The changing epidemiology of food allergy—implications for New Zealand

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Abstract
Food allergy (FA) is recognised as an important public health problem in developed countries. Recent studies suggest a significant proportion of the general population has a definable FA. The methods used to study FA influence published estimates of incidence and prevalence. In particular, studies relying on self-assessment are likely to overestimate the condition compared to studies using a comprehensive approach including symptoms, allergy testing, rigorously conducted laboratory tests, and food challenges. Currently there are no reliable data on the prevalence of FA in New Zealand. This has had several adverse consequences including the lack of public hospital services for patients with severe allergies. In this article we summarise the epidemiological data on FA and discuss the implications for New Zealand.

Food allergy background
Food allergy (FA) is a common adverse reaction to food mediated by the immune system. The condition can result in a wide variety of clinical manifestations that involve IgE or non-IgE mediated mechanisms, or sometimes both (e.g. eosinophilic oesophagitis). In contrast, food intolerances can be considered adverse non-allergic responses to foods. This is best illustrated by lactase deficiency, where cow’s milk can cause gut symptoms as a result of undigested lactose.1

The gastrointestinal tract is important not only in the absorption of nutrients but also in the protection against microbial invasion through appropriate immune responses. Oral tolerance develops when there is down-regulation of the immune response to non-harmful antigenic substances.2

Allergic reactions to food are largely thought to be due to genetic factors and can occur when oral tolerance is impaired.2 The severity of FA can vary from trivial abdominal discomfort to death from anaphylaxis. FA accounts for a significant proportion of anaphylaxis and severe allergic reactions in children.3–5 Much less is known about the pattern of FA in older adults.6

Most allergic reactions to food originate in childhood and few treatment options have the potential to alter their natural course.7 Both genetic and environmental factors are likely to be involved in the pathogenesis of FA, but the interactions are complex with considerable gaps in knowledge.7 Studies of identical twins indicate high concordance pointing to genetic predisposition, but inter-related environmental factors such as feeding practices are also likely to be important.8

Many children who develop allergy to food may outgrow their allergies.9–12 For example, in a study of 118 children with cow’s milk allergy (CMA), 42 (35.6%) with
non-IgE mediated CMA were found to be free of their allergy by the age of 5 years. However 13 children (15% of the cohort) had persistent CMA at the age of 8.6 years. Thus, contrary to previous perceptions, CMA may persist into late childhood in a significant minority of patients.12

Accurate diagnosis and appropriate management of food allergy is critical. Failure to identify the offending food allergen(s) correctly may place the person at risk of recurrent anaphylaxis. On the other hand, inappropriate and unsupervised dietary elimination can increase the risk of nutritional deficiencies. This was recently illustrated by the case of a 14-month-old child with CMA who presented with rickets due to poorly managed dietary exclusions, resulting in deficiencies in Vitamin D, dietary calcium, and phosphate causing impaired bone mineralisation and growth.13

Therefore, FA sufferers are doubly challenged to find a diet that will not result in an adverse reaction, but which is nutritionally balanced, in order to maintain good health.14

In addition to the clinical symptoms, severe FA can pose a significant socioeconomic burden to families as diet and lifestyle may be adversely affected. Unfortunately, some of the commonest allergenic foods are also of high nutritional value (e.g. milk, eggs, and peanuts) relative to their cost. The financial burden of substituting alternative dietary options can be substantial.13 FA can also limit social activities and school attendance in children, and young adults may have restricted career options.15

FA can generate considerable anxiety in affected families and the community, and some patients suffer post-traumatic stress disorder after a severe episode of anaphylaxis. Indeed, a recent study suggested that having a child with severe food allergy had the same adverse impact on the quality of life as having a child with Type 1 diabetes.15

**Prevalence of food allergy: problems in ascertainment**

FA is acknowledged to be a significant public health problem in developed countries, but there are major gaps in knowledge regarding the population burden of the condition as highlighted in a recent meta-analysis funded by the European Commission (part of the EuroPrevall research project).

Of the 934 papers that investigated the prevalence of allergy from January 1990 to December 2005,16 only 54 met the authors’ criteria for inclusion, and only 19 included the double-blind placebo-controlled food challenge (DBPCFC) method of diagnosis (considered to be the gold standard method14,16–18).

The articles that met the review criteria were classified by the diagnostic methods used; self-reported FA (SRFA), specific IgE (IgE cut-off levels varied between studies), skin prick test, a combination of SRFA and IgE or skin prick test, and SRFA and DBPCFC. The authors found widely varying estimates of prevalence depending on the method used. For example, the prevalence of CMA ranged from 1.2 to 17%, egg allergy from 0.2 to 7%, and peanut allergy from 0 to 2%.16 Not surprisingly, studies based only on self-reported FA have tended to provide the highest estimates of prevalence.16
Inconsistent study design

The variability in reported results was subsequently highlighted by Keil, who critically reviewed published studies on the epidemiology of FA between October 2005 and January 2007. Only six published studies were identified that met the review criteria for study design, recruitment process, assessment methods of FA outcomes, and interpretation. These included two well-designed birth cohort studies from the Isle of Wight in the United Kingdom (UK).

The first of these studies found that the prevalence estimates of FA (based on clinical history, skin prick testing, open food challenges and DBPCFC) in the first year of life varied between 2.2% and 5.5%, which were considerably lower than the estimates based on parental reports (between 5.5% and 14.2%).

In the second Isle of Wight study, FA prevalence was determined in a cohort of 6 year-olds. Adverse reactions to food were reported by 11.8% of the cohort. This is higher than the prevalence confirmed by clinical history, skin prick tests, and open food challenge (2.2%) and DBPCFC (1.6%).

The propensity to over-estimate adverse reactions to food based on self-reported symptoms has also been observed among teenagers. For example, Pereira et al found that in contrast to the prevalence of self-reported symptoms among 11 year olds (11.6%) and 15 year olds (12.4%), only 2.2% had a diagnosis confirmed by food challenges. Similar rates may also be perceived by adults; in a study of 1483 adult subjects in the Netherlands, 12.4% reported FA but only 0.8% were confirmed as FA by DBPCFC.

Inconsistent study design has been identified as a problem in the Global Allergy and Asthma European Network (GA² LEN) review of 18 on-going European birth cohort studies. It is hoped that through the co-operation of participating research teams that some data may be pooled and common analyses used for endpoints such as the natural history of FA.

Laboratory factors may influence the diagnosis of FA, including food-specific IgE cut-off values. Limitations also exist due to a lack of standardisation of the skin test allergens used to assess sensitisation. A survey of the participating research teams in the GA² LEN study found that different standard panels of allergens are used across Europe.

There may be variability in physician diagnosis which further complicates the perception of increasing FA prevalence. Responses to a questionnaire sent to 7000 United States physicians indicated that non-allergist physicians diagnosed FA at a higher rate than allergy specialists. This is the first study to report differences in FA diagnosis between physicians. This survey suggests there may be a need for further training in this area.

The establishment of accurate data on FA prevalence is problematic because most estimates of prevalence are based on methods other than a comprehensive approach including symptoms, allergy testing, and the gold standard DBPCFC.

It is difficult to predict clinical reactivity to an allergen based purely on the measurement of IgE antibodies in serum and mast cell reactions by SPT. Positive results from either method, especially with low levels of food-specific IgE, do not
mean that an allergic reaction is inevitable on consumption of the food.\textsuperscript{24} The significance of other methods such as kinesiology, hair testing, and ‘electroacupuncture according to Voll’ (EAV) are unknown.

One approach that could address the problems described is to recruit a large unselected birth cohort, where regular clinical assessments and allergy testing is undertaken. Children suspected of having FA then undergo DBPCFC. Such studies are, however, limited by expense and logistical complexities, and may not provide time-dependent-information (such as changing population demographics and changing dietary practices), and do not provide information about adults with FA. Furthermore, there may be ethical concerns with undertaking DBPCFC in children.

Alternatively, monitoring the change in patterns of food allergy (using the same research tools used to detect changes in prevalence of peanut allergy\textsuperscript{18} and asthma\textsuperscript{25}) would be a simpler and less expensive approach, and could provide relevant, useful information.

**Is the incidence of food allergy increasing?**

The extent to which the burden of FA has changed over time is contested. While some studies do not support evidence of increasing incidence of FA,\textsuperscript{14,16,19} the well-designed Isle of Wight birth cohort studies showed an increase in prevalence of peanut allergy (from 0.5 to 1.0\%) and peanut sensitisation (from 1.1 to 3.3\%) from 1989–1994 to 1994–1996.\textsuperscript{26}

By using the same research instrument (nationwide, cross-sectional, random telephone survey with a standardised questionnaire), Sicherer et al found self-reported peanut allergy doubled in children less than 5 years of age from 1997 to 2002 in the US.\textsuperscript{18} Clinical reports of children with food-related anaphylaxis have also reportedly increased in Australia.\textsuperscript{27,28} The explanations for these observed increases were not investigated in these studies.

**Food allergy in non-European populations**

FA reactions appear to occur at a higher rate in Asian children in Westernised countries.\textsuperscript{29,30} A cohort study produced important results on self-reported wheeze in European children and south Asian children born in the UK.\textsuperscript{29} Parental reports of food and drink triggered-wheeze were significantly higher in the south Asian children compared to the Europeans and doubled over a 5-year period.\textsuperscript{29} While this was a clinically significant finding due to the impact on health services, the reasons for these differences were not reported.

Moreover, FA may be more common in Asian countries than previously suspected.\textsuperscript{8} In Singaporean children (identifying with Chinese, Malay, Indian, and Eurasian ethnic groups) the most common foods causing allergies were peanuts, shellfish, and egg.\textsuperscript{8}

In this study of FA, which was determined by SPT and questionnaire, peanut allergy was seen in a third of children. While Singaporean children develop shellfish allergy at an older age than peanut or egg allergies, it is the second most common allergen.\textsuperscript{8}
This finding for Singaporean children was considered to be different to paediatric norms in the United States and Western Europe where the major allergenic foods are milk, egg, and peanuts. The high incidence of peanut allergy was also in contrast to previous results. It had been thought that the low incidence of peanut allergy in Chinese populations was due to different processing methods. FA appears to be of concern in Asian countries, and the authors recommended that large-scale epidemiological studies be carried out there.

These studies highlight the changing epidemiology of food allergy and underscore the importance of environmental factors in food allergy.

**Food allergy in New Zealand: what is known?**

Recent publications have included limited data on FA prevalence in New Zealand. In the first study, information was from the early 1990s and was part of the European Community Respiratory Health Study. Data were collected from 1148 New Zealanders by a brief questionnaire about respiratory health, which included four questions regarding dietary intake.

From this study 11.4% of subjects reported illness from food, although it is unclear if the FA diagnosis was supported by allergy tests. In another paper the prevalence of CMA amongst New Zealanders was reported to be about 11% based on child and parental reported data from a cohort of 155 children aged 3 to 10 years in Dunedin.

The burden and characteristics of FA in New Zealand are likely to have changed over time in view of the demographic changes (e.g. substantial increases in the proportions of Asian and other immigrants in the last two decades) and changes in the diversity and production of foods available to consumers.

Several species of shellfish are endemic to New Zealand. Allergic reactions to shellfish and molluscs may be highly cross-reactive, which is thought to be due to the conserved nature of amino-acid sequences in the allergenic protein tropomyosin across species.

The relationship between FA and New Zealand’s unique species of shellfish may also require further investigation. Infant feeding patterns and genetic predisposition are also likely to vary in different ethnic communities. While equivalent data for FA are not available, Pacific children who migrate to New Zealand from countries such as Samoa and Tonga have been noted to experience an increased incidence of asthma compared to children in their home countries.

The incidence of FA in Māori is unknown. In order to fully understand the aetiology of FA and initiate primary prevention and treatment strategies in New Zealand, it is important to identify any disparities between Māori and non-Māori.

Māori have on average the worst health status of any ethnicity in New Zealand. The Māori population has a higher growth rate compared to Europeans, and between 2006 and 2021 the Māori population is expected to grow by 20% compared to only 5% in Europeans. Therefore the paucity of information on FA in Māori limits our ability to...
predict the future disease burden and plan the most appropriate delivery and access to health resources over the coming decades.

Overseas research has identified FA as a risk factor for life-threatening asthma attacks in children. Māori experience greater morbidity associated with asthma and Māori are twice as likely to be hospitalised for their asthma as non-Māori. In asthma and other atopic diseases, FA may have an important role in the health disparities we see between Māori and non-Māori.

Lower socioeconomic status is a well documented predictor of poor health outcomes and a barrier to care; it is well documented that Māori are more likely to live in more deprived areas than non-Māori. Therefore, the collection and analysis of up-to-date, accurate epidemiological data and the development of specific health strategies must remain an ongoing priority in order to tackle these inequalities.

Consequences of the limited data on food allergy in New Zealand

Anecdotal evidence shows that the public hospital system in New Zealand experiences substantial constraints in responding to the needs of those affected with FA.

Children with the potential for outgrowing FA need to be reviewed regularly so that they are not confined to an unnecessarily restricted diet, while adults with FA also need to be reviewed particularly after experiencing a severe reaction.

With no national guidelines for the provision of allergy services there is an *ad hoc* approach by district health boards (DHBs) including the availability of specialists and purchase of laboratory tests.

Few New Zealand hospitals currently offer specialist allergy services for adults, and services for children are particularly limited from a national perspective. Indeed, many patients with complex allergic disorders have to fly long distances for diagnosis and treatment, often at their own expense. Similar shortages of allergy specialists and primary health care services are also seen in the UK and in Australia.

Access to laboratory tests in some parts of the country is also restricted. In Wellington, for example, patients of private specialists are required to pay for laboratory tests.

Better epidemiological data may assist health boards in prioritising the need for allergy/immunology services and ensure robust coordination and continuity of care across primary, secondary, and (where necessary) tertiary care services. Tertiary hospital-based multidisciplinary teams would ideally include specialist allergists, nurses, dietitians, and facilities for food challenges and immunotherapy.

A better understanding of the epidemiology of FA may also identify the gaps in established protocols and school services. The *ad hoc* approach to severe food allergy in New Zealand’s schools may place some students at increased risk of reactions while attending school.

Currently, adrenaline auto-injector devices—the primary treatment for acute anaphylaxis in the community—are not publicly funded in New Zealand. Ensuring an up-to-date supply of this life-saving medication (e.g. EpiPen®)—the commonly used...
formulation—has a shelf-life of 12–16 months) can place an unacceptably high financial burden on families with severe FA. Better data on the prevalence of severe allergies may assist funding these devices.

Compliance with food-allergen labelling regulations is a significant issue for the food industry including manufacturers, the food service, and hospitality sectors. Mistakes can be costly for both the industry and consumers. Better data on the prevalence of food allergy would assist the food industry both in compliance and in producing food suitable for people with FA.

Studies of FA can provide useful information that is relevant to the national economy. New Zealand is heavily dependent on agricultural exports and the development of new foods. Recently, the kiwi fruit gold variety was identified as being as allergenic as the green variety in Europe.

The inadvertent development of highly allergenic foods may inflict damage to New Zealand’s international reputation as an exporter of high quality foods. On-going FA studies have the potential to identify these foods at an early stage, or ensure appropriate processing and labelling to mitigate the risk to vulnerable individuals.

While many advances have been made in the last two decades, much has yet to be learned about FA. More targeted research elucidating the burden, barriers to effective treatment, and related factors in New Zealand is necessary to ensure better services and support for all children and adults with food allergy, and improved safety for those at risk of severe reactions.

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