

available orally administered selective pulmonary vasodilator, and the search goes on.

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Raed A Dweik

Department of Pulmonary and Critical Care Medicine,
Cleveland Clinic Foundation, Cleveland, OH 44195, USA
(e-mail: dweikr@ccf.org)

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Breast is best for preventing asthma and allergies—or is it?

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One of the major changes in thinking over the past decade has been the growing realisation of the importance of early life events in the development of many childhood and adult diseases, especially asthma and allergies. Genetic susceptibility certainly has a substantial role in determining who develops asthma, but is alone not sufficient. Environmental factors are clearly important and that they interact with genetic susceptibility is well accepted. However, this gene-environment model is not sufficient to describe the

initiation phase of a complex disease such as asthma; the developmental stage at which this interaction occurs is critical to outcome.¹ Both the physiological and immunological seeds for asthma that persist into adolescence and adulthood are determined by early life events. In particular the programming of aberrant pattern(s) of immunological memory specific for inhalant allergens, and inflammatory damage to lung and airway tissue occurring during the critical phase of growth in early childhood, have serious long-term consequences for the way lungs and airways function. One of the important exposures in early infancy is breastfeeding. Although it would take a brave paediatrician to argue against the benefits of breastfeeding, there is no consensus about whether breastfeeding protects against the development of asthma and allergies.

Exposing infants to food allergens, especially cows' milk protein in early life, has been claimed to increase the likelihood of developing atopy and asthma.² These views led to a number of studies, typified by those on the Isle of Wight pioneered by the late David Hide,³ which failed to demonstrate a convincing reduction in the prevalence of allergic sensitisation and asthma from dietary restrictions of infants, nursing mothers, or pregnant women. Similarly, the effects of breastfeeding on the risk of developing asthma and allergies are conflicting. Recent studies from birth cohorts in Perth³ and Tucson⁴ highlight this conflict. Oddy and colleagues,³ studying a community-based birth cohort of about 3000 children, reported that introduction of milk other than breastmilk before the age of 4 months increased the risk of wheezing outcomes. The non-breastfed infants had a 25% increased risk of doctor-diagnosed asthma at age 6 years (odds ratio 1.25, 95% CI 1.02–1.52), and a 30% increased risk of having a positive skin-prick test to at least one aeroallergen (1.30, 1.04–1.61). This cohort was recruited antenatally and not selected on any asthma, atopy, or respiratory variables.⁵ Breastfeeding had previously been reported to decrease the incidence of acute respiratory infections in early life, in particular those due to respiratory syncytial virus.⁶ In the Perth study at least half the protection against wheezing by breastfeeding could be attributed to fewer lower respiratory illnesses associated with wheezing in the first year of life. Such wheezing was a major risk factor for wheezing outcomes at age 6 in this population. But this factor did not explain all of the effect.⁷ Wright and colleagues,⁴ reporting from the Tucson cohort study (1246 people), showed that the relation between breastfeeding, asthma, and wheeze at age 13 years differed with the presence of maternal asthma and atopy in the child: atopic children with asthmatic mothers were more likely to have asthma if they had been exclusively breastfed in early life (8.7, 3.4–22.2), even after adjusting for confounders. This effect was seen whether the duration of exclusive breastfeeding was under or over 4 months, but was not seen in children from non-asthmatic mothers.⁴ There was no effect of paternal asthma on this relation.⁴ Like the Perth study,³ Wright and colleagues⁴ also showed that breastfeeding was associated with a lower prevalence of wheeze in the first 2 years of life (0.45, 0.2–0.9).

In today's *Lancet*, Malcolm Sears and colleagues report the long-term outcome of a longitudinal study of children born in Dunedin, New Zealand, in the early 1970s, and show an increased risk of asthma in children who were breastfed. Initially 1661 children were included in an intensive neonatal study⁸ and 1037 (91%) of 1139 eligible children at the age of 3 years were enrolled for

follow-up. The investigators classified children as being breastfed if feeding lasted at least 4 weeks and found that the 504 breastfed children were significantly more atopic at age 13 to several common allergens than the 533 non-breastfed children. Breastfeeding also significantly increased the likelihood of current asthma at age 9 years (10.8% *vs* 4.6%) and at 21 years (18.8% *vs* 13.4%). Defining children as being breastfed if they received any breastmilk (feeding for 8 or 12 weeks), the investigators found essentially the same results, which indicates that the length of breastfeeding was not an important determinant of outcome. Neither the prevalence of breastfeeding in the population nor a family history of asthma or atopy explained the increased risks of atopy and asthma in the breastfed children—ie, this is not an example of reverse causation. The fact that the increased risk of asthma occurred in children both with and without mothers with asthma contrasts with the Tucson study. There are no obvious reasons for this difference. The beneficial effects of breastfeeding on decreasing asthma at 6 years reported from the Perth cohort were not dependent on family history.

To date no plausible mechanism explains how breastfeeding could increase the risk of asthma. If this effect was only seen in infants fed by asthmatic mothers, one might speculate that some factor, or lack of some factor, passing to the child in breastmilk might be responsible. This concept would not, however, be consistent with the data presented by Sears and colleagues.

These studies highlight the difficulties facing patients and asthma researchers at present. The effect of breastfeeding on asthma and atopy is not consistent between studies and changes with the age of the child. Paediatricians are beginning to recognise at least three wheezing syndromes in children: transient infantile wheeze, viral-associated wheeze, and atopic asthma. Although these are distinguishable in epidemiological studies, the particular phenotype is not always apparent when faced with an individual wheezing child. The apparent protective effect of breastfeeding reported by Oddy and colleagues³ may relate more to viral-associated wheeze than to atopic asthma; however, the decreased risk of atopic sensitisation suggests that the results cannot be explained this simply. Although there are many valid reasons for encouraging breastfeeding during the first 4–6 months of life, based on the current evidence the prevention of asthma and allergies is not one of them.

*Peter D Sly, Patrick G Holt

Telethon Institute for Child Health Research and Centre for Child Health Research, West Perth 6872, Perth, Western Australia (e-mail: peters@ichr.uwa.edu.au)

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Will the Global Fund help roll back malaria in Africa?

Malaria imposes a profound burden on global public health and inhibits economic growth, particularly in sub-Saharan Africa where at least 90% of infections and deaths occur.¹ Commitment to malaria control has been renewed over the past 3 years through the establishment of the Roll Back Malaria (RBM) global partnership by WHO and its partner agencies.² RBM seeks to halve malaria deaths by 2010. More than 40 African heads of state endorsed this goal at the Abuja Malaria Summit in April, 2000, and set measurable interim targets.³

By the end of 2001, many malaria-endemic countries had developed plans to scale-up equitable access to key interventions for malaria prevention and management, largely through mechanisms that are already in place. Country-led RBM partnerships engage the public, the private sector, non-governmental organisations, community organisations, and donors.

The stage is set, but successful implementation will depend on a massive increase in funding to countries with the heaviest malaria burdens. Minimum packages should include the management of children at health clinics with artesunate-based combinations of antimalarial drugs, two presumptive doses of sulphadoxine/pyrimethamine to pregnant women, provision of insecticide-treated nets for pregnant women and their newborn children, and house-spraying in areas prone to epidemics. At least US\$1.3 billion each year is required to support basic commodities, the minimum package of essential supplies for the prevention and treatment of vulnerable groups. However, the amount for commodities in existing international support is insufficient.² The Global Fund to fight AIDS, Tuberculosis and Malaria (GFATM) seeks to redress this deficiency.^{4,5}

A key feature of the Fund is its potential to rapidly channel global resources to support individual country's programmes. By removing the constraints related to financing commodities, the fund should assist national programmes to move to national level implementation. The World Bank's adjustable programme loans, the various bilateral and multilateral grant programmes, and debt-relief mechanisms for highly indebted poor countries operate more slowly and generally address malaria only minimally, and many countries with well-developed RBM plans have not had ready access to these funds.

The GFATM appears to provide a novel and much-needed mechanism specifically for poor countries. This optimism was reflected in the large number of country applications generated by the first call for proposals in January, 2002. More than 300 proposals were received and 200 were evaluated by a Technical Review Panel. In April, 2002, US\$378 million was awarded by the Fund for 40 proposals from 31 countries.⁴ About 70% of this disbursement went to HIV/AIDS, 20% to tuberculosis, and only 10% to malaria. Proposals from six African countries were awarded only US\$14.3 million for antimalaria activities, representing US\$0.04–0.42 a head (panel). The funded plans are for a few at-risk communities or a single intervention. 18 other proposals (only Zambia's was for malaria) for US\$238 million were recommended for deferred funding. The total award for malaria in Africa is US\$22.7 million.

Over the lifetime of these malaria awards, African countries, which experience more than 90% of the global malaria burden, will have access to only 56% of the total global malaria resources made available by the GFATM.