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Dr. Paina is a consulting allergist & clinical immunologist in Kitchener, Ontario. She completed her residency in Paediatrics at McMaster University in Hamilton and her fellowship in Clinical Immunology and Allergy at University of Manitoba in Winnipeg. She has a MS in Medical informatics and Biostatistics from University of Medicine and Pharmacy Cluj-Napoca, Romania. Between 2017 and 2018 she acted as Chief Fellow for the Distributed Academic Half Day for six Clinical Immunology & Allergy training programs in Vancouver, Winnipeg, London, and Halifax. In 2016, she was granted an award from the Canadian Society of Allergy and Clinical Immunology for her research abstract on Nasal Polyps & Biomarkers in Children with Cystic Fibrosis. Dr. Paina's recent clinical and research interests are focused on food allergy and eczema in children. She has authored and coauthored posters, synopsis, and abstracts on food allergy prevention for scientific meetings in Canada and USA.

UNDERSTANDING, PREVENTING AND MANAGING FOOD ALLERGY IN PRESCHOOL CHILDREN: PART 1

This 3-part series will discuss food allergy prevention in preschool children through early nutrition and eczema management. In Part 1, the prevalence of food allergy along with factors contributing to its rise and its impact on quality of life are presented. Part 2 in this series will examine the topic of food allergy prevention through early infant nutrition and early management of eczema. Finally, in Part 3, we will focus on adverse food reactions in children, symptoms of immunoglobulin E (IgE)-mediated food allergy in preschool children, food-specific IgE testing and management of food allergy.

PREVALENCE OF FOOD ALLERGY IN CHILDREN

The incidence of allergic diseases has increased, especially in children.[1] Food allergy is one of the most common chronic and potentially life-threatening conditions during childhood. While food-related anaphylaxis remains an uncommon cause of death and its prevalence varies according to the definition used, a significant proportion of these deaths are preventable.[2]

Food allergy is a public health concern, especially in an urbanized world, with increasing emergency department visits and hospitalizations for food-induced anaphylaxis events (**Figure 1**).[1,2]

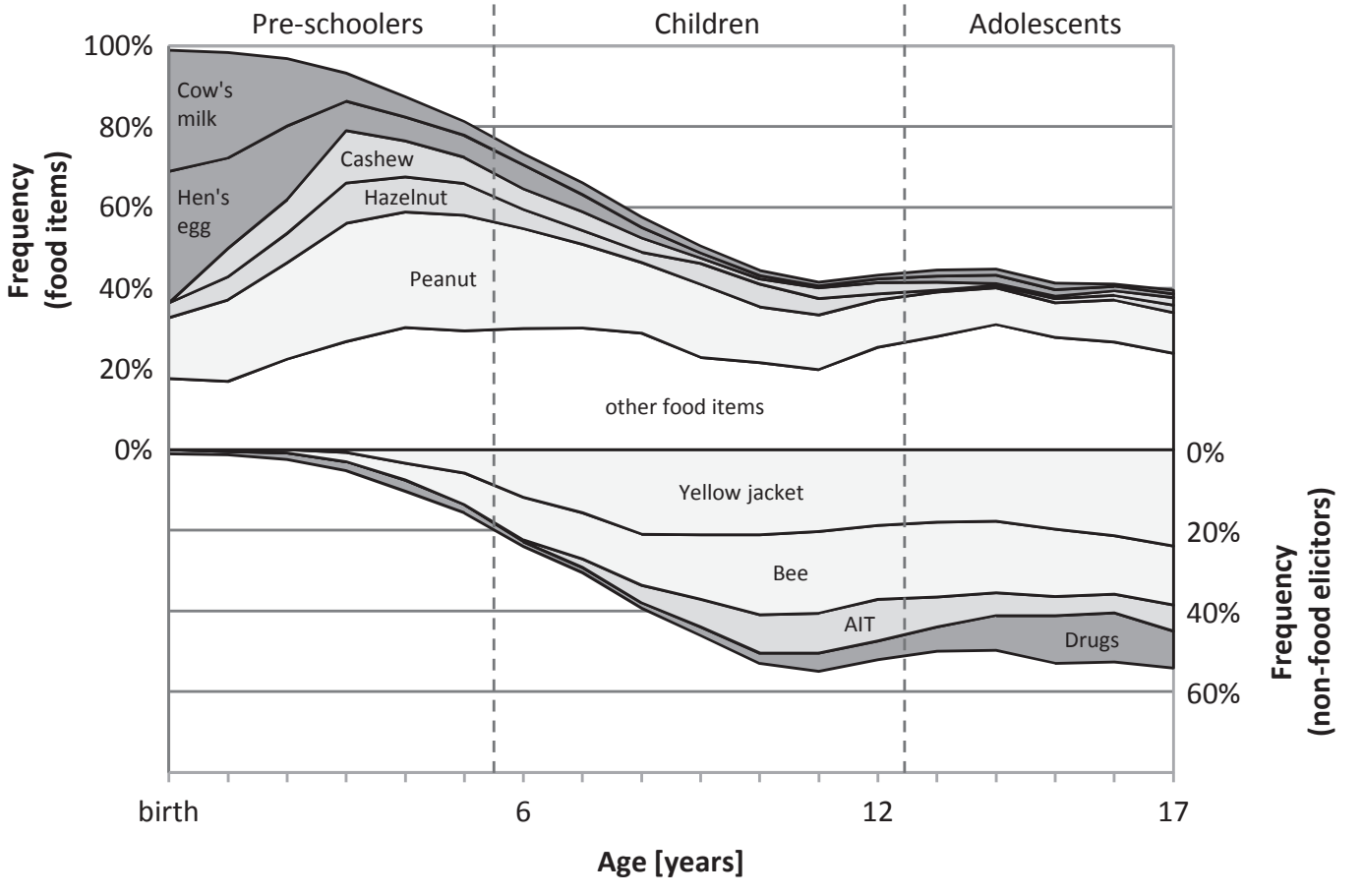

Figure 1. Elicitors of anaphylaxis by age (only for known common elicitors) in Europe. AIT, Allergen immunotherapy (from Grabenhenrich et al. 2016)[1]

Word-wide, food allergy affects about 10% of children in industrialized countries from North America (most common being peanut), Europe (most common being cow's milk) and Australia (most common being shellfish) and seems to be rising in other parts of the world, such as Asia (United Arab Emirates, China, Vietnam) and South Africa. Interestingly, children of East Asian or African descent born in a Western environment are at higher risk of food allergy compared to Caucasian children.

In the USA, the estimated prevalence of food allergy in children was 7.6%, after excluding 4% of children whose parent-reported food reactions were inconsistent with IgE-mediated food allergy. About 1 in 13 children have food allergies, affecting about 2 school-aged kids per classroom. Of these, approximately 40% were reported to be allergic to multiple foods and 42% had experienced at least one severe reaction requiring an emergency visit, and 40.7% had a current epinephrine autoinjector prescription.[2]

In Canada, the estimated prevalence was 6.7%, when excluding 2% of children with unconfirmed reports of IgE-mediated food allergy (e.g., lactose intolerance, gluten sensitivity). There has been an increase in probable milk allergy in children and adults and in probable wheat allergy in adults, which may relate to increasing dietary trends for the elimination of milk-based formula, dairy, and gluten in the general population.[3] Based on physician-reported data from 2018, only 33.7% of children diagnosed with food allergy had an epinephrine autoinjector prescription.[4]

About 50% of Canadian households are impacted by food allergy, directly or indirectly. Self-reported rates of food allergy are much higher than the true prevalence, and the perceived disease burden may have significant economic and psychosocial impact on young patients/families who may have not yet seen an allergist.

WHY IS FOOD ALLERGY ON THE RISE?

Numerous genetic and environmental factors contribute to the development or loss of food allergy. The immune system is supported in mounting strong and long-lasting adaptive immune responses by many environmental triggers, including bacteria, particularly the colonizing bacteria of normal gut, skin, and airway. These benign microorganisms act to shape and train a person's immunological and metabolic functions. While the causal link between microbial 'exposome' (in utero, ex utero) and development of chronic inflammatory diseases later in life continues to be explored, evidence suggests that the risk for developing food allergy is multifactorial.[5]

Increasing industrialization, urbanization and pollution appear to affect the microbial exposome and contribute globally to increased prevalence of food allergies, eczema, and asthma.

One established risk factor for food allergy is early onset eczema. Dry, cold climate, filaggrin gene mutations, elevated skin pH caused by frequent washing and soaps, are contributing factors to xerosis.

Delaying introduction of allergenic foods inhibits development of early oral tolerance, promoting development of food allergy. A likely contributor to the current food allergy epidemic was the 2000 North American recommendations to delay food allergen introduction in infants until after age 3 years and avoid food allergens in maternal diet during pregnancy.[6] These recommendations were revised in 2008, but practice did not effectively change until 2015, when it was found that proactive early and weekly exposure to peanut during infancy fosters the development of peanut tolerance at school age.[7]

Currently, there is no evidence supporting dietary restrictions in breastfeeding mothers for the prevention of childhood food allergies. A diverse balanced diet containing dairy, vegetables, fruit, and whole grains is recommended for both mother and infant to promote a healthy microbiome. Gut colonization and the diversity and intensity of microbial exposure may play a role in inducing food tolerance to dairy. Studies supporting a preventive role with early, mostly between 2 and 4 weeks of age, regular cow's milk formula ingestion, suggest the possibility of a different mechanism of sensitization to cow's milk protein than for other food allergens (**Figure 2**).[8]

Exposure to the specific maternal microbiome and outside pollutants starts in utero. The microbiome of formula-fed infants born via caesarian section is different compared to breastfed vaginally delivered infants, but the impact on future food allergy is unclear. Complete avoidance of exposure to regular cow's milk protein in the first months of life through exclusive breastfeeding, use of hydrolyzed formulas, and avoidance of regular cow's milk formula does not appear to reduce the risk of cow's milk protein allergy. Concurrently, temporary supplementation with regular cow's milk formula in breastfed infants in the first week of life may actually increase the risk of cow's milk allergy[9,10], while starting ingestion in the second week of life could be the most protective. Additional studies to establish optimal timing for cow's milk protein introduction are needed.

Other factors contributing to the unique pattern of bacterial exposures include housing and living

conditions, the presence of pets in the household, urbanization versus living rurally, and use of antibiotics. Later in life, microbial colonization is heavily influenced by the type, structure, and composition/diversity of the food.[5]

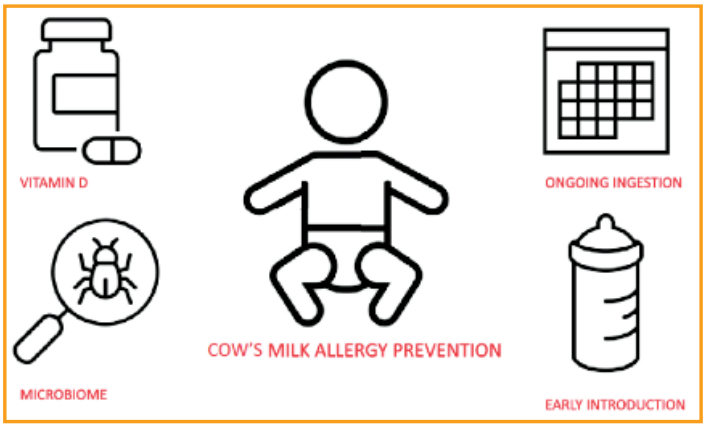

Figure 2. Possible factors involved in the pathogenesis of cow's milk allergy (from Abrams MA, Sicherer SH. 2021)[8]

These multiple contributing factors have been summarized as the "5Ds" and integrate three hypotheses of how food allergy develops: dual allergen exposure hypothesis (**d**ry skin and **d**iet, where skin exposure to food allergen precedes allergenic food ingestion), hygiene hypothesis (lack of exposure to **d**og, **d**ribble) and vitamin D hypothesis (both too low and too high[11,12] levels of vitamin **D** appear to be unfavorable)(**Figure 3**).[5]

The dual allergen exposure hypothesis suggests that non-ingestion exposures to allergenic foods via the skin, especially on inflamed skin of allergy-prone infants with early-life atopic dermatitis, combined with a lack of early oral exposure, can result in early allergic food sensitization.[13] Mounting evidence supporting this has resulted in recent changes to clinical practice and public health policy for food allergy prevention.

While beneficial for preventing eczema, starting infant skin moisturization right after birth does not on its own prevent food allergy. Ongoing trials of exposure to allergenic solids and vitamin D supplementation are anticipated to inform further preventative strategies.

QUALITY OF LIFE IN CHILDREN WITH FOOD ALLERGY/ANAPHYLAXIS

Food allergy is not a lifestyle choice and should be viewed as a public health concern.[14]

There is no definite curative treatment for food allergy. The risk of near-fatal or fatal anaphylaxis is unpredictable and difficult to study, as it usually occurs outside the home or hospital environment. Uncontrolled asthma and delayed adrenaline injection are associated with fatal outcomes, but timely adrenaline alone may be insufficient at times, possibly due to insufficient dose/needle length or limited administration technique. This uncertainty about accurate prediction of future severe reactions and overall prognostic outcome substantially impairs the quality of life for young patients with food allergies[15] and for their families, comparable to children/families living with type-1-diabetes.

Food allergies bring a complex pattern of requirements and emotions throughout a person's life, with early and strict eating rules, diligent reading of food labels and avoidance of triggering food(s). As the most common food allergens are often staple foods and highly prevalent in the Western diet (including trace amounts in packaged foods labelled as "May contain allergenic foods"), patients and families, but also daycares and schools, must remain vigilant. This may lead to maladaptive coping strategies such as maximisation (extreme levels of food avoidance, and hypervigilance) or minimisation behaviours (denial, risk taking behaviour) in patients and their families.[16]

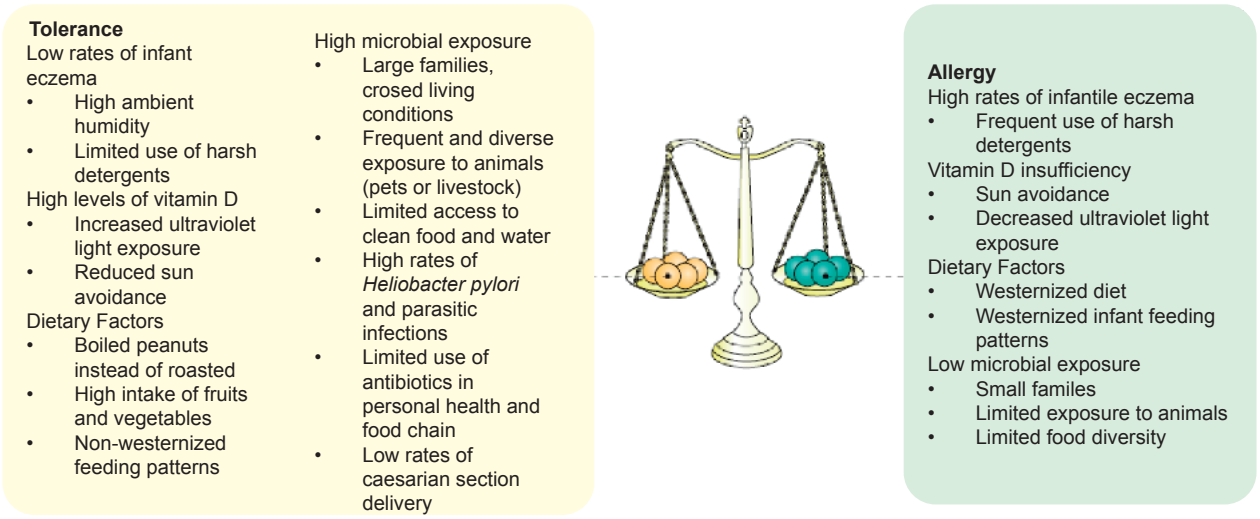

Figure 3. Integrated hypotheses of food allergy (from Renz et al. 2018)[5]

Living with uncertainty, strict food-related rules, and a feeling of being different from peers, together with an ever-present risk of accidental exposures, can lead to constant stress, fear of reactions, embarrassment, relational difficulties, anxiety and depression.[17] Since 2020, the coronavirus pandemic has added an additional negative layer to the quality of life, with increasing difficulty accessing "safe" foods and food allergy-related health services.[18]

Children with food allergies and their families are in constant pursuit of normalcy and control over personal safety. Given this, educating new parents about food allergy prevention measures, such as infant skin care and early nutrition, by family physicians is equally important as an accurate diagnosis by an allergist to avoid unnecessary food restrictions, nutritional deprivation, and anxiety.

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