

Finding a Path to Safety in Food Allergy

Assessment of the Global Burden,
Causes, Prevention, Management,
and Public Policy

Committee on Food Allergies: Global Burden, Causes, Treatment,
Prevention, and Public Policy

Food and Nutrition Board

Health and Medicine Division

Virginia A. Stallings and Maria P. Oria, *Editors*

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This report has been reviewed in draft form by individuals chosen for their diverse perspectives and technical expertise. The purpose of this independent review is to provide candid and critical comments that will assist the institution in making its published report as sound as possible and to ensure that the report meets institutional standards for objectivity, evidence, and responsiveness to the study charge. The review comments and draft manuscript remain confidential to protect the integrity of the deliberative process. We wish to thank the following individuals for their review of this report:

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Although the reviewers listed above have provided many constructive comments and suggestions, they were not asked to endorse the conclusions or recommendations nor did they see the final draft of the report before its release. The review of this report was overseen by **Robert S. Lawrence**, Johns Hopkins Bloomberg School of Public Health, and **Huda Akil**, University of Michigan. They were responsible for making certain that an independent examination of this report was carried out in accordance with institutional procedures and that all review comments were carefully considered. Responsibility for the final content of this report rests entirely with the authoring committee and the institution.

Preface

As pediatricians in training, we learned about life-threatening anaphylaxis and that prompt, appropriate treatment with a simple drug, epinephrine, saves lives. We mostly worried about anaphylaxis triggered by an undiagnosed drug allergy, or maybe by multiple bee stings. Food allergy was not well appreciated and was confused in our minds and those of parents with food intolerance, food sensitivity, and family reports of food reactions. Prevention of severe allergic reactions from peanut exposure in schools and airplanes was not discussed.

Food allergy is a complicated, multifactorial disease whose causes, mechanisms, and effects are not yet fully understood. The evidence on the true prevalence of food allergy is obscured by insufficient or inconsistent data and variable methodology. Despite these obstacles, public concern has grown in response to the apparent rising global prevalence of food allergies, and many health care experts who provide care to patients agree that any real increase in food allergies that has occurred is unlikely to be due simply to an increase in awareness. Numerous stakeholders are concerned about this rise in food allergies, including the general public, policy makers, regulatory agencies, the food industry, scientists, clinicians, and especially families of children and young people suffering from food-related allergies.

This consensus study is the result of a planning meeting that was held by the National Academies of Sciences, Engineering, and Medicine in response to broad public interest in the health aspects of food allergy, the relevance to public health, health care, and society, and the current lack of solutions both for preventing and managing food allergies. The goal of this consensus study is to review the science and management practices of food

allergies. Our committee intends that this report will clarify the nature of the disease, its causes, and its current management; highlight gaps in knowledge; encourage the implementation of food allergy management tools at many levels and among many stakeholders; and delineate a roadmap to safety for those who have, or are at risk of developing, food allergies, as well as for others in society who are responsible for public health.

This committee had the unique opportunity to hear directly from an advisory panel made up of nine parents of children with food allergies and one individual with food allergy. Members of the advisory panel were invaluable to the committee as meaningful examples of the sentiments and struggles of living with food allergies. We heard about the anxiety they feel in restaurants, schools, airplanes, and other settings where they are fearful about unintentional exposure to a food that can cause a life-threatening allergic reaction. The advisory panel asked for clear and consistent guidelines for diagnosing and managing food allergies and for treating reactions. We also heard their desire for more clarity in food labeling, appropriate training for emergency personnel, and greater access to epinephrine. And we heard their plea for a roadmap to safety so that people with food allergy and their family and friends can participate fully in the world without the fear of a severe or fatal food allergy reaction.

Drawing on insights from the advisory panel, as well as expert testimony, comprehensive literature reviews, committee expertise and deliberations, the committee recognized that preventing and treating food allergy and creating a roadmap to safety is a multifaceted undertaking that must take into account many interacting systems that influence both risks and safety over the life course. To address this, the committee decided that this report would benefit from taking an ecological and developmental perspective. This ecological-developmental model emphasizes the importance of developmental timing for food allergy exposures and for safety planning. The committee used this approach to delineate the issues, organize the evidence, draw conclusions, make recommendations, and communicate conclusions. The committee recognized that many sectors at multiple levels of organization in private and public life must be considered to understand and protect the individuals from the risks posed by food allergies.

The current paradigm of prevention and treatment is changing. As this report was being written, new evidence on the potential benefits of early introduction of allergens was emerging to dismantle previous views about the benefits of delaying introduction of allergens until 1 year of age or even later. These new studies are causing leading organizations to rethink the current recommendations and consider promising new prevention approaches. Understandably, these changes can lead to confusion among those at risk of food allergy and even among health care providers.

Thoughtful policies at many different levels, including guidelines and

regulations, can help protect public health. Although many nongovernmental organizations and governments provide tools, guidelines, and policies to promote greater safety in various settings (e.g., food industry practices, regulatory agencies, child care settings, schools, higher education, and public transport), their implementation and enforcement varies greatly across the United States. Moreover, policies and guidelines may not be keeping pace with the science.

This report is meant to be a review of scientific questions. In addition, this report reviews some of the management approaches that are in place to improve health and quality of life for individuals with food allergy and their caregivers. Finally, the committee envisions that this report will serve as a tool for all the stakeholders and the public to recognize the importance of this disease as well as to join forces in efforts to improve markedly our ability to understand, effectively manage, and ultimately cure food allergy, and to make the world safer for those afflicted with this disease.

The committee responsible for the report is varied in expertise, with members chosen for their experience in allergic diseases, immunology, pediatric medicine, epidemiology, genetics, epigenetics, public health, nutrition, food science, and the food industry. The chapters are authored jointly by committee members, who contributed their expertise to appropriate areas, subject to review and comment from the entire committee. Committee members volunteered countless hours to long but productive days of meetings in Washington, DC, and to research, deliberations, and preparation of the report. Many other people contributed significant time and effort to support the preparation of the report during open committee sessions and through presentations at a workshop. We are grateful for their efforts.

The committee could not have done its work without the initiative and collaboration from the Board on Children, Youth, and Families and superb guidance and support provided by the Food and Nutrition Board staff: Maria Oria, Study Director; Alice Vorosmarti, Research Associate; Anna Bury, Research Assistant; and Kyra Cappelucci and Noa Nir, Senior Program Assistants. The committee also benefited from the overall guidance of Ann Yaktine, Director of the Food and Nutrition Board. The committee is also especially thankful to Anne Rodgers, who edited this report.

Lastly, as chair, I express my sincere appreciation to each member of this committee and staff for their extraordinary commitment to the project and to the wonderful opportunity to work with them on this important task to improve the health and future of people around the world with food allergy.

Virginia Stallings, *Chair*
Committee on Food Allergies:
Global Burden, Causes, Treatment, Prevention, and Public Policy

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Summary

Food allergy, an adverse health effect arising from a specific immune response that occurs reproducibly on exposure to a given food, affects the health and quality of life of individuals and their caregivers across a range of dimensions. A food allergy can cause skin, respiratory, and gastrointestinal reactions. The quality of life of individuals with food allergy is diminished as their social interactions and routine life activities are affected. For some individuals, a food allergy can lead to severe allergic reactions and death. Food allergies typically develop within the first year of life but they can also develop later in life. Eight food groups are considered to be major allergens. These are milk, egg, peanut, tree nuts, wheat, soy, fish, and crustacean shellfish.

Questions persist about whether food allergy prevalence has been on the rise within the past two decades and why. The current data do not unequivocally support the occurrence of such a rise. Multiple hypotheses have been generated about potential genetic and environmental factors that lead to food allergies and a potential rise in food allergy cases. Concomitant with a widespread perception of an increase in prevalence, the public and other stakeholders frequently misinterpret a food allergy and its symptoms, how to differentiate a food allergy from other immune and gastrointestinal diseases, and what effective management and prevention approaches to use. For example, lactose intolerance symptoms can be misinterpreted as a food allergy, when in fact their physiological origin and management approaches are vastly different.

Food allergy is a complex disease at the molecular and cellular level and although much research data have accumulated, many fundamental

questions remain. For example, researchers are struggling to identify factors in utero and during the first year of life, such as the timing of introduction of solid foods or breastfeeding duration, that could lead to the onset of allergies. Overall, gaps in knowledge at the mechanistic level represent barriers to developing strategies for disease prevention and management. Not surprisingly then, recommendations by public health authorities or professional associations for preventing or managing a food allergy are limited by the scarce or inconsistent research findings. Although promising therapeutic approaches are being tested, no effective treatments currently exist for patients with food allergies.

In the absence of approved treatments, patients are advised to avoid the allergen, which can be very difficult, especially in some circumstances. For example, under the Food Allergen Labeling and Consumer Protection Act, food allergens must be listed in the ingredient list of a packaged food. Unfortunately, during production or manufacturing, cross-contamination may occur, resulting in the food product having a hidden allergen that does not appear on the label. In addition, food service establishments are not required to list food allergens, so an individual's safety depends on clear communication and on employees' knowledge of the allergen content of the food being served and on the establishment's management practices. Even with the most stringent management practices, accidents, such as cross-contact events, can still occur when people with a food allergy eat outside of the home. Concerted efforts by policy makers, industry leaders, and others are necessary to bring about a safe environment for those with food allergy.

In summary, many stakeholders, including policy makers, the food industry, scientists, clinicians, and especially individuals with food allergy and their caregivers, are concerned about the misunderstandings, and the lack of effective treatment and clear approaches to prevent food allergy. This report collects and evaluates the scientific evidence on the prevalence, origins, diagnosis, prevention, and management of food allergy and makes recommendations to stakeholders to maximize safety and to increase research activities related to food allergy.

THE TASK AND COMMITTEE'S INTERPRETATION

An ad hoc committee of 15 experts was selected to respond to the statement of task (see Box S-1). The plan for the study included an advisory panel made up of nine parents of children with food allergy and one individual with food allergy. This panel was asked to present to the committee at public meetings; their testimonies were invaluable as examples of the challenges and burden of living with food allergies.

Given the misunderstandings related to food allergy, a first assignment

BOX S-1

Statement of Task

A committee will be formed to examine critical issues related to food allergy, including the prevalence and severity of food allergy and its impact on affected individuals, families, and communities; and current understanding of food allergy as a disease, and in diagnostics, treatments, prevention, and public policy. This consensus study will engage a broad array of stakeholders, including government agencies, organizations, academic institutions, industries, policy makers, and patient organization groups; to bring together leading investigators from relevant fields, clinicians, and parents; and to develop a framework for future work; and to recommend actions by both government and nongovernment agencies. The committee's review of the evidence will consider the following key questions:

1. What are current trends in food allergy prevalence?
 - What is an appropriate definition of food allergy to use in measuring prevalence?
 - What data or methods are most appropriate to use in measuring prevalence and how may they be implemented?
 - Should there be an effort to assess prevalence for allergens other than the eight most common that are required to be disclosed on food packages? If so, should the same methods be used for these allergens?
2. What are the key prenatal/early life determinants of food allergy?
 - For example, are there dietary factors that impact development of food allergy and are these modifiable?
3. What are the current data gaps in understanding the diagnosis and prognosis for food allergy?
 - What new approaches are being developed to address these data gaps?
4. What steps can be taken to educate providers and the public in order to create safe environments for food allergic children both within and outside the home?
 - What and where are the most risky food scenarios and how can these be better managed?
 - What guidance can be given to individuals about exposure to low levels of allergens in food products?
5. What is the status of assessing allergen thresholds in individuals? What additional methods or tools are needed?
6. What research gaps need to be filled in order to provide better guidance to health care providers and policy makers?

The committee will develop a framework for future direction in understanding food allergy and its impact on individuals, families, and communities; recommending steps to increase public awareness of food allergy; promoting research on both disease causation and management; and informing preventive approaches to food allergy. Research gaps will be identified and recommendations made to fill them.

for the committee was to define the types of food allergies to address in this report. Food allergy, as opposed to a food intolerance, which does not have an immunologic component, arises from a specific immune response. Food allergy has two key classifications: immunoglobulin E (IgE)-mediated or non-IgE-mediated. The recommendations in this report focus on IgE-mediated food allergies, which have better defined underlying cellular mechanisms and physiological reactions. Other food-related diseases, such as celiac disease, food intolerances (e.g., lactose intolerance) are not covered. However, other non-IgE-mediated food allergies are mentioned when appropriate, particularly while discussing diagnostic methodologies. With a focus on the United States, many recommendations could apply in other countries.

A DEVELOPMENTAL AND ECOLOGICAL PERSPECTIVE ON FOOD ALLERGY

For every individual, the risks and protections from food allergies vary over the life course, depending on individual genetic factors, biological development, exposures to allergens, and the contexts in which the individual lives (i.e., a developmental perspective). Before birth, a fetus interacts indirectly with systems because influences (e.g., diet) are mediated by maternal biological function. After birth, children continue to develop and they interact directly with numerous new systems, including peers, schools, social media, workplaces, and social contexts. But individuals are influenced by many additional systems beyond their proximal interactions, through cultural practices and governmental or nongovernmental policies or rules. The safety and well-being of individuals with potential food allergies, then, require recognition that risks and protections for public safety are spread across many systems, including food production and distribution systems, health care systems, and education systems (i.e., an ecological perspective). The committee developed a model to depict those important interactions (see Figure S-1).

THE ROADMAP TO SAFETY

In mapping the road to greater public safety regarding food allergy, in addition to the health care system, the committee selected the following settings for their relevance to the task at hand: food establishments, early care and education, schools, higher education, and the travel industry. These settings vary in policies and practices, and many improvements are both feasible and would likely contribute to preventing and managing severe allergic reactions and improving quality of life.

The committee's roadmap to safety is multifaceted, involving many

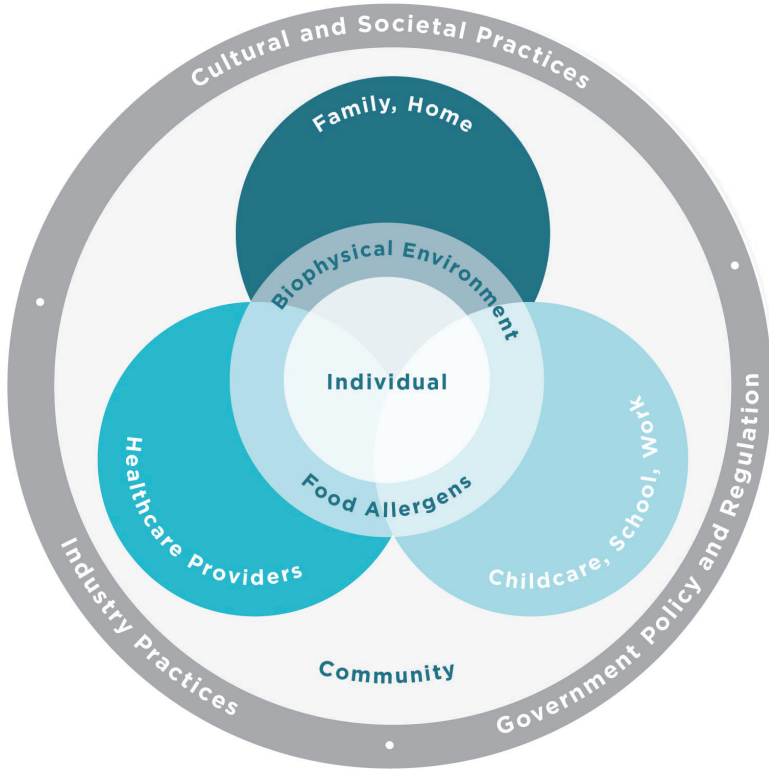


FIGURE S-1 Ecological-developmental model for food allergies. Different systems that an individual interacts with are depicted as proximal (e.g., food, biophysical environment) and distal (e.g., industry, government).

NOTES: **Industry practices** refers to all the manufacturing processes and allergen control plans followed during food production, distribution, preparation or cooking, and serving. They also refer to mandatory and voluntary labeling of food allergens and to recall procedures followed when a product is contaminated with a food allergen. **Cultural and societal practices** refer to the particular diets and foods of regions and countries. **Biophysical environment** refers to the external proximal environment (e.g., air) while **Individual** refers to all systems internal to a developing human, including genome, epigenome, proteome, metabolome, central nervous system, immune system, microbiomes, and many other self-regulatory systems involved in adaptation and sustaining life. **Health care providers** include the persons (e.g., physicians, dieticians) and the institutions that protect individual and public health. **Child care, school, work** includes all proximal settings that interact with an individual at different life stages. Finally, **family, home** refers to the system of people, relationships, routines, and practices occurring at home. Interactions (e.g., communication, physical contact) occur between and among all those systems and the individual to support (or not) food safety.

stakeholders and the following actions (see Figure S-2): (1) obtain accurate prevalence estimates, (2) use proper diagnostic methods and provide evidence-based health care, (3) identify evidence-based prevention approaches, (4) improve education and training, (5) implement improved policies and practices to prevent the occurrence of severe reactions, and (6) expand research programs. This section summarizes these actions and related recommendations.

Obtain Accurate Prevalence Estimates

To prioritize food allergy as a public health concern and ensure that adequate resources are directed at the issue, the extent of the problem must be defined. No study in the United States has been conducted in a systematic manner, with sufficient sample size, and in various populations to determine the true prevalence of food allergy. Because of the low quality of data, particularly the use of self-reported data instead of the gold standard oral food challenge (OFC)¹ method, the true prevalence of food allergy is likely overestimated in most published studies.

The committee recommends that the Centers for Disease Control and Prevention obtain prevalence estimates on food allergy in a systematic and statistically sound manner.

Prevalence should be assessed in a systematic fashion in a sufficiently large population, with consideration given to using stratified sampling for cost-efficiency, with frequency-weighting used to obtain population-wide estimates. Prevalence estimates should be conducted in both children and adults and in groups defined by race, ethnicity, and socioeconomic status to determine differences in diagnosis and prevalence within these subgroups. To support population risk assessments, the committee also recommends that the dietary intake history of those reporting food allergy be compared to those who do not, particularly for the specific foods of interest.

Although a new study design (or the use of other data surveillance systems) is possible, the National Health and Nutrition Examination Survey (NHANES) is a feasible option to systematically examine the prevalence of food allergy by collecting data on

¹ Oral food challenge is a feeding test that involves gradual, medically supervised ingestion of increasingly larger doses of the food being tested as a possible food allergen. The test is positive when the individual experiences food allergy symptoms, such as skin, respiratory, and gastrointestinal reactions.

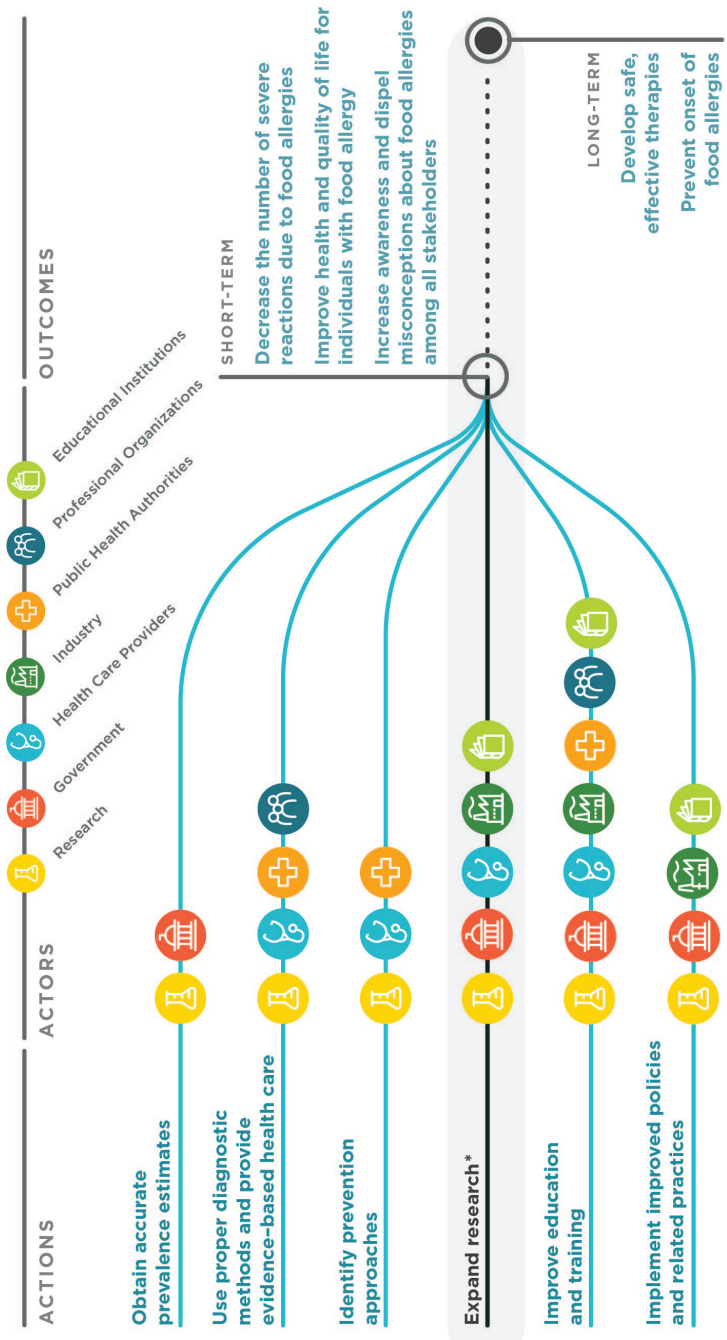


FIGURE S-2 Roadmap to food allergy safety in six actions.

* Research is needed to achieve all other actions and to reach the short- and long-term goals (see Chapter 9 for all specific areas of research). The actors represent the primary stakeholders that will be involved in implementing the actions.

self-reported food allergies, food-specific immunoglobulin E concentrations, food-specific skin prick test results, and oral food challenge results.² Specific suggestions for use of NHANES (or other data surveillance systems), such as oversampling of young children (<6 years) as an important group, are included in Chapter 3.

Use Proper Diagnostic Methods and Provide Evidence-Based Health Care

No simple diagnostic tests exist for food allergy, and the selection and interpretation of tests depend upon the nature of the disorder and the individual medical history. The OFC carries risk and expense and is underused. The medical history and other test results (e.g., skin prick test) can suggest the likelihood of a food allergy, but in some cases an OFC is needed to confirm the presence of a clinical disease.

The committee recommends that physicians use evidence-based, standardized procedures as the basis for food allergy diagnosis and avoid nonstandardized and unproven procedures (e.g., applied kinesiology, immunoglobulin G panels, electrodermal testing). When food allergy is suspected, a patient should be evaluated by a physician who has the training and experience to select and interpret appropriate diagnostic tests.

Although this process often may include an initial evaluation by a primary physician, it is important that those with suspected food allergy be diagnosed appropriately, which is likely to involve referral to or consultation with a physician specialist who can diagnose, comprehensively evaluate, and manage the food allergy.

Food allergy evaluation procedures include a medical history and physical examination, and also may include a food-specific skin prick test, food-specific serum immunoglobulin E test, diagnostic food elimination diet, and OFC. Selection of the specific tests needs to be individualized based on the medical history of each patient. Health care providers trained in food allergy, leaders of health care facilities, and health care payor groups can facilitate the appropriate use of OFCs, including personnel, facilities, and safety guards, so that physicians are not deterred from performing

² The gold standard OFC is an expensive method and must be administered in a clinic and under supervision of a trained physician. The testing sequence, therefore, is meant to lead to a population sample that is enriched with individuals reporting food allergy and that minimizes cost and effort.

the types of diagnostic testing that are appropriate for the patient's diagnosis and care.

Identify Evidence-Based Prevention Approaches

Although many factors have been postulated to contribute to the onset of food allergy, strong evidence is lacking about any association, mainly due to methodological limitations and variations in study designs. The strongest data derive from recent studies supporting the dual allergen exposure hypothesis, which proposes that a food allergy may occur through exposure to low doses of allergen through damaged skin (such as in eczema) followed by oral exposure to these allergens through consumption early in infancy. The hypothesis proposes that the practice of delaying the introduction of allergens may have contributed to the presumptive rise in food allergy prevalence.

The committee recommends that public health authorities and clinical practice guidelines include consistent, clear, and evidence-based advice for families and health care providers, including dietitians, about the potential benefits of introducing allergenic foods (e.g., peanut products, egg, dairy, and wheat) in the first year of life to infants, when an infant is developmentally ready (around 6 months of age), but not before 4 months of age, particularly to those at high risk of allergy. Guidelines also should include information about the circumstances in which health care providers should advise their patients about the safest way to introduce in their diet peanut products (and/or other foods, as determined by the results of ongoing research).

Improve Education and Training

Public Health Authorities, Health Care Providers, and Their Patients and Caregivers

The committee generally supports current guidelines and U.S. practice parameters for food allergy management and emphasizes those areas where improvements would lead to significant changes in the quality of life of patients and their caregivers, such as training and education.

The committee recommends that the Centers for Disease Control and Prevention work with other public health authorities to plan and initiate a public health campaign for the general public, individuals with food allergy, and all relevant stakeholders to increase

awareness and empathy as well as to dispel misconceptions about food allergy and its management.

For example, as part of that campaign and taking advantage of the popularity of digital media among the public, particularly children and adolescents, public health authorities could develop effective media engagement programs. To plan for this campaign and develop media programs, public health authorities could conduct formative research with all potential audiences.

The committee recommends that public health authorities, such as the National Institutes of Health and the World Health Organization, and professional organizations, such as the American Academy of Pediatrics; the American Academy of Allergy, Asthma & Immunology; American Academy of Family Physicians; and the Academy of Nutrition and Dietetics, regularly update guidelines on diagnosis, prevention, and management of food allergy based on strong scientific evidence, as emerging scientific data become available.

For example, current evidence is insufficient to associate any of the following behaviors with prevention of food allergy: food allergen avoidance diets for pregnant or lactating women, prolonged allergen avoidance in infancy, vaginal delivery, breastfeeding, infant formulas containing extensively or partially hydrolyzed protein, and supplementation with specific nutrients (e.g., vitamin D, folate, fatty acids) in children or adults.

The committee recommends that medical schools as well as residency and fellowship programs and other relevant schools include training for health care providers in the management of food allergy and anaphylaxis. Health care providers, including dietitians and mental health professionals, also should receive training on approaches to counseling patients and their caregivers. Counseling training is envisioned to be provided, in part, by professional organizations through various means, including the Internet.

The following elements of food allergy training are appropriate for all health care providers, including emergency medical technicians, emergency room staff, nurses, dietitians, and others:

- *Emergency management.* This includes training to recognize and manage an anaphylaxis emergency, such as the use

of intramuscular epinephrine as a first line of emergency management for episodes of anaphylaxis.

- *Counseling on food allergy management and anaphylaxis.* This includes identifying food allergies as well as managing and treating them in various settings (e.g., home, school, restaurants), as well as emergency management of anaphylaxis.

As appropriate, physicians and other health care providers also may receive training to provide the following:

- *Nutrition counseling.* This includes discussion of safe and nutritionally adequate avoidance diets to individuals with food allergies, particularly children and their caregivers. The training also could include offering referral to a dietitian when needed and as part of reimbursable care. In addition, dietitians may receive training in providing individualized dietary advice to people with food allergy and their caregivers.
- *Psychosocial counseling.* This includes identifying and discussing with patients and caregivers psychosocial concerns (e.g., bullying), validation of feelings, and balancing management with participation in daily activities. Training also could include offering referral to a mental health professional when needed and as part of reimbursable care. In addition, mental health professionals may receive training in counseling individuals with food allergy and their caregivers.

The committee recommends that health care providers counsel patients and their caregivers on food allergy following the most recent food allergy guidelines and emphasizing the need to take age-appropriate responsibility for managing their food allergy. Counseling is particularly important for those at high risk of food allergy and severe food allergy reactions, such as adolescents, young adults, and those with both food allergy and asthma.

The committee recommends that health care providers and others use intramuscular epinephrine (adrenaline) in all infants, children, and adults as a first line of emergency management for episodes of food allergy anaphylaxis. The Food and Drug Administration should evaluate the need for, and, if indicated, industry should

develop an auto-injector with 0.075 mg epinephrine specifically designed for use in infants.

Current auto-injectors have 0.15 mg or 0.30 mg epinephrine, which is not suitable for infants. Consensus is currently lacking on first aid management using available auto-injectors when managing infants. A dose of 0.075 mg from an auto-injector could fill this gap. Labeling the auto-injectors in a standard manner to differentiate doses also could be beneficial.

Training First Responders and First Aiders

Food anaphylaxis can occur in any setting, and proper emergency management can be life-saving. The public, particularly first responders and first aid personnel, need to be prepared to assist with food-related severe reactions. Overall, food allergy anaphylaxis is not included in training curricula of organizations that offer certifications on emergency training or specialized training for professionals, such as pediatric specialization for early care and education providers.

The committee recommends that organizations, such as the American Red Cross or the National Safety Council, who provide emergency training (e.g., first aid training, basic life support) to the general public and to first responders and first aid personnel in various professions and workplaces, include food allergy and anaphylaxis management in their curricula.

Training Food Industry Personnel

The committee found deficiencies in the knowledge of food industry personnel, including poor communication within the establishment, staff failure to prevent cross-contact, and lack of knowledge about hidden ingredients.

The committee recommends that food industry leaders provide the necessary resources for integrating food allergy training (e.g., food allergen identification and preventive controls, effective risk communication with customers) into existing general food safety and customer service training for employees at all levels and stages in the food industry, as appropriate, encompassing processing, retail food and grocery stores, restaurants, and other food service venues.

Training for employees could be offered through, for example, supporting conferences, workshops, or webinars to share best practices related to allergen preventive controls, food allergen risk communication, and other food allergen safety topics. State health departments could develop a certification process for allergy awareness and management in restaurants modeled after the letter grading system that rates their food safety performance.

Implement Improved Policies and Practices to Prevent the Occurrence of Severe Reactions

Policies Regarding Labeling of Packaged Foods

The food processing industry and the federal government have an essential role in informing individuals at risk of food allergy about the presence of allergens in foods. There are two types of allergen labeling: (1) mandatory, when the allergen is added as an ingredient; (2) voluntary, when the allergen might be inadvertently in the food as a result of cross-contact.

The list of major allergens to be labeled in food packages, which has been adopted by many countries, has not been reviewed since it was developed by the Codex Alimentarius Commission (CAC) in 1999. Also, some U.S. labeling policies are not effective in informing consumers about the risks from food allergens.

In terms of voluntary labeling, unintentional allergens at levels that could cause a reaction can be identified on the labels of packaged foods using precautionary allergen labels (PALs) with wording such as “X may be present.” Currently, PALs bear no relationship to risk. To improve the labeling of unintentional allergens, the Allergen Bureau of Australia and New Zealand has developed the VITAL[®] (Voluntary Incidental Trace Allergen Labeling) program, which is based on risk assessment principles.

The committee recommends that the Codex Alimentarius Commission and public health authorities in individual countries decide on a periodic basis about which allergenic foods should be included in their priority lists based on scientific and clinical evidence of regional prevalence and severity of food allergies as well as allergen potency.

For example, in the United States, some foods listed by the Food and Drug Administration as tree nuts (i.e., beech nut, butter-nut, chestnut, chinquapin, coconut, ginkgo nut, hickory nut, lichee nut, pili nut, shea nut) could be removed from the current priority

list based on the paucity of data or low frequency of allergic reactions. In addition, evidence of the allergy prevalence and reaction severity to sesame seeds may warrant their inclusion on the priority allergen list in the United States.

The committee recommends that the Food and Drug Administration makes its decisions about labeling exemptions for ingredients derived from priority allergenic sources based on a quantitative risk assessment framework.

A quantitative risk assessment is based on knowledge of the detectable level of protein, its presence in the ingredient, exposure levels to the ingredient, and threshold dose-distributions for individuals allergic to the food.

The committee recommends that the food manufacturing industry, the Food and Drug Administration (FDA), and the U.S. Department of Agriculture (USDA) work cooperatively to replace the Precautionary Allergen Labeling system for low-level allergen contaminants with a new risk-based labeling approach, such as the VITAL program used in Australia and New Zealand.

To meet this risk-based approach, the following three steps are recommended:

1. The FDA and the USDA should establish Reference Doses (thresholds) for allergenic foods, where possible. The committee concludes that at this time, sufficient data exist on milk, egg, peanut, certain tree nuts (i.e., cashew, walnut, hazelnut), wheat, soybean, fish, and crustacean shellfish (shrimp) to establish Reference Doses. The FDA and the USDA should review the Reference Doses periodically, with particular attention to the remaining tree nuts for which data to establish Reference Doses are not currently available (i.e., almond, Brazil nut, macadamia nut, and pine nut).
2. Once Reference Doses are established, a food product would carry an advisory label (e.g., “peanut may be present”) only in situations when ingesting the product would expose the individual to a level above the Reference Dose for that allergen. The FDA should restrict the number of allowable advisory labels to one phrase. Because this labeling is voluntary, the product should clearly inform the

consumer, through labeling as appropriate, as to whether a risk-based approach (such as VITAL) has been followed for each specific product. The FDA and the USDA should educate health care providers and consumers about the meaning of such a food allergy advisory statement.

3. The FDA and the USDA, together with the food industry and the analytical testing industry, should develop and validate detection methods and sampling plans for the various food allergens for which Reference Doses are established. A common unit of reporting also should be established, such as parts per million of protein from the allergenic source, so that comparisons can be made between methods and between levels in the food and clinical threshold values.

Policies at Specific Settings

The FDA Food Code provides advice from the FDA for uniform systems and practices that address the safety of food sold in food establishments. The 2013 FDA Food Code includes provisions on preventing food allergic reactions but it has not been adopted by all states.

The committee recommends that all state, local, and tribal governmental agencies adopt the 2013 Food and Drug Administration Food Code, which includes provisions for food establishments on preventing food allergic reactions. Working in collaboration with other stakeholders, the agencies also should propose that the next Food Code requires that the person in charge in food establishments pass an accredited food safety certification program that includes basic food allergy management in order to decrease or prevent the risk of food allergen exposure. In addition, agencies should develop guidance on effective approaches to inform consumers with food allergies in food service establishments.

Guidance on effective approaches to inform consumers with food allergens in food service establishments could include menu designations of allergens and posters, and other forms of displaying information about food allergens in food establishments.

The CDC *Voluntary Guidelines for Managing Food Allergies in Schools and Early Care and Education Programs* (the CDC Food Allergy Guidelines) includes essential management approaches, such as preparing for food allergy emergencies, but they have not been implemented widely in all schools. Higher education institutions do not have similar guidelines.

Although reports of severe reactions while flying are rare, accidents can occur and improving policies and practices might prevent them. In response to its task, the committee developed specific recommendations for ways to assure that appropriate guidance and education are in place to create a safe public environment for individuals with food allergy. In doing so, the committee recognized that its task did not include recommendations for therapeutic intervention or clinical management of food allergies.

The committee recommends that, within the next year, relevant federal agencies (e.g., the Food and Drug Administration [FDA], the Centers for Disease Control and Prevention [CDC], the Federal Aviation Administration) convene a special task force that includes participants from the medical community, food companies, and advocacy stakeholder groups to establish and implement policy guidelines to:

- Assure emergency epinephrine capabilities are in place for children and adults in public venues, including schools, early care and education facilities, and on-board airlines;
- Provide standardized food allergy and anaphylaxis first aid training (e.g., identification of major food allergens, signs and symptoms of allergic reactions, and emergency treatment protocols) to appropriate school and university health staff, early care and education providers, and on-board flight crews; and
- Implement education standards for responding to and managing food allergy emergencies in schools and early care and education facilities (e.g., CDC Food Allergy Guidelines), and on airlines.

The committee recommends that the FDA continue to work together with other relevant federal, state, and local agencies to develop and implement labeling policies specific to allergenic ingredients in packaged and prepared foods that are distributed through airlines and other public venues, including schools and early care and education facilities.

Expand Research Programs

The committee lists research needs in areas of mechanisms of action, better diagnostic tools, effective educational approaches, and evidence-based guidelines for all stakeholders, and prospective and clinical trials to support or refute current hypotheses on the development of food allergies. In addition, although the committee did not review emerging therapeutic

approaches to cure food allergies, it included development of effective and safe therapies as a key long-term goal. The details of the research needs are in Chapter 9.

The committee envisions that this report will reach many stakeholders, including consumers, patients, health care providers, school leaders, food manufacturers, and food establishment managers, and serve as guidance for future understanding and management of food allergies. The committee also has confidence that the recommendations in this report, if implemented, will stimulate progress in the understanding of food allergies, reduce further uptakes in prevalence, and improve the quality of life of those with this chronic disease and their caregivers.

1

Introduction

FOOD ALLERGIES: CHARTING A ROADMAP TO SAFETY

Over the past 20 years, public concerns have grown in response to the apparent rising prevalence of food allergy and related atopic conditions,¹ such as eczema. Although evidence on the true prevalence of food allergy is complicated by insufficient or inconsistent data and studies with variable methodologies, many health care experts who care for patients agree that a real increase in food allergy has occurred and that it is unlikely to be due simply to an increase in awareness and better tools for diagnosis. Many stakeholders are concerned about these increases, including the general public, policy makers, regulatory agencies, the food industry, scientists, clinicians, and especially families of children and young people suffering from food allergy.

Food allergy has important implications not only for those individuals directly affected but also for their families, day care and school settings, and society (Gupta, 2014; Pawanker et al., 2011). Some children naturally grow out of a food allergy, while other children or adults develop a food allergy for the first time later in life. In either case, having a food allergy is a chronic disease that can influence a person's quality of life throughout the lifespan and, in some unfortunate individuals, lead to death. The human stories of food-related anaphylaxis and the heavy burden of protecting children from foods that might initiate such serious allergic conditions are

¹ The atopic conditions of childhood consist of the triad of asthma, allergic rhinitis, and atopic dermatitis. All share a common pathogenesis, being mediated by immunoglobulin E (IgE), and are frequently present together in the same individual and family.

BOX 1-1
Statements from Children or Their Caretakers

Statements from children and adolescents (6-15 years old) with food allergy in focus groups (DunnGalvin et al., 2009)

“There’s always food around you know . . . it doesn’t have to be a food party”

“When I take a first bite, there’s a moment when you think, is this it?”

“Nearly everything says ‘may contain’ so what can you eat?”

“Unlike my friends, I always have to be on [my] guard. . . . I envy them not having to be.”

“They say you’re just looking for attention.”

“. . . the same thing again and again . . . be careful, be careful . . . do you have your pen . . . watch what you eat . . . I need to have a life.”

“I was at a barbecue and Mum forgot to ask what was in the burger . . . there were eggs in the burger and my eyes and lips swelled up and it was scary.”

“You feel like you are choking; you have to get given the pen and then go to the hospital.”

“I get lumps in my stomach and my eyes get red and I’m in agony.”

“You know your throat is meant to be this size [indicates] and it swells to about this size [indicates]. It gets really hard to breath. . . . I can’t get my breath . . . and you feel scared . . . so scared.”

“I only go to friends’ houses who I know for ages . . . it’s safer that way”

particularly compelling. This burden includes fear of accidental consumption, difficulties with missing (or misunderstood) food labels, and bullying at school. Those not afflicted with such a disorder may have difficulty even imagining what life is like for severely food-allergic individuals, some of whom are allergic to multiple commonly encountered foods, such as milk, eggs, peanuts, tree nuts, and shellfish. To illustrate some of these issues, Box 1-1 includes real-life example statements from children, adolescents (DunnGalvin et al., 2009) and caretakers (Kahn, 2014; Monaco, 2015) as

“The girl next to me in school always has nuts . . . and I feel worried but I don’t like to say anything; nobody needs to know.”

“On Halloween they throw nuts at me but you can’t tell the teacher or they’ll say you’re a whiney baby; you only tell your best friends; I only told my best friend but she told everyone . . . and then I was teased.”

“It’s not the teasing . . . it’s the isolation . . . that’s what gets you.”

Statement from a caretaker

“. . . at seven months old, he was diagnosed with food allergies. The diagnosis was not to just one, but to four different food allergens: dairy, wheat, eggs and peanuts. . . . This was no mere intolerance. These were life-threatening allergies. . . . What I can do is to make sure that, as my baby grows, he learns to protect himself. . . . As a parent of a child with food allergies, I always have to be prepared. This is no simple feat. I carry emergency medications such as epinephrine auto-injectors, antihistamines, and an asthma inhaler. I vigilantly stay prepared with food. You never know when you will wind up somewhere that does not have a safe choice, such as a friend’s house where they cannot accommodate your child’s allergies.”

By Adrienne Kahn; posted on September 11, 2014, at AllergicLiving.com.

“Ever since my children were diagnosed with these [food] allergies, each moment has been a growing educational (and often empowering) experience. My husband and I felt it was very important from the initial diagnosis to be honest with Vincent about what would happen if he ingested peanuts, tree nuts, or anything that was cross-contaminated with them. We taught him how to carry and use the epinephrine auto-injector, how not to accept food from anyone but family, and never to take off his medical ID bracelet.”

By Meghan Monaco; posted on June 9, 2015, at AllergicLiving.com.

they describe quality-of-life impacts and hazards of having a severe food allergy.

Ultimately, answering questions about the actual prevalence of food allergy, the mechanisms underlying allergen sensitization and the development of food allergy, and how to estimate the severity of disease in affected individuals, among many other research questions, requires adequate support from research funding sources. Similarly, protecting those with food allergy from accidental exposure and providing appropriate treatment for

those who develop reactions, demand effective governmental policy and consumer protections across multiple sectors, including agricultural production, the food industry, product labeling, regulatory authorities, and the food and entertainment industries. At the present time, however, despite a mounting body of data on the prevalence, health consequences, and associated costs of food allergy, this chronic disease has not garnered the level of societal attention that it warrants. Moreover, for patients and families at risk, recommendations and guidelines have not been clear about preventing exposure or the onset of reactions or for managing this disease.

In brief, the scientific knowledge about food allergy has significant gaps and, for those at risk, few or no reliable prevention strategies or treatments exist. How did we get to this situation? First, the accepted gold standard for identifying a food allergy—the oral food challenge (OFC)—has not been used widely due to difficulties of the procedure (e.g., risk of a severe reaction, length of procedure, the need to standardize the food), especially in research where large numbers of study participants are needed.

Second, conducting research on food allergy presents various types of practical barriers: studies are very costly due to the long duration of typical therapeutic studies (e.g., 2 to 4 years); the heterogeneity of participants; difficulty recruiting participants; and notably, too few research centers and researchers equipped to conduct high-quality studies.

Third, food allergy is a complicated, multifactorial disease and researchers do not fully understand its causes, mechanisms, and effects. Except for having atopic parents (i.e. parents with a predisposition to allergic reactions), the contributions of various factors to food allergy remain unclear and under investigation. Genetics, time, route of allergen exposure, diet, factors related to pregnancy and lactation, and the microbiome all are being studied as potential influences on the development of food allergy. The fact that food allergy develops in infants makes the research difficult, as conducting trials during pregnancy or in infants could be unethical.

Finally, few effective therapies for food allergy currently exist. The gaps in scientific understanding have impaired the development of effective therapies, although many promising ones are being investigated.

Professional medical associations continue to update their practice guidelines for food allergy despite limitations in the evidence, based on the most recent knowledge on diagnosis, prevention, treatment, and management. Yet, unlike other chronic diseases related to diet, such as diabetes or cardiovascular diseases, where specific strategies for prevention or management have been established (ADA, 2015; Goff et al., 2014), recommendations by governments or professional associations for preventing the onset of a food allergy have been hampered by limited or inconsistent data. Recent and ongoing research and clinical progress on assessment, diagnosis, and treatment of food allergy hold the promise of improving future practice

and management strategies. These advances include the safe use of OFCs as the gold standard for diagnosis, emerging data on the role of early exposure to potential allergens for favoring prevention, and high-quality studies of effective therapies. Indeed, based on the latest findings in food allergy prevention science, and particularly the latest findings on the protective effects of early exposure to peanut, leading organizations are rethinking the current recommendations and considering promising new approaches. Still, new thinking and approaches can have the unintended consequence of confusing parents and all the institutions that interact with people with food allergy, including schools, airlines, and restaurants.

For individuals who are already diagnosed, complete avoidance is still the only established method for preventing a reaction and, as indicated in Box 1-1, it is not easy to achieve. This is particularly the case when effective policies and practices are not implemented in places where foods are purchased or consumed (e.g., the hospitality and food service industries). Likewise, policies to ensure that relevant settings are prepared to identify and treat a severe reaction are not always enacted, implemented, or enforced. For example, epinephrine may not be available in relevant places, such as early care and education centers, schools, afterschool programs, camps, or airplanes. To promote greater safety in such settings, nongovernmental organizations are creating tools and guidelines to increase awareness, help parents and children with strategies for avoiding allergens, advocate for better policies, and/or increase the effectiveness of research efforts. Likewise, professional organizations of various industry sectors (e.g., manufacturers, retailers, food service) have created guidelines and training programs for their stakeholders. Federal, state, and local governments also are beginning to include allergy management as an element of their food safety policies. However, despite all the policies and guidelines for the various settings (e.g., food industry practices, regulatory agencies, early care and education centers, schools, higher education, and public transport), their development may not be keeping pace with the science and their implementation and enforcement varies greatly across the United States.

In addition, food allergy is a major global challenge and prevention strategies are needed across the globe. Although the prevalence and implementation of policies will vary by country, similar management approaches could be adopted across countries.

For all of these reasons, it was thought to be timely and important, in the interest of public health, for the National Academies of Sciences, Engineering, and Medicine to conduct a consensus study to review the science and management practices of food allergy. The committee intends that this report will (1) clarify the nature of the disease, its causes, and its current management, (2) highlight gaps in knowledge, (3) encourage the implementation of management tools at many levels and among many stakeholders,

and (4) delineate a roadmap to safety for those who have, or are at risk of developing, food allergy, as well as for others in society who are responsible for public health.

STATEMENT OF TASK

This study originated as a result of the broad public interest in the health aspects of food allergy; the relevance to public health, health care, and society; and the current lack of solutions both for the prevention of food allergy and its management. The apparent increase in food allergies, and concerns about a lack of good management strategies, prompted informal discussions that resulted in a planning meeting in Washington, DC, under the auspices of the National Academies of Sciences, Engineering, and Medicine on May 24, 2014. Various experts gave presentations on what is known about food allergy prevalence, causes, and risk determinants; perceptions regarding food labeling; and treatment approaches. Representatives from stakeholder groups with an interest in food allergy also attended. The group discussed the concerns related to those topics and provided comments about questions that would be of value to include in a consensus study from the National Academies. Following this meeting, a Statement of Task (see Box 1-2) was developed with contributions from all stakeholders.

APPROACH OF THE COMMITTEE

Expert Committee and Advisory Panel

An ad hoc committee of 15 experts was selected and nominated to respond to the statement of task. Committee members were drawn from a broad range of disciplines, including food allergens and methods of detection, pediatrics, clinical medicine, immune-related illness, genetics, epigenetics, the microbiome, epidemiology, biostatistics, nutrition/dietetics, food safety, public education, public health policy, clinical trials, prediction and prevention of food allergy, and child development. To expand the geographical context and experiences, food allergy experts from the United Kingdom and Australia were included in the committee. The committee held one public session on June 22, 2015, and one public workshop on August 31-September 1, 2015, to gather information. The committee also met on five occasions in closed sessions to discuss the findings, draw conclusions, and craft recommendations. The public session and workshop were valuable in providing the committee with the perspectives of sponsoring organizations and with information regarding diverse aspects related to the task (see Appendix A for public sessions and workshop agenda).

In order for the committee to consider the perspectives of those affected

BOX 1-1

Statement of Task

A committee will be formed to examine critical issues related to food allergy, including the prevalence and severity of food allergy and its impact on affected individuals, families, and communities; and current understanding of food allergy as a disease, and in diagnostics, treatments, prevention, and public policy. This consensus study will engage a broad array of stakeholders, including government agencies, organizations, academic institutions, industries, policy makers, and patient organization groups, to bring together leading investigators from relevant fields, clinicians, and parents; and to develop a framework for future work; and to recommend actions by both government and nongovernment agencies. The committee's review of the evidence will consider the following key questions:

1. What are current trends in food allergy prevalence?
 - What is an appropriate definition of food allergy to use in measuring prevalence?
 - What data or methods are most appropriate to use in measuring prevalence and how may they be implemented?
 - Should there be an effort to assess prevalence for allergens other than the eight most common that are required to be disclosed on food packages? If so, should the same methods be used for these allergens?
2. What are the key prenatal/early life determinants of food allergy?
 - For example, are there dietary factors that impact development of food allergy and are these modifiable?
3. What are the current data gaps in understanding the diagnosis and prognosis for food allergy?
 - What new approaches are being developed to address these data gaps?
4. What steps can be taken to educate providers and the public in order to create safe environments for food allergic children both within and outside the home?
 - What and where are the most risky food scenarios and how can these be better managed?
 - What guidance can be given to individuals about exposure to low levels of allergens in food products?
5. What is the status of assessing allergen thresholds in individuals? What additional methods or tools are needed?
6. What research gaps need to be filled in order to provide better guidance to health care providers and policy makers?

The committee will develop a framework for future direction in understanding food allergy and its impact on individuals, families, and communities; recommending steps to increase public awareness of food allergy; promoting research on both disease causation and management; and informing preventive approaches to food allergy. Research gaps will be identified and recommendations made to fill them.

by food allergy, the study also included an advisory panel made up of nine parents of children with food allergies and one individual with food allergy. The advisory panel members were selected from a group of approximately 50 individuals recommended by the sponsor organizations. All members of the advisory panel live with the challenges of food allergy on a daily basis and some are active advocates in their communities, participants in policy work and public speaking, or mentors for families who are new to food allergy. Although their opinions may not represent those of all people with the disease, they were invaluable to the committee as good examples of the sentiments and burden of living with food allergy. Some of the concerns brought up by this panel included the need for more clarity in food labeling, appropriate training for emergency personnel, access to epinephrine, and for improvements in well-being and safety at specific settings, such as schools, camps, restaurants, and transportation.

Boundaries and Clarifications About the Task

As mentioned above, food allergy, as a chronic disease, shares characteristics with other conditions and diseases. It is therefore necessary to be very clear about the task and its interpretation by the committee. The committee focused its efforts on the questions in the statement of task as they refer to the definition of food allergy by the National Institute of Allergy and Infectious Diseases (NIAID) of the National Institutes of Health (NIH). This definition states that food allergy is “an adverse health effect arising from a specific immune response that occurs reproducibly on exposure to a given food.” Food allergies fall into two major types—immunoglobulin E (IgE)-mediated and non-IgE-mediated—and the committee focused mostly on IgE-mediated food allergies (see Chapter 2 for definitions). Some of the discussions, where appropriate, also pertained to non-IgE-mediated food allergies, such as food protein-induced enterocolitis, particularly when discussing diagnostic methodologies that are unique for each type of food allergy. However, the literature reviews, findings, conclusions, and recommendations reviewed in this consensus study refer exclusively to IgE-mediated food allergies. Other food-related diseases, such as celiac disease, or food intolerances, such as lactose intolerance, or toxicity of food additives, are not covered in this report because they were beyond the scope of the statement of task.

Although any protein can be allergenic, certain proteins and specific foods that contain them (e.g., Ara h 2 in peanut) are characteristically allergenic and have been recognized as such because of the frequency or severity of the symptoms they cause in individuals at risk. The list of common allergenic foods varies by country. This variation is often due to the nature of diets or native foods in a given region but also to different criteria that are used

to qualify a food for inclusion in the list. The committee's literature reviews were conducted from the perspective of foods that are considered allergenic in the United States. However, global evidence was considered to the extent that it informed the central issues the committee reviewed. Moreover, most recommendations also apply to any allergenic food today or those that may become clinically important allergens in the future. The committee did not review the scientific or regulatory aspects of the potential for proteins from genetically modified foods to be allergenic. The reader is referred to the 2016 National Academies of Sciences, Engineering, and Medicine report *Genetically Engineered Crops: Experiences and Prospects* for a review and recommendations on this topic (NASEM, 2016).

Although the study is meant to have a global perspective, it would not be feasible to answer all the questions in the statement of task from the perspective of all countries. Research data are being generated worldwide but implementation of research findings depends on contextual factors that would be different for each country or region. When it was valuable and feasible to do so, data collected about implementation in the United States, as well as in other countries, were used to guide the committee's deliberations and recommendations. It should be noted that while the recommendations are focused on the United States, many could be implemented in other regions of the world.

This report is not meant to duplicate or replace important guidelines that have been developed in the past and that will continue to provide essential information about progress in diagnosis, treatment, and management of food allergy in the United States. Instead, this report is meant to be a call for unified action among all stakeholders and the public, both to recognize the importance of this disease and to join forces in efforts to markedly improve our ability to understand, effectively manage, and ultimately, cure this disease, and to make the world safer for those afflicted with it. Rather than conducting evidence-based reviews for all topics relevant to the task, the committee offered the support of specific guidelines where appropriate. In addition, the committee has conducted selected evidence-based reviews of the scientific literature where recent developments or the need for reinforcement deemed it necessary. Moreover, the committee did not review therapeutic approaches that are currently being investigated and instead recommended more research efforts in this area. These key guidelines include the following: 2010 NIAID/NIH-sponsored *Guidelines for the Diagnosis and Management of Food Allergy in the United States: Report of the NIAID-Sponsored Expert Panel* (Boyce et al., 2010), the European Academy of Allergy & Clinical Immunology (EAACI) *Food Allergy and Anaphylaxis Guidelines* (Muraro et al., 2014), two Practice Parameters (Lieberman et al., 2015; Sampson et al., 2014), and two Clinical Reports (Sicherer et al., 2007, 2010). Table 1-1 includes the guidelines (and system-

TABLE 1-1 Food Allergy Guidelines and Systematic Reviews

| Title | Organization | Authors and Date | Referenced in This Report as |
|---|---|---|--|
| <i>Guidelines for the Diagnosis and Management of Food Allergy in the United States: Report of the NIAID-Sponsored Expert Panel</i> | National Institute of Allergy and Infectious Diseases (NIAID)/ National Institutes of Health (NIH) | Boyce et al., 2010 | NIAID/NIH-supported Guidelines |
| <i>Food Allergy and Anaphylaxis Guidelines</i> | European Academy of Allergy & Clinical Immunology (EAACI) | Systematic review: Chafen et al., 2010 Muraro et al., 2014 | RAND systematic review EAACI Guidelines |
| | | Systematic reviews: <ul style="list-style-type: none"> • de Silva et al., 2014 • Dhimi et al., 2014 • Nwaru et al., 2014 • Panesar et al., 2013 • Salvilla et al., 2014 • Soares-Weiser et al., 2014 | EAACI systematic reviews |

| | | | |
|--|--|------------------------|--------------------------|
| <i>Food Allergy: A Practice Parameter Update</i> | Joint Task Force on Practice Parameters representing the American Academy of Allergy, Asthma & Immunology (AAAAI) American College of Allergy, Asthma & Immunology (ACAAI) Joint Council of Allergy, Asthma & Immunology (JCAAI) | Sampson et al., 2014 | AAAAI Guidelines |
| <i>Anaphylaxis—A Practice Parameter Update</i> | Joint Task Force on Practice Parameters, representing AAAAI, ACAAI, and JCAAI | Lieberman et al., 2015 | AAAAI Practice Parameter |
| <i>Clinical Report—Management of Food Allergy in the School Setting</i> | American Academy of Pediatrics (AAP) | Sicherer et al., 2007 | 2007 AAP Clinical Report |
| <i>Self-Injectable Epinephrine for First-Aid Management of Anaphylaxis</i> | AAP | Sicherer et al., 2010 | 2010 AAP Clinical Report |

atic reviews on which they were based) and the names by which they are referred to in this report.

Gathering the Evidence

In addition to holding the public session and the information gathering workshop mentioned above and detailed in Appendix A, the committee used various approaches to respond to the questions in the statement of task. For example, it was possible to rely on the scientific literature to answer some of the questions. However, for questions related to current practices in the various settings encountered by those with food allergies, the committee relied more often on information gathered at workshops and/or by consulting the “gray literature” (published reports or research outside the traditional peer-reviewed scientific journals and commercial publications).

For example, to answer questions related to the prevalence of food allergy and the key prenatal and early life determinants of food allergies, evidence-based reviews were conducted as described in the report. To answer questions related to the definition, diagnosis, and prognosis of food allergy, as well as those related to managing food allergy in the health care setting, the committee did not conduct an extensive review of the literature because relevant recommendations have already been addressed in very recent authoritative reports. In such cases, primary resources for the findings, conclusions, and recommendations of the committee were derived from the 2010 NIAID/NIH-sponsored Guidelines (Boyce et al., 2010); the 2014 EAACI Guidelines and systematic review (de Silva et al., 2014; Dhimi et al., 2014; Muraro et al., 2014), as well as the 2015 American Academy of Allergy, Asthma & Immunology (AAAAI) Guidelines (Lieberman et al., 2015), the 2014 AAAAI Practice Parameter (Sampson et al., 2014), and the two American Academy of Pediatrics (AAP) Clinical Reports (Sicherer et al., 2007, 2010). Additional searches in scientific databases were performed to identify specific items in the literature to supplement the discussion about specific topics, paying special attention to papers published after the aforementioned reports.

A DEVELOPMENTAL AND ECOLOGICAL PERSPECTIVE ON FOOD ALLERGY

During its review and deliberations, the committee recognized that addressing the task and goals of the consensus study would benefit from taking a developmental and ecological perspective. Preventing and treating food allergy, and delineating a roadmap to safety are a multifaceted undertaking that must take into account many interacting systems that

influence both risks and safety. For every individual, the risks and possible protections for food allergy vary and change over the life course, depending on individual genetic factors, biological development, exposures to allergens, and the nature of the contexts in which the individual lives. From a societal and public health perspective, the safety and well-being of many potential individuals with food allergy requires recognition that risks and protections for public safety are spread across many systems, including food production and distribution systems, health care systems, and education systems, among others. This section explains how the committee undertook a developmental and ecological approach toward the health and safety of individuals with food allergy.

Ecological Models of Individual Development

Ecological models of individual human development emphasize that the individual interacts with many social, cultural, and environmental systems throughout life and these interactions shape the development, health, and well-being of the individual over the life course (Boyce and Kobor, 2015; Bronfenbrenner and Morris, 2006; Gottlieb, 2007; IOM, 2005; Lickliter, 2013; Overton, 2013). These interactions span genetic to societal levels (Gottlieb, 2007; Lerner, 2006; Lickliter, 2013; Overton, 2013). The importance of taking a relational developmental systems approach to health promotion also has been applied by others (Halfon et al., 2014). From this perspective, the health and well-being of a developing individual is constantly changing as the individual interacts with the physical and biological environment, schools, family, and other contexts throughout life.

Proximal ecological systems (i.e., the social, cultural, and physical contexts) with which individuals interact directly over the life course have been termed “microsystems” in Bronfenbrenner’s bioecological model (Bronfenbrenner, 1979; Bronfenbrenner and Morris, 2006). In general, the health and well-being of individuals and populations with respect to food allergy are influenced by biological systems within individuals, including the microbiome, as well as human biological systems, and also their interactions with their physical contexts, including the built environment, plants, animals, microbiotic organisms, water quality, or climate, that could influence food allergy risk and/or protective processes.

Throughout the life course, however, the systems with which a person interacts vary. Before birth, a developing fetus interacts indirectly with systems in the broader context because the mother’s body is the entire proximal context and essentially all current extrinsic influences (e.g., diet or psychological trauma) are mediated by processes linking the fetus to the mother’s biological function. After birth, the caregiving system (i.e., parents and other caregivers) plays a primary role in mediating the experiences

of a baby, but now the child has additional direct experiences with other people and physical environments (e.g., health care, early care and education centers, and the social environments). As children continue to develop, they join and interact directly with numerous new systems, including peer groups, schools, and community services for children and families. Eventually, children begin to interact directly with social media, workplaces, and social and recreational contexts, such as sport teams, and religious or other cultural contexts.

Individuals also are influenced by many additional systems beyond their proximal interactions, through the influences of cultural practices and governmental or nongovernmental policies or rules that shape their contexts and experiences within societies and social groups. These relatively distal systems in the social ecology that influence individual development indirectly have been termed “macrosystems” (Bronfenbrenner, 1979; Bronfenbrenner and Morris, 2006). In the context of food allergy, for example, macrosystems include the laws and regulatory systems that affect food or the transportation industries and health care systems, religion, or mass media.

Human individuals adapt to the contexts of their development in multiple ways. An organism can adapt to a wider range of environments because developmental plasticity makes it possible for the developing phenotype to adjust to the environment in which it will live (Boyce and Kobor, 2015; Del Giudice et al., 2011; Hochberg et al., 2011; Szyf and Bick, 2013). For example, many of the adaptive systems that sustain health and well-being, including immune functions, stress responses, and language development, require some calibration for effectiveness within a given environment. It is conceivable that changes in modern life, including urbanization, mobility, and rapid environmental change, may have disrupted some processes of adaptive calibration, such that an individual could be “tuned” for one environment but live in or move to a radically different context. For example, exposure to microorganisms may trigger different responses depending on the timing. Growing up on a farm in a context of exposure to a rich assortment of microorganisms early in life may have protective influences on the risk for developing asthma. However, initial exposure to the same organisms later in life can trigger allergic responses (Figueiredo et al., 2013; Guerra and Martinez, 2008; von Mutius and Radon, 2008). The *developmental timing* of a person’s interactions with his or her context is an important consideration for understanding the origins and prevention of food allergy. Research is revealing that the timing of exposure to potential allergens can be a key determinant of whether or not food allergy develops in those at risk. The development and vulnerabilities to food allergy likely depend on an array of sensitivities to context that also may be shaped by the timing of exposures to potential allergens and other environmental fac-

tors. The committee considers these to be vital factors in promoting health and well-being for those at risk of developing food allergy.

From the perspective of an individual person or that person's caregivers, a roadmap for safety in regard to food allergy must include a developmental understanding of current individual vulnerabilities and risks, informed by individual history, plus a detailed analysis of the risks and protective factors embedded in the contexts in which that person lives. A parent or caregiver actively protects a child with an allergy until that individual can manage on his or her own. As Box 1-1 illustrates, management of food allergy at the individual level can be challenging and complex. However, the task of a society to protect all its members with food allergy is even more complicated.

Complex Adaptive Systems in the Prevention, Treatment, and Management of Food Allergy

Health care and public safety systems have been described as examples of complex adaptive systems (Hammond, 2009; IOM and NRC, 2015; Lipsitz, 2012; Reiman et al., 2015). A complex adaptive system is composed of many heterogeneous elements whose interactions drive the system in ways that cannot be easily understood from considering only the separate elements. The elements can be social, physical, or biological. Specific properties characterize a complex adaptive system: individuality and adaptation, feedback and interdependence, heterogeneity, spatial complexity, and dynamic complexity (IOM and NRC, 2015).

Considering public risk, adaptation, and safety in relation to food allergy, examples of complex adaptive system features include the independent behavior of many individuals or their parents acting to avoid allergen exposure in the diet of self or child (adaptation and independence); the diverse responses of individual consumers to labels about allergens in food and to the experience of severe reactions to specific foods (independence, adaptation, heterogeneity); the actions of many independent businesses to customer concerns about allergies (independence, adaptation, heterogeneity, feedback) or to implementation of new state and federal regulations governing food production or sales (adaptation); the variation in sensitivity of individuals to the same potential allergen (adaptation, heterogeneity); the fact that different foods are considered allergenic in different countries (spatial complexity); and immunological changes during early development (dynamic complexity).

Efforts to change the safety of complex adaptive systems are complicated, whether the target of change is the entire public health care system, the commercial transportation systems, or the food production and service industries. Change is likely to require attention to issues of leverage,

resistance, cascading effects, and unanticipated consequences, as well as recognition that a single strategy is unlikely to change a large and multifaceted adaptive system. Changing one element in a complex system can have unanticipated consequences that raise problems in another part of the interconnected systems network. Moreover, it is difficult to move a complex system in the desired direction due to the complexity, heterogeneity, independence, and dynamic nature of its many component systems. Thus, solving problems in a complex adaptive system involves consideration of multiple levels and systems, multiple sectors, and multiple strategies. From this perspective, managing food allergy would include consideration of the roles of diverse actors, a multiplicity of processes, nonlinear and unexpected-emergent effects, counter-regulatory feedback loops, and many systems operating at different levels to achieve disparate goals. Examples of the many actors and settings (i.e., elements) that have a role in preventing and treating food allergy are individuals, families, schools, workplaces, food and transportation industries, and health care systems. As Reiman et al. (2015) stated, “Safety management of complex adaptive systems presents a great challenge” (p. 90). It may require appreciation of complexity in understanding and addressing the issues, distribution of adaptive capacity across levels, a balance of rules and flexibility, and an interactive process to steer the system toward greater safety.

ORGANIZATION OF THE REPORT

This introductory chapter describes how and why the study originated, the charge to the committee, and the developmental and ecological context. Chapter 2 is a background chapter that describes the definition of food allergy that the committee adopted, explains common food allergy signs and symptoms, summarizes common allergenic foods, and explains the mechanism of food allergy. It also comments on the misinformation among the many stakeholders in regard to what a food allergy is and how to prevent and manage it. Chapter 3 summarizes what is known about the prevalence of food allergy in the United States and abroad, highlighting the limitations in methods, especially in regard to prevalence trends. Chapter 4 includes the current diagnostic and prognostic methods used and others that are under investigation. Chapter 5 presents current knowledge about prenatal and early life determinants of food allergies, including genetic and environmental factors. Chapters 6, 7, and 8 contextualize the ways in which food allergy is currently managed in the health care system (Chapter 6), the food manufacturing industry (Chapter 7), and other settings such as schools and restaurants (Chapter 8). Chapter 9 includes all the committee’s recommendations for research. Finally, Chapter 10 culminates with the committee’s vision of a roadmap to safety, discussing how food allergy

can be prevented and managed based on evolving knowledge, taking into consideration the roles and responsibilities of the many actors and settings that an individual interacts with throughout the life course.

The committee envisions that this report will reach the many stakeholders, including the general consumer, patients, health care providers, school leaders, food manufacturers and establishment managers, and serve as guidance for future understanding and management of food allergies. The committee also has confidence that the recommendations in this report, if implemented, will stimulate progress in the understanding of food allergies, reduce further uptakes in prevalence, and improve the quality of life of those with this chronic disease and their caregivers.

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