The food blamed for fatal reactions was catered (18), domestically prepared (6), packaged/labeled (16), sold loose/unlabeled (2), whole nuts (3), and unknown (3). Fourteen patients were thought not to have been avoiding the culprit food; avoidance was graded as casual for 16, careful for 7, extremely careful for 6, and unknown for 5. Even with the most diligent avoidance, lapses occurred during festive eating, foreign travel, or when distracted by disruption to routine. Just as much as they need to recognize foods that will cause them to react, patients should be made aware of these potentially dangerous circumstances and be supported in assessing them and in developing appropriate coping strategies with increased vigilance in hazardous situations.

Deaths typically occurred in those whose previous reactions had been mild, which supports the concept that severity of subsequent reactions cannot be predicted from the reaction history.4,5 Contrary to previous recommendations,6 1 fatality was supported upright after she lost consciousness; most patients died from respiratory arrest. Data from the first 7 years of the registry suggested that overuse of salbutamol, lack of daily inhaled steroid, and asthma exacerbation might be associated with fatal food reactions. The pattern has been similar in the second 7 years: 43/48 took daily treatment for asthma, and 3 were known to avoid inhaled steroids. The state of health on the day of death is known for 32: 10 had varying degrees of asthma exacerbation leading up to the fatal reaction, which suggests this may be a cofactor for severity. In a few cases, a flare-up of eczema or ill-defined malaise may have signified a change in cytokine levels predisposing to a severe reaction.7 We conclude that patients with a food allergy should take extra care if they feel unwell.

We think over half of those dying had had no professional advice about their food allergy; a few we think had been poorly advised. Improved education of patients with food allergies, their caregivers, doctors, and the food industry might help prevent deaths.

We conclude that the effectiveness of self-injectable epinephrine cannot be guaranteed and should not be relied on; moreover, most of those patients dying had such trivial previous reactions they would have had little motivation to carry a pen or to remember how to use it. After adoption of a properly informed allergen avoidance strategy and optimal daily asthma management, patient alertness to additional risk factors may be the most important component of managing food allergy.

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Probiotics during the first 7 years of life: A cumulative risk reduction of eczema in a randomized, placebo-controlled trial

To the Editor:

Innate immunity represents a front line protection against invading pathogens, functioning as a microbe sensor. For that task, the mucosal lining in the gastrointestinal tract senses molecular patterns shared by pathogens and nonpathogenic commensal microbes. Toll-like receptors act as transmembrane signaling receptors whose activation by pathogens triggers signaling pathways leading to production of inflammatory cytokines. In contrast, commensals in the healthy gut have been shown to use several different mechanisms to turn the same signaling cascades down. Indeed, a recognition of commensal gut microbiota by Toll-like receptors is a sine qua non for intestinal homeostasis and prevention of allergic inflammation.1,2 These data together suggest that control of inflammatory responses by nonpathogenic stimuli during early critical developmental stages may have a long-term beneficial effect on health. In accordance with the gut microbiota hypothesis of atopic disease,3 we have recently shown that perinatal probiotic supplementation reduced significantly the incidence of eczema at 2 and 4 years of life in at-risk children.4,5

To evaluate the cumulative effect of the probiotic intervention during the first 7 years of life, we re-examined the study cohort at the age of 7 years. The original study design has been described in detail elsewhere.4 Briefly, 159 mothers were randomly assigned to receive 2 capsules of placebo (microcrystalline cellulose) or 1 × 1010 colony-forming units of Lactobacillus rhamnosus strain GG (ATCC 53103; Valio Ltd, Helsinki, Finland) daily for 4 weeks before expected delivery. After delivery, capsules were taken postnatally for 6 months. Altogether, 132 of 159 (83%) children completing the 2-year follow-up were invited to the 7-year follow-up visit. The invitation
The letter included a questionnaire concerning possible allergic symptoms and medications during the previous 3 years. The diagnosis of eczema was made in a blind fashion on the basis of both a questionnaire and a clinical examination. In particular, diagnosis of eczema was confirmed if there had been pruritic eczematous lesions with typical location and with relapsing or chronic course during the last 12 months; that of allergic rhinitis with nasal discharge, blockage, sneezing, and itching related to allergen exposure and sensitization; and that of asthma if a child had been qualified by the Social Insurance Institution of Finland for a special reimbursement for asthma medication. Skin prick tests to cow’s milk, egg white, wheat flour diluted 1/10 (wt/vol) with 0.9% (wt/vol) sodium chloride, gliadin diluted 1/1000 (wt/vol) with 0.9% (wt/vol) sodium chloride, cod, soya bean, hazel nut, peanut, birch, mugwort, alder, 6 local grasses, cat, dog, and Dermatophagoides pteronyssinus allergen Der p 1 (ALK-Abelló, Horsholm, Denmark), and latex (Stallergens, Marseille, France) were conducted as previously described. A test was considered positive if a wheal of 3 mm or larger was observed in response to any of the allergens in the presence of an appropriate response to the positive control (10 mg/mL histamine dihydrochloride; ALK-Abelló) and no response to the negative control (allergen diluent; ALK-Abelló).

The incidence of atopic diseases in the Lactobacillus GG group was compared with that in the placebo group using the relative risk estimate (RR). The χ² test was used to compare the proportions. The proportions of children without eczema at the age of 2, 4, and 7 years were given as Kaplan-Meier curves. The log-rank test was used to compare the curves. Cox regression analysis was used to compare the groups with respect to diagnosis of eczema. In these 2 analyses, we included all children who completed the 2-year follow-up (n = 132). Subjects who withdrew prematurely without eczema from the study were treated as censored cases. The results are given as odds ratios with 95% CIs.

The 7-year follow-up was completed by 116 of 159 (73%) children, 62 of 82 (76%) in the placebo and 53 of 77 (69%) in the Lactobacillus GG group. The cumulative risk for developing eczema during the first 7 years of life was significantly lower in the Lactobacillus GG group than in the placebo group (42.6% vs 66.1%; RR, 0.64; 95% CI, 0.45-0.92) in the group of children completing the 7-year follow-up. According to Cox regression, the risk of eczema was significantly reduced in the Lactobacillus GG group compared with the placebo group (odds ratio, 0.58; 95% CI, 0.35-0.94; P = .027). The proportions of children without eczema at the ages of 2, 4, and 7 years are presented in Fig 1. Skin prick test reactivity at 7 years of age was detected in 35 of 109 (32%) children. The overall frequencies were comparable between the placebo group, 19 of 57 (33%), and the Lactobacillus GG group, 16 of 52 (31%; RR, 0.92; 95% CI, 0.53-1.60). The majority of the children (23/35 [66%]) reacted to at least 2 different antigens. The most common antigens to give positive reactions in skin prick tests were birch (18/35), cat (17/35), alder (16/35), and local grasses (11/35). There were 17 of 116 (15%) cases of allergic rhinitis (6 cases in the placebo and 12 cases in the Lactobacillus GG group; RR, 2.30; 95% CI, 0.93-5.70) and 12 of 116 (10%) cases of asthma (3 cases in the placebo and 9 cases in the Lactobacillus GG group; RR, 3.44; 95% CI, 0.98-12.1) at 7 years of age.

We demonstrated here that the overall risk for developing eczema during the first 7 years of life was significantly decreased in the Lactobacillus GG group in accordance with our earlier findings with shorter follow-up. Allergic rhinitis and asthma tended to be more common in the probiotic group, calling for further studies in other populations and with other probiotic strains designed for this target to scrutinize the issue. Again, the frequency of atopic sensitization was similar between the groups, suggesting that the preventive effect on eczema was not IgE-mediated.

Indeed, the role of atopic sensitization in childhood eczema remains obscure. It is neither a prerequisite nor a uniform cause of the disease. Consequently, the term eczema (instead of atopic eczema) has been used to describe skin pathology of the study according to the World Allergy Organization nomenclature committee’s recommendations and further supported by novel findings. Moreover, we invite revisitation of original theory of eczema as a skin barrier dysfunction defect leading to atopic sensitization to environmental antigens. A recent study demonstrated that 2 loss-of-function mutations of the epidermal barrier protein filaggrin are major predisposing factors for atopic eczema, suggesting the importance of normal skin barrier function in the prevention of both eczema and atopic sensitization. The issue may also hold true for the gut barrier function. We have earlier shown that antigen transfer through the gut mucosal barrier is increased in children with atopic eczema. Our previous studies further demonstrate that alterations in the gut microbiota, an essential component of the gut mucosal barrier, precede atopic sensitization. Indeed, restoration of the gut barrier function has been taken as a target in probiotic interventions, offering a potential mechanistic...
Letters to the Editor

Characterization of allergens from the fish bait Galleria mellonella

To the Editor:

Larvae of insects and worms used as live fish bait can be a cause of allergy in amateur fishers and occupationally exposed workers. Asthma, rhinitis, and contact urticaria have been associated with exposure and sensitization to Galleria mellonella larvae (bee moth) in anglers and breeders.1-4 Villalta et al5 described that bee moth’s allergenic proteins are thermolabile, and their presence depends on the stage of the larval development, the bee moth’s hemolymph being the most likely source.

We report on a 49-year-old amateur fisher with a history of smoking and a fixed-drug eruption to tetracycline. In the previous 4 years, he had experienced several acute episodes of sneezing, nasal itching, watery nose, and tearing. During the previous year, he had also developed exercise-induced asthma. He employed only bee moth as bait. His symptoms were so bothersome that he had to stop fishing on some occasions, but he took no medications.

Physical examination and blood tests results were normal. Total serum IgE concentration was 152 IU/mL. Skin prick tests with common Aeroallergens were positive to grass pollen. A skin prick test was performed by puncturing the live wax moth larvae and then pricking the subject’s skin with the same lancet (“prick-by-prick” technique). A positive skin response (15-mm diameter wheal) was obtained in the patient, whereas it was negative in 10 healthy control subjects not exposed to the bee moth.

Spirometry was normal. Because of the possible exercise-induced asthma, a methacholine inhalation test was performed, which showed no airway hyperresponsiveness (PC20 > 16 mg/mL). Induced sputum was obtained and analyzed by flow cytometry as previously described.5 At baseline, induced sputum showed 1.14% eosinophils, 53.35% neutrophils, 1.13% lymphocytes, 42.62% macrophages, 0.02% eosinophilic precursors, and 0.70% activated basophils. Real-time polymerase chain reaction in induced sputum cells (Applied Biosystems, Foster City, Calif) revealed relative mRNA expression of IL-5 (0.47), IL-10 (0.47), IL-11 (1.22), IL-13 (0.36), and vascular endothelial growth factor (VEGF) (1.13). mRNA values were normalized with rRNA gene used as endogen.

Specific inhalation challenge (SIC) with wax moth extract was performed as previously described6 in the patient and in 1 control nonatopic subject after obtaining written informed consent. The starting concentration for SIC was that eliciting a 3-mm wheal by end-point skin titration (0.01% weight/volume [wt/vol]). FEV1 was then measured at 30 seconds, 5 minutes and 10 minutes after inhalation of the extract. Then, the extract concentration was duplicated until an FEV1 fall of 20% or greater in the first 60 minutes was obtained. Rhinorrhea, tearing, and sneezing together with a 20% fall in FEV1 was observed 30 minutes after the challenge (2.5% wt/vol). Subsequently, FEV1 was monitored with a computerized asthma monitor (AM1 Jaeger, Hoechberg, Germany) every hour for the following 24 hours, and no late asthmatic response was obtained. SIC was negative in the control subject.

Twenty-four hours after SIC, bronchial hyperresponsiveness to methacholine increased (PC20, 3.5 mg/mL) only in the patient. The development of bronchial hyperresponsiveness to methacholine after SIC may explain why the patient experienced exercise-induced asthma, which may be related to recurrent exposures to bee moth when fishing.

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