

**DEMOGRAPHIC & CLINICAL
CHARACTERISTICS OF FOOD -
INDUCED ANAPHYLAXIS IN ATOPIC
CHILDREN, AGED 0-5 YEARS:
A CASE-CONTROL STUDY**

A major project submitted in partial fulfilment of the requirement for
the award of the degree of

**BACHELOR OF NUTRITION AND DIETETICS
UNIVERSITY OF WOLLONGONG**

by

RACHEL MYHILL

Supervisors:

Katherine Jukic (Dietician)
Dr. Velencia Soutter (Paediatrician)
Dr. Robert Loblay (Director)
Dr. Anne Swain (Chief Dietician)

ALLERGY UNIT
DEPARTMENT OF CLINICAL IMMUNOLOGY
ROYAL PRINCE ALFRED HOSPITAL
October 2007

ACKNOWLEDGEMENTS

I would like to thank all the staff at the RPAH Allergy Unit for all their advice and encouragement. Your time and knowledge was greatly appreciated. Thank you for making my experience an extremely enjoyable one.

A very special thank you to Katherine for all your help, patience and support. Your time and knowledge was extremely appreciated.

Many thanks to Velencia and Rob for their time and knowledge. I feel truly privileged to have worked under such inspiring individuals.

Thank you to Anne for all your encouragement and support. Your bubbly and cheerful nature certainly helped me in times of stress.

Special thanks to our lecturers Karen Walton and Kelly Lambert for their guidance throughout the semester.

A very special thank you to my project partner Alison. I had a really great time working with you. Thanks for the great company and entertainment. It wouldn't have been the same without you.

ABSTRACT

Introduction: The incidence of food allergy and occurrence of food-induced anaphylaxis is increasing. Understanding the epidemiology of anaphylaxis has been challenged by inconsistencies in definition, and lack of a universal grading system. This study defined anaphylaxis as ‘a severe, life threatening allergic reaction, characterised by signs of cutaneous, gastrointestinal, respiratory and cardiovascular compromise’. To date, literature concerning anaphylaxis has primarily researched clinical symptoms, risk factors (typically asthma) and management associated with the reaction. The primary aims of this study was to analyse demographic and clinical characteristics of atopic children who have had an anaphylaxis.

Methods: This retrospective case-control study was carried out at the RPA Allergy Unit in Sydney. Children were recruited if they were atopic and aged 0-5 years on presentation at the Allergy Unit. The patient database and files of 672 subjects were reviewed, and cases (n=218) were identified, i.e. if the child had a history of anaphylaxis according to our definition. Characteristics of children who had an anaphylaxis (graded as mild, moderate or severe) were pre-determined and analysed. Such characteristics included: symptoms of the reaction; age and sex of the child; presence or history of asthma; the type, form and SPT of the causative allergen; and administration of adrenaline.

Results:

Characteristics: The majority of cases had a mild or moderate anaphylactic reaction (85%), and were aged between 1 and 3 years. Skin symptoms occurred in 90% of all reactions. The main food allergens that caused anaphylaxis were peanut (42%), egg (21%) and milk (17%), and their corresponding SPT size most commonly ranged between 6 mm and 8 mm. The allergen was consumed as a whole food in approximately two-thirds of cases, rather than as an ingredient or component of a food.

Conclusion: Establishment of a universal grading system would enable improved clinical observation and management of anaphylaxis, and better comparison of the results of this study with other studies.

INTRODUCTION

The incidence of food allergies appears to be increasing, particularly within the pediatric population (Sampson, 1996). Current epidemiological data indicate that the prevalence of food allergy is most common in young infants (5-8%), but continues to affect about 1-2% of the general population (Sampson, 1996; James, 1992; DunnGalvin et al, 2006; Peng & Hershel, 2004).

Despite greater awareness and recognition of food allergy among physicians and patients, many allergists believe that the actual prevalence of allergy has risen substantially over the past decade, similar to the rise in prevalence of other atopic conditions such as asthma and allergic rhinitis (Kagan, 2003). This rise is presumably due changes in feeding patterns within the western world with widespread use of protein additives in commercially prepared foods (Sampson, 1996, Gern et al, 1991).

Definitions

Food allergy, defined as an IgE mediated reaction to a food protein can manifest clinically in a number of ways. The most serious manifestation being anaphylaxis. Anaphylaxis is a severe and potentially life-threatening allergic reaction which often involves more than one body system (Novembre et al, 1998). Food induced anaphylaxis is defined as an immunologically mediated group of symptoms that occur after the ingestion of a food to which the reacting individual has previously been sensitized (Shimamoto & Bock, 2002). The number of deaths caused by anaphylactic reactions to food is increasing each year (Yunginger et al, 1988) and with increasing hospital admissions for allergic disease, it is likely that the prevalence will continue to rise (Brown, 2004).

Skin prick testing is used to diagnose a food allergy in combination with clinical examination and dietary modification (Clarke et al, 1996). The presence of a positive Skin Prick Test (SPT) indicates that the child has been sensitized to that food protein. A positive SPT is considered significant if wheal diameter on skin is greater than 3mm. A negative SPT has a predictive accuracy of 95% and therefore, is a useful, supportive, and safe test for excluding food allergy (Sampson, 1988).

Theoretically, any food containing a protein could potentially elicit an allergic reaction. However, eight common proteins are responsible for greater than 90% of food allergies in children (Hefle et al. 1996); they include egg, milk, peanut, tree nut, wheat, soy, fish and seafood. Unlike allergy to foods such as milk, egg, soy, and wheat, allergic sensitivities to peanut and tree nut are rarely outgrown, with approximately 80% persisting into later life (Sicherer et al, 1998). Anaphylaxis to peanut and tree nuts is of particular concern because of its life-threatening potential and the propensity for life-long sensitivity (Emmett et al, 1999).

Anaphylaxis often occurs in poorly maintained environments outside a hospital (Simon & Brown, 2004). In a study among pediatric patients, it was found that 57% of anaphylaxis episodes occurred at home, 12% outdoors, 5% at restaurants and less than 1% in a school setting (Novembre et al, 1998). In the event of an anaphylactic reaction, adrenaline is the preferred treatment, and should be administered rapidly, before symptoms have progressed to the point where the outcome may be fatal (Muraro et al, 2007). The onset of symptoms associated with anaphylaxis varies widely between individuals, ranging from within seconds of an ingested allergen, to a few hours after exposure, but typically involves the respiratory, cardiovascular, cutaneous and gastrointestinal organ systems (Shimamoto & Bock, 2002).

The understanding of the epidemiology of anaphylaxis is challenged by inconsistencies in definition. Currently there is no universally accepted definition of anaphylaxis nor a common severity grading system. Also, within the literature, there appears to be a lack of information or data corresponding to the characteristics of an individual and their

anaphylactic episode. Therefore, the difficulty in defining anaphylaxis, especially within the pediatric age group, has presented problems for those involved in clinical observation and management of the condition itself, as well as those involved in research.

The aim of this study was to analyse pre-determined demographic and clinical characteristics of atopic children aged 0-5 years who have had an anaphylaxis.

METHODS

This retrospective case-control study was conducted at the Royal Prince Alfred Allergy Unit in Camperdown, Sydney. Subjects were recruited at the clinic from the patient database of paediatrician Dr Velencia Soutter, if they were aged 0-5 years on presentation at the clinic, and were considered atopic.

The medical records of 672 patients were reviewed (from an initial study population of 904 patients) to determine each child's history and nature of anaphylaxis. Patients were considered to have had an anaphylaxis if the paediatrician had stated so in the patient file or if they had met our definition of anaphylaxis - "a severe life-threatening allergic reaction, characterised by signs of cutaneous, gastrointestinal, respiratory and cardiovascular compromise". To classify an event as an anaphylaxis, signs and symptoms of the reaction were required and included difficulty breathing or talking, rapid swelling of the lips, face, eyes, tongue and/or throat, wheeze or persistent cough, hives or welts, acute distress, loss of consciousness and/or collapse, light-headedness, weakness, paleness or floppiness. Clarification of any questionable patient histories was obtained through correspondence with the paediatrician.

All information regarding the anaphylactic episode(s), including signs and symptoms, and food ingested and therefore causative allergen was tabulated for further analysis against each 'case'.

Grading & Symptoms of the Reaction

A simplified grading system, based on Clark et al (2007) was used to determine if the anaphylactic reaction was considered mild, moderate or severe. 'Mild' reactions were those that solely involved the cutaneous system, that is no reported respiratory and/or cardiovascular symptoms (R-C-). 'Moderate' reactions were 'mild' reactions with respiratory symptoms (R+C-). For a reaction to be 'severe' a cardiovascular symptom

had to be present, with or without cutaneous and respiratory symptoms (R+/- C+). Refer to table in *Appendix 1* which details symptoms that were used to identify skin gastrointestinal, respistaory and cardiovascular outcomes.

Skin reactions

The table in *Appendix 1* also outline signs and symptoms that constitute skin reactions. For the purpose of this study, a local skin reaction was defined as a reaction that involved the face; Non-local was defined as a skin reaction that involved any other part of the body besides the face.

Anaphylaxis – causative Allergen

Once a ‘case’ was determined, patient notes were further used to determine the allergen that cuased reaction (1), the way in which the allergen was consumed, that is whole food or as an ingredient/component in a food (2), the SPT size of the allergen corresponding to the date the patient was seen. (3), and whether the patient’s SPT was taken before or after the anaphylaxis episode (4).

A positive SPT was defined as a weal of at least 3mm x 3mm (mean) diameter greater than the negative saline control. Each SPT was recorded as a mean wheal diameter (mean of the longest diameter and the diameter perpendicular to it).

Regarding tabulation and proper interpretation of results, SPTs corresponding to the causative allergen that were ‘negative’ or not taken on the date seen, were excluded.

Anaphylaxis - Administration of Adrenaline

Patient files were also used to determine if adrenaline was administered at any point in time during or after the anaphylaxis episode, for each ‘case’.

Age, Sex and Asthma History of the Child

The patient database and patient files were referred to, to determine the age at which each child had their anaphylaxis, their sex, and if there was a presence or history of asthma.

Data Analysis

Quantitative variables as indicated above were calculated and expressed as percentages of the corresponding case group, and severity/grading group. SPT results were graphed using GRAPHPAD PRISM version 3.00 for Windows, (GraphPad Software, San Diego, CA, USA)

RESULTS

Refer to Appendix 2 for all tables.

Study population, Grading & Symptoms of the Reaction

A total of 218 cases were determined to have had an anaphylaxis; of those 138 (63%) were considered to have a ‘mild’ (R-C-) reaction, 48 (22%) a ‘moderate’ (R+C-) reaction and 32 (15%) suffered from a ‘severe’ (R +/- C+) reaction.

Skin Reactions

Independent of severity grading, cutaneous features were present in 91% of all cases; 63% experiencing a localized reaction (Table 1).

Causative Allergen

Food allergens that were responsible for the anaphylactic reactions are listed in Table 2. The main food allergens causing a reaction were peanut (42%), egg (21%) and milk (17%), and their corresponding SPT size most commonly ranged between 6 mm and 8 mm (Figure 1). The allergen was consumed as a whole food in 67% of cases, and as an ingredient/component of a food in 33% (Table 3). 73% of cases experienced a reaction before they were skin prick tested, whilst 27% had a reaction after they were tested (Table 4).

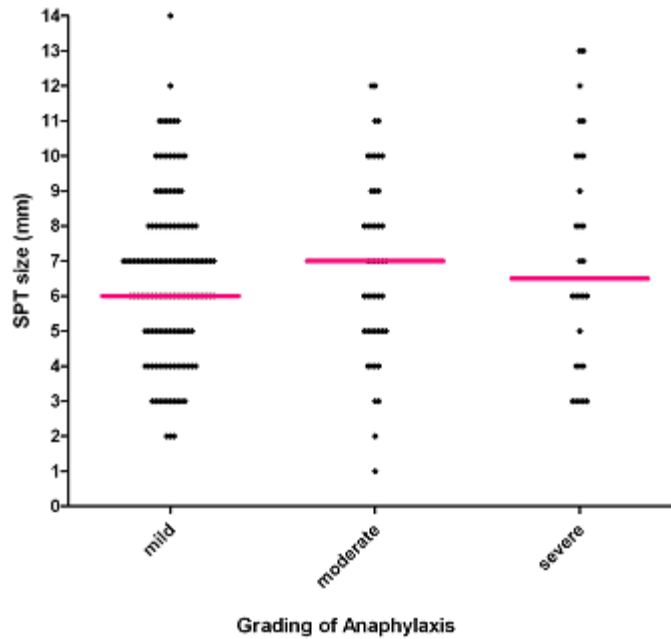


Figure 1: SPT size (mm) vs. Anaphylaxis Grading

Administration of Adrenaline

Adrenaline was administered in 20 (9%) of the anaphylactic episodes (Table 5).

Age, Sex and Asthma History of the Child

The median age for anaphylaxis was 24 months. One-hundred and sixty-six (76%) of reactions occurred in those aged 0-3 years (Table 6). One-hundred and twenty-seven (58%) of the patients were male, 91 (42%) were female (Table 7).

The prevalence of asthma in patients experiencing anaphylaxis was 72 (33%). 28 (39%) of those with asthma experienced respiratory symptoms during the reaction (Table 8).

DISCUSSION

Grading and Symptoms of the anaphylaxis

Symptoms of anaphylactic reactions were graded ranging from urticaria ('mild') to cardiovascular compromise ('severe').

Of the 218 cases of anaphylaxis in this study, 63% suffered a 'mild' reaction involving cutaneous features, 22% experienced a 'moderate' reaction with wheeze and laryngeal oedema being most commonly reported and 15% experienced a 'severe' reaction involving collapse or unconsciousness. (Refer to *Appendix 2*). Other studies involving anaphylaxis in children have shown respiratory involvement ranging from 69-93% (Novembre et al, 1998; Sicherer et al, 1998; Braganza et al, 2006). Respiratory features have been said to be more common in children than adults, which may be due to the higher frequency of atopy and asthma in children and/or the fact that food-induced anaphylaxis is more common in children and tends to cause respiratory involvement (Braganza et al, 2006). Cardiovascular symptoms have been described in 8-26% of anaphylactic reactions in children (Braganza et al, 2006; Macdougall et al, 2002).

The 'mild', 'moderate', 'severe' grading system used for this study was adapted from Clark et al (2007) however several severity grading systems have been described throughout the literature. Approaches range from simple descriptions of key symptoms (Yocum, et al, 1999), to complex 'two or more' rules (Muraro et al, 2007), or physiological parameters that may not be available when assessing a reaction outside monitored environment (Brown & McKinnon, 2001). Others have classified anaphylaxis on the basis of a five-levelled (I-IV) grading system (Sampson et al, 2006). Until a widely accepted definition is devised, care must be taken in interpreting results within and between studies

Skin Reactions

Skin symptoms were the most frequent clinical manifestation reported in this study. Independent of severity grading, 91% of all children experienced some form of cutaneous involvement at the time of anaphylaxis, with facial angioedema and hives/urticaria being the most common symptoms reported. Furthermore, two thirds (67%) of all skin cases

were classified as localised, (Table 1), that is, swelling, hives or a rash present on the face. A recent retrospective case study of Australian children presenting to a paediatric emergency department found similar results with 82% of anaphylactic reactions experiencing some form of cutaneous symptoms (Braganza, 2006). Other studies involving anaphylaxis in children have shown skin symptoms to vary between 78-93% (Novembre et al, 1998; Sicherer et al, 1998; Wang & Sampson, 2007).

Causative allergen

The most common food allergens to cause an anaphylaxis was peanut, egg and milk. This pattern is fairly typical within the pediatric population with similar results have been observed in other studies (Sampson, 1996, Macdougall et al, 2002). Approximately 90% of all allergic reactions in the pediatric population are due to egg, milk, peanut, soy, wheat and fish (Sampson, 1996). More recently however, allergy to cashew nuts is increasingly being recognized in young children. (Clark et al, 2007; Ewan, 1996). Certain foods pose a much greater risk than others. The increasing prevalence of peanut and tree nut allergy is of great concern, particularly due to the often severe nature of reactions and the persistence of the allergy into adulthood (Grundy et al, 2002, Sampson, 1996, Sicherer et al, 1998). Unlike allergy to foods such as milk, egg, soy, and wheat, allergic sensitivities to peanut and tree nut are rarely outgrown, with approximately 80% persisting into later life. (Sicherer et al, 1998).

Skin Prick Testing

This study found that the SPT corresponding to the causative allergen most commonly ranged between 6mm to 8mm, independent of the severity grading (Figure 1) Therefore, the size of the skin prick wheal diameter does not correlate with the severity of the reaction, but merely indicates a possible association between the allergen tested and the patient's reactivity to that specific allergen. This finding has also been noted by Simons et al (2007). In clinical practice, a SPT is a useful measure of assessing a child's sensitivity to a specific allergen, but cannot be used as a reliable guide to determine whether someone will suffer a mild, moderate or severe reaction. Taking plasma IgE levels or

undertaking food challenges is therefore thought to be a more reliable biomarker for assessing food allergies (Simons et al, 2007).

The majority (73%) of children experienced a reaction before the allergen was known to them, thus prevention was impossible. Approximately two thirds (67%) of allergens were consumed as the whole food, whereas 33% had been consumed as an ingredient/component within a food (Table 3).

On the other hand, 27% of cases experienced a reaction having been aware of their allergen. In 59% of these cases, the recurrent reaction was caused by the same allergen as in the previous episode, being ingested as a component/ingredient in a food two-thirds (68%) of the time, possibly due to the allergen being a 'hidden' ingredient or contaminant. The high rate of accidental ingestions has been documented in many studies. Bock & Atkins (1989) found that among 32 patients with peanut allergy followed for up to 14 years, 75% experienced accidental ingestion. Sicherer et al (1998) found that accidental ingestion to peanut occurred in 55% of patients over five years, with an average of two accidents per patient. The results of this study demonstrates that despite avoidance, accidental ingestion remains likely. 'Masked' allergens cause many cases of severe anaphylaxis. This is particularly the case with peanut, because of its relative ubiquity as well as the wide distribution of contents, despite vigilant attempts to avoid peanut-containing foods (Bock and Atkins 1989; Vander Leek et al. 2000).

Sicherer et al (1998) found that the modes of this accidental exposure to peanut included hidden ingredients in processed foods, cross-contamination, sharing food and skin contact with peanut butter in school and classroom projects. Sampson et al (1992) point out in their study, that attempts at strict avoidance of allergens are often unsuccessful; none of the patients studied were aware that the implicated allergen was present in the food that they consumed. Complete avoidance of any allergen, is a great challenge and requires the vigilance of the patients and adult carers (Bock and Atkins 1989; Jones et al, 1992; Vander Leek et al, 2000). These children require special care and attention, and parents and carers should be educated on how to avoid or reduce the risk of exposure to

allergens, what procedures are necessary in the event of accidental exposure to the food allergen.

Age, Sex and Asthma history of the child

In population-based studies, sex differences in atopy and the prevalence of food allergy have been reported throughout childhood. Rates in girls have been shown to be lower than in boys up to 15 years of age (DunnGalvin et al, 2006). This was the case for this study where there were a greater number of males experiencing anaphylaxis than females (127 vs. 91 respectively). On the other hand, retrospective studies have reported that food anaphylaxis is more prevalent in females (Brown, 2004; Mullins, 2003). This study found that slightly more females suffered a 'severe' reaction (18 vs 14 respectively). Similarly, in a Norwegian study on severe allergic reactions to food, it was found that the sex distribution of severe reactions showed a 60:40 female:male ratio in adolescence and adulthood (Lovik et al, 2004). The authors suggest that either severe food allergy is more common in females or females may have a different food allergen exposure than males (Lovik et al, 2004)).

Regarding the finding of this study, there appeared to be a relationship between age and incidence of anaphylaxis, with most reactions occurring in the first 3 years of life, with a median age of 2.1 years. Studies have shown that the prevalence of food allergy is greatest in the first year of life, affecting about 4-5% of young infants, and then falling to about 2% by the end of the first decade as children "outgrow" their sensitivity (Sampson, 1996, Emmett et al, 1999, Dowdee et al, 2007). Allergies to milk, egg, soy and wheat, typically present in infancy, are outgrown and usually resolve by school age (Sampson, 1996).

This study found that the prevalence of asthma in patients with anaphylaxis was 33%. This result is similar to that of Braganza et al, (2006) where it was found that asthma was reported in 37% of cases. Asthma has widely been thought to be a risk factor for the

development of an anaphylactic reaction (Roberts et al, 2003; Wang & Sampson, 2007) Bock et al (2001) strongly links the association of asthma with fatal reactions. Macdougall et al (2002) found that among young children, the more severe the reaction, the greater chance the patient had co-existing asthma. However, according to the results of this study it was found that having a presence/history of asthma did not necessarily mean the child would suffer a more severe reaction, nor that a reaction would involve respiratory symptoms (Table 7).

Administration of adrenaline

Regarding medical treatment for all children, only 9% were given adrenaline. Adrenaline, although the absolute first-choice treatment in anaphylaxis, appears to be insufficiently used even in the medical setting (Yocum et al, 1999; Pumphrey, 2000). The failure to recognize the severity of these reactions and to administer adrenaline promptly increases the risk of a fatal outcome (Sampson et al, 1992). Pumphrey (2000), in a UK study of 164 fatalities found that adrenaline was only used in 62% of all reactions and only in 14% before cardiorespiratory arrest. Pumphrey's study demonstrates the necessity among children and adults for greater awareness of when and how to use adrenaline in anaphylaxis, as it has been found that recovery from anaphylaxis is most likely if adrenaline is given within 30 minutes (Pumphrey, 2000). The relatively low administration of adrenaline in this study could be attributed to the lack of knowledge of the food allergy, and therefore the importance of adrenaline, when it occurred. Since most of the reactions in this study occurred before the child had been tested for their food allergy, most had only become aware of the allergy as a result of the reaction. Therefore, a more structured and protocol system regarding the use of this drug, especially in children where its effectiveness is associated with minimal cardiovascular side-effects, should be promoted and enforced among general, hospital and paediatric physicians.

Limitations

As previously mentioned, studies which look at allergic reactions and anaphylaxis are limited by the lack of a diagnostic standard definition of anaphylaxis and grading system. This not only has potential implications on research but also resulted in flaws in the way anaphylaxis is clinically and consistently diagnosed and managed among physicians (Brown et al, 2006) (Muraro et al, 2007).

Diagnosing a reaction as an anaphylaxis rather than as a major food allergy reaction, predominately based on cutaneous symptoms alone is debatable. Whilst some studies choose to define cutaneous symptoms as mild anaphylactic reactions (Clark et al, 2007), some studies choose to define reactions limited to the skin as an ‘acute allergic reaction’ and reserving the term ‘anaphylaxis’ for those with additional gastrointestinal, respiratory, cardiovascular or neurological features (Sturn et al, 2002; Sampson et al, 2006) (from clinical features and severity grading). In addition, the definition proposed by the Australasian Society of Clinical Immunology and Allergy (ASCI) describes a generalized allergic reaction characterized by one or more symptoms of skin and/or gastrointestinal involvement without respiratory and/or cardiovascular involvement. The majority of cases in this study were classified as ‘mild’ reactions which only involved the cutaneous system, thus, the case population in this study may have been an overestimation of the incidence of anaphylaxis. The results of this study could therefore not be accurately compared to previous study findings.

This study included only paediatric patients who attended a single allergy clinic, and therefore results may not be able to be extrapolated to those over 5 years of age.

Literature has observed differences in the types of allergens causing reactions among adults and children, as well as differences in the symptoms reported (Braganza et al, 2006).

Other limitations may be related to misreporting and bias due to data being collected retrospectively. This study relied on accurate and complete medical records taken by a physician which was based solely on the parents’ observation, hence relying on memory

and subject to bias. Many reaction characteristics are likely to have gone unnoticed or undocumented. Adrenaline treatment may have altered subsequent development of other symptoms, which may have affected the grade of anaphylactic reaction the child had, therefore altering the results.

Conclusion

This research project was conducted with the aim to analyse the demographic and clinical characteristics of anaphylaxis in atopic children aged 0-5 years. It was found that most young children suffer from cutaneous symptoms, with very few experiencing severe life-threatening complications. These young children were most commonly found to react to peanut, egg and milk, the majority experiencing reactions within the first three years of life, with the allergen being unknown to them at the time. Skin prick testing was found not to be a reliable indicator in determining reaction severity. Thus, further studies should look at ways to identify children at risk of developing food allergies and their related complications.

Unfortunately, there will always be some degree of risk for a food allergic individual having an anaphylaxis. Improved education and more stringent food-labeling may help reduce the occurrence and severity of food-induced anaphylaxis. Ultimately this can be accomplished by ongoing attention to the subject of food-induced anaphylaxis by the medical profession as well families, carers and schools. Patients must be given extensive education regarding food avoidance, signs/symptoms of anaphylaxis and the use of self-injectable adrenaline. Until a universally accepted definition for anaphylaxis is developed, there will continue to be inconsistencies when comparing the literature, as well as in diagnosing and managing the condition.

REFERENCES

1. ASCIA Epipen prescription guidelines 2004, *Anaphylaxis Management Plan* [Brochure], ASCIA Anaphylaxis Working Party, Australia
2. Bock SA, Atkins FM. 1989. 'The natural history of peanut allergy'. *Journal of Allergy and Clinical Immunology*, vol. 83, pp.900–904.
3. Brown A, McKinnon D & Chu K. 2001. Emergency department anaphylaxis: a review of 142 patients in a single year, *Journal of Allergy and Clinical Immunology*, vol. 108, pp. 861-866.
4. Brown S, 2004, 'Clinical features and severity grading of anaphylaxis', *Journal of Allergy and Clinical Immunology*, vol. 114, pp. 371-376
5. Brown, S Mullins, R & Gold, M 2006 'Anaphylaxis: diagnosis and management', *Medical Journal of Australia*, vol. 185, no. 5, pp. 283-288
6. Clark A, Anagnostou k & Ewan P. 2007. Cashew nut causes more severe reactions than peanut: case-matched comparison in 141 children. *Allergy* Vol 62; pp. 913-916
7. Dowdee, A & Ossege, J 2007, 'Assessment of childhood allergy for the primary care practitioner', *Journal of the American Academy of Nurse Practitioners*, vol. 19, no. 2, pp. 53-63
8. DunnGalvin A, Hourihane J, Frewer L, Knibb R, Elberink J & Klinge I. 2006. Incorporating a gender dimension in food allergy research: a review, *Allergy*, vol. 61, pp. 1336-1343.
9. Emmett, S Angus, F Fry, J & Lee, P 1999, 'Perceived prevalence of peanut allergy in Great Britain and its association with other atopic conditions and with peanut allergy in other household members', *Allergy*, vol. 54, pp. 380-385

10. Gavalas M, Sadana A & Metcalfe S 1998 'Guidelines for the management of anaphylaxis in the emergency department', *Journal of Accident Emergency Medicine*, vol. 15, pp.96-98
11. Gern J, Yang E, Evrard H 1991 'Allergic reactions to milk-contaminated "nondairy" products', *Journal of New English Medicine* vol.324 pp.976-979
12. Grundy J, Matthews S, Bateman B, Dean T, Arshad SH. 2002. 'Rising prevalence of allergy to peanut in children: data from 2 sequential cohorts'. *Journal of Allergy and Clinical Immunology*, vol. 110, pp.784-789.
13. Hefle S, Nordlee J, Taylor S. 1996. 'Allergenic Foods'. *Critical Review Food Science Nutrition*, vol 36(suppl) pp.S69-S89.
14. Jones RT, Squillace DL, Yunginger JW: Anaphylaxis in a milk-allergic child after ingestion of milk-contaminated kosher-pareve-labeled "dairy-free dessert." *Ann Allergy* 1992; 68: 223-227
15. Kagan R. 2003. 'Food Allergy: An Overview', *Environmental Health Perspectives*, vol. 111 pp. 223-225.
16. Lovik M, Namork E, Faeste C & Egaas E. 2004. 'The Norwegian National Reporting System and Register of severe allergic reactions to food'. *Norsk Epidemiology*, vol. 14, pp. 155-160.
17. Macdougall C, Cant A & Colver A. 2002 'How dangerous is food allergy in childhood? The incidence of severe and fatal allergic reactions across the UK and Ireland'. *Archives Dis Child*, vol 86, pp. 236-239

18. Muraro A, Roberts G, Clark A, Eigenman P, Halten S, Lack G, Moneret-Vautrin A, Niggemann B & Rance F 2005 'The management of anaphylaxis in childhood: position paper of the Europe academy of allergy and clinical immunology, *Allergy*, vol, 62, pp.857-871.
19. Novembre E, Cianferoni A, Bernardini R, Mugnaini L, Caffarelli C, Cavagni G, Giovane A and Vierucci A. 1998. 'Anaphylaxis in Children: Clinical and Allergologic Features'. *Pediatrics* vol. 101, pp.e8
20. Peng M & Hershel J. 2004. 'A population-based study of the incidence, cause, and severity of Anaphylaxis in the United Kingdom', *Archives of International Medicine*, vol. 164, pp. 317-319
21. Pumphrey R. 2004. 'Anaphylaxis: can we tell who is at risk of a fatal reaction?', *Current opinion in Allergy and Clinical Immunology*, vol. 4, pp. 285-290.
22. Roberts, G Patel, N Levi-Schaffer, F Habibi, P & Lack, G 2003, 'Food allergy as a risk factor for life-threatening asthma in childhood: A case controlled study', *Journal of Allergy and Clinical Immunology*, vol. 112, no. 1, pp. 168-174
23. Sampson H. 1988. Comparative study of commercial food antigen extracts for the diagnosis of food hypersensitivity. *J Allergy Clin Immunol* 82:718–726.
24. Sampson H. 1996. Epidemiology of food allergy. *Pediatr Allergy Immunol* 7:42–50.
25. Sampson H, Mendelson L & Rosen J. 1992. 'Fatal and Near-Fatal Anaphylactic Reactions to Food in Children and Adolescents', *New England Journal*, vol. 327, pp.380-384

26. Sicherer S, Burks A, Sampson H. 1998. 'Clinical features of acute allergic reactions to peanut and tree nuts in children', *Pediatrics*, vol, 102 pp.e6.
27. Shimamoto & Bock. 2002. Update on the clinical features of food-induced anaphylaxis, *Current opinion in Allergy and Clinical Immunology* vol. 2, pp. 211-216.
28. Simon G & Brown A, 2004. Clinical features and severity grading of anaphylaxis, *Journal of Allergy and Clinical Immunology*, vol. 114, pp. 371-376.
29. Simons F, Frew A, Igancio J, Ansotegui J, Bochner B, Golden D, Finkelman F, Leung D, Lotvall J, Marone G, Metcalfe D, Muller U, Rosenwasser J, Sampson H, Schwartz L, van Hage M & Walls A. 2007. 'Risk assessment in anaphylaxis: Current and future approaches', *Journal of allergy and Clinical Immunology*, vol. 120, pp. S2-S24.
30. Vander Leek TK, Liu AH, Stefanski K, Blacker B, Bock SA. 2000. 'The natural history of peanut allergy in young children and its association with serum peanut-specific IgE'. *Journal of Pediatrics*. Vol. 137:749-755.
31. Yocum M, Butterfield J, Volcheck G, Schroeder D & Silverstein M. 1999, Epidemiology of anaphylaxis in Olmsted Country: A population-based study, *Journal of Allergy and Clinical Immunology*, vol. 104, pp. 489-594
32. Yunginger JW, Sweeney KG, Sturner WQ et al: Fatal food-induced anaphylaxis. *JAMA* 1988; 260: 1450-1452)
33. Wang, J & Sampson, H 2007, 'Food Anaphylaxis', *Clinical and Experimental Allergy*, vol. 37, pp. 651-660

APPENDIX 1

Table 1. Clinical features of anaphylaxis

BODY SYSTEM	CLINICAL OBSERVATION
Cutaneous	Urticaria, angioedema, Flushing, rash, pruritus, Erythema, Edema, itching
Gastrointestinal	Oedema of the lips/tounge, nausea, vomiting, diarrhoea, abdominal pain, loss of bowel control
Respiratory	Nasal congestion, Laryngeal oedema, sneezing, rhinorrhea, difficulty swallowing,persistent cough, wheeze, chest tightness, noisy breathing
Cardiovascular	Tachycardia, arrhythmia, hypotension, shock, pale & floppy, chest pain, cardiac arrest
Neurologic	Anxiety, headache, seizure, loss of consciousness, dizziness

Source: Wang & Sampson (2007)

APPENDIX 2

Table 1. Skin reactions; Local vs. non-local

	Severe(R±C+) <i>n</i>	Moderate(R+C-) <i>n</i>	Mild (R-C-) <i>n</i>	TOTAL <i>n</i>	%
Skin	23 (11%)	37(17%)	138 (63%)	198	91
- Local	15	27	93	135	
- Non local	8	10	45	63	
No Skin	9 (4%)	11 (5%)	0	20	9
TOTAL	32 (5%)	48 (22%)	138 (63%)	218	

Table 2. Causative Allergen

	MILD (R-C-)		MODERATE (R+C-)		SEVERE (R±C+)		TOTAL ANAPHYLAXIS	
	<i>n</i>	%	<i>n</i>	%	<i>n</i>	%	<i>n</i>	%
Peanut	59 (63%)	63.44	23	24.73	11	11.83	93	42.30
Walnut	1 (33%)	33.33	1	33.33	1	33.33	3	1.36
Cashew	6 (67%)	66.67	3	33.33			9	4.09
Pistachio	2	100					2	0.91
Brasil	1	100					1	0.45
Hazelnut	2	40	3	60			5	2.27
Macadamia	1	100					1	0.45
TOTAL NUT	73	63.16	30	26.32	12	10.53	114	51.82
Egg	34	72.34	4	8.51	9	19.15	47	21.36
Milk	21	53.85	12	30.77	6	15.38	39	17.73
Other	11	55	4	20	5	25	20	9.10
TOTAL	139	62.73	50	22.73	32	14.55	220	

*other = soy, buckwheat, fish, sesame, wheat, seafood, beef/lamb, potato, kiwi fruit

Table 3. Whole food allergen vs. allergen ingredient

	MILD (R-C-)	MODERATE (R+C-)	SEVERE (R±C+)	TOTAL
Whole food allergen	93 (67%)	31 (63%)	17 (53%)	141 (64%)
Allergen ingredient	45 (33%)	18 (37%)	15 (47%)	78 (36%)
TOTAL	138	49	32	219

Table 4. Allergen tested before or after date seen

	MILD (R-C-)	MODERATE (R+C-)	SEVERE(R±C+)	TOTAL
	<i>n</i> (%)	<i>n</i> (%)	<i>n</i> (%)	<i>n</i> (%)
Before date seen	107 (67%)	31 (19%)	21 (13%)	159(73%)
After date seen	31 (53%)	17 (29%)	11(19%)	59 (27%)
TOTAL	138 (63%)	48 (22%)	32 (15%)	218

Table 5. Use of adrenaline

	MILD	MODERATE	SEVERE	TOTAL ANAPHYLAXIS
	<i>n</i>	<i>n</i>	<i>n</i>	<i>n</i>
ADRENALINE	10 (50%)	5(25%)	5 (25%)	20 (9%)
TOTAL				218

Table 6. Age of Anaphylaxis

Age (months)	<i>n</i>	%
≤12m	78	36%
13 to 36m	88	40%
37 to 60m	31	14%
≥61m	21	10%
TOTAL	218	
Mean age	60months	
Mode age	24months	
Median age	13 to36months	

Table 7: Male vs. Female

	Male		Female	
	<i>n</i>	%	<i>n</i>	%
Mild	82	64.57	56	61.54
Moderate	31	24.41	17	18.68
Severe	14	11.02	18	19.78
TOTAL	127		91	

Table 8. Prevalence of Asthma; Respiratory symptoms (R+) vs. No Respiratory(R-)

	R + C +		R + C -		R+	R - C +		R - C -		R-	Total
	<i>n</i>	%	<i>n</i>	%		<i>n</i>	%	<i>n</i>	%		
Asthma	6	8.33	22	30.56	28	9	12.50	35	48.61	44	72
No Asthma	5	3.42	26	17.81	32	12	8.22	103	70.55	115	146
TOTAL	11	5.05	48	22.02	60	21	9.63	138	63.30	159	218

