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 IgG 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...
1% cream or placebo for initial symptoms, and more potent topical corticosteroids were used for flares not prevented by pimecrolimus 1% cream. Patients were vaccinated at normal scheduled times (4 doses of tetanus and diphtheria and 1 or 2 doses of measles and rubella). Response was evaluated at months 18 and 24 of the 2-year period.

RESULTS. The seropositivity rates of 93.6% for tetanus, 88.6% for diphtheria, 88.5% for measles, and 84.4% for rubella were comparable with those reported in the literature. Seropositivity was not significantly affected by the use of pimecrolimus at the time of vaccinations (+28 days). These seropositivity rates were within the ranges of 87% to 100% for tetanus, 83.3% to 99.3 for diphtheria, 60.5% to 97.1% for measles, and 55.6% to 88.1% for rubella, similar to those reported in age-matched pediatric populations.

CONCLUSION. Topical pimecrolimus in the treatment of atopic dermatitis had no effect on the response to routine childhood vaccination.

REVIEWER COMMENTS. Topical pimecrolimus, similar to topical tacrolimus (J Am Acad Dermatol. 2005;53[2 suppl 2]:S206–S213), had no effect on routine childhood vaccination. These topical calcineurin inhibitors did not affect basic B-cell function as measured by postvaccination titers.

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Efficacy and Safety of Tacrolimus Ointment Treatment for up to 4 Years in Patients With Atopic Dermatitis

PURPOSE OF THE STUDY. This study was designed to evaluate the long-term safety and efficacy of 0.1% tacrolimus ointment in adult and pediatric patients with atopic dermatitis (AD).

STUDY POPULATION. A total of 408 adult and 391 pediatric patients with moderate-to-severe AD who had participated in a previous clinical trial of tacrolimus ointments. The pediatric patients were from 2 to 15 years of age (185 patients aged 2–6 years, and 206 patients aged 7–15 years), and 93.5% of the patients had severe AD.

METHODS. Tacrolimus ointment 0.1% was applied twice daily either intermittently or continuously to the affected areas. Efficacy and safety assessments included percent body surface area affected, Eczema Area and Severity Index score, individual signs of AD, and the incidence of adverse events. Patients were treated for a range of 1 to 1186 days (median: 982 days). A total of 37.5% of the patients in the study were treated for >3 years.

RESULTS. Improvements in efficacy parameters were observed within 1 week of treatment and continued for the duration of the study. Common adverse events included skin burning, pruritus, skin infection, skin erythema, flu-like symptoms, and headache. The incidence of adverse events, including cutaneous infections, did not increase with time on treatment.

CONCLUSION. Tacrolimus ointment therapy is a rapidly effective and safe treatment for the management of AD in pediatric and adult patients for up to 4 years.

REVIEWER COMMENTS. This study shows no long-term adverse effects of this topical calcineurin inhibitor in the treatment of AD. Most patients had >2½ years of treatment without increase in the number or incidence of infections. If these drugs were systemically immunosuppressive, the number of cutaneous or systemic infections would have been expected to increase.

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Efficacy and Tolerability of Pimecrolimus and Tacrolimus in the Treatment of Atopic Dermatitis: Meta-analysis of Randomised Controlled Trials

PURPOSE OF THE STUDY. To determine the efficacy and tolerability of topical pimecrolimus and tacrolimus compared with other treatments for atopic dermatitis.

METHODS. Randomized, controlled trials of topical pimecrolimus or tacrolimus reporting efficacy outcomes or tolerability from the Cochrane Library, Medline, and Embase were identified. Eligible trials were evaluated for efficacy, identified as investigators’ global assessment of response; patients’ global assessment of response; proportions of patients with flares of atopic dermatitis; and improvements in quality of life. Trials were also evaluated for tolerability, identified as overall rates of withdrawal, withdrawal resulting from adverse events, and proportions of patients with burning of the skin and skin infections.

RESULTS. A total of 4186 of 6897 participants in 25 randomized, controlled trials received pimecrolimus or tacrolimus. Both drugs were significantly more effective than a vehicle control. Tacrolimus 0.1% was as effective as potent topical steroids at 3 weeks and more effective than combined treatment with hydrocortisone butyrate 0.1% plus hydrocortisone acetate 1% at 12 weeks (num-
Long-term Treatment of Atopic Dermatitis With Pimecrolimus Cream 1% in Infants Does Not Interfere With the Development of Protective Antibodies After Vaccination

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