Most group 1 children (96%) demonstrated sensitization \( \text{in general}, \) but this difference was not significant. The food-sensitized groups required more medication, higher rates of hospitalization and steroid medication use. The food-sensitized groups were associated with the highest specific IgE levels. Patients who were sensitized to at least one food had sensitization to foods and sensitization to aeroallergens, correlating with sensitization to soy, wheat, and peanut. Forty-five percent of study patients were sensitized to at least one food (groups 1–3): 4% of the participants were categorized to group 1, 26% to group 2, and 14% to group 3. Fifty-five percent were not sensitized to any of the 6 foods (group 4). Food allergy to egg and peanut were associated with the highest specific IgE levels. Patients who were sensitized to at least one food had higher rates of hospitalization and steroid medication use. The food-sensitized groups required more medications in general, but this difference was not significant. Most group 1 children (96%) demonstrated sensitization to >1 food, with 25% of the patients sensitized to all 6 foods tested. Most group 2 patients (75%) and 19% of group 3 patients were sensitized to multiple foods. There was a significant increase in hospitalizations for asthma in children sensitized to >1 food. When specific foods were examined, a correlation between higher asthma morbidity and sensitization to fish or soy was noted.

**RESULTS.** There was a significant correlation between sensitization to foods and sensitization to aeroallergens, with sensitization to the highest number of aeroallergens correlating with sensitization to soy, wheat, and peanut. Forty-five percent of study patients were sensitized to at least one food (groups 1–3): 4% of the participants were categorized to group 1, 26% to group 2, and 14% to group 3. Fifty-five percent were not sensitized to any of the 6 foods (group 4). Food allergy to egg and peanut were associated with the highest specific IgE levels. Patients who were sensitized to at least one food had higher rates of hospitalization and steroid medication use. The food-sensitized groups required more medications in general, but this difference was not significant. Most group 1 children (96%) demonstrated sensitization to >1 food, with 25% of the patients sensitized to all 6 foods tested. Most group 2 patients (75%) and 19% of group 3 patients were sensitized to multiple foods. There was a significant increase in hospitalizations for asthma in children sensitized to >1 food. When specific foods were examined, a correlation between higher asthma morbidity and sensitization to fish or soy was noted.

**CONCLUSIONS.** Food sensitization correlated with increased asthma severity in the study population. The prevalence of food allergy was not determined because of the nature of the study (anonymous serum samples and lack of blinded food challenges); however, on the basis of the study results, the authors predicted that inner-city children with asthma were more likely than the general population to have food allergy. The association of increased asthma morbidity with at least 1 food sensitization, and findings that patients with sensitization to multiple foods had significantly more asthma morbidity than those with single-food sensitization, suggest that food sensitization is a marker for increased asthma severity.

**REVIEWER COMMENTS.** This study suggests that the prevalence of food sensitization, and possibly food allergy, is increased in patients with asthma and may be a useful marker for increased asthma severity. Health care providers should consider screening for food sensitization in patients with severe or poorly controlled asthma.

**Risk of Celiac Disease Autoimmunity and Timing of Gluten Introduction in the Diet of Infants at Increased Risk of Disease**


**POURPOSE OF THE STUDY.** Patients with HLA-DR3 or DR4 alleles are at increased risk for the development of celiac disease. However, not all genetically susceptible individuals develop celiac disease. The objective of this study was to investigate whether there was an association between the timing of exposure to gluten and subsequent development of celiac disease autoimmunity (CDA) in children with a genetic predisposition for celiac disease.

**STUDY POPULATION.** Children \( (n = 1560) \) were identified in the Denver, Colorado, metropolitan area with an increased risk for celiac disease (or type 1 diabetes), defined as having either a first-degree relative with type 1 diabetes or positive cord blood screening for HLA-DR3 or DR4 alleles. This study was conducted over 10 years with a mean follow-up of 4.8 years.

**METHODS.** This was a prospective, observational study. Infant diet data were collected during telephone or face-to-face interviews at 3, 6, 9, 12, and 15 months of age. No dietary advice was given to the families. Children had blood drawn at 9, 15, and 24 months and annually thereafter for the measurement of the celiac disease autoantigen, and tissue transglutaminase (tTG). After 1 or 2 positive tTG autoantibody results, small-bowel biopsy was offered to the families, although not all had this procedure performed. The primary outcome of the study was the time to development of CDA defined as the presence of tTG autoantibodies on 2 consecutive results or a positive small-bowel biopsy after a single tTG-positive test.

**RESULTS.** Fifty-one children developed CDA. Children exposed to foods containing wheat, barley, or rye in the first 3 months of life had a 5 times increased odds ratio \( (P = .02) \) of CDA as compared with children first exposed to gluten at 4 to 6 months of age. Twenty-five of the CDA-positive children had biopsy-proven celiac disease. In these children, exposure to gluten in the first 3 months of life had a 23 times increased risk \( (P = .001) \) of CDA. In the biopsy-proven cohort, children not exposed to gluten until >7 months of age also had a significantly increased risk of CDA (odds ratio: 4; \( P = .04 \)). There was...
no association between the development of CDA and the timing of introduction of oats or rice. No protective effect of breastfeeding was found with the development of CDA. Although all children in the cohort were exposed to gluten by 12 months of age, the first positive tTG autoantibody test did not occur until 2 years of age, with a mean age of positive conversion of 4.7 years.

CONCLUSIONS. In children at increased risk of developing celiac disease, timing of gluten exposure in the diet is associated with the appearance of CDA. Exposure to gluten in the first 3 months of life is thought to be associated with increased risk because of immature or incomplete intestinal barrier function. The authors speculate that late gluten exposure may have been associated with CDA because of greater amounts introduced in the older infants.

REVIEWER COMMENTS. It is important to understand that this study population was specific children with genetic and family history characteristics at increased risk for the development of celiac disease and may not be generalizable to the entire population. Mean follow-up of this population was just under 5 years, and long-term follow-up of these patients is needed to determine if earlier exposure to gluten simply leads to earlier appearance of CDA and that many (if not all) exposed at-risk children would eventually develop CDA. This study also does not address the relationship between CDA and celiac disease.

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A National Prospective Study on Childhood Celiac Disease in the Netherlands 1993–2000: An Increasing Recognition and a Changing Clinical Picture


PURPOSE OF THE STUDY. To investigate whether the incidence of diagnosed celiac disease (CD) is increasing in the Netherlands and whether the clinical presentation is changing.

STUDY POPULATION. Children between the ages of 0 and 14 years with newly diagnosed cases of CD from 1993–2000.

METHODS. Diagnosis of CD was based on biopsy of the small intestine. The following data were collected: age, gender, weight, height, and aspects of the presenting clinical picture.

RESULTS. The overall crude incidence rate for CD from 1993–2000 was 0.81 per 1000 live births. There was a significant linear increase of the crude incidence from 1993–2000. During the period of 1993–2000 there was a significant increase in the diagnosis of CD with partial villous atrophy of the small-bowel mucosa and a relative decrease in the diagnosis with subtotal villous atrophy. Fewer children are presenting with abdominal distention, chronic diarrhea, and failure to thrive, and more children are presenting with weight <10th percentile, abdominal pain, and lassitude.

CONCLUSIONS. The increase in newly diagnosed cases of CD seems to represent greater awareness of the disease and the availability of serologic tests. The increase in the number of children with CD diagnosed with small-bowel biopsy specimens showing partial villous atrophy suggests increased recognition of milder cases.

REVIEWER COMMENTS. In the United States, CD now seems to affect ~0.5 to 1.0% of the population (10 times higher than previous estimates). In the past, diagnosis of CD has taken an average of 10 years. Serologic screening (eg, tissue transglutaminase immunoglobulin A antibodies) should be considered for children with symptoms of diarrhea, abdominal cramping, pain, and distention as well as short stature and delayed puberty; individuals with Down syndrome or type 1 diabetes mellitus; and first-degree relatives of patients with biopsy-proven CD. Positive serologic tests should be followed up by small-bowel biopsy. Increased awareness of CD allows earlier diagnosis and institution of a gluten-free diet.

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ATOPIC DERMATITIS

Long-term Treatment of Atopic Dermatitis With Pimecrolimus Cream 1% in Infants Does Not Interfere With the Development of Protective Antibodies After Vaccination


PURPOSE OF THE STUDY. To examine if pimecrolimus 1% cream in the treatment of atopic dermatitis would have any effect on vaccinations.

STUDY POPULATION. A total of 91 children with mild-to-severe atopic dermatitis (AD), aged 3 to 23 months at enrollment.

METHODS. Children were enrolled in a 1-year double-blind study (76 children received pimecrolimus, and 15 children received placebo). All 91 children were enrolled in a 1-year open-label extension study of pimecrolimus 1% cream. Patients were treated with either pimecrolimus...
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