of severe rhinoconjunctivitis or severe eczema.⁵ The strengths of this study include its large global sample size (206,453 children from 32 countries including 103,716 children with complete data) from a school-based random sample⁶ as well as the extent to which the ISAAC questionnaires have been translated into multiple languages and validated around the world.^{7,8} The fact that the multivariable models included adjustment for maternal smoking during infancy is also important, as maternal smoking may modify any effects of breast feeding on risk of lower respiratory tract infections and asthma.^{9–12}

Unfortunately, several elements of the study design prevented the authors from definitively putting this controversy to rest. First, as mentioned by the authors, data on breastfeeding were limited to a yes/no response to the question “Was your child breast fed?” Such a limited ascertainment of breastfeeding precludes any ability to identify a dose-response or a threshold of exposure necessary to detect an

effect. Does exclusive breast feeding confer more protection compared to breastfeeding supplemented with formula? Is a specific duration (4 months being the standard in most studies) required for a beneficial impact? Perhaps. Second, family history of atopy was not included. As multiple studies have asserted^{13,14} there may be a differential effect of breastfeeding on the risk of developing asthma and/or allergies depending on whether or not the mother herself is atopic.

In a prospective birth cohort of 2602 children in Western Australia, exclusive breastfeeding for at least 4 months was associated with a decreased risk of asthma at age six years, regardless of maternal history of asthma.¹⁵ Data from over 4000 children in a prospective birth cohort in Sweden suggest that the association between breastfeeding and asthma was not as strong in those with a family history of allergic disease (OR 0.73, 95% CI 0.43–1.20) as in those without a family history (OR 0.58, 95% CI 0.38–0.88).¹⁶ In another study in Tucson, AZ, USA, breastfeeding was inversely associated with recurrent wheeze at age two years (regardless of maternal history of atopy) but positively associated with asthma at age 6 years among children with maternal history of asthma (asthma prevalence among those with: exclusive BF > 4 months = 46%, BF < 4 months = 23.5%, never BF 9.1%, $p < 0.005$).¹⁴ Furthermore, data from the same cohort show that at age 16 years, children of asthmatic mothers who were exclusively BF for >4 months had lower lung function on spirometry than those who were not BF.¹⁷ In contrast, the Isle of Wight prospective birth cohort showed that exclusive breastfeeding for >4 months was associated with increased lung function (higher FVC, FEV1, and peak expiratory flow rates) at age 10 years, regardless of maternal history of asthma and/or atopy.¹⁸

Why have there been such disparate findings across studies? What are the potential mechanisms that underlie both the protective effects of breastfeeding seen in some cohorts and the increased risk associated with breastfeeding demonstrated in others? The answers to these questions may depend on individual level factors rather than what can be assessed in large population-based observational studies. For example, data from intervention trials suggest that food allergen avoidance (including dairy, egg, nut, soy, etc.) by lactating mothers of children at high risk for

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atopy may reduce antigen exposure for those infants and thus be beneficial in reducing later risk of food allergy and atopic eczema.^{19,20} In addition, Verhasselt et al. found that compared to mice breastfed by unexposed mothers, mice breastfed by mothers with exposure to airborne allergen (ovalbumin) during lactation developed antigen-specific tolerance and reduced airway hyper-reactivity and allergic inflammation in response to ovalbumin challenge.²¹ In addition to effects of antigen exposure, investigators have looked at other aspects of breast milk composition. Studies focusing on long chain n-3 fatty acids (LCFA, which may have immunomodulatory effects) have found that maternal dietary intake has little impact on LCFA content in breast milk²²; that there are minimal differences in LCFA content of breast milk between allergic and non-allergic mothers^{23,24}; and that higher LCFA levels in breast milk may actually be associated with increased rather than decreased risk of atopy in high-risk infants.²⁴ From a methodological standpoint, some have argued that observational studies showing an increased risk of allergy among exclusively breastfed infants may be influenced by "reverse causation" (an increased tendency of mothers of high-risk children to exclusively breastfeed their children for longer duration because of well-publicised perceived protective benefits of breastfeeding).^{25,26}

Future studies in this field should include as detailed a prospective ascertainment of breastfeeding as possible (including information on exclusivity and duration), collection of breast milk for composition analysis (including antigens, immunological factors, and potentially toxic exposures), ascertainment of potential mediators of effects on asthma (including viral infections during early childhood and environmental tobacco smoke exposure)^{9–11} and clearly defined outcomes based on objective diagnostic criteria (e.g., allergy markers, lung function measures) Ongoing and future clinical trials of early versus delayed introduction of foodstuff during breast feeding should help elucidate the relation between breastfeeding and asthma or allergies.

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