Committee on Toxicity of Chemicals in Food, Consumer Products and the Environment

PEANUT ALLERGY

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Chairman
&
Chairman of the Working Group on Peanut Allergy:
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Executive Summary

1.1 Peanut allergic individuals can undergo a severe, life-threatening reaction following exposure to peanut allergens. Due to the severity of this reaction and the possibility that the incidence of peanut allergy is increasing in the UK, a Working Group of the Committee on Toxicity of Chemicals in Food, Consumer Products and the Environment was established to advise whether there is an association between early exposure to peanuts and peanut products and the incidence of peanut allergy in later life. If so, the Working Group was asked to give advice on the consumption of peanuts and peanut products by pregnant and lactating women, infants and children. The Working Group prepared a report which was considered and endorsed by the Committee.

1.2 It was noted that, although crude peanut oil can contain peanut allergens, refined peanut oil is a neutralised bleached deodorised product which contains no proteins detectable by immunoassay and which has not caused reactions in peanut-allergic individuals. It was considered that the use of the refined oil in food and medicinal products is without risk to sensitive individuals. Refined peanut oil is therefore not included in the category of 'peanut products'in the advice below.

1.3 There is some support for the suggestions that peanut allergy in an infant can result from exposure in utero or during lactation. However, following a review of the scientific literature, it was decided that the data on the relationship between peanut consumption by pregnant and lactating women and the incidence of peanut allergy in their offspring were inconclusive. With regard to the mechanism of sensitisation and allergy such a link is, however, possible. It was decided therefore that it would be unwise to discount sensitisation of offspring resulting from exposure of the mother.

1.4 Because of this uncertainty we have recommended a number of topics for further research, a detailed list of these can be found in section 13 of this report.

1.5 It was noted that peanut allergy occurs in individuals who have atopic eczema, asthma, hayfever or other manifestations of allergic disease (known as atopy) or who have parents, brothers or sisters with atopy. Overall, in common with other atopic diseases, the evidence indicates that the prevalence of peanut allergy is increasing. Given that exposure of sensitive individuals to peanut allergens can result in anaphylaxis, a life-threatening reaction, the advice given is precautionary.

1.6 It is advised that:

(i) pregnant women who are atopic, or for whom the father or any sibling of the unborn child has an atopic disease, may wish to avoid eating peanuts and peanut products during pregnancy;

(ii) breast-feeding mothers who are atopic, or those for whom the father or any sibling of the baby has an atopic disease, may wish to avoid eating peanuts and peanut products during lactation;

(iii) a) in common with the advice given for all children, infants with a parent or sibling with an atopic disease should, if possible, be breast-fed exclusively for four to six months;

b) during weaning of these infants, and until they are at least three years of age, peanuts and peanut products should be avoided;

(iv) infants or children who are allergic to peanuts should not consume peanuts or peanut products.

1.7 It is also recommended that the parents or those charged with the care of peanut allergic infants and children should:

(i) be vigilant in reading labels on all multi-ingredient foods and should avoid any for which doubt exists about the ingredients;

(ii) be aware that even minute amounts of peanut allergens may result in severe reactions. They should therefore be alert to the possibility of accidental exposure and should ensure that cross contamination of foodstuffs with peanut allergens does not occur;

(iii) be aware of the treatment for anaphylaxis should inadvertent exposure occur at, for example, school or the homes of other children.

1.8 The Committee would encourage the labelling of foodstuffs to indicate the presence of any peanuts or peanut products even where this is not specifically required under existing labelling legislation.

Introduction and Background

2.1 Recent publications in the scientific literature have suggested that the incidence of peanut allergy in the United Kingdom is increasing.[1-4] It has been proposed that this may be due to (i) a general increase in atopic diseases over the past 10 to 20 years, and/or (ii) an increased consumption of peanuts by pregnant and breast-feeding mothers resulting in sensitisation at an early age.[4] In addition, there is a greater awareness of the possible problems caused by peanuts. Regardless of the route of sensitisation and subsequent exposure, peanut allergy is increasingly recognised as a potentially serious health hazard which may result in fatal anaphylaxis. Sampson[1] and Hourihane and colleagues[4] suggested that, in order to halt this apparent increase in the prevalence of peanut allergy, infants identified as "at risk", i.e. those from atopic families, should have peanuts and peanut products eliminated from their diets and, furthermore, breast-feeding mothers should eliminate peanuts and peanut products from their own diets. In the light of the publications mentioned above, a Working Group of the Department of Health's Committee on Toxicity of Chemicals in Food, Consumer Products and the Environment was established to review the available scientific literature and to advise on the consumption of peanuts and peanut products by pregnant or breast-feeding women, infants and young children.

The Peanut

3.1 Peanuts are also known as ground nuts, earth nuts and monkey nuts. Within this report only the term peanut will be used. Reference to the word nut, without qualification, will refer to tree nuts such as brazil, hazel, or almond and not to the peanut. The peanut plant, Arachis hypogaea, belongs to the botanical family Leguminosae. The plant bears pods which contain seeds, commonly known as peanuts. Other foodstuffs which come from plants of the same botanical family include green peas, soya beans, kidney beans, and lentils.

3.2 The peanut, as a legume, is not related botanically to nuts such as brazil, hazel or almond. It is a native of South America but is cultivated in, for example, North America, Africa, Europe, and India. Typical nutritional composition figures for peanuts are 46% fat, 26% protein (albumins and globulins) and 13% carbohydrate[5] The globulin proteins are divided into arachidonic and non-arachidonic fractions, both of which have been separated into a number of subunits with molecular weights varying from 10-71,000 Daltons as compared with native arachin protein which has a molecular weight of >600,000 daltons. The albumin protein fraction consists of agglutinins, lectin-reactive glycoproteins, protease inhibitors, Gkα-amylase inhibitors and phospholipases.

3.3 Some peanut proteins can cause a serious form of food allergy (hypersensitivity) in susceptible individuals and, in some instances, this may be fatal. Such proteins are referred to as peanut allergens. Sachs and co-workers[6] first isolated a major peanut allergen which they designated “Peanut 1”. Further work by Burks and co-workers[7] resulted in the isolation of 2 major peanut allergens designated Ara h I and Ara h II. These are glycoproteins with isoelectric points and molecular weights of 4.55 and 63,500 Daltons and 5.2 and 17,000 Daltons respectively. Other results suggest that several proteins are recognized by up to 50% of IgE from peanut allergic individuals, demonstrating that such proteins are also major allergens.[8] A recent study concluded that peanut proteins contain multiple allergens of which six were classified as being major allergens.[9] However, in the group of peanut allergic patients participating in this study none had IgE-containing plasma which reacted with a protein identified as Ara h I.

Peanut Consumption and other Routes of Exposure

4.1 Peanuts were introduced into the UK at around the time of the Second World War, providing a history of consumption and exposure over the last 50 years. The consumption of whole peanuts and peanut butter accounts for approximately 80% of total peanut and peanut product consumption. Peanuts and peanut oil are also used in the manufacture of a wide range of foods including biscuits, cakes, pastries, desserts, ice cream, breakfast cereals, cereal bars, nut butters and spreads, confectionery, vegetarian dishes, Chinese, Thai and Indonesian dishes, curries, satay sauce and salad dressing.

4.2 Oils extracted from nuts can be defined as “crude” or “refined”. The crude oils, also known as “gourmet” oils within industry, are manufactured to retain the flavour of the nut. Such oils may contain sufficient quantities of protein to induce an allergic reaction whereas refined oils, which are neutralised, bleached and deodorised peanut oils, contain no protein detectable by immunoassay,[10,11] nor do they possess allergenic activity. The allergenicity of crude and refined peanut oil in peanut allergic subjects has been investigated.[12-14] In one study,[14] 6 of 60 peanut allergic individuals underwent mild reactions to crude peanut oil challenge (Table 1), whereas, when individuals were challenged with refined peanut oil, no adverse reactions were reported. It has been estimated that the likelihood of refined oil causing an allergic reaction is very small and even crude peanut oil is unlikely to produce a severe reaction.

4.3 Following publication of these reports, the Seed Crushers and Oil Processors Association (SCOPA) produced a code of practice for its members on the production and labelling of peanut oil. This states that Good Manufacturing Practice (GMP) and Hazard Analysis Critical Control Point (HACCP) procedures must be observed during the production of refined peanut oil to prevent contamination of refined oil with crude oil. The Code of Practice also stipulates that crude peanut oil should always be labelled as such and makes clear that it is unsuitable for those who have peanut allergy.

4.4 Limited information on consumption of peanuts is available from dietary surveys. National Diet and Nutrition Surveys (NDNS) were undertaken in Britain in 1986/7 of adults (16-64 years) and in 1992/3 of pre-school children (1½-4½ years).[15,16] A survey was also undertaken of different age groups of schoolchildren (10 to 11 years and 14 to 15 years) in 1983 [17] and of infants (6 to 12 months) in 1986.[18] The use of different methodologies in these surveys prevents direct comparisons and the pattern of peanut consumption may have changed in the period since the earlier surveys were undertaken. However, Tables 2 to 5 contain estimates for the consumption of peanuts and peanut products derived from the results of these surveys. Using the combined total daily consumption of all types of peanuts and peanut products, the average consumption for a child aged 1½-4½ was estimated to be 0.7 g/day and for an adult 1.8 g/day. Individuals eating considerably more than the average (the 97.5th percentile consumers) ingest 18 g/child/day and 29 g/adult/day.

Table 1: Mild reactions to crude peanut oil suffered by 6 subjects of 60 tested during Double Blind Placebo Controlled Food Challenge, data from reference 14

Subject	Skin prick test weal size (mm)	Dose of crude oil ingested (ml)	Reaction
1	9	5	Oral itch
2	10	5	Oral itch
3	12	1	Wheeze
4	7	10	Oral itch
5	12	5	Throat itch
6	10	5	Lip swelling

Table 2: Consumption of peanut and peanut products by British Infants aged 6-12 months, 1986 survey data from reference 18

Food	% of survey consuming peanuts or peanut products	Average consumption over whole population (ie including non-consumers) (g/person/day)	Average consumption of those eating peanuts or peanut products (g/person/day)	Consumption at 97.5 percentile of consumers (g/person/day)	Average of maximum amounts of peanuts or peanut products consumed on one occasion (g/person/day)	Highest amount recorded for consumption of peanuts or peanut products in one day (g/person/day)
Whole peanuts	NC	-	-	-	NC	NC
Peanuts in mixes	NC	-	-	-	NC	NC
Peanut butter and spreads	3.4	0.1	2.5	5.5	10.8	25.7
Coated peanuts	NC	-	-	-	NC	NC
Peanuts in chocolate or cereal bars	NC	-	-	-	NC	NC
Peanuts in dishes	NC	-	-	-	NC	NC
TOTAL *	3.4	0.1	2.5	5.5	10.8	25.7

NC = no consumers

* The total amount of peanuts or peanut products eaten by the high level (97.5th percentile) consumer or by the average consumer is not equal to the sum of the consumption from the individual products. It refers to a consumer eating one or any combination of the foods and these values are derived from a distribution of the consumers'eating patterns of these foods.

- not calculated (no consumers recorded)

Table 3: Consumption of peanut and peanut products by British Pre-schoolchildren aged 1½-4½ years, 1992/93 survey data from reference 16

Food	% of survey consuming peanuts or peanut products	Average consumption over whole population (ie including non-consumers) (g/person/day)	Average consumption of those eating peanuts or peanut products (g/person/day)	Consumption at 97.5 percentile of consumers (g/person/day)	Average of maximum amounts of peanuts or peanut products consumed on one occasion (g/person/day)	Highest amount recorded for consumption of peanuts or peanut products in one day (g/person/day)
Whole peanuts	1.6	0.1	7.7	24.9	23.8	53.6
Peanuts in mixes	0.5	0	1.8	3.9	7.5	21.9
Peanut butter and spreads	10.1	0.5	4.7	17.2	11.6	29.5
Coated peanuts	0.6	0	4.5	11.4	23.4	40.7
Peanuts in chocolate or cereal bars	3.2	0.1	1.7	4.5	6.2	10.9
Peanuts in dishes	0.1	0	2.6	3.4	12.0	19.3
TOTAL *	15.2	0.7	4.6	17.6	12.5	40.9

NC = no consumers

* The total amount of peanuts or peanut products eaten by the high level (97.5th percentile) consumer or by the average consumer is not equal to the sum of the consumption from the individual products. It refers to a consumer eating one or any combination of the foods and these values are derived from a distribution of the consumers'eating patterns of these foods.

- not calculated (no consumers recorded)

Table 4: Consumption of peanut and peanut products by British Schoolchildren aged 10-11 years and 14-15 years, 1983 survey data from reference 17

Food	% of survey consuming peanuts or peanut products	Average consumption over whole population (ie including non-consumers) (g/person/day)	Average consumption of those eating peanuts or peanut products (g/person/day)	Consumption at 97.5 percentile of consumers (g/person/day)	Average of maximum amounts of peanuts or peanut products consumed on one occasion (g/person/day)	Highest amount recorded for consumption of peanuts or peanut products in one day (g/person/day)
Whole peanuts	6.4	0.5	7.4	23.9	43.0	120.3
Peanuts in mixes	1.3	0	1.8	10.1	10.9	55.7
Peanut butter and spreads	7.2	0.5	6.2	22.6	24.6	59.4
Coated peanuts	NC	-	-	-	NC	NC
Peanuts in chocolate or cereal bars	19.5	0.6	3.2	10.2	15.7	34.8
Peanuts in dishes	NC	-	-	-	NC	NC
TOTAL *	30.3	1.6	5.2	20.0	23.7	69.1

NC = no consumers

* The total amount of peanuts or peanut products eaten by the high level (97.5th percentile) consumer or by the average consumer is not equal to the sum of the consumption from the individual products. It refers to a consumer eating one or any combination of the foods and these values are derived from a distribution of the consumers'eating patterns of these foods.

- not calculated (no consumers recorded)

Table 5: Consumption of peanut and peanut products by British Adults aged 16-64 years, 1986/87 survey data from reference 15

Food	% of survey consuming peanuts or peanut products	Average consumption over whole population (ie including non-consumers) (g/person/day)	Average consumption of those eating peanuts or peanut products (g/person/day)	Consumption at 97.5 percentile of consumers (g/person/day)	Average of maximum amounts of peanuts or peanut products consumed on one occasion (g/person/day)	Highest amount recorded for consumption of peanuts or peanut products in one day (g/person/day)
Whole peanuts	9.2	0.8	8.9	29.1	49.5	150.9
Peanuts in mixes	4.9	0.2	4.5	24.5	19.8	72.2
Peanut butter and spreads	4.0	0.3	7.2	25.1	26.2	73.3
Coated peanuts	NC	-	-	-	NC	NC
Peanuts in chocolate or cereal bars	15.2	0.5	3.1	10.9	14.1	30.0
Peanuts in dishes	1.1	0.0	2.6	15.5	14.0	78.3
TOTAL *	28.8	1.8	6.4	28.6	28.2	100

NC = no consumers

* The total amount of peanuts or peanut products eaten by the high level (97.5th percentile) consumer or by the average consumer is not equal to the sum of the consumption from the individual products. It refers to a consumer eating one or any combination of the foods and these values are derived from a distribution of the consumers'eating patterns of these foods.

- not calculated (no consumers recorded)

4.5 Besides being a source of human nutrition, peanut and peanut products are used in animal and bird feeds, and in the manufacture of plastics, adhesives, shampoos and linoleum.[19] Peanut oil may be contained in creams for dermal application, including those used for nipple care by mothers during breast feeding and for babies with cradle cap.[20-25] The skin, particularly damaged or abraded skin, may be an important route of sensitisation but, given that such creams contain refined oil, dermal sensitisation is unlikely.

4.6 Intrauterine immunological sensitisation can occur, but the mechanisms by which this is achieved, and the relationship to the development of allergic disease, are uncertain.[1,26,27] It is also recognised that some food allergens (eg ß-lactoglobulin, ovalbumin) can be transmitted to infants via breast milk during lactation in an undegraded form in highly variable amounts (1-1000 µg/l breast milk) and this may also be a route for neonatal sensitisation.[28] There are no reports on the uptake of peanut proteins after ingestion, but data on milk and egg protein absorption suggest that systemic uptake of immunoreactive proteins is about 1/1000 to 1/10,000th of the administered dose within 1-6 hours after ingestion.[28-30] Allergen exposure of infants by inhalation of volatile components, or following handling by an individual who has been in contact with peanuts, is also possible.[31] Since it is reported that individuals react on their first known exposure to peanut allergens, sensitisation must have already occurred when the presence of peanut allergens was not obvious. Concern was expressed that it was not always possible to know from the ingredients list if peanuts or peanut products were contained in manufactured foods (see paragraph 5.1 below).

Labelling and Ingredients

5.1 Food labelling regulations require ingredients and most additives to be listed in descending order of weight at the time of their use in the preparation of the food. Additives are listed by chemical name, or by an approved EC number (E number), usually with their function noted e.g. “preservative”. There are, however, a few exceptions to these rules:

- Foods sold unpackaged need not carry ingredient lists, but meat, fish, cheese and delicatessen items have to indicate near the display that they contain certain types of additives, ie antioxidant, colour, flavouring, flavour enhancer, preservative, sweetener;

- If an ingredient of a food is itself made up of more than one ingredient (sometimes called a compound ingredient), the label need not list the ingredients used in the compound ingredient (other than the additives it contains) if the compound ingredient constitutes less than 25% by weight of the final product. An example of a compound ingredient could be muesli, where it was used as the base of a cheesecake. If the muesli was sold as such, then the nuts present would need to be listed. However, as the base of a cheesecake constituting less than 25% of the finished product, the individual ingredients of the muesli, including the nuts, need not be listed;

- There are no requirements for flavouring additives or peanut oil used as a carrier to be listed individually on labels at present;

- A food manufacturer may use generic names such as “vegetable oil”, although the oil may be from different sources and may contain peanut oil.

5.2 It was noted that some food manufacturers often declare the presence of peanuts in their products even though the “25% rule” does not require them to do so. The Committee considered that this practice should be encouraged, though it noted the problems that could arise if there were to be “defensive labelling” of products which might not, in fact, contain any peanut.

5.3 The Committee welcomed the initiative under the EU Scientific Cooperation Procedure to seek information on which to base changes in the EU labelling rules on allergens and noted that the EU Commission had already initiated discussions on possible legislative changes.

5.4 The rules on the labelling of medicines require that the active ingredients and those excipients which have a known effect be shown on the labelling of all medicines. Peanut

oil (arachis oil) is included in the list of excipients which are known to have a pharmacological effect and will always appear on the labelling of medicinal products containing this material. This requirement became effective on 1 September 1997 and will be introduced as marketing authorisations (licences) come up for renewal. Arachis oil BP and peanut oil BP are refined oils as defined in Section 4.2 above.

5.5 Cosmetic products containing peanut oil are required to disclose ingredients under the 6th Amendment to the European Union Cosmetic Directive (1993) which had an implementation date of December 1997. “Arachis hypogaea” is defined as the International Nomenclature Cosmetic Ingredient (INCI) name for peanut oil and will be used in the list of ingredients.

The Development of Allergy and the Allergic Response

6.1 Allergy is defined as the adverse health effects that may result from the stimulation of a specific immune response. Allergic disease may take many forms and normally develops in two phases. The first phase, sensitisation, occurs when a susceptible individual is exposed for the first time to an inducing allergen in sufficient quantities to stimulate a primary immune response. If the sensitised individual is exposed to the same allergen on a subsequent occasion, then an accelerated and more aggressive immune response may be provoked, resulting in an inflammatory hypersensitivity reaction in the relevant target organ or organs (the second phase). The quantities of allergen necessary to either induce or elicit an allergic response are usually unknown.

6.2 Allergic responses differ little from protective immune responses with respect to the basic immunobiological events that are induced following receipt of the immunogenic signal. For instance, immune reactions to parasitic worm infections of the gastrointestinal tract in man are associated with eosinophilia and high levels of IgE, these being characteristic also of the allergic response.[32] Allergen must be encountered in sufficient quantity and in a form appropriate for recognition by responsive T lymphocytes. The activation of these cells is dependent on the delivery of an immunogenic stimulus, together with the necessary costimulatory signals, by specialised antigen-presenting cells (APC). Probably, the most important APCs are dendritic cells (DC) which drive the induction of the primary immune response and development of allergic sensitisation. These cells are found in small numbers in lymphoid tissue and also in the epithelial layers of the skin (Langerhans cells) as well as the respiratory and gastrointestinal tracts. In these latter tissues, DC serve as sentinels of the immune system. They internalise and process antigen and, subsequently, present it in an immunogenic form to responsive T lymphocytes.[33]

6.3 Whereas most foreign proteins are potentially immunogenic, only a proportion are able to stimulate the quality of immune response necessary for allergic sensitisation. In order to understand the mechanisms of allergy, it is necessary to consider the characteristics of allergic responses and how they are induced and regulated.

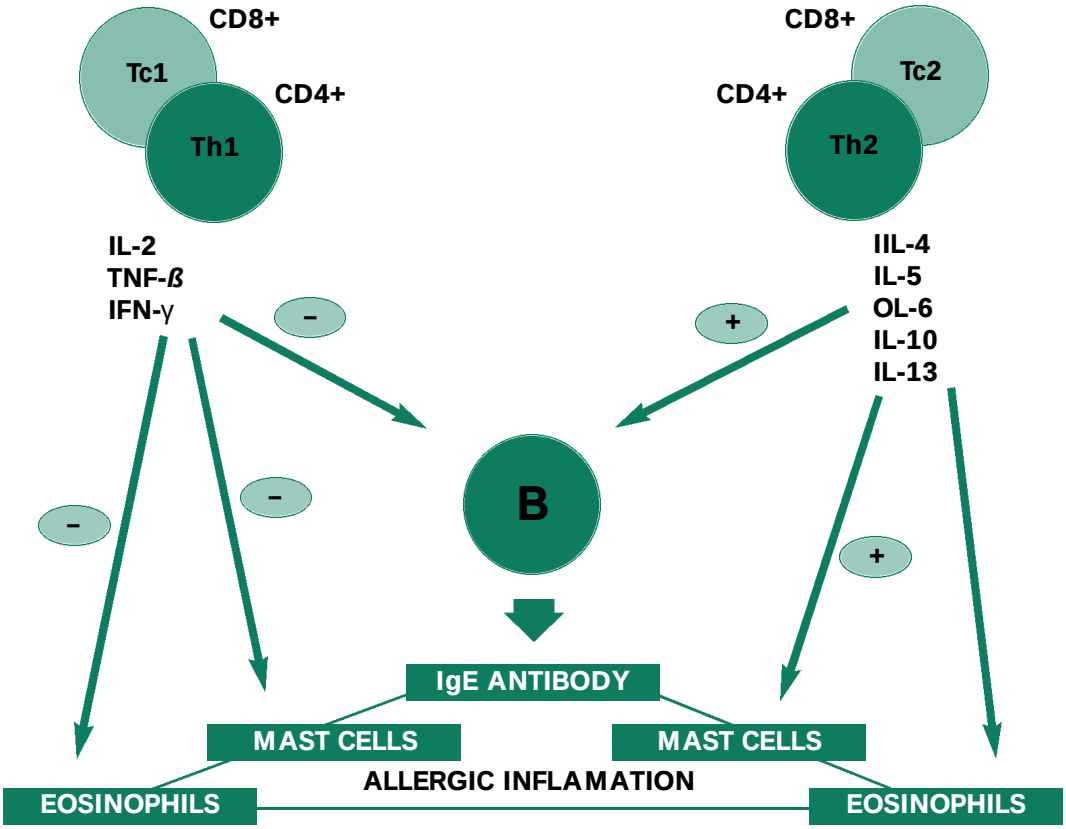
6.4 Many forms of allergic reaction, particularly those that are characterised by an immediate onset such as peanut allergy, are effected by an antibody (immunoglobulin) of the IgE class. Following first exposure to the inducing allergen, the susceptible individual will mount a specific IgE antibody response. These antibodies distribute systemically and associate with mast cells, including those in the gastrointestinal and respiratory tracts. At this point, the individual is sensitised and subsequent exposure to the inducing allergen will provoke an immediate-type hypersensitivity (allergic) reaction. The allergen cross-links IgE antibodies bound to high affinity receptors on mast

cells which results in mast cell degranulation and release of both preformed and newly synthesised mediators. These act together to cause vasodilation, bronchoconstriction and other features characteristic of the allergic reaction.

6.5 The production of IgE antibody is dependent upon T lymphocytes and is highly regulated. Cognate interaction between T lymphocytes and B lymphocytes and regulatory cytokines influence the initiation and maintenance of IgE responses. Of particular importance is interleukin 4 (IL-4), a cytokine that has been shown in mice to be required for normal IgE responses.[34] Mice that lack a functional gene for IL-4 fail to exhibit IgE responses,[35] whereas mice that have a transgene for this cytokine display increased serum concentrations of IgE and mount more vigorous IgE antibody responses.[36] A balance is provided by interferon gamma (IFN-γ), a cytokine that antagonises the production of IgE antibody.[37] These same cytokines also serve to regulate reciprocally the stimulation of IgE responses in humans,[38] although in man another cytokine, interleukin 13 (IL-13), which shares some homology with IL-4, also plays an important role as a promoter of IgE production.[39] Although it is the cytokines quoted above that, in normal circumstances, have the most profound influence on the initiation and vigour of IgE responses, there are other cytokines and other cellular interactions that have also been shown to affect the production of IgE by human lymphocytes or the stimulation of IgE responses in mice. Moreover, there is evidence that other physiological processes may also have some impact, notably the interactions between the neuroendocrine and immune systems involving neuropeptide release.

6.6 While cytokines are produced by a wide variety of immunologically competent cells, it is the T lymphocyte cytokine microenvironment that is probably of greatest importance for IgE production and the regulation of allergic responses. Of particular relevance to the stimulation of qualitatively distinct immune responses are functional subpopulations of T lymphocytes and their cytokine products. Over ten years ago, it was reported that in mice the T helper (Th) cells, characterised by their expression of the CD4+ membrane determinant, display functional heterogeneity.[40] Two main populations are recognised, designated Th1 and Th2, that differ in their cytokine secretion patterns. Some cytokines, such as interleukin 3 (IL-3) and granulocyte/macrophage colony-stimulating factor (GM-CSF) are produced by both cell types. In mice, however, Th1 cells produce IFN-γ, interleukin-2 (IL-2) and tumour necrosis factor ß (TNF-ß), whereas Th2 cells produce interleukins 4,5,6 and 10.[41] Heterogeneity among CD4+T lymphocytes has also been described in humans.[42] The significance of this functional heterogeneity with regard to the induction and maintenance of IgE responses is that under conditions in which Th2-type responses predominate, IgE antibody production will be favoured, whereas Th1-type responses inhibit IgE production. Figure 1 summarises the inter-relationship between different cell types and the production and action of cytokines.

Figure 1: Cellular and Molecular Mechanisms of Allergy



There exists functional heterogeneity among differentiated T lymphocyte populations. Two main types of CD4+T helper cells are recognised and these are designated Th1 and Th2. A similar dichotomy has been described for CD8+ cytotoxic T lymphocytes: Tc1 and Tc2 cells. Type 1 cells produce interleukin 2 (IL-2), tumour necrosis factor ß (TNF-ß) and interferon γ (IFN-γ), whereas type 2 cell products include interleukins 4, 5, 6, 10 and 13 (IL-4, IL-5, IL-6, IL-10 and IL-13). These cytokines exert reciprocal effects on IgE antibody responses, and on the development, localisation and function of those cells (mast cells and eosinophils) that together with IgE antibody effect immediate-type allergic hypersensitivity reactions and more chronic inflammatory reponses.

6.7 In addition to promoting IgE responses, cytokines produced by Th2 cells augment the development, localisation and activation of mast cells and eosinophils, cells that play pivotal roles in immediate-type hypersensitivity reactions and the more chronic inflammatory responses associated with them.[43]

6.8 It is believed that differentiated subpopulations of $CD4^+$ cells are derived from a common precursor during the evolution of an immune response. It is apparent that a number of factors can influence the preferential development of differentiated $CD4^+$ cells including the nature of the antigen itself, the route, extent and duration of exposure, the characteristics of antigen-presenting cells, the co-stimulatory molecules that they express and the context within which antigen is displayed to responsive T lymphocytes. One of the most important determinants of Th cell development appears to be the local cytokine microenvironment in association with other co-stimulatory factors produced by APC. Broadly, it is Th1-type cytokines that drive the development of Th1 cells, while

IL-4, IL-10 and other products of Th2 cells favour Th2 responses. Indeed, Th2 cell responses fail to develop in IL-4 gene knockout mice.[44] These same cytokines are also reciprocally antagonistic insofar as IL-10 inhibits cytokine synthesis by Th1 cells and IFN-γ inhibits the proliferation of Th2 cells. The cytokines that are of the greatest importance as determinants of selective Th cell development are IL-10 and interleukin 12 (IL-12), the latter being a product of dendritic cells, macrophages and B lymphocytes. IL-12 promotes Th1 cell development and also inhibits Th2-type immune responses.[43]

6.9 It has become apparent more recently that there also exists functional heterogeneity among another subpopulation of T lymphocytes. These T cytotoxic (Tc) cells are characterised by their expression of the CD8 membrane determinant. Two populations, designated Tc1 and Tc2, have been described that display selective cytokine secretion patterns comparable, respectively, with Th1 and Th2 cells. Tc1-type cells may play a particularly important role in the negative regulation of IgE responses.[45] Taken together, the available evidence suggests that an important determinant of allergy is the development with time of discrete functional subpopulations of T lymphocytes and their production of cytokines that direct the quality of immune responses.

6.10 As mentioned in section 4.6, exposure to a specific allergen may take place early in life and possibly prior to birth.[46] In those children who progress to develop milk and egg allergy, T cells from the cord blood obtained at birth not only proliferate in response to these allergens, but also display impaired production of IFN-γ. This will remove a potentially important negative influence which normally constrains the development of the Th2-driven allergic responses.[47] After an initial phase in which allergy to milk/egg predominates and is linked to the development primarily of atopic eczema or gastrointestinal symptoms, the clinical expression of allergy may regress completely or there may be the subsequent development of sensitisation to various air-borne allergens such as house dust mite, cat and dog dander, mould, and pollen from grass and trees.[48]

6.11 Once an individual is sensitised to allergens, such as those found in peanut, the IgE generated provides a very sensitive pathway for triggering an acute allergic response. The IgE binds to high affinity receptors on the surface of mast cells and basophils [49] in such a way that contact between only a few cell bound IgE molecules and the allergen triggers the release of a large number of highly active mediators of inflammation (eg. histamine, proteolytic enzymes, leukotrienes and prostaglandins) from the cells' granules.[49,50] Together, these mediators cause urticaria, angioedema, hypotension, acute asthma and sometimes systemic anaphylaxis.

6.12 In addition to this immediate response, release of mediators and cytokines from activated mast cells results in the recruitment of neutrophils, eosinophils and basophils into the area of inflammation. These mediator-secreting leukocytes are slowed as they pass along blood vessels and then pass through the blood vessel wall into the tissue

(transendothelial migration).[51,52] Once in the perivascular space, the neutrophils, eosinophils and basophils migrate into the tissue, attracted by cytokines and chemokines [53] where they release a further cascade of mediators which are responsible for the "late phase" of the allergic response. With additional allergenic stimulation, Th2 cells and monocytes are recruited which, through appropriate cytokine secretion, maintain the inflammatory response.

6.13 It is not known whether increased permeability of the gastrointestinal tract in infancy is one reason why egg and milk allergy are more common in infants than in older children. Besides maturation of the gut, shifting of the immune system towards a protective mechanism and away from Th2 type responses could also explain this phenomenon.[54] This is associated with a reduction in specific IgE titres and positive skin prick tests (SPTs) and an increase in specific IgAantibody production together with a shift towards a Th1 profile.[55] The failure of such a shift to be made may contribute to a persistent allergic reaction.[48]

Characteristics of Peanut Allergy

7.1 It is clear that in peanut sensitive subjects, specific IgE is generated against particular peanut allergens. The range of allergens from peanuts recognized by allergic subjects differs between individuals. Many of these allergens are heat stable and their allergenicity is not diminished by heating or processing. Thus, an allergic response can be elicited following ingestion of either raw or heat-treated peanuts and peanut products.

7.2 De Jong and co-workers [56] have shown that peanut specific T cells from the blood of patients with peanut allergy occur with an increased frequency in comparison with non-allergic control subjects. Supernatants derived from peanut allergen-stimulated peripheral blood mononuclear cells from peanut allergic individuals contained significantly less IFN-γ than control cultures, the implication being that regulation of IFN-γ is important in the pathogenesis of peanut allergy.

7.3 Higgins et al [57] examined T lymphocyte responses in vitro to peanut and tree-nut allergens. Peanut-reactive T cell clones proliferated in vitro in response to peanut extract and, with one exception, showed cross-reactivity with either brazil or hazel nut allergens. The peanut-specific T cell clones produced high levels of IL-4, but only low levels of IFN-γ; a profile consistent with a selective Th2-type phenotype and the development of IgE mediated responses. Similar findings were reported by Laan et al [58] who found that, compared with controls, peanut allergic patients had an increased frequency of peanut-responsive $CD4^+$ T lymphocytes and that these cells produced increased IL-4, but reduced levels of IFN-γ. Taken together, the evidence suggests that peanut allergy is associated with the development of Th2-type cells that produce high levels of IL-4.

Clinical Presentation of Peanut Allergy

8.1 Peanut sensitive individuals can undergo a variety of clinical reactions following exposure by skin, mouth contact, ingestion or inhalation of allergen. Immediate reactions that are not life-threatening include bowel discomfort and exacerbation of atopic eczema. Many allergic individuals, particularly children, have an intense dislike for the taste of peanut and immediately experience a tingling sensation on the lips, tongue and palate. Other comparatively mild symptoms include nausea, abdominal distension, colicky pain and diarrhoea. Within a few minutes of exposure, generalised urticaria can develop.

8.2 Other immediate reactions can be severe and life-threatening. In such cases, a reaction can cause angioedema which results in swelling of the tongue, palate, and the back of the throat. Complete obstruction of the upper airway is possible. Anaphylactic shock,[59] the most severe allergic reaction, is characterised by a rapid fall in blood pressure which has been attributed to peripheral vasodilation, enhanced vascular permeability, plasma leakage and intravascular volume depletion. Coma and death may result. Anaphylaxis may well start with burning of the throat and mouth, generalised urticaria as well as laryngeal oedema, bronchospasm and fainting. In general, this reaction is treated by immediate intramuscular adrenaline injection.[60] Rapid transfer to hospital for resuscitation is imperative.

8.3 Asthmatic reactions to peanuts can occur in isolation or in association with anaphylaxis. A severe asthmatic reaction may also be life threatening. Asthma may be treated with appropriate anti-asthma therapy such as bronchodilators and corticosteroids. However, this treatment is much less effective than adrenaline injection and if any doubt exists about the outcome of the allergic reaction, adrenaline should be administered without delay.

Testing for Sensitisation

9.1 The diagnosis of peanut allergy should be made in a specialist referral centre and, in the first instance, with the clinical history. For peanut allergic individuals, this often produces a classical picture of immediate reaction to the allergen, in which case the use of SPTs, with or without additional in vitro tests to detect peanut specific IgE, is all that is required. However, when the clinical history is unclear and/or the results of in vitro tests are equivocal, it is necessary to proceed to the use of elimination diets and subsequent controlled challenges (see below in paragraph 9.3). It should be noted that SPTs are not generally available and are usually performed by paediatricians, respiratory physicians or at the specialist testing centre.

9.2 A questionnaire based diagnosis of peanut allergy in adults revealed a 14% false-positive rate based on subsequent skin prick test and peanut challenge.[4] In many individuals with a false positive history, the symptoms reported are unusual and often develop over hours instead of the more usual immediate responses. In some cases, reactions are to other allergens but have been wrongly attributed to peanuts. Objective testing is, therefore, an important adjunct to the clinical history. Provided they are carried out with a specific pure allergen, SPTs are highly sensitive but not, in themselves, conclusive. Specific IgE antibody measurements in the blood, such as the radioallergosorbent test (RAST), the enzyme linked immunosorbent assays (ELISA) or immunoblot assays, are available but the sensitivity and specificity of these tests have not been investigated fully for peanut allergy.

9.3 If doubt still exists, a double blind placebo controlled food challenge (DBPCFC) is the best available method [55] since such studies should eliminate doctor and patient bias. However, masking of foods is not always possible and encapsulation of the food may prevent upper gastrointestinal tract reactions. It is also difficult to account for exercise, infection and other factors which are known to affect the allergic response. Comprehensive reviews of methodology have been reported elsewhere.[61] Generally, DBPCFCs are rarely required in cases of peanut allergy.

Trends in Atopic Disease and Peanut Allergy

10.1 Prevalence data on food allergy are limited but prevalence is reported to be in the range of 1-3% for the population, lower than estimates of prevalence of asthma (4-20%), atopic eczema (5-16%) and hay fever (11-17%).[63-67] The prevalence of food allergy in children ranges between 2-8%, but, as mentioned in section 6, children can and do lose responsiveness. Thus, prevalence of food allergy can decline with age.[68-73] However, individuals who are allergic to peanuts rarely lose clinical reactivity.[55,74] There are no sequential data which accurately report the prevalence of peanut allergy in the UK population.[19] Many reports are not epidemiologically based, but state the clinical and immunological responses in individual cohorts in whom diagnosis of peanut allergy has already been made.

10.2 The prevalence of peanut allergy varies among countries and cultures.[25] Since the introduction of the peanut into the USAand countries such as France, peanut allergy has been estimated to be the commonest cause of food allergic reaction.[25,55] Similarly, fish allergy is common in the Nordic countries where fish and fish products are commonly ingested.[61,75] Conversely, peanut allergy is rare (or not recognised) in African and Asian countries. This apparent lack of allergic response may be due to genetic differences between populations or to the development of tolerance. It is also noteworthy that although peanut allergic individuals may also clinically react to tree nut allergens, they generally do not react to allergens from other legumes [76-78] suggesting that sequence homology of the allergens between species of the same botanical family is not important in this instance.

10.3 In common with other atopic allergic disease, the available evidence indicates that the prevalence of peanut allergy is increasing.[19,25,64,65,68] It is of interest to note, that the general increase in atopic disease appears to be linked to the Western lifestyle.[79] Reduction in parasite load, changes in the nature of air pollution and reduced consumption of antioxidants in the diet have all been advanced as possible causes for the rise in asthma prevalence.[80] The reduced number of bacterial and viral infections (potent stimulators of Th1 responses)[81,82] may also account for the relationship between atopic disease and socioeconomic class.[48,83,84] The introduction of novel allergens, such as latex, may also account in part for this increase.

Clinical Studies of Atopic Disease and Peanut Allergy

Environmental factors

11.1 There has been a number of studies over the past decade on the sensitisation of individuals to environmental and other allergens at a young age.[61,85,86] The effect of environmental factors on infants in the Isle of Wight was studied in a prospective population-based study for one year.[87] A positive SPTfor house dust mite occurred more frequently in infants fed formulae than in those who were breast-fed. At one year of age, more infants in lower socioeconomic groups were reported to have developed asthma than infants in higher socioeconomic groups. Development of the reported asthma was associated with maternal smoking and time of year when born, with those born in summer more likely to develop asthma than those born in winter. Although the authors of this paper refer to the development of asthma, they were in fact describing wheezing which, at this age, may not necessarily lead to the development of asthma.[88] This may explain an apparent inconsistency between the results of this study and of others as regards the influence of socioeconomic status.[83]

General food allergies

11.2 Since atopic individuals are at risk of developing food allergies, the effect of exclusion diets on subsequent development of allergy has been investigated. In one such intervention study 120 children, identified at birth as high risk for atopy, were assigned to either (i) a prophylactic group who received breast milk from mothers on an exclusion diet or (ii) a control group who received cows' milk-based infant formulae.[89] "At risk" subjects were chosen on the basis of a positive family history of allergy in both parents, two siblings or a parent and a sibling, or a single first degree relative plus cord IgE levels of greater than 0.5 kU/l. The diet for the breast-feeding mothers in the prophylactic group excluded dairy products, eggs, fish and nuts (unspecified) from their diet. Breast-fed infants in the prophylactic group were supplemented, if necessary, with a soya-based protein hydrolysate infant formula. Dairy products, eggs, wheat, unhydrolyzed soya, oranges, fish and nuts were excluded from the infants' diet until 9 months of age. Mattresses were covered and carpets treated in an effort to control exposure to house dust mites in this same group. At examination at 10-12 months, allergic disorders were reported in 25 (40%) of the control infants and 8 (13%) of the prophylactic group. The prevalence of asthma and atopic eczema were significantly greater in the control group (odds ratio 4.13, 95% confidence interval 1.1-15.5 and odds ratio 3.6, 95% confidence interval 1.0-12.5 respectively). Parental smoking was a significant factor for the prevalence of all allergies at 12 months. The benefits reported were still apparent at 2 and 4 years of age in the prophylactic group, although differences in the prevalence of asthma were no longer statistically significant.[90,91] Similar results have been reported by others.[92] In this latter study, mothers with their infants were randomised into a prophylactic and control group, such that the mothers in the prophylactic group avoided cows'milk, eggs

and peanuts in the last trimester of pregnancy and during lactation. The infants were not given cows'milk for up to one year of age, eggs for up to two years of age, and fish and peanuts for up to 3 years of age. The control group followed normal feeding practices. Although the prophylactic group had significantly reduced food allergy and milk sensitisation at 2 years of age, by 7 years of age there were no differences between the groups. The presence and extent of allergy in the infant was influenced by genetic factors, gender (males more susceptible than females), and parental smoking. Although there were benefits in the short-term for the infants and young children, in the long-term the benefits were greatly diminished.

Peanut allergy

11.3 As discussed in sections 2 and 4 above there have been some suggestions that peanut allergy in a young child may result from exposure to allergenic proteins either in utero or in breast milk.[3,4] However, as is made clear in these papers the evidence is not conclusive.

11.4 Other studies have reported specifically on peanut allergy in infants and young children. Tariq and coworkers[2] reported on peanut and tree nut sensitisation in 4 year olds from an Isle of Wight cohort. Of the 1218 children contacted at 4 years of age, 981 underwent SPTs. On the basis of clinical history and SPTs, 8 children were identified as having peanut or nut allergy (6 were allergic to peanuts and one each were allergic to hazelnuts and cashews) while 7 had positive SPTs but no clinical reaction. For those allergic to peanuts the age of first reaction ranged from 7 to 30 months. A family history of atopy was associated with peanut sensitisation and all children sensitive to peanuts were atopic. Other risk factors associated with peanut allergy were male gender and egg allergy. However, maternal ingestion of peanuts during pregnancy or lactation or both did not increase peanut sensitisation in the children. This may have been because mothers were not questioned about their consumption of peanuts during pregnancy and lactation until their offspring were 4 years of age.

11.5 Results from one allergy clinic in the UK have shown that peanuts were the most common cause of allergy in young atopic children.[3] Peanut allergic individuals commonly reacted to tree nuts such as brazil, almond and hazel. In some, sensitisation had occurred within the first year of life and the first allergic reaction had occurred by the second birthday. The most common manifestation of peanut allergy was facial angioedema. Respiratory involvement varied from mild sensation in the throat to laryngeal oedema and asphyxia. Others have also reported that atopic infants can have a positive RAST to peanut before their second birthday (21 of 33 individuals) even though they have not knowingly been exposed to peanuts or peanut products.[93]

Risk factors for peanut allergy

11.6 Peanut allergy in relation to heredity, maternal diet and other atopic diseases has been studied by questionnaire.[4] Subjects were those known to have peanut allergy, those referred by the Anaphylaxis Campaign (a parent and adult self-help group for sufferers of anaphylaxis) and those who responded to local advertisements. From the 622

completed questionnaires, it was apparent that all forms of atopy were more common in successive generations and were more common in maternal than in paternal relatives. As with other manifestations of atopy, the maternal environment for early life would seem to be especially important. All self-reported peanut allergic individuals were also atopic. Fifty children, under 5 years of age, with reported peanut allergy underwent SPT. Seven were negative and five did not have peanut allergy as assessed by open challenge. A total of 14 subjects with peanut allergy had a positive SPT to tree nuts. Commenting on this study, Clifford [94] suggested that the apparent increase in peanut allergy was a reflection of increased consumption of peanuts in mothers over the last 10 years.

Severity of the allergic reaction

11.7 Severity of the allergic reaction is difficult to predict. In one study, 50% of peanut allergic individuals considered that the severity of reaction was similar on successive occasions, while 38% considered the reaction worse. Only 2.5% considered the reaction had decreased.[95] An adjuvant effect of exercise was noted in 2.9%, whereas 0.8% reported amelioration of symptoms with exercise. A further study attempted to identify a threshold of peanut allergen.[96] A DBPCFC was conducted in 14 peanut allergic individuals with doses ranging from 10 µg to 50 mg. Two individuals reported mild, subjective reactions such as lip tingling, scratchy throat, facial flushing and lip swelling following challenge with 100 µg, 2 subjects reported the same symptoms following challenge with 2 and 5 mg. Four subjects reported the same mild reactions to 50 mg only, whereas 5 subjects tolerated doses up to 50 mg. Only one subject had a severe reaction and that followed challenge with 5 mg.

Fatalities and their prevention

11.8 Fatal and near fatal anaphylactic reactions following peanut ingestion (and other known food allergens) have been reported in the scientific literature. Collectively the reports demonstrate the benefits of administering adrenalin immediately after the onset of anaphylaxis. In one report,[97] seven such cases involving 5 males and 2 females aged 11 to 43 years were reported over a sixteen month period. All were atopic and had suffered non-fatal episodes prior to the fatal event. The foods incriminated were peanut (four individuals), pecan (one individual), crab (one individual) and cod (one individual). Importantly, in 6 cases, the adverse event occurred away from home. Factors contributing to the severity of the reaction included concomitant intake of alcohol, administration of oral antihistamines and adrenal suppression by chronic glucocorticoid therapy for co-existing asthma. In no case was adrenaline administered immediately after the onset of the symptoms. Another investigation reported 6 fatalities and 7 near fatalities over a 14 month period in children and adolescents after ingestion of certain foods.[98] The age of the children was 2 to 17 years and 12 had well controlled asthma. All had recognised food allergies, but had unknowingly ingested the foods responsible for the reactions. Four were allergic to peanuts, six to tree nuts, one to egg, and two to milk. The initial onset of symptoms in the six fatalities (5 females and one male, aged 2 to 16 years) occurred within 3 to 30 minutes of ingestion of the allergen and death occurred within 95 to 300 minutes. Only 2 received adrenaline within the first hour. Of the seven

near-fatalities, all showed initial symptoms within 5 minutes of allergen ingestion and all but one received adrenaline within 30 minutes. This investigation also demonstrates that the failure to administer adrenaline at the first sign of symptoms increases the risk of a fatal outcome.

Conclusions and Advice

12.1 The development of allergy or an allergic disease, such as asthma, hayfever or atopic eczema, in an individual is associated with that individual being atopic. Atopy is a condition in which there is a genetic predisposition to the development of an enhanced production of immunoglobulin E in response to exposure to some allergens. Therefore it is likely to occur in individuals who have at least one close relative who is atopic. In adulthood peanut allergy is likely to be associated with allergic responses to other materials, whereas in childhood sensitisation to peanuts alone may occur. There are many possible routes of sensitisation. Sensitisation in utero or of the neonate during breast-feeding is possible, although there are no data supporting this mechanism with regard to peanut allergens.

12.2 There are no robust data on the prevalence of peanut allergy since peanuts were introduced into the UK approximately 50 years ago. However, the available evidence indicates that, in common with other atopic disease, the prevalence of peanut allergy is increasing. Peanut allergy, unlike allergy to other food allergens such as cows' milk protein, rarely resolves with age. Although some individuals have mild allergic reactions, severe reactions, including life-threatening anaphylaxis, are possible. In view of this, a precautionary view was taken in formulating advice on peanut consumption by pregnant and breast-feeding women, infants and young children.

12.3 In the main body of the report reference is made to 'refined peanut oil'. As explained in Section 4 above this is neutralised bleached deodorised peanut oil which contains no protein detectable by immunoassay and has not produced any reaction in peanut allergic individuals. Arachis oil BP or peanut oil BP, as used in medicinal products, are refined peanut oil. Because there is no evidence of reaction in allergic individuals refined peanut oil is excluded from the peanut products referred to in the advice.

12.4 For pregnant women our advice is directed to those who are themselves atopic, or to those for whom the father or any sibling of the unborn child has an atopic disease. We advise that, during the pregnancy, these individuals may wish to avoid eating peanuts and foods containing peanut products.

12.5 For breast-feeding mothers our advice is directed to those who are themselves atopic, or to those for whom the father or any sibling of the baby has an atopic disease. We advise that, during lactation, these individuals may wish to avoid eating peanuts and foods containing peanut products.

12.6 For infants with a parent or sibling with atopic disease, we advise that:

(i) in common with the advice given for all children, they should, if possible, be breast-fed for four to six months;

(ii) during weaning, and until at least three years of age, the diets of these children should not include peanuts and foods containing peanut products as these may increase the risk of sensitisation and should be avoided.

12.7 For the infant or child who is already allergic to peanuts, the consequences of exposure to peanut allergens are potentially serious and therefore we advise that they should not consume any peanuts or foods containing peanut products.

12.8 The parents or those charged with the care of peanut allergic infants and children should:

(i) be vigilant in reading the labels of pre-packaged multi-ingredient foods and avoid any if doubt exists about the ingredients;

(ii) be aware that even minute amounts of peanut allergens may result in severe reactions. They should therefore be alert to the possibility of accidental exposure and should ensure that cross contamination of foodstuffs with peanut allergens does not occur;

(iii) be aware of the treatment for anaphylaxis should inadvertent exposure occur at, for example, school or the homes of other children.

12.9 We also advise that parents of sensitised children should first seek advice from their general practitioner and an allergy specialist about prevention of allergic reactions and emergency treatment. Sensitised children should be encouraged to wear a MedicAlert emblem or other similar identification so that, if they are exposed away from those mainly charged with their care, others will be aware of the management of their medical problem.

12.10 We welcome the Ministry of Agriculture, Fisheries and Food's initiative to increase awareness within the catering industry of anaphylaxis and the needs of peanut allergic individuals.

12.11 We advise that, because of the problems of peanut allergy, there is a need for clear and informative labelling of foodstuffs that contain peanut products. We would welcome the encouragement of measures to bring this about, even in instances when legislation does not specifically require it.

12.12 We stress that our advice to pregnant women or lactating mothers is precautionary and directed at those whose baby may be atopic. This may arise when the mother, the father, or a sibling of the baby are atopic or have experienced an allergic disease. We do not discourage those pregnant or nursing mothers who do not fall into this category from

eating peanuts.

12.13 Irrespective of any family history of allergy, we stress that whole peanuts should not be given to children until the age of 5 years because of the possibility of choking.

Recommendations for Further Research

13.1 During the discussions and review, it became apparent that there were many gaps in the understanding of peanut allergy. There are few data on the routes of sensitisation of infants and young children to peanuts or on the mechanisms of the development of clinical tolerance. Therefore, a number of areas of research in which clinical studies would add to current knowledge are recommended and are listed below. Investigation or characterisation of:

(i) In utero sensitisation/tolerance to peanut allergens;

(ii) Sensitisation to peanut allergens via breast milk;

(iii) Routes other than those mentioned in (i) and (ii) above which may lead to peanut sensitisation of infants;

(iv) The nature of the associated reaction of peanut allergic individuals and botanically unrelated tree nuts;

(v) Therapeutic measures that may modify peanut sensitisation and/or ameliorate the symptoms of peanut allergy;

(vi) The basis for the marked severity and persistence of the peanut allergy in comparison with other food allergens;

(vii) The peanut proteins responsible for the allergic response.

It was also suggested that a prospective, longitudinal study be undertaken to determine whether or not the advice given in Section 12 influences the incidence of peanut allergy.

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Appendix 1

Glossary of Terms and Abbreviations

Adrenaline	A catecholamine used for the treatment of anaphylaxis. Also known as epinephrine
Allergen	Substance capable of inducing an allergic immune response
Allergy	Immune response in sensitive individuals which results in an adverse reaction
Anaphylaxis	Acute form of allergy characterised by urticaria (qv), shortness of breath, rapid fall in blood pressure and swelling of the throat and lips. Without immediate treatment, which consists of intramuscular injection of adrenaline (qv), anaphylaxis can be fatal
Anaphylactic shock	see Anaphylaxis
Angioedema	Presence of fluid in subcutaneous tissues or submucosa particularly of the face, eyes, lips and sometimes tongue and throat in anaphylactic reaction
Antibody	Immunoglobulin which is specific for an antigen or allergen
Antigen	Substance capable of inducing an immune response
APC	Antigen-presenting cells
Arachis hypogaea	Botanical name for the peanut plant
Arachis oil	Peanut oil
Ara h I and Ara h II	Peanut allergens
Asthma	Chronic inflammatory disease of the airways which renders them prone to narrow too much. The symptoms include paroxysmal coughing, wheezing, tightness and breathlessness. The inflammation is commonly associated with allergy and, therefore, occurs in individuals who are genetically predisposed to produce IgE antibodies
Atopy	A genetic predisposition toward mounting IgE antibody responses. Atopy

	is associated with allergic disease and, in practice, atopic individuals are commonly defined as those who exhibit sensitisation to two or more allergens
Bronchodilator	Drug that reduces the tone of smooth muscles thereby increasing the diameter of the airways
B lymphocyte	Bursa-equivalent lymphocytes. After maturation into plasma cells they produce antibodies (immunoglobulins) during humoral responses in immunological reactions
Crude oil	Unrefined oil that may contain sufficient quantities of protein to induce an allergic reaction. May be known as “gourmet oil”
COT	Committee on Toxicity of Chemicals in Food, Consumer Products and the Environment. A committee composed of independent experts which advises Government on the human health risk of chemicals in food, consumer products and the environment
Cytokines	Mediators which influence immune, inflammatory and other biological responses. Produced and secreted by T and B lymphocytes, macrophages and other cells
DBPCFC	Double Blind Placebo Controlled Food Challenge. An in vivo test in which the patient and doctor do not know which food is being tested until after the tests and the recording of responses have been completed. Often regarded as the “gold standard” of allergenicity testing but infrequently used in peanut allergy due to the severity of any reaction induced
DC	Dendritic cells
ELISA	Enzyme linked immunosorbent assay
Epinephrine	see Adrenaline
Epitope	Peptide sequence within an antigenic molecule which is recognized by either lymphocytes or antibodies
Glycoproteins	Proteins conjugated with a carbohydrate group
GM-CSF	Granulocyte/macrophage colony-stimulating factor
Gourmet oils	see Crude oil. They retain their flavour for use in cooking, e.g. walnut oil

GMP	Good Manufacturing Practice
Ground nut	Peanut
HACCP	Hazard Analysis Critical Control Point
Hypersensitivity	Heightened responsiveness induced by allergic sensitisation. There are several types of response including that associated with allergy (see immediate-type hypersensitivity)
IFN-γ	Interferon gamma. Produced by Th1 and other cells. Antagonises IgE antibody production
IgE	One of five classes of human immunoglobulin. IgE is involved in allergy and anaphylaxis as well as protecting against intestinal parasites
IL	see Interleukin
Immediate-type allergy/ hypersensitivity	IgE-mediated hypersensitivity characterised by release of mediators such as histamine
INCI	International Nomenclature Cosmetic Ingredient
Incidence	The number of new cases of a disease that occur during a particular time in a defined population
Interleukins	Soluble polypeptide mediators, produced by activated lymphocytes and other cells during immune and inflammatory response
Mast cells	Cells found predominantly in connective tissue, although a specialised population of mast cells is found in mucosal sites (e.g. the gut). Containing histamine (amongst other compounds) released during an allergic reaction. These chemicals form part of the inflammatory and allergic processes
Monkey nut	Peanut
NDNS	National Diet and Nutrition Survey
Peanut	Also known as the groundnut or monkey nut. Comes from the legume family. Related botanically to peas and beans. Not related to tree nuts such as brazil, hazel or almond. Used in a number of foodstuffs and also used to produce peanut oil

Peanut oil	Also known as arachis oil. Used in foods and other products such as skin creams
Prevalence	Total number of cases of a disease in existence at a certain time in a designated population (including new and old cases)
RAST	Radioallergosorbent test, for measurement of specific IgE antibodies in the blood
Refined oil	Contains no detectable protein and therefore unlikely to cause an allergic reaction
SCOPA	Seed Crushers and Oil Processors Association
SPT	Skin Prick Test. A test of allergenicity commonly used in allergy clinics
T helper cells	In general, T cells which help B lymphocytes to produce antibodies. Two principle subtypes exist. Th1 cells produce IFN-γ amongst other cytokines and antagonise the IgE responses. Th2-type cells produce interleukins that promote IgE production and allergic sensitisation
T lymphocytes	Thymus-dependent lymphocytes which, amongst other functions, help B lymphocytes during immunological responses and provide protection from intracellular microbial infection. Distinct sub-populations have been characterised - see T helper cell above
Tc	T cytotoxic cells
Th1 cells	T helper lymphocytes of the type 1 subgroup which produce cytokines such as IFN-γ. In general, their actions antagonise the IgE response
Th2 cells	T helper lymphocytes of the type 2 subgroup which produce cytokines that promote IgE hypersensitivity reactions
TNF- ß	Tumour necrosis factor ß
Urticaria	An intensely itchy rash which results from inflammation and leakage of fluid from the blood into the superficial layers of the skin in response to various mediators, e.g. ‘hives’or ‘nettle rash’.

Appendix 2

Terms of Reference of the Working Group

To advise the Committee on Toxicity of Chemicals in Food, Consumer Products and the Environment on:-

i whether there is an association between early exposure to peanuts and peanut products and the incidence of peanut allergy later in life, and, if so,

ii what advice should be given about the consumption of peanuts and peanut products by pregnant and lactating women, infants and young children.

Appendix 3

Membership of the Working Group on Peanut Allergy

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Professor Warner's research team has received funding from the Seed Crushers and Oil Processors Association and from the Ministry of Agriculture, Fisheries and Food. It was agreed that, since this work has been published in peer-reviewed journals, the working group could use these papers without there being any conflict of interest.

Appendix 4

Membership of the Committee on Toxicity of Chemicals in Food, Consumer Products and the Environment

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