The past 3 decades have witnessed remarkable changes in our basic understanding of food allergic disorders, which have elevated food allergy from a collection of unsubstantiated anecdotes largely ignored by “serious” clinicians to a science generating hundreds of publications annually in high-impact scientific journals. This increase in interest and activity in food allergy research has paralleled an apparent increase in the prevalence of food allergy. Thirty years ago food allergies were believed to affect 0.2% - 0.3% of the pediatric population (even fewer adults) whereas today food allergies appear to affect up to 10% of young children\(^1,2\) and perhaps 3% - 4% of adults.\(^3\) Severe food-allergic reactions were rare 30 years ago, but now represent the single leading cause of anaphylaxis treated in emergency departments in the US,\(^4\) and have accounted for over a 3.5 fold increase in pediatric hospital admissions for food-related disorders.\(^5\) While this increase in the prevalence and severity of food allergy has been confined to industrialized countries with westernized lifestyles, the reason for this increase remains enigmatic.\(^6\) Certain potential factors, such as the microbiome, were barely discussed 3 decades ago, whereas today new technology has enabled investigators to focus on this new frontier, with recent studies in animal models demonstrating that susceptibility to food allergy has a specific gut microbiota signature that can transfer this susceptibility.\(^7\) Foods responsible for the majority of allergic reactions have not changed over the past 30 years, but peanut and tree nut allergy have become much more prevalent, tripling in the US between 1997 and 2008.\(^8\)

Although many of the same tools are used to diagnose food allergy that were utilized 3 decades ago, these tools have been refined and are providing more precision. Thirty years ago skin tests and patient history were used to diagnose food allergy by most allergists, even though May and Bock had demonstrated the imprecision of this approach and called for the use of double-blind placebo-controlled food challenges.\(^9\) Food-specific IgE measurements (radioallergosorbent tests) were utilized by a minority of allergists to diagnose food allergy because of their even poorer specificity.\(^10\) Since that time, the quantitative value of food-specific IgE measurements and prick skin tests was demonstrated,\(^11,12\) and today the quantitative measurement of food protein-specific IgE\(^13\) and food allergenic epitopes\(^14\) show promise in providing more information about a patient’s clinical reactivity to a food.\(^4\) Three decades ago few allergists performed oral food challenges, whereas today it is the accepted “gold standard”\(^4\) and efforts have been made to standardize the procedure so that research results can be accurately compared.\(^15\)

The management of food allergy today is not much different than it was 3 decades ago, but practices changed considerably in the intervening period. Food allergic patients were told to avoid foods to which they were allergic, but there were no organizations such as FAAN to assist patients and their families, food labels were not very informative, and self-injectable epinephrine was not typically prescribed. Until recently, it was believed that strict allergen avoidance was the only hope for “outgrowing” food allergies, although many food-allergic patients were probably ingesting some allergen-containing products unknowingly because of poor labeling or lack of information. The concept of patients with different allergic phenotypes, i.e. reacting differently to conformational and sequential epitopes, was not known. Today the majority of milk- and egg-allergic patients are encouraged to ingest baked-products where conformational epitopes have
been destroyed since the addition of these products to their diets actually accelerate the acquisition of tolerance.\(^{16;17}\) Although the first case of oral immunotherapy was published in 1908,\(^{18}\) no forms of immunotherapy were being pursued 30 years ago. However, in the past decade, many investigators have been evaluating oral immunotherapy and several other immunotherapeutic strategies,\(^{19}\) but at the present time it is felt that oral immunotherapy shows the most promise,\(^{20;21}\) although considerable evidence regarding safety and long-term efficacy are needed before it is ready for general clinical practice.\(^{4;22}\) Thirty years ago there were no specific recommendations for trying to prevent the development of food allergies. In the intervening period, various organizations recommended eliminating major food allergens from the mothers’ diets during the third trimester of pregnancy and during lactation, and withholding major allergens from susceptible newborns, e.g. milk for one year, eggs for two years and peanut until three years of age.\(^{23}\) Subsequently it was concluded that there was insufficient information to make any strong recommendations regarding prevention diets in high risk children,\(^{4;24}\) and some recent association studies suggested that early introduction of allergens may actually prevent the development of allergies in high risk infants.\(^{25;26}\)

The number of investigators in the field of food allergy has increased from less than a dozen 30 years ago to several hundred today, and the number and quality of published articles has increased exponentially. Nevertheless, many questions remain to be answered: (1) Why is food allergy largely a product of westernized countries and why is it increasing? (2) Why do some patients have significant levels of food-specific IgE and yet never react to the food? (3) Why do some patients experience multiple mild food allergic reactions and then experience a near-fatal or fatal reaction, i.e. what mechanisms are responsible for severe anaphylaxis? (4) Why don’t serum tryptase levels rise in the vast majority of patients experiencing food allergic reactions? (5) Why are some foods so allergenic, e.g. peanuts, fish, shellfish, and others rarely cause allergies, e.g. corn? (6) What are the basic underlying mechanisms responsible for tolerance to foods? (7) What are the best therapeutic strategies for treating (curing) food allergy? (8) What are the immunologic mechanisms responsible for non-IgE-mediated food allergy? (9) What are the best strategies for preventing food allergy? (10) What mechanisms are responsible for exercise-, NSAID- and alcohol-associated, food-induced anaphylaxis? (11) What biomarkers will better predict clinical reactivity to IgE- and non-IgE-mediated food allergies? (12) What genetic and epigenetic factors are involved in the development of food allergies? While tremendous progress has been made in the diagnosis and management of food allergy over the past 3 decades and new information has dramatically altered our concept of food allergy, many more questions remain and will likely keep investigators occupied for at least the next three decades.
References


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