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American Academy of Pediatrics recommendations on the Effects of Early Nutritional Interventions on the Development of Atopic Disease

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Abstract

Purpose of review—This article reviews the AAP's statement on early nutritional interventions on the development of atopic disease in infants and children.

Recent findings—Recent findings suggest that restriction of maternal diet during pregnancy and lactation does not play a major role in the development of allergic disease. In high risk infants exclusive breastfeeding for at least 4 months prevents or delays atopic dermatitis, cow milk allergy, and wheezing early in life. There is evidence that supplementing breastfeeding with a hydrolyzed formula protects against atopic disease, especially atopic dermatitis in at risk infants. Finally there is little evidence that delaying the introduction of complimentary foods beyond 4 to 6 months of age has any protective effect against allergy. There is insufficient data that any dietary intervention beyond 4 to 6 months of age has any protective effect against developing atopic disease.

Summary—In high risk infants there is evidence for exclusive breastfeeding for at least 4 months and delaying of complimentary foods until 4 to 6 months prevents the development of allergy. There is some evidence that supplementing hydrolyzed formulas in high risk infants may delay or prevent allergic disease. There is no convincing evidence that maternal manipulation of diet during pregnancy or lactation, use of soy products, or infant dietary restrictions beyond 4 to 6 months has any effect on the development of atopic disease.

Keywords

Atopic disease; breastfeeding; nutritional interventions; diet restrictions; allergy

Introduction

The incidence of atopic disease (asthma, eczema, allergic rhinitis, and food allergy) has significantly increased in recent history. In western societies serial prevalence studies have shown an increasing trend in the prevalence of childhood asthma and airway hyperresponsiveness [1]. Some estimates state that lifetime prevalence of atopic dermatitis in school children in western countries is now in the range of 10% to 20%. In the United States, the prevalence of asthma rose from 30.7 per 1000 in 1980 to 53.8 per 1000 in 1993–1994 [2]. Most of the available interventions include treating the diseases with medication or immunotherapy. This rise in disease incidence and prevalence affects patients, families, and clinicians.

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It is clear that there is a genetic as well as environmental basis for these diseases It has been postulated that early dietary intervention may influence atopic disease progression [3**]. This review describes the latest statement by the American Academy of Pediatrics (AAP) published in January of 2008 on early nutritional interventions on the development of atopic disease and the evidence that supports these suggestions. Specifically discussed will be the role of maternal diet restrictions during pregnancy, breastfeeding, timing of solid food introduction, and the use of hydrolyzed formula. Evidence published since that time will also be presented. The official AAP statement will be shown at the end of the review.

Dietary restrictions for pregnant and lactating women

There is no conclusive evidence for any dietary manipulations or restrictions in the pregnant women that will help prevent or delay atopic disease development in children [3**]. Previous AAP guidelines have suggested that pregnant mothers avoid peanut in their diet, since that time evidence has surfaced to the contrary. A Cochrane Review done is 2006 concluded that an antigen avoidance diet in high risk woman during pregnancy is unlikely to substantially reduce the risk of atopic diseases in the child (with the possible exception of atopic dermatitis) and that this kind of diet could have adverse repercussions on nutrition for both the mother and child [4]. In 2003 Lack et al. used data from the Avon Longitudinal Study of Parents and Children and found that in peanut allergic children there was no evidence of prenatal sensitization from the maternal diet, and peanut-specific IgE was not detectable in the cord blood [5]. There have been multiple studies showing evidence for and against an association between diet interventions during breastfeeding and allergy development [3**]. There are a large number of studies on this topic, but not all were randomized or included dietary restrictions during breastfeeding. These studies showed no significant impact on the development of allergic disease, especially when follow up was greater than 4 years. Muraro et al. in 2004 performed an extensive review of the available literature; they concluded that there was no convincing evidence for a preventive effect of maternal diet during pregnancy or lactation on preventing the development of atopic disease [6].

Role of human milk and exclusive breastfeeding on the development of atopic disease

The overall beneficial effects of breastfeeding an infant has been well documented, but its role in prevention of atopic disease is controversial. There is substantial evidence of the protective effect of breastfeeding on the development of asthma and wheezing in early infancy and childhood [7,8], but the evidence for its protective effect on other allergic disease is not as conclusive [9*]. The following section will review the evidence for the protective effect of breastfeeding for atopic dermatitis, asthma, and food allergy.

In 2001 Gdalevich et al. conducted a systematic review with meta-analysis of prospective studies that evaluated exclusive breastfeeding during the first 3 months after birth and atopic dermatitis. They found that exclusive breastfeeding during the first 3 months of life was associated with lower incidence of atopic dermatitis during childhood in children with a family history of atopy (infants with at least one first-degree relative [parent or sibling] with allergic disease), but this relationship did not hold true for those children without a family history of atopy [10]. There have been multiple studies that contradict the findings that breastfeeding for less than 4 months has any protective effect on the incidence of atopic dermatitis regardless of family history of atopy [11,12]. Kull et al. did show that exclusive breastfeeding for more than 4 months reduced the risk of atopic dermatitis at 4 years of age in children with a family history of atopy [12]. There has been data from the German Infant Nutritional Intervention (GINI) Program that also found that exclusive breastfeeding decreases the incidence of atopic dermatitis [13-15]. These results are from a prospective trial of a large number of children with

high risk of developing atopic disease. All of the children were enrolled in the study by 14 days of life and were exclusively breastfed at enrollment. The risk of atopic dermatitis in infants who were exclusively breastfed (OR 0.64; 95% CI 0.45-0.90) or breastfed and supplemented with a hydrolyzed (either partial or extensive) formula for at least 4 months (OR 0.53; 95% CI, 0.32-0.88) was significantly lower than those infants who were breastfed and supplemented with a cow milk based formula [13-15]. The same conclusion cannot be made for children not at high risk for allergic disease. In the non-interventional arm of the GINI Program (infants not at high risk of developing atopy) exclusive breastfeeding did not show a significant protective effect on atopic dermatitis compared with conventional cow milk formula [13].

The evidence for the protective effect of exclusive breastfeeding and asthma development is more controversial [3**]. Gdalevich et al. in 2001 found that in their meta-analyses the odds ratio for the protective effect of breastfeeding for the first 3 months of life was 0.70 (95% CI 0.60 to 0.81) and the effect was greater in studies of children with a family history of atopy (OR 0.52) than in studies of a combined population (OR 0.73) [7]. But in 2002 a Cochrane review concluded there was no benefit of exclusive breastfeeding beyond 3 months of age on the incidence of asthma in infants who were not pre-selected for high risk [16]. In a cohort study of children followed from birth to 13 years of life, Wright et al. found that exclusive breastfeeding was associated with protection against recurrent wheeze early in life, but for atopic children with asthmatic mothers, breastfeeding was associated with an increased risk of asthma and recurrent wheeze beginning at the age of 6 years [17]. Since the publication of the AAP's new statement more analysis has been done on the relationship between breastfeeding and later asthma and allergy outcomes by using data from the Avon Longitudinal Study of Parents and Children, a large birth cohort in the United Kingdom [9*]. They found that breastfeeding was protective for wheeze in the first 3 years of life, but not wheeze or bronchial hyperresponsiveness at ages 7 to 8 years [9*].

As with asthma, the relationship between breastfeeding and food allergy is not clear. In 2004 an analysis of published peer-reviewed observational and interventional studies found that feeding exclusively human milk for at least 4 months was associated with a lower cumulative incidence of cow milk allergy until 18 months of age [6]. But a Cochrane review (which included 1 study because it had a blinded challenge) from 2002 came to a different conclusion [16]. It stated that exclusive breastfeeding for 4 months did not protect against food allergy at 1 year of age [16]. The AAP could not make any firm conclusions about the role of breastfeeding and development of food allergy (except cow milk allergy) based on this evidence [3**].

Role of Hydrolyzed Formula on the development of atopic disease

Table 1 lists the commercially available hydrolyzed formulas in the United States. A Cochrane review from 2006 (which included 14 studies) concluded that there was no evidence to support feeding with a hydrolyzed formula for the prevention of allergy compared to exclusive breastfeeding, but in high risk infants who are unable to be completely breastfed, there was limited evidence that prolonged feeding with a hydrolyzed formula compared to a cow milk formula reduced the development of infant and childhood allergy [18]. After the publication of the latest AAP recommendations, it was found that scientific fraud had been committed in four of these trials and that these studies had to be excluded from the original Cochrane meta-analysis, but no changes have been made in their conclusions at this time [19]. In the interventional arm of the GINI Program (mentioned earlier) they found that the incidence of allergic manifestation was significantly reduced by using extensively hydrolyzed casein based formula compared with cow milk based formula (OR 0.51; 95% CI, 0.28-0.92), and the incidence of atopic dermatitis was significantly reduced by using extensively hydrolyzed casein based formula (OR 0.42; 95% CI, 0.22-0.79) and partially hydrolyzed whey formula (OR 0.56;

95% CI, 0.32-0.99) [15]. But the incidence of allergy overall with the other formulas was not as impressive as that of the extensively hydrolyzed casein based formula and the incidence of atopic dermatitis was not significantly reduced with extensively hydrolyzed whey based formula [15]. This data could indicate that the extensively hydrolyzed casein based formula is advantageous over the other formulas in preventing allergic disease, but this advantage may not be as abundant with partially hydrolyzed formulas. If atopic disease with cow milk allergy is present, partially hydrolyzed formulas are not recommended because they can contain cow milk proteins [3**]. The amino acid based formulas have not been studies in this area. A meta-analysis from 2004 concluded that feeding with a soy formula should not be recommended for the prevention of allergy in infants at high risk of developing atopic disease [20].

Role of the introduction of complementary foods on atopic disease

Since the publication of the last AAP recommendations on the introduction of complimentary foods in infants, new studies have been published that warranted a change in the statement. In 2004, Zutavern et al. enrolled 642 children before birth and followed them to the age of 5 ½ years [21]. They found was no evidence of a protective effect of late introduction of solids for the development of wheezing, atopy, or eczema; and there was no statistical evidence of feeding practices playing a different role in the development of asthma and eczema after stratification for parental asthma and atopy status [21]. The same author in 2006 found in an ongoing birth cohort study of 2612 infants no evidence supporting a delayed introduction of solids beyond the sixth month of life for the prevention of atopic dermatitis and sensitization [22]. They also could not rule out that delaying the introduction of solids for the first 4 months of life might offer some protection which has been seen in older studies [22,23]

The 2008 official statement from the American Academy of Pediatrics states [3**]:

1. At the present time, there is lack of evidence that maternal dietary restrictions during pregnancy play a significant role in the prevention of atopic disease in infants. Similarly, antigen avoidance during lactation does not prevent atopic disease, with the possible exception of atopic eczema, although more data are needed to substantiate this conclusion.
2. For infants at high risk of developing atopic disease, there is evidence that exclusive breastfeeding for at least 4 months compared with feeding intact cow milk protein formula decreases the cumulative incidence of atopic dermatitis and cow milk allergy in the first 2 years of life.
3. There is evidence that exclusive breastfeeding for at least 3 months protects against wheezing in early life. However, in infants at risk of developing atopic disease, the current evidence that exclusive breastfeeding protects against allergic asthma occurring beyond 6 years of age is not convincing.
4. In studies of infants at high risk of developing atopic disease who are not breastfed exclusively for 4 to 6 months or are formula fed, there is modest evidence that atopic dermatitis may be delayed or prevented by the use of extensively or partially hydrolyzed formulas, compared with cow milk formula, in early childhood. Comparative studies of the various hydrolyzed formulas have also indicated that not all formulas have the same protective benefit. Extensively hydrolyzed formulas may be more effective than partially hydrolyzed in the prevention of atopic disease. In addition, more research is needed to determine whether these benefits extend into late childhood and adolescence. The higher cost of the hydrolyzed formulas must be considered in any decision-making process for their use. To date, the use of amino acid based formulas for atopy prevention has not been studied.

5. There is no convincing evidence for the use of soy based infant formula for the purpose of allergy prevention.
6. Although solid foods should not be introduced before 4 to 6 months of age, there is no current convincing evidence that delaying their introduction beyond this period has a significant protective effect on the development of atopic disease regardless of whether infants are fed cow milk protein formula or human milk. This includes delaying the introduction of foods that are considered to be highly allergic, such as fish, eggs, and foods containing peanut protein.
7. For infants after 4 to 6 months of age, there are insufficient data to support a protective effect of any dietary intervention for the development of atopic disease.
8. Additional studies are needed to document the long term effect of dietary interventions in infancy to prevent atopic disease, especially in children older than 4 years and in adults.

Conclusion

The latest AAP statement has significant changes from previous reports. The current statement is more similar to past and current reports from European professional groups [24*]. The latest report avoids making recommendations and instead gives statements presented with the evidence of its efficacy [24*]. The lack of data for some of the interventions studied does not indicate that the approach is disproven; rather it means more research is needed to clarify whether or not these have an effect on the development of atopic disease.

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** Of outstanding interest

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