CHAPTER 3

Developmental Trajectories in Food Allergy: A Review

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Contents

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Abstract

Increasing recognition of the importance of the relationships between perceptions, emotions, behaviors and health has changed the way health and disease are portrayed and researched. A chronic condition may affect and/or interact with already existing normative demands and changes in socialization. Although the prevalence of food allergy and anaphylaxis have been reportedly increasing, the emotional and social impact of growing up with food allergy has received little emphasis.

In this paper, we present current findings on the biopsychosocial impact of food allergy on children in order to gain insight into the food allergy experience, from the perspective of the child, teen, and parent living with food allergy, with particular attention to developmental aspects. Due to the scarcity of publications on the psychosocial dimensions of food allergy, we also draw on selected literature on children's and parent's experience of, and coping with chronic disease that may inform research into food allergy. To this end, we review some general developmental mechanisms that may underpin and explain normative age-graded shifts in patterns of coping across childhood and adolescence. We also highlight gaps in the literature and assess implications of current research in food allergy and other chronic diseases for intervention and prevention of negative short and long term outcomes.

I. BACKGROUND

The growing prevalence of allergic diseases present an increasing challenge for populations and health care systems around the world and food allergies constitute a notable part of this increase (Sicherer, 2002). The emotional and social aspects of food allergy have not received much attention to date although an association between allergy and anxiety disorders in children and adolescents have been found to persist into adulthood (Katon *et al.*, 2004a,b), and evidence linking psychological stress to the expression of asthma and atopy continues to grow (Wright, 2005). In child/adolescent populations with asthma, up to one third may meet criteria for comorbid anxiety disorders (Bender-Berz *et al.*, 2005; Ortega *et al.*, 2002).

Thoughts, feelings, and behaviors affect our health and well-being. Recognition of the importance of these influences on health and disease is consistent with evolving conceptions of mind and body and represents a significant change in medicine and the life sciences. Recent developments include the idea that emotional processes, such as stress, moderate activity in nearly all systems of the body and can directly influence the pathophysiology of disease. Discovery of these and other relationships between behavior and health has changed the way health and disease are portrayed. This interest is also reflected in the rapid development of health psychology and its more multidisciplinary cousin, behavioral medicine.

These fields grew rapidly in the 1980s and now constitute major endeavors in most university and medical center settings (Barlow *et al.*, 2002a). The movement coincides with the growing recognition of the importance of children's views of their experiences that has begun to permeate many areas of research (Hill, 2006). Methods for research with children are, however, relatively underdeveloped, emphasizing the need to develop and document methods for research with children (Hennessy and Heary, 2004).

Within the basic and clinical scientific community, there is increasing recognition that developmental trajectory frameworks offer a conceptual model for health development and a more powerful approach to understanding diseases. A developmental trajectory or pathway may be understood as a lifelong process of developmental integration that involves complex interactions between biological and environmental factors that influence the phenotypic expression of physiology, psychology, and behavior (Halfon and Hochstein, 2002).

The health of children is a product of complex, dynamic processes produced by the interaction of external influences, such as children's family, social, and physical environments, and their genes, biology, and behaviors. Because children are rapidly changing and developing in response to these interactions, the developmental process plays an important role in shaping and determining their health.

A. Transition points: neurocognitive development

Developmental pathway models can take account of the cumulative and interactive contribution of physiological and environmental variables. They may also delineate sensitive or transition points in development when physiological or environmental variables associated with a chronic condition may have a relatively greater impact and/or interact with already existing normative demands and changes in socialization (Halfon and Hochstein, 2002). One key transition point occurs at between 4 and 7 years in most cultures and involves entry into formal education. Children's social networks start to change from networks in which children primarily interact with adults to networks in which children primarily interact with other children, with consequent exposure to social comparison and competition in school classrooms and peer groups (Dixon and Stein, 2006). The clinical literature suggests that children's patterns of social functioning in middle childhood is predictive of relationship patterns at later points in development (Gifford-Smith and Browning, 2003). Furthermore, there is evidence of shifts in cognitive development in which enhanced memory, new reasoning abilities, and new strategies for recall emerge (Dixon and Stein, 2006). Adolescence marks a similar transition point. Growth of primarily physiologically based processes, such as attention, perception, and information processing, provide the foundation for important social and emotional changes that occur during these years that contribute to children's growing sense of identity and self-esteem (Harter, 1997).

Research in chronic disease in childhood may be particularly apposite, as children who grow up with a chronic illness not only have to meet their age-related developmental tasks, but they also have to manage their disease, which leads to a heightened risk of maladaptation (Hill, 2006). A chronic condition may affect and/or interact with already existing normative demands and changes in socialization (Schmidt, 2003). Thus, although most children follow normative developmental pathways and encounter predictable transition points, disease-specific pathways may be embedded within these trajectories and influence the phenotypic expression of physiology, psychology, and behavior.

B. Research with children

Children are increasingly acknowledged to have rights in the determination of medical decisions that affect them. This has encouraged research to be undertaken with children themselves to understand their own views on the impact of a disease on their experiences and relationships. It has become increasingly important for researchers and healthcare professionals to understand how the perceptions, experience, and impact of a chronic disease might influence a patient's interpretation and response to it, so that we, in turn can respond more appropriately.

Related to this, the role of psycho-educational interventions in facilitating adaptation to chronic disease has received growing recognition and is in keeping with policy developments advocating greater involvement of patients in their own care (Barlow *et al.*, 2002a)

II. PREVALENCE, MECHANISMS, AND CLINICAL MANIFESTATIONS OF FOOD ALLERGY

Atopy may be defined as a genetically and environmentally determined predisposition to clinically expressed disorders, including allergic rhinitis, atopic dermatitis or eczema, food allergy, and allergic asthma, regulated through immune phenomena in which many cells (i.e., mast cells, eosinophils, and T lymphoctytes) and associated cytokines, chemokines, and neuropeptides play a role.

Atopy identifies allergic diseases such as atopic dermatitis (eczema), bronchial asthma, and hayfever, which tend to cluster in families and are associated with the production of specific IgE antibodies to common environmental allergens (Sicherer, 2002). The ''atopic march' refers to the natural progression of allergic conditions, characterized by a typical pattern of sensitization and manifestation of symptoms appearing at certain ages, persisting over years or decades, but often spontaneously resolving with age (Sampson, 2003). Epidemiological studies have attempted to disentangle the various phenotypes, focusing on single manifestations at certain age windows, since different specific phenotypes may be induced or modulated by different genetic, environmental, or lifestyle factors. Most investigators seem to agree that a complex interaction between genetic and environmental factors regulates development of different atopic features, however much of the natural history of atopic diseases and its determinants are still not well understood (Johannson *et al.*, 2004). Food allergy is defined as an adverse immune response to food allergens.

The growing prevalence of allergic diseases present an increasing challenge for populations and health care systems around the world and food allergies constitute a notable part of this increase (Sicherer 2002; Sicherer *et al.*, 2001; von Berg *et al.*, 2003). The most common food allergens are peanuts, tree nuts, seafood, eggs, and milk, however, the list is constantly growing (Sampson, 2003). Several studies have confirmed the increase in prevalence of food allergies, especially peanut allergy and as a disease burden throughout the world; however, they seem to increasingly affect countries with a formerly low prevalence and is becoming a growing public health problem (Hourihane, Smith and Strobez, 2002). These findings were substantiated by Al-Muhsen and colleagues (2003) suggesting that peanut allergy now accounts for the majority of severe food-related allergic reactions. There appears to be a correlation between the increased consumption of a novel food and the risk of allergic reactions. Examples of foods introduced into the North American diet which consequently began to provoke allergic reactions as consumption increased include kiwi, mango, avocado, and other exotic fruits (Burks, 2006; Sampson, 2003).

Food allergy affects ~6–8% of young children and 3–4% of young adults in the UK, US, and Europe (Eggesbo *et al.*, 2001; Sampson, 2005; Sicherer and Sampson, 2006). In contrast, food intolerance describes an abnormal physiological response to an agent which is nonimmune-mediated (Johansson *et al.*, 2004). The prevalence of food allergies vary between countries. The only comprehensive permanent nationwide reporting system and register for severe allergic reactions to food was instituted in Norway in 2000 (Lovik *et al.*, 2003), and so more quantitative estimates are difficult to provide. In Ireland, Hourihane (1998) estimates that there are 16,000 children with peanut allergy; however, there has been no formal prevalence study undertaken to date. In addition, current data on severe and fatal reactions may be misleading because anaphylactic reactions are often mislabeled as asthma deaths, because of a lack of antecedent history or information. In effect, inadequate diagnosis of food allergy may, in part, reflect the lack of adequate provision of relevant health services.

The European Academy of Allergy and Clinical Immunology has proposed a revised nomenclature for allergic and related reactions (Johansson *et al*., 2004). According to this proposal adverse reactions to food should be termed "food hypersensitivity." The term food allergy should be used when immunological mechanisms have been demonstrated, and includes both IgE- and non-IgE-mediated reactions. All other reactions, which have sometimes been referred to as "food intolerance," should be termed nonallergic food hypersensitivity (Fig. 3.1).

Adverse reactions to foods were first described over 2000 years ago by Hippocrates, who is credited with the observation that cow's milk could cause urticaria and gastric upset, and, 500 years later Galen also described a case of allergy to cow's milk (Kimber and Dearman, 2002). Adverse reactions to foods were published intermittently during the twentieth century, but it is only during the last 20–30 years that an increasing awareness of food allergy has emerged in western industrialized societies.

Food allergy occurs when the body's immune system mounts an exaggerated response against the offending food, which acts as an allergen. It is a type of hypersensitivity reaction. It can be either:

- A type I, IgE-mediated reaction: This is the usual cause of food allergy. After initial sensitization, the release of mediators such as histamine are triggered each time a person is exposed to the food. It is these mediators that cause the symptoms.

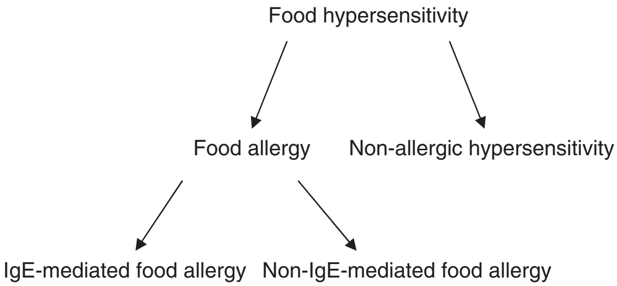

FIGURE 3.1 Continued

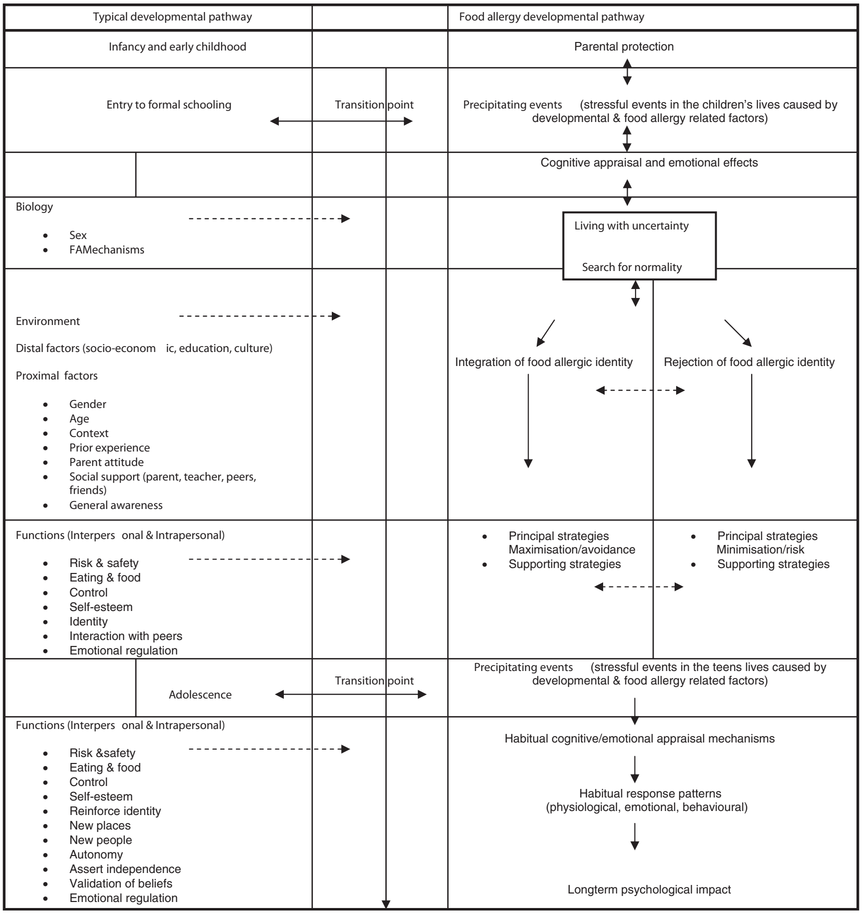

FIGURE 3.1 Nomenclature proposed by the European Academy of Allergology and Clinical Immunology (Johansson *et al.*, 2004). The developmental pathway in food allergy. Our developmental model outlines the content of stressors (e.g., social events, restaurants, food, allergic reactions, concern for risk and safety, concern for identity); modifying variables on appraisal (e.g., attitudes of others, low general awareness, poor labeling, age, sex, context; parental attitude); specific resources (e.g., types of social support; restaurants; labelling); emotional impact (uncertainty, difference); psychological impact (e.g., generalized anxiety, low self-efficacy); functions (e.g., reducing uncertainty; "fitting-in") and consequences for behavior and participation (e.g., principal, supporting).

- A delayed, type IV-mediated reaction: These reactions are mediated mainly by T cells. They typically affect the gastrointestinal tract or skin, for example, exacerbation of eczema in children after milk ingestion.

In an IgE-mediated reaction, symptoms involving the oropharynx and gastrointestinal tract may occur within minutes of ingesting a food allergen. Itching and swelling of the lips, tongue, and soft palate as well as nausea, abdominal pain, vomiting, and diarrhea have all been demonstrated secondary to food allergy (Sampson, 2003).

Anaphylaxis refers to a sudden, severe, potentially fatal, systemic allergic reaction that can involve skin, respiratory tract, gastrointestinal tract, and cardiovascular system (Sampson, 2003). The term anaphylaxis is derived from the Greek words meaning ''without'' (ana) and ''protection'' (phylaxis). The most dangerous symptoms include breathing difficulties and a drop in blood pressure, or shock, which are potentially fatal. Symptoms of anaphylaxis may develop within seconds or a few hours after ingestion of a food allergen, with the vast majority of reactions developing in the first hour. Symptoms can include swelling (especially lips, tongue, or throat), difficulty breathing, abdominal cramps, vomiting, diarrhea, circulatory collapse, coma, and death. Typical allergy medications such as antihistamines work too slowly and cannot reverse the effects of chemical mediators. Adrenaline or epinephrine, therefore is the treatment of choice and must be administered by injection promptly.

Food allergy, particularly to peanuts, is the most common cause of anaphylaxis outside hospital (Bock *et al.*, 2001), yet there are other common food causes such as shellfish, fish, milk, soy, wheat, and eggs (Asero *et al.*, 2007). These foods may not only cause fatal or near-fatal reactions, and they also tend to induce ''persistent sensitivity'' in most patients, in contrast to other foods such as milk, eggs, and soybeans, which are frequently associated with milder reactions and are usually ''outgrown.''

The life-threatening nature of anaphylaxis ''makes prevention the cornerstone of therapy,'' (Sampson, 2003). Avoidance of the responsible food allergen and emergency management in the form of injectable epinephrine (Epipen, Anapen, or Twinjet) in case food allergen is accidentally ingested is the only reliable therapy offered to those living with food allergy.

Anticipatory guidance measures form the cornerstone of advice, including; reading food ingredient labels, concern for cross-contamination, vigilance in a variety of social activities, and immediate access to the Epipen (Munoz-Furlong, 2003). However, avoidance is complicated by the fact that peanuts, nuts, soy, can be found in many foods (e.g., breads, muffins, pastries, biscuits, cereals, soups, icecreams, seasoning, sauces) and in different forms as an emulsifier or thickening agent.

A growing number of families must live and cope with food allergy on a day to day basis, socio-emotional impact of food allergy on children, and adolescents has been little researched to date (DunnGalvin *et al.*, 2007). Although researchers in the field of food allergy have stated that the scarcity in psychological and social literature on the experience of living with food allergy demands attention, the majority of research in food allergy has been biomedical in orientation, focusing on issues such as the molecular structure of allergens, or methods of diagnosis (see DunnGalvin *et al.*, 2007).

More recently, there has a growing interest in the development of questionnaires to measure the impact of food allergy on health-related quality of life (De Blok *et al.*, 2007). Health related quality of life (HRQL) is a multidimensional construct, consisting of physical, psychological, and social components (Eiser and Morse, 2001).

III. THE IMPACT OF FOOD ALLERGY ON HRQL

Most studies to date used generic HRQL questionnaires to investigate the impact of food allergy on quality of life. However, a disease-specific questionnaire is necessary because generic measures although useful for comparison across diseases, do not incorporate issues directly related to the patients condition and therefore lack the sensitivity necessary to detect changes as a result of treatment interventions (Fayers and Machin, 2000). Further generic measures lack the detail that is required to assess how different subgroups are impacted by food allergy (De Blok *et al.*, 2007).

A. Research using generic HRQL measures

Primeau and colleagues (2001) studied a sample of 301 patients and evaluated the quality of life and family relations of children and adults with peanut allergy, compared to that of children and adults with rheumatological disease. Their study was the first on the subject and they compared HRQL in rheumatology and food allergy patients. It was shown that the parents of allergic children believed that their children had difficulties in many areas. Remarkably, their children had more impairment, especially in daily activities and in their familial social interactions, compared to children with significant rheumatological disease. The authors found that families with peanut allergic children experience significantly more disruption in their familial and social interactions/activities than families with a child with CRD and suggested that this may be due to the constant risk of sudden death in the peanut allergy group leading to greater parent restriction of activities.

The comparison was criticized by Avery *et al.* (2003) because children with rheumatological diseases have other symptoms to include severe pain and chronic physical disabilities, which exceeds experiences of children with peanut allergy. Primeau *et al.* (2000), at the time of their study, recognized and acknowledged this comparison as a potential compromise. They admitted that their choice was influenced by the accessibility to available data.

Sicherer *et al.* (2001) measured the parental perception of physical and psychological functioning. The authors randomly selected 400 members of the food and anaphylaxis network, with families of children aged 5–18 years old and had 253 responses. Results indicated that peanut allergy impacted significantly on general health, parental distress, and family activities. Those with two or more food allergies scored significantly lower, depending on how many foods they were avoiding. There was also evidence to suggest that the educational and emotional support needs of these families are not being met.

Avery *et al.* (2003) assessed the effect of peanut allergy on the quality of life in children aged 7–12 years old and contrasted this with experiences of children with insulin-dependant diabetes mellitus (IDDM). They recruited 20 children with peanut allergy and 20 children with IDDM (ages ranging from 7 to 12 years). Their results indicated that children with IDDM have similar problems as children with peanut allergy. This includes, food choices, social restriction, issues relating to school, the carriage and use of a syringe and the chronic nature of the condition. The results also suggested that children with peanut allergy are more anxious and parents feel that their needs are not taken into account. Results showed that children with peanut allergy had a poorer quality of life and are more anxious concerning accidental ingestion of peanut than children with diabetes are of having a hypoglycemic reaction.

Another generic questionnaire-based study, among 1451 adolescents, indicated that 19% of the participants reported that they had a perceived adverse reaction to food, however their condition was not physician-diagnosed (Marklund *et al.*, 2004). When compared to adolescents without such conditions, this kind of allergy-like condition, regardless of the underlying mechanisms, was associated with lower HRQL.

B. HRQL Research using disease-specific measures

The first validated HRQL food allergy specific measure; the Food Allergy Quality of Life–Parental Burden (FAQL-PB) questionnaire (Cohen *et al.*, 2004) measures the parental burden associated with having a child with food allergy. Scores in the food-allergic cohort were significantly lower for general health perception, parental distress and worry, and interruptions and limitations in usual family activities, than in healthy controls. Scales were also lower in subjects with multiple food-allergies.

More recently, several measures have been developed to assess quality of life in parents, children and teens, propelled by Europrevall. Europrevall has initiated/propelled a leap in research.

Europrevall is Europrevall is an EU project which aims to improve quality of life for parents, children, teenagers and adults with food allergy (De Blok *et al.*, 2007; Dunn Galvin *et al.*, 2007). Europrevall multidisciplinary integrated project (IP) involving 17 European member-states, Switzerland, Iceland, and Ghana. Of the 63 partners, there are 15 clinical organisations and six small-medium sized enterprises (SMEs) as well as the leading allergy research organisations in Europe. Since the project began in 2005, new partners have also joined from New Zealand, Australia, Russia, India, and China.

By integrating information and developing tools for the use of European food allergy scientists, health professionals, food and biotech industries, and consumers it is Europrevall's hope that causes of food allergy can become better understood, diagnosis of food allergy can become swifter and the quality of life of food allergy sufferers improved.

Two food allergy specific questionnaires have been developed and published under the auspices of Europrevall. The first measures HRQL in children aged 0–12 years and is parent administered; ''Food Allergy Quality of Life'' questionnaire (FAQLQ-PF; DunnGalvin *et al.*, 2008) and the second measures quality of life in teens (FAQLQ-TF; Flokstra-DeBlok *et al.*, 2008).

The FAQLQ-PF and -TF were developed and validated in four stages: (1) item generation using focus groups with both children and parents, expert opinion, and literature review; (2) item reduction, using clinical impact and factor analysis; (3) internal and test-retest reliability and construct validity were evaluated; and (4) cross-cultural and content validity was examined by administering the questionnaire in a US sample (FAQLQ-PF, only).

Both studies found a severe impact of food allergy on HRQL in relation to psychosocial aspects of children's and teens everyday lives. For example, in the initial focus groups put in place to generate items for the FAQLQ-PF, parents suggested that the anxiety associated with the risk of a potential reaction has more profound effects on emotional and social aspects of a child's everyday life, than clinical reactivity induced by food intake. The importance of a subscale assessing this aspect of anxiety was subsequently confirmed using clinical impact and factor analytic methodologies.

In addition, multivariate analysis showed an interaction between sex and age group for impact of general emotional impact on HRQL scale, in effect, parents of boys reported higher mean scores up to the age of 6 years; parents of girls reported higher mean scores in the 6–12 years age group.

Studies using these measures have thrown light on the everyday burden of living with food allergy.

It has therefore been well established that food allergy can have a profoundly negative impact on quality of life, extending well beyond the immediate clinical effects of the individuals condition. However, very little is known about the attitudes, beliefs, and coping strategies of food allergic children about food allergy generally and their condition specifically and little attention has been paid to the most effective methods of communication with this group (Miles *et al.*, 2006).

IV. THE PSYCHOLOGICAL BURDEN OF FOOD ALLERGY

Although it appears that food allergy leads to intrapersonal (e.g., anxiety) and interpersonal (e.g., social restrictions) problems in adaptation, there has been little research into the socio-emotional impact of food allergy on psychological and social functioning. Indeed, in most studies on chronic diseases, usually psychological maladjustment factors such as behavior problems or depression are studied, but social maladjustment factors, such as social anxiety or social skills, have rarely been included (Meijer *et al.*, 2002).

The literature also lacks well-designed studies describing the psychological burden of food allergy. Studies are scarce and are often carried out in a mixture of diagnoses, reflecting the difficult field of adverse reactions to food. Many of the studies that have been undertaken are limited because they rely only on questionnaires, on the particular questionnaire selected, and on prestudy or preexisting hypotheses which limits novel findings. Questionnaire studies produce findings on ''how often'' or ''how many'' but are very limited in answering ''why.''

For example, patients attending allergy clinics were found to have higher levels of depression when compared with the general population, (e.g., Kova'cs *et al.*, 2003). In a community sample, Knibb *et al.* (1999) found that women with a perceived food intolerance or allergy have significantly higher scores for somatic symptoms, anxiety and insomnia, and severe depression than women with no reported food allergy or intolerance. Vatn (1997), found that patients identifying themselves as sensitive to food or chemicals had high scores for depression, anxiety, shyness, and defensiveness.

Coping has been defined as ''action regulation under stress'' and refers to how individuals ''mobilize, guide, manage, energize, direct behavior, emotion, and attention and how they fail to do to'' (Skinner and Wellborn, 1994, p. 113) under stressful conditions.

However, it appears that literature on adjustment or coping in chronic illness focuses mainly on coping in illness-specific situations. However, general coping styles may be more predictive for the psychosocial development of chronically ill children and teens than illness-related coping because these styles reflect how children cope with developmental tasks (Meijer *et al.*, 2002). General coping styles (e.g., in social situations) may be particularly relevant in food allergy because it is the anxiety associated with the risk of a potential reaction that has more profound effects on emotional and social aspects of a child's everyday life, than clinical reactivity induced by food intake (DunnGalvin *et al.*, 2008). In addition, food allergy, once diagnosed and after restrictions are put in place, may be primarily asymptomatic. Living with peanut allergy places increased stress on the child and the child's parents and siblings (King *et al.*, 2008). It also causes differing levels of anxiety throughout the family. The authors found that mothers of children with peanut allergy feel that they have significantly poorer HRQL and suffer more anxiety and stress than the father.

However, clinicians assume that "appropriate" levels of anxiety is adaptive in children and parents living with food allergy. Primeau *et al.*, 2000 and Avery *et al.*, 2003 suggest that the high level of stress in families with a peanut allergic child may have beneficial effects on coping strategies. Only one study, using a study-specific questionnaire, suggested that deprivation due to restrictions in lifestyle may lead to social anxiety in food allergy (Bollinger *et al.*, 2006).

Adaptational processes of children and adolescents with chronic conditions are of utmost importance because of the long-term consequences of childhood conditions. For example, in child/adolescent populations with asthma, up to one third may meet criteria for comorbid anxiety disorders (Bender-Berz *et al.*, 2005). In adult populations with asthma, the estimated rate of panic disorder ranges from 6.5% to 24% (Katon *et al.*, 2004a,b). Children with any chronic condition have twice the risk of developing mental health disorders of healthy children without an accompanying physical disability (Schmidt, 2003). A recent paper (Knibb *et al.*, 2008) may provide another clue to the impact of living with food allergy on long term adjustment. The authors used the Illness Perception Questionnaire (Moss-Morris *et al.*, 2002) to measure the extent to which illness perceptions and coping strategies are associated with levels of psychological distress among 156 adults with food allergy. Results showed that a strong illness identity and emotional representations of food allergy in adults were associated with higher levels of psychological distress; as were less adaptive coping strategies such as focusing on and venting of emotions. Strong personal control beliefs were associated with the lower levels of distress, as were adaptive coping strategies such as positive reinterpretation and growth. Coping skills partially mediated the link between the illness perceptions and the outcome; however, illness identity, emotional representations, and personal control retained an independent significant association with psychological distress.

V. THE INFLUENCE OF PARENTS ON CHILD ADJUSTMENT

Parental perceptions can have a profound impact on the way that children themselves perceive their own health and illness and on how they interpret risk associated the disease (Noojin and Wallander, 1997). Although the impact of any condition on a child's life varies according to the specific characteristics of the disease, the chronically ill child is often more dependent on parents with adolescents complaining more often a delay in independent life-styles (Wallander and Varni, 1998).

An important developmental issue relates to the fact that children and adolescents are dependants, largely reliant on adults for significant aspects of illness behavior. This behavior includes the way in which symptoms are responded to, including the extent to which medical consultation and lifestyle alterations are undertaken. Parents and carers are powerful in responding to (or ignoring) children's physical complaints, attributing significance (or reassurance) to these complaints, facilitating (or otherwise) the children's use of health care facilities and their involvement in (or withdrawal from) normal life activities (Noojin and Wallander, 1997). Thus, parental distress, response to diagnosis and consequent coping strategies will have implications for how children themselves cope and manage food allergy along developmental trajectories.

We could only find one published study that looked at the impact of parent influence in food allergy. Recent findings by Bollinger *et al.* (2006, p. 419) suggests that "children with food allergy may be at an increased risk of social-emotional developmental difficulties." Many parents admitted to overprotecting their children through an understandable desire to ensure their children's safety. However, such restrictions can stunt children's social and emotional development and increase children's perception of "illness intrusiveness." Keating and Miller (2005) discuss research findings on infant distress which suggests two socioemotional roots of competence, with possible interactions between them: age-specific emotion regulation style; and parental response and facilitation. They use the term "habits of mind" to describe the increasing coordination and integration of the competence and regulatory system trajectories over the course of development.

Our research group have carried out a study (submitted) on parent stress triggers using a specially designed Implicit Association Test (IAT). The IAT measures associative links between environmental triggers and psychological states. Explicit or "self-report" questionnaires have given rise to concerns related to the influence of conscious self-presentational biases which often result in inaccurate answers (Greenwald *et al.*, 1998; Nosek, 2007). In addition, the very act of completing the self-report measure may change emotions attitudes and beliefs about the construct under investigation (Greenwald *et al.*, 1998). Therefore, the IAT was used to measure the differential association of a target category (environmental stimuli) with an attribute dimension (anxious vs. relaxed) in parents of food allergic children ($N = 60$) and matched controls ($N = 30$). A study specific questionnaire (SSQ) was used to measure explicit attitudes. The IAT targets the specific concerns/attitudes/beliefs parents of food allergic children while minimizing confounders. In contrast, the perceived threat of social situations where food may or may not be present (a central concern of parents of food allergic children) is incomprehensible to parents of nonfood allergic children. Results showed that parents are significantly more anxious when they believe they are not in control of their child's environment. In contrast, there were no significant results with regard to parents of nonfood allergic children. It is clear therefore that parents face a difficult balancing act between encouraging growing children's independence and ensuring their safety that may have implications for children's own perception of control in living and coping with food allergy.

VI. SOCIAL SUPPORT

Not only interpersonal functioning, but also interpersonal needs of children with chronic conditions differ from those of healthy children. Social support is understood as a ''resistance'' or ''buffering'' factor in chronic diseases. Studies with children have shown that higher stress increases risk for adjustment problems, such as greater anxiety and depressive symptoms, while higher social support reduces the risk for adjustment problems (e.g., Wallander and Varni, 1998). Although many studies aggregate social support variables, the sources and types of available to children may differentially predict psychosocial adjustment (Schreurs and de Ridder, 1997). In addition, classmate support (contrasted with parent, friend, and teacher support) was found to be the strongest predictor of adjustment in children with limb deficiencies (Varni *et al.*, 1991), cancer (Varni *et al.*, 1994a,b,c), and pediatric rheumatic disease (Von Reiss *et al.*, 2002). However, other studies have found that family social support, but not peer support, was a significant predictor of adjustment in children juvenile rheumatoid arthritis (Varni *et al.*, 1988).

The diverse findings may occur because social support needs differ as a function of the particular disease. However, given the sparse literature on support in chronic disease in children in general, and food allergy in particular, further research is needed to examine the relative importance of different sources and types of support on the adjustment of children. For example, in a recent qualitative study into children's, teens, and parents perceptions of living with food allergy (DunnGalvin *et al.*, 2009), we found that social support, *per se*, does not necessarily protect against emotional distress, but rather how the individual perceives and interprets his or her social network. In children with generalized avoidance strategies, friends or parents may actually reinforce children's beliefs of a generally unfriendly world. Our findings show that parental distress, threat perception, and coping strategies reflect how children themselves respond to and manage food allergy. Parental influence and beliefs may have greatest impact during sensitive (psychological) or critical (physiological) periods of development when children and adolescents are most vulnerable, for example, during middle childhood and/or adolescence. This type of specificity permits precise empirical guidance in the development of our educational interventions for children, teens, and parents with food allergy.

In addition, we found that different dimensions of social support may reflect different dimensions of adjustment, for example, children who spoke about classmate support or teacher support appeared more in control and much less anxious about food allergy, compared to those who referred only to support from parents and close friends. Those who did not seek (or receive) instrumental or emotional support from friends or teachers appeared to engage in much riskier behavior. These differential relationships underline what Varni (1994b, p. 35) refers to as the ''specificity of the relationship between resistance factors and outcomes.''

VII. THE IMPACT OF STRESS ON BIOPSYCHOSOCIAL DEVELOPMENT

From a physiological viewpoint on development, we find that environmental stress may be important in perinatal programming (Wright, 2005). Studies in rodents and primates have shown that environmental manipulations that increase maternal stress result in elevated cortisol levels and dysfunctional behaviors in offspring that are mediated, in part, through effects on gene expression (Meaney and Szyf, 2005). Wright and colleagues (2005) found that higher caregiver stress in the first 6 months after birth was associated with increases in the children's allergen-specific proliferative response (a marker of the allergic immune response) higher total IgE levels, and increased production of TNF-α and reduced IFN-γ in a birth cohort of children predisposed to atopy. Therefore, during T cell maturation when the atopic phenotype is being determined by exposure to allergens, stress may be an additional factor.

During an immune response, the brain and the immune system communicate with each other in order to maintain homeostasis (Knonfol and Remick, 2000). Two major pathways, the HPA-axis and the CNS are involved in this bi-directional interaction (Elenkov *et al.*, 2000). The effects of stress on neuroimmuregulation in turn may modulate the hypersensitivity response in developing children. Cytokines play a crucial role in the pathogenesis of allergic diseases. In addition to acting as chemical messengers between immune cells, cytokines can serve as mediators between the immune system and the brain (Dantzer, 2001).

Catecholamines, glucocorticoids, and proinflammatory cytokines (TNF-α) are considered to be the principal messengers between the immune system and the nervous system in the stress response. For example, chronic stress enhances the production of TNF-α, in turn increased TNFa levels can activate the HPA axis. For example, increased numbers of regulatory T cells in peripheral blood were observed in both atopic and nonatopic students under exam stress, as well as skewed Th1/Th2 ratio and reduced NK cell numbers that were unique to atopic students (Kang and Fox, 2000). Although some studies (e.g., Wright, 2005) have examined the impact that the activity of the stress system may have on immune activation and symptoms, very few studies have considered whether immune activation and the experience of having an atopic disease, particularly during childhood, influences the long-term responsiveness of the HPA axis. For example, Rosencrantz *et al.*, 2005 used fMRI during antigen challenge to examine regional brain activation in adults with mild allergic asthma and identified activity in the anterior cingulated cortex (ACC) in response to asthma associated emotion words (e.g., wheeze). After antigen challenge, increased levels of IL-1 and IL-6 have been noted (Marshall *et al.*, 2002). Depression has also shown to be associated with excessive secretion of proinflammatory cytokines such as IL-1 and IL-6 (Maddox and Pariante, 2001).

VIII. THE IMPACT OF SEX AND GENDER IN FOOD ALLERGY

The relationship of sex and gender to health and disease is complex, and varies across an individual's lifespan, and between cultures and different social contexts. Attention to sex and gender in biomedical and health sciences research is being actively promoted by the European Union Commission under their research policy of ''mainstreaming gender equality''(Klinge and Bosch, 2005). Sex denotes the differences attributed to biological origins alone, while gender refers to the social and cultural influences that lead to differences between women and men (DunnGalvin *et al.*, 2007). One consequence of variables related to both sex and gender is that potentially differing patterns of disease prevalence, different degrees of severity, and different patterns of mortality and morbidity may be identifiable between men and women (e.g., Wizeman and Pardue, 2001).

A. The influence of sex

In population based studies sex differences in atopy (assessed as skin test reactivity to one or more of a panel of allergens) have been reported throughout childhood and into early adulthood, such that rates in girls are lower than in boys up to at least 15 years of age, in most studies up to 25 years of age, but are not consistently observed thereafter (Forde *et al.*, 2003). In contrast to the sex differences in atopy assessed as skin test positivity which vary and change direction across the human lifespan, sex differences in atopy assessed as total serum IgE levels are consistent across the lifespan, with levels in females being lower than those in males (Burney *et al.*, 1997). With reference to asthma and food allergy, prevalence is higher in boys before puberty, while this sex ratio is reportedly reversed after puberty (Becklake and Kauffman, 1999). Physiological pathways for these sex differences have been discussed with reference to ''immune dimorphism,'' the term given to differences in immune responses and regulation between the sexes.

The mechanistic involvement of sex hormones in immune reactions has increasingly been acknowledged in recent years (Osman, 2003). Testosterone and oestrogen affect diverse cellular processes including protein synthesis, cell division and migration, neuronal growth and axonal branching, and synaptic remodeling. Receptors for sex steroids have been identified on lymphocytes, monocytes, and mast cells (e.g., Balzano *et al.*, 2001). Lymphocytes are known to express both testosterone and estrogen receptors (Osman, 2003) whereas androgens enhance CD8+ lymphocyte activity and are correlated with the activation of IFN-γ-secreting cells in healthy adults (Balzano *et al.*, 2001). In allergy, sex hormone receptors on lymphocytes and leukocytes may modulate the type of immune reaction and regulate inflammation. For example, estrogens have a receptor-mediated effect on the releasibility of mast cells influencing the threshold levels in the effector phase of allergy (Da Silva, 1999).

Different patterns of cytokine responses between males and females may be implicated in gender specific effects. Mechanisms linking psychological stress, personality, and emotion to neuroimnoregulation as well as increased risk of atopy have been increasingly elucidated (Wright, 2005). We already know that components of stress and the stress response differ between men and women. The tend-and-befriend response, mediated by oxytocin and endogenous opioids, may be more applicable to women than the fight-or-flight response, which was based largely on studies of men (Wright, 2005). Even within the flight-or-flight response pattern there are sex-based differences. The HPA axis interacts with reproductive function, such as menstruation.

For example, when challenged by psychosocial stressors, males have been found to show a significant increase in glucocorteroid sensitivity but decreased proinflammatory plasma cytokine production, whereas females show a significant decrease in glucocorticoid sensitivity but unchanged proinflammatory plasma cytokine production (Rohleder *et al.*, 2001). Furthermore, these sex differences were found only under active mental stress, not under passive cold stress. This raises the possibility that sex differences in self-reporting (see DunnGalvin *et al.*, 2006) and even prevalence in some diseases could at least in part be explained by sex differences in the nature of the physiological response to stress, and, further that the nature of stressors may also influence sex differences in immune reactivity to stress (Kang *et al.*, 2004) involving a complex interaction between biology and environment. For example, there are gender differences in the *types* of stressors to which an individual is likely to be exposed.

The complexity of these sex and gender based interactions may explain the more adverse effects of food allergy on female over male general emotional well-being. For example, females with food allergy were found to be at increased risk of negative socio-emotional outcomes (Bollinger *et al.*, 2006). Patients attending allergy clinics reported higher levels of depression compared to the general population (Kova'cs *et al.*, 2003). A birth cohort study in Finland (Timonen, 2003) revealed that, at epidemiological level, skin prick test positive females exhibited up to an 1.8-fold greater risk of developing lifetime depression when compared with skin prick test negative subjects. In addition, the corresponding risk increased up to 2.7-fold among females, who had a positive skin prick test together with self-reported allergic symptoms. Maternal atopy alone almost doubled the risk of lifetime depression in female probands when compared with families in which no maternal atopy existed. In contrast, parental atopy did not predict any type of depression in male probands. However, as previously discussed, social adjustment or social anxiety was not investigated; therefore, we only have results on more extreme or clinical psychological or behavioral disorders, such as those described in the DSM-IV.

B. The influence of gender

There has been little psycho-social research on the influence of gender in the context of food allergy (see DunnGalvin *et al.*, 2007). Marklund and colleagues (2004) investigated the extent to which females and male adolescents experience perceived allergy-like conditions and the impact of these on everyday life. They found that adolescent females reported allergy-like conditions more frequently than adolescent males. Although all adolescents with allergy-like conditions reported significantly lower HRQL in seven of eight health scales that measured bio-psycho-social functioning, however, females reported more severe HRQL-deterioration compared with males. This is consistent with research that shows an excess of psychological vulnerability in adolescent girls with chronic conditions when compared to boys suffering from the same conditions, including epilepsy and asthma (Austin *et al.*, 2000), insulin dependent diabetes mellitus (La Greca *et al.*, 1995a,b), and cerebral palsy (MaGill and Hurlbut, 1986). Of the allergy conditions reported by Marklund, more than 50% of the adolescents stated they had food hypersensitivity with positive allergy tests. However, a sex and/or gender breakdown for confirmed food hypersensitivity or method of diagnosis was not included. Thus, it is not possible to determine if there is a gender difference in perceived versus actual food allergy for these individuals. However, work by Knibb and colleagues (1999) has demonstrated a gender bias in reporting self-diagnosed food allergy and intolerance, with significantly more females self-reporting than males.

Differences in self-reports of ill-health and psychological distress have also been observed in adolescents in the general population. For example, Sweeting and West (2003) found that self-reported general ill-health and physical symptoms, as well as psychological distress was significantly higher and increasing from age 11 for females compared to males. This increased with age and by age 15, there was a female excess in general ill-health, including psychological distress and ''malaise,'' limiting illness, poor self-rated health, headaches, stomach problems, and dizziness. This may also explain possible gender differences in self-assessed health in the context of perceived food allergy.

This has been explained by the concept of ''illness centrality'' (Wiebe *et al.*, 2002), or the level at which particular illness has been integrated into the self-concept. In a recent study (DunnGalvin *et al.*, 2009), we found that as the child develops, the level of integration of food allergy into the self concept also develops in a mostly gender-specific manner and has consequences for the child's understanding of food allergy and everyday management of the condition. We found that girls tend to incorporate food allergy into their self-concept, making it a defining part of who they are, whereas males ''contain'' the illness by minimizing its importance. Interestingly, although boys evinced lower anxiety levels because of this tendency, they were more prone to ''risky'' behavior (e.g., not bothering to read labels), whereas girls were more anxious, but also demonstrated more self-care behaviors.

IX. RISK BEHAVIOR IN FOOD ALLERGY

Risk is considered as the probability of a negative event occurring and can be quantified. However, this form of risk can be understood as ''danger.'' The perception of risk is a socially constructed phenomenon, and is more difficult to measure. Psychological risk is based on perception rather than fact, and is therefore based on qualitative, not quantitative characteristics of the hazard being considered. For example, when one individual feels a sharp pain, he/she may interpret it as a possible ''heart-attack'' and phone for an ambulance, whereas another individual might just reach for an indigestion remedy. As already discussed, food allergy has an impact on quality of life, due in part to the constant vigilance required on the part of the allergic individual, or their caregiver, to ensure accidental ingestion of food allergens does not occur. However, limited research exists in risk perception in food allergy and there is no research to date on process variables and/or causal pathways involved in the initiation, treatment, and cessation of health risk behaviors in food allergy.

Research looking at the incidence of severe allergic reaction has suggested that adolescents and young adults are more at risk. In a Norwegian study on severe allergic reactions to food, the main risk group was comprised of young adults aged 20–35 (Lovik *et al.*, 2003). Teenagers represent a high-risk group for anaphylactic fatalities caused by food allergy, accounting for 53% of a group of UK fatalities (Pumphrey, 2000).

A recent paper by Sampson and colleagues (2006) found that adolescents and young adults appear to be at an increased risk for fatal food allergic reactions, and suggested that they may adopt more risk-taking behaviors with regard to their food allergy; however, gender differences or possible causal mechanisms were not explored. The study population included persons with a high degree of severity of food-induced allergic disease, with numerous food allergies, and frequent and severe reactions, however, 37% with severe symptoms did not receive epinephrine, and 38% did not have it with them during severe reactions. The authors suggestions for intervention was to encourage clinicians to emphasize to patients that food is often a part of all group activities, and an accidental exposure could occur, making it necessary and safest to always have an epipen available. They also suggested teaching parents to remind teenagers about carrying epipens to social events. It is clear, therefore, that research is needed to establish underlying emotional risk factors associated with risk taking.

Perception of risk in adults is usually described, or interpreted, with reference to health belief models (HBMs) (Ajzen and Fishbein, 1980; Janz and Becker, 1984). Individuals are more likely to engage in health behaviors if they perceive: vulnerability to health threats; that the consequences are severe; that treatment or preventive measures will be successful. Although there are variants to the framework, the different models share many of the same elements. In effect, theories assume that individuals rationally weigh benefits and costs and act according to the outcome of this analysis. Subsequent modifications to the models include the addition of perceived social or monetary barriers to the adaptive response. A cue to action which can be internal (e.g., symptoms) or external (e.g., health communication) is hypothesized to trigger these cognitive processes. Of course, demographic and sociopsychological variables may influence perceptions and indirectly affect the likelihood of the response (van der Pligt, 1994, 2002). Although the HBM have been found to predict children's expectations to use medicines to treat illnesses (Bush and Iannotti, 1990), there is limited support for the model and for components of the model predicting children's health behaviors. This is especially evident for perceived vulnerability to health threats. For example, early research revealed mostly negative relations between children's health behaviors and perceived vulnerability to risk (e.g., Gochman and Saucier, 1982) and initial findings were later extended to adolescents (Greening and Stoppelbeim, 2000), thus challenging the hypothesis postulated by HBM that greater perceived risk is related to adaptive behaviors in children and adolescents.

Such findings suggest that risk perception is a complex process that warrants a deeper understanding from both health educators and researchers. For example, in light of the incongruence between knowledge and action in terms of compliance and risk, there is an increasing recognition of the need to qualitatively explore people's experiences, perceptions, and understandings of what it is like to live with a chronic condition, including its management, in order to better understand the decisions people make about managing their condition.

Developmental factors are also important when considering risk perception in food allergy. For example, in middle childhood, as processes relating to the impact of social comparison develop, children may be tempted to reject safety rules in order to ''fit-in.'' Adolescents and young adults frequently eat away from home, they face growing peer pressure, and alcohol consumption may be high. The latter may both impair their ability to assess risk and augment the physiological effects of allergen encounter such as vasodilation (Sampson, 2004). For many adolescents, the social pressure for psychosexual autonomy directly clashes with the prolonged dependence on family, which may be particularly pronounced in chronic diseases such as food allergy. Researchers in the field of allergy suggest that teenagers should be a priority group for the development and evaluation of interventions to improve their adherence to management plans. However, interventions will not prove successful unless we know the disease-specific developmental trajectory by which some teenagers become high risk and others do not.

X. DEVELOPMENTAL PATHWAYS IN FOOD ALLERGY

All these studies represent outcomes, but, there has been little, if any, research in allergic diseases in general and food allergy in particular, into the developmental pathways that lead to these observable consequences.

This limits the ability of clinicians, researchers, and policy makers to predict and evaluate cognitive and emotional development in the food allergic child, with implications for prevention, treatment, intervention and health policy. For example, allergists assume, but have never confirmed, that high levels of vigilance in children performs an adaptive protective function and psycho-social outcomes have not been investigated to date. Furthermore, a developmental perspective has the potential to provide an explanatory framework for previous disparate findings of the impact of food allergy on children and adolescents.

The way in which children and adolescents cope with chronic health conditions is considered as an increasingly important predictor of health in clinical and psychosocial research (Schmidt, 2003). Consideration of the developmental perspective is not only useful when studying children, but also helps to explain cognitive processes in response to stressors in adulthood. However, coping has been studied less frequently in children and adolescents than in adults. Researchers contend that this may be due to the difficulty in assessing developmental processes that are occurring simultaneously in children and teens (Schmidt, 2003). The interrelatedness of coping and development implies that coping is a process that is shaped by developmental organization and, likewise, development is shaped by coping processes (Schmidt, 2003; 214).

However, early adopted strategies of coping with chronic disease may serve as a buffer against these disease-related consequences, even if a certain stability of coping strategies across situations and developmental stages cannot be assumed. Coping has not only been shown to be related to patient well-being, but mediates health behavior as well as health care utilization (Barlow *et al.*, 2002b). For health care providers, there is socioeconomical interest to support the development of adaptive and active coping strategies in children with chronic conditions as early as possible.

A recent study (DunnGalvin *et al.*, 2009), under the aegis of Europrevall, represents a first attempt to provide an integrated developmental framework to explain the onset, development, and maintenance of food allergy related cognitions, emotions and behavior. 62 children/teenagers aged 6–15 years took part in 15 age appropriate focus groups, 52% of children were female. Parents were also interviewed. All children were physician diagnosed with IgE-mediated food allergy and had been issued with an anapen/epipen.

Through qualitative enquiry, a framework for evaluating children with food allergy was developed. Developmentally appropriate techniques were designed to stimulate discussion, maintain interest, and minimize threat to the child's self-esteem. Six main themes emerged from the analysis that encompassed precipitating events (stressful events in the children's lives caused by food allergy related factors); psychological impact (cognitive appraisal and emotional effects); and behavioral consequences or coping strategies. Findings indicate that coping in food allergy is more than simply a strategy, it is a cumulative history of interactive processes (both age, gender, and disease specific) that are embedded in a child's developmental organization.

Our findings show that food allergy is a central ''lens'' in children's lives through which they interpret experiences. When children and teens are confronted with a stressful event, such as a birthday party, a novel situation, an allergic reaction, or making new friends, the way in which they appraise the event, and its attendant emotional impact are viewed through this lens. How this lens is constructed and its psychological impact (uncertainty, anxiety, confusion, difference) on individual children is modified by age, gender, context, prior experience, attitudes of parents, attitude of peers, and level of general awareness.

Age is an important factor in determining the type of event children are likely to encounter from structured events such as birthday parties in younger children to more unstructured and unplanned events as children become more independent.

Children live within the context of their families, which have interaction patterns, rules, organizing principles, and general belief systems, as well as those specifically regarding health and disorder. Parental stress and perceptions of level of threat and consequent anxiety has a profound impact on the way that children themselves perceive risk and control. In focus groups with parents, many admitted to overprotecting their children through an understandable desire to ensure their children's safety. Teens used very similar language and phrases when talking about aspects risk and control that younger children ascribed to their parents—and that parents themselves used in focus groups.

In most children under the age of 8 years, there is a certainty of parental and adult knowledge and a consequent sense of control of events relating to food allergy. Children in the 6–8 years age group described the food they eat as ''special'' and also described themselves in this manner. In addition, younger children are more confident in social situations because of the protective presence of the parent. However, a transition point occurs around >8 years when children begin to describe themselves as different and the term special is ascribed to parents and takes on a negative connotation. At this time, children also begin to learn or feel that they cannot conclusively prevent an allergic reaction from occurring, giving rise to a state of uncertainty, and impacting on children's perception of autonomy and self-belief in their ability to control events in their lives.

Older children have to learn to live with constant uncertainty, often reinforced by parent's own anxiety about safety. This sense of uncertainty continues to grow as children develop and when children were asked ''when do you have a reaction,'' many recounted stories of accidental ingestion of allergic foods when visiting relatives, at school, or at social events "even though I was careful."

This state of uncertainty is also reinforced as children and teens encounter a widespread lack of awareness that encompasses teachers, schoolfriends, classmates, shops, restaurants, coffeeshops, afterschool activities, social events, and other parents. Therefore, children become aware, both through parents or through direct experience that a clear dichotomy exists between safe places and people and risky places or people, perceived by participants as "those who understand and those who don't." This directly impacts on perception of control and illness intrusiveness. In addition, difficulties in adapting concrete rules often results in a perception of external control over a particular event, particularly in the transition period between parental and "self" control.

A food allergic child's identity appears to be closely tied to the dietary and social restrictions that come with their condition. In middle childhood as peer comparison begins to appear, children with food allergy begin to make causal connections between experiences in the world at large and inner feelings, a strong negative association can develop between appraisal in terms of an objective health threat and appraisal in terms of the emotional response to a health threat. This perception of "difference" is isolating and has consequences for how children perceive themselves and how they feel they are perceived by others. Indeed, teens speak about social events mostly in terms of their restrictions.

Events are appraised in the context in which they occur and an awareness of expected behavior. For example, whereas an allergic reaction which takes place in the home may be regarded as a low-anxiety event, one which takes place in school can be appraised a highly stressful because it impacts on the child's goal to "fit-in." This goal confronts children with the difficult balancing act of protecting their ego and managing risk. He or she learns to appraise (and weight) threats to personal safety with threats to social identity. The stress appraisal process may result in children "just chancing it will be ok" and deliberately eating an allergic food when in the company of others, whereas others protect their self-esteem by avoiding novelty as much as possible. With regard to risky behavior, another important factor emerged as a motivation for deliberately eating an allergic food. It appears that some older children attempt to determine their own risk thresholds; "I would have a little bit... and see what happens... you might get a bit sick only." This may be a way to gain some control over feelings of uncertainty that are integral to growing up with food allergy.

Levels of anxiety appear to range from mild anxiety in a situation where the allergic food is present to more severe "trait-like" anxiety. About 20% of the participants mentioned being anxious "a lot of the time," the majority of which were girls. Coping strategies were found to lie on an maximization/avoidance to minimization/risk continuum. The majority of girls were found to use ''avoidant'' strategies to cope with living with food allergy. Many clinicians assume that these strategies are necessary and adaptive, if they are proportionate. However, results showed high levels of anxiety, vigilance, and generalized avoidance of situations and people not directly related to food consumption are associated with maladaptive avoidant strategies. A surprising finding was that anxious children and teens are not necessarily those who experience the most or recent reactions. For example, many of the children who described themselves as anxious or worried about food allergy could not remember ever having had a serious reaction. ''Minimizing'' strategies, such as not reading labels, not telling others that you are food allergic in risky situations and deliberately eating an allergic food (mostly found in boys), are also maladaptive in that children who use them are more vulnerable to experiencing an allergic reaction. Opportunities to engage in risky behavior increase as children enter their teens. Teenagers represent a high-risk group for anaphylactic fatalities caused by food allergy, accounting for 53% of a group of UK fatalities (Pumphrey, 2000).

A. Transition points in development for food allergic children

With reference to transition points in development, a negative representation of food allergy can result in psychological distress, which may accompany, or follow, transition (or sensitive) points in the developmental pathway, for example, when children learn that they (or their parents) cannot conclusively prevent an allergic reaction.

In the middle childhood years, children must begin to gain autonomy and self-belief in their ability to control events in their lives. Appraisal processes outlined above may result in increasing attention being given to processing information relating to food allergy, accompanied by emotional arousal and consequent increased detection of threat, whether social (self-concept) or personal (safety). However, recent experience of a reaction is not a necessary precondition for this.

Because food allergy places particular limitations on children's lives and frequently leads to restrictions in a variety of activities, there is the potential for these perceived illness-induced limitations to generalize to disease- unrelated events as children progress along the development pathway. For example, we have evidence of an over-interpretation of ambiguous information in terms of processing of potential threat not directly related to food; ''you'd be worried if you were somewhere new... that you weren't before; 'when other kids see an advert for a circus, they think fun, I think danger.''

In adolescence we encounter another transition point, when teens encounter unstructured ''novel situations'' and peers and their automatic response patterns are challenged resulting, as before, in increased attention to threat. This appears to apply particularly to those with avoidant coping strategies at the middle to high points of the avoidance/risk continuum and has an impact on cognitions, emotions and ultimately behavior. Although many teens appear to accept an ongoing conflict between personal safety and social self-concept, others resolve this by intensifying previous behaviors, whether minimization/risk or maximization/avoidant, moving them up or down the continuum. Finally, increasing coordination and integration of regulatory systems (e.g., information processing, and appraisal processes) over the course of development means that by the time children reach their teens, self-perception, emotional reactions, and cognitive appraisal mechanisms have become relatively stable and consistent.

B. Parental views and management of food allergy

Food allergy adds an extra element to the ordinary challenges of parenting. There was to considerable overlap between parent and children/teen focus group findings. Both parents and children spoke of feelings of anxiety, frustration, anger, difference, embarrassment, and uncertainty in response to situations stemming from food allergy. In addition, parents spoke about the difficulty of balancing the needs of their nonallergic children against those of the child with food allergy, and negotiating the precarious line between supporting children's independence and keeping them safe. These challenges sometimes led to conflict between parents and children and between father and mother which, in turn, impacted on the quality of family life. Furthermore, the sense of huge responsibility, over and above that felt by the parent of a "normal" child, and guilt, means that levels of stress often continue for significant periods of time.

In order to keep their children safe, and cope with their own anxiety, a substantial proportion of mothers, in particular, appear to micromanage their young children's lives, which may lead to dependence and low self-efficacy in some teens and, in contrast, to rebellion and risky behavior in others. On this point, as in the child/teen transcripts, there appears to be gender differences, with parents reporting that boys tend to hide their food allergy from others and girls rely largely on parents, and longstanding friends as they enter adolescence, to manage social situations involving food. There are also gender differences between fathers and mothers, although this difference may pertain to language style and role expectations, in that mothers were more likely to talk about feelings of anxiety and helplessness.

Parents had different concerns at different developmental points, for example, when children were young parents keenly felt the burden of responsibility in managing risk in their children's lives, but were less anxious about children's safety because of higher perceived control. Parents were particularly anxious in the transition period from primary to secondary school. In primary school, classes are generally smaller and parents are familiar with friends, however, in secondary school children encounter new social and peer pressures, and hence an increased risk. Parents worried that children would not carry their ''pens,'' would take risks with food in response to peer pressure, or would not inform others of their food allergy.

XI. DISCUSSION AND IMPLICATIONS FOR FUTURE RESEARCH

Because food allergy is only sporadically symptomatic, the anxiety and uncertainty associated with a potential reaction has more profound effects on a child's everyday life than physiological symptoms; therefore, children with food allergy may be at increased risk of negative short- and long-term socioemotional outcomes. Low general awareness encountered in the social world appears also to contribute to the later development of psychological distress and/or to risky behavior. Additionally, variables, such as personality traits and gender are likely to moderate individual impact. Findings also demonstrate the need for health professionals to work closely with the understandings individuals have about their food allergy, about 'compliance' and about risks associated with the condition.

Studies to date show that many of the issues around food allergy reported by participants and their parents are operative at an emotional level. As such, they fall outside the responsibility or indeed the capacity of family doctors or allergists to address in a direct way, entailing the need for an educational intervention specific to food allergy. Many existing interventions in chronic diseases focus only on disease management and information and fail to address the wider psychosocial consequences of living with chronic disease (Barlow and Ellard, 2004; Gage *et al.*, 2004). Although it is very important that children and their families understand the condition and its treatment, Gibson and colleagues (2004) maintain that asthma education limited to information transfer alone is ineffective. Further, research suggests that the goal of an intervention should not only to be change the mean level of a particular coping strategy but also to create a stable growth dynamic by including issues that are food allergy specific, as well as age and context specific. Research in food allergy suggests that greater support and clear information is important at time of diagnosis and at the different transition points along the development pathway. Greater emphasis is needed on the social and emotional aspects of food allergy, on knowing ''what to expect,'' and on enhancing the self-management skills of children and their families. In addition, public information on food allergy is needed in general, and in health, education, catering, and retailing, in particular.

Food allergic children appear to experience disease-specific stressors and use particular coping strategies that evolve in response to age-, gender-, and context-specific stressors. Particular issues revealed by the literature are summarized below:

- For young children particular issues include: how to feel part of social occasions such as birthday parties while being and feeling safe; how to communicate with friends, restaurant staff, and other children and adults in novel situations; how to deal with difficult people and situation (e.g., teasing and bullying); how to create a positive self-image that includes food allergy.
- For older children and young teens particular issues include: how to balance peer pressure and positive self-perception while staying safe; how to communicate in novel situations such eating out and making new friends; how to manage feelings such as embarrassment, self-consciousness, difference, managing the removal of the parental safety net, and development of effective self-care.
- For older teens particular issues include: how to deal with going out independently with friends, starting to drink alcohol, the first independent holiday, romantic relationships, and attending clubs or discos.
- For parents particular issues include: anxiety; teaching children to be independent and safe, what to expect as children grow, managing the removal of the parental safety net and helping children develop effective self-care.
- Gender specific issues include: how to deal with gender roles (e.g., boys do not seek social support; girls find it difficult to be assertive).

Over the last 20 years, new lifecourse frameworks have been developed which offer a conceptual model for health development and a more powerful approach to understanding diseases (Halfon and Hochstein, 2002). Such models are germane in the field of food allergy since biological hypersensitivity to environmental stimuli is a central feature of atopic disorders. Although it is recognized that allergen contact can elicit symptoms at higher and lower dose at different time points, rendering different thresholds in allergen provocation tests within the same individual, there is only a limited understanding of the mechanisms involved in the developmental course of food allergies.

A developmental framework has the potential to link formerly disparate concepts such as health-related quality of life, the maturation of the immune system, and delineate mechanisms linking psychological stress, personality and emotion to neuroimmunoregulation as well as to increased risk of negative impact. Such a model may be used to explain both physiological and psychological phenomena, and their interaction, and consequently provide a shared language as a basis for multidisciplinary studies in food allergy.

A growing appreciation of the interactions between behavioral, neural, endocrine, and immune processes have underlined the need for a multidisciplinary approach. For example, it is possible that psychological distress and atopy have overlapping biological contributors, increasing the likelihood of ''trait'' anxiety. Mechanisms linking psychological stress and emotion to neuroimnoregulation as well as increased risk of atopy have been increasingly elucidated (e.g.,Wright, 2005). Stress early in life can, for example, result in long-term alterations of the function of the HPA-axis (Helm *et al.*, 2002). In addition, an association between TNF-α and the cognitive affective subscale of the Beck Depression Inventory, which measures depressed mood independent of physical symptoms, demonstrated a negative affect-specific activation of proinflammatory cytokines that may actually promote disease progression (Knonfol and Remick, 2000).

A biopsychosocial framework may reveal new links between physiological and psychological systems that, in turn, may provide new insights to guide future explorations that result in novel clinical or therapeutic treatments that relieve the burden of food allergy. Such a framework entails the adoption of methodologies that illuminate pathways in development such as qualitative methods and structural equation modeling.

One of our aims in ongoing research is to move beyond quantitative reports of HRQL impact to an examination of the underlying mechanisms. A developmental framework, such as that illustrated (Fig. 3.1), has the potential to link formerly disparate concepts such as health-related quality of life, the maturation of the immune system, cytokine secretion, to the influence of sex and gender variables, as well as to increased risk of negative physiological or psychological impact. Such a model may be used to explain both physiological and psychological phenomena, and their interaction, and consequently provide a shared language as a basis for multidisciplinary studies in food allergy. Longitudinal studies are necessary when the goal is to investigate cause and effect. At present Europrevall is conducting a birth cohort study in food allergy, that includes clinical and psychological measures. Such studies may also lead to novel treatment options in the future.

For clinicians, the early recognition and incorporation of a developmental framework into a treatment plan is essential and sets the stage for an effective medical care and the eventual transition from paediatric to adult care. For health care providers, there is socio-economical interest to support the development of adaptive and active coping strategies in children with food allergy as early as possible, targeted at specific transition points, and with age and gender relevant content.

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