Adverse reactions to foods

David H. Allen, Sheryl Van Nunen, Robert Loblay, Lesley Clarke and Anne Swain

ABSTRACT: The discovery of IgE in the mid-1960s resulted in a widespread view that allergy was the basis of most adverse reactions to food, but it is becoming increasingly clear that other, as yet poorly understood, mechanisms are responsible in the overwhelming majority of cases. This, together with the proliferation of popular literature on "food allergy" has resulted in considerable confusion in the minds of both the public and the medical profession on the subject. In the majority of patients presenting with food intolerance, recognized or otherwise, symptoms are precipitated by various small, non-immunogenic organic molecules present in the food as natural or added ingredients. These reactions are pharmacological rather than immunological in nature, although in some situations they may share a final common pathway with true allergic reactions, resulting in similar symptoms.

IDIOSYNCRATIC REACTIONS to food have been recognized since Hippocratic times,[1] but systematic approaches to diagnosis and therapy have only begun recently with the introduction of elimination diets by Rowe[2] and the double-blind food challenge by May and Bock.[3] The discovery of IgE in the mid-1960s resulted in a widespread view that allergy was the basis of most adverse reactions to food, but it is becoming increasingly clear that other (as yet poorly understood) mechanisms are responsible in the overwhelming majority of cases (Table 1).[4] This, together with the proliferation of popular literature on "food allergy", has resulted in considerable confusion in the minds of both

Departments of Thoracic Medicine and Dietetics, The Royal North Shore Hospital and Departments of Immunology and Dietetics, Royal Prince Alfred Hospital, Sydney.
David H. Allen, MB BS, PhD, FRACP, Visiting Thoracic Physician.
Sheryl Van Nunen, MB BS, FRACP, Assistant Physician.
Robert Loblay, MB BS, PhD, FRACP, Senior Lecturer.
Lesley Clarke, BSc, Dietitian.
Anne Swain, BSc, Dietitian.
Reprints: Dr D.H. Allen, 2/82 Pacific Highway, St Leonards, NSW 2065.

the public and the medical profession on the subject.

Food components can be divided into two categories for the purposes of this discussion: nutrients (proteins, fats, carbohydrates, vitamins and minerals), and small organic molecules (secondary metabolites, as well as additives used in processing and cooking). Particular components can make susceptible individuals sick for various reasons (Table 1). Inborn and acquired errors in the metabolism of nutrients are well-characterized, and will not be discussed here. True allergic reactions are rarely seen in clinical practice, but are well-documented, and are due to an exaggerated IgE response to certain protein antigens. Reactions to foods mediated through other immunological mechanisms (eg, immune complexes) have yet to be convincingly demonstrated. In the majority of patients presenting with food intolerance, recognized or otherwise, symptoms are precipitated by various small, non-immunogenic organic molecules present in the food as natural or added ingredients. These reactions are pharmacological rather than immunological in nature, although in some situations they may share a final common pathway with true allergic reactions, thus resulting in similar symptoms.

TABLE 1: Mechanisms of adverse reactions to foods

1. Metabolic	Inborn or acquired errors in metabolism of nutrients (eg, diabetes, phenylketonuria, lactase deficiency, favism)
2. Pharmacological	Adverse reactions to small, biologically active food chemicals (natural as well as added)
3. Allergic	Specific immunological hypersensitivity (usually to food proteins)

The chemical compounds commonly involved (Appendix 1) are small, biologically active organic molecules widely distributed in plants and other organisms, including those commonly consumed as foods. In many instances, artificial food additives (eg, salicylates and benzoic acid, a common preservative) are identical to naturally occurring compounds found in plants. A diet rich in fruits and vegetables may provide several hundred milligrams of these compounds on a daily basis.[5]

Clinical features

True food allergy is an uncommon cause of adverse reactions to food (less than 1% of patients presenting to the Royal Prince Alfred Hospital (RPAH) Allergy Clinic with food-related symptoms), and, when present, is usually easily diagnosed from the history (Table 2). Patients tend to be children with an atopic background, and only one or two foods (eg, eggs, nuts, milk, seafood) are involved. Local swelling, itch, and burning around the mouth and pharynx are common, and may be followed by nausea, vomiting, abdominal cramps and diarrhoea. Systemic anaphylaxis is a rare but dramatic complication.

Pharmacological food idiosyncrasy is much more common and tends to run in families, although the inheritance is different from that of the atopic diathesis. When both occur in the same individual the symptoms can be more severe, and food ingredients may aggravate atopic eczema, asthma or rhinitis. The chemical constituents responsible are widespread (Appendices 1 and 6), and the reactions are often delayed (from between 1 and 2 hours up to 48 hours). Therefore, recognition of the relationship between symptoms and a particular food is often difficult for both patient and physician. When such a relationship is recognized, multiple foods are usually incriminated. Reactions to each constituent exhibit a dose-response relationship, with a triggering threshold that depends partly on recent intake, so that an individual food does not necessarily produce the same reaction on each occasion.

TABLE 2: Clinical features of adverse reactions to foods

Pharmacological	Allergic
Common	Uncommon
All ages	Mostly children
Non-atopic	Atopic
Many foods	One food
Delayed	Immediate
Difficult diagnosis	Easy diagnosis

The symptoms of pharmacological food idiosyncrasy can involve the skin, gastrointestinal tract, respiratory tract or central nervous system, and frequently resemble drug side-effects (see below). The best recognized syndromes are recurrent urticaria/angio-oedema, irritable bowel syndrome, and migraine, although it should be emphasized that there are other causes for each of these conditions. Symptoms may occur in isolation or in any combination, and one or other syndrome may have been dominant at different stages in the past history. In very sensitive patients, other factors, both exogenous and endogenous (eg, drugs, fumes and other environmental chemicals, hormonal changes, inflammatory mediators, or physical and emotional factors) may provoke similar symptoms. Such individuals are sometimes inappropriately labelled as suffering from "total allergy syndrome".

Diagnosis

True food allergy is diagnosed principally by a careful history and physical examination. In doubtful or difficult cases skin-prick tests or the RAST test for specific IgE can provide useful information, particularly for suspected milk, codfish or peanut allergy; when doubtful, the diagnosis can be confirmed by oral challenge. Since there is a high incidence of IgE and IgG specific to food antigens in normal blood donors, a positive skin- or RAST test is of no significance in the absence of clinical symptoms.[6]

Pharmacological food idiosyncrasy cannot be diagnosed accurately by any currently available skin or blood test, and the responsible chemical components are best identified by systematic elimination and oral challenge. Since each compound is present in many foods, and each patient is usually sensitive to several compounds, an elimination diet must be comprehensive. Inadvertent consumption of an offending chemical often prevents complete resolution of symptoms, and may render challenge results invalid. Furthermore, since each food can contain several suspect chemicals in widely varying doses, it is desirable to challenge with the purified individual components where possible, rather than with the food itself. This enables the common denominators to be identified with a minimum number of challenges, and ensures standardization of the challenge protocol. Challenges should be spaced by at least 48 hours to allow for delayed reactions, and any response to challenge should be followed by a pause of at least three symptom-free days, since patients often experience a temporary refractory period during which they are unresponsive.

A number of controversial techniques are currently used in the diagnosis of "food allergy". These include cytotoxic

food testing, provocative subcutaneous testing, and sublingual testing with food extracts. A recent position statement issued by the American Academy of Allergy indicated that all three techniques were of unproven validity, and recommended that their use be limited to well-designed clinical trials.[7] In our own experience, review of the results of cytotoxic food tests performed elsewhere shows a very poor correlation with challenge results, with a high incidence of both false-positives and false-negatives. Recommendations based on such tests frequently result in unnecessary or inappropriate dietary restriction, and do not reliably identify "masked food allergies".

Specific reactions to ingested chemicals

Research over the past few years has identified an increasing number of ingested chemicals capable of provoking acute severe asthma or urticaria and angio-oedema. The mechanisms by which these chemicals provoke asthma or urticaria are largely unknown and possibly different. Both asthma and urticaria are rarely provoked in the one patient, and the time of onset, duration of reaction, and other clinical features suggest that different mechanisms are operative. We shall, therefore, consider the ingested chemical provocation of these two conditions separately.

Asthma

Aspirin, tartrazine and other azo dyes have been recognized for many years as provokers of asthma. A common preservative, metabisulphite, has been reported by ourselves[8] and others.[9-12] Provocation of asthma by monosodium-L-glutamate (MSG), a widely used flavour enhancer, has recently been reported.[13]

Monosodium glutamate is the sodium salt of glutamic acid, a non-essential amino acid that forms 20% of dietary protein. Free glutamate is also present in our diet as MSG, the majority of which is artificially added to enhance the flavour of foods. Although it may appear difficult to fault a substance that is one of the building-blocks of proteins, considerable evidence exists that MSG, as an additive in food, can cause symptoms. Perhaps because glutamate is a naturally occurring substance, it is listed by the US Food and Drug Administration as "generally regarded as safe", along with sugar, salt and pepper. However, MSG is both neuroexcitatory and neurotoxic in animals, and, in man, added MSG is reported to cause epileptic-like shudder attacks in children, and the Chinese Restaurant Syndrome. (This syndrome, occurring within hours of a Chinese restaurant meal, is characterized by headaches, a burning sensation along the back of the neck, chest tightness, nausea and sweating.)

During the past three years 32 patients, a number of whom had experienced severe asthma following Chinese restaurant meals, have been challenged at The Royal North Shore Hospital (RNSH) with MSG. The patients received an additive-free diet for 5 days prior to the challenge, and were challenged in hospital after an overnight fast with capsules of MSG. Twelve patients reacted, and they fell into two groups: Group 1 consisted of patients who developed asthma and symptoms of the Chinese Restaurant Syndrome 1–2 hours after ingestion of MSG; Group 2 patients did not develop symptoms of Chinese Restaurant Syndrome, and their asthma was delayed 6–12 hours after ingestion of MSG.

The reaction to MSG is dose-dependent and may be delayed up to 12 hours, making recognition difficult for both patient and physician. We recommend that challenges with MSG be performed in hospital because of the potential severity of the reaction. In view of the possibility of delayed reactions, they should be performed in the early morning following an overnight fast. In potentially sensitive individuals the dose should be 0.5 g. Most patients will react to the 1.5–2.5 g level; however, a dose of 5 g should be administered before excluding MSG as a provoker. Appendix 2 contains the detailed dosage schedule used for challenging patients at RNSH.

Patients sensitive to MSG need to know not only which foods contain added MSG, but also the amount contained in a particular food or meal, as it is meals containing 5–10 g of MSG that are likely to provoke severe asthma. The information is at present difficult, if not impossible, to obtain with the unrestricted addition of large amounts of MSG to manufactured and restaurant foods.

In contrast to MSG, asthmatic reactions to ingestion of metabisulphite-containing foods or beverages are usually rapid, frequently within 1 and 2 minutes of ingestion. Our challenge studies, with both acidified solutions of metabisulphite and capsules containing metabisulphite, show that the acidified solution challenges correlate better with a history of reactions to metabisulphite-containing foods or beverages, and more closely reproduce the clinical food-induced reactions. Furthermore, we have recently shown that a 3-second mouthwash with an acidified solution of metabisulphite will provoke asthma in most sulphite-sensitive individuals.

Metabisulphite-containing foods and beverages which commonly produce asthmatic reactions are shown in Appendix 3. It is our standard practice to challenge with both capsules of metabisulphite and solution (see Appendix 2 for challenge doses). Patients are allocated to mild, moderate, severe or very severe groups according to previous clinical reactions. For example, severe asthma, following aspirin or a Chinese meal would rate a "very severe" classification; no history of reaction to ingested substances and mild asthma would rate a "mild" classification.

The yellow dye, tartrazine, and other dyes are also known to provoke asthma. Studies performed at RNSH indicate that up to 14% of asthmatic patients are sensitive to tartrazine.

A questionnaire used by one of us (D.H.A.) to help identify reactions to ingested substances is shown in Appendix 4; history-taking for ingested chemical sensitivity requires specific questions such as these. General, non-specific questions (eg, "do foods or beverages provoke your asthma?") will generally elicit a negative response. Patients tend to forget the pickled onion or sweet white wine that provoked their asthma a year or two previously. Further evidence for provocation of asthma by ingested chemicals can be obtained by monitoring a patient's asthma while on a normal diet for two weeks, and subsequently on a general elimination diet for a similar period. This diet, as shown in Appendix 5, but with the omission of milk, excludes common foods and ingested chemicals known to provoke asthma. Improvement on the elimination diet is suggestive of provocation by ingested substances. Particular foods or chemicals are then identified by single-blind, placebo-

controlled oral challenge studies performed in hospital.

In summary, ingested chemicals as a group are common provokers of asthma, with more than 50% of asthmatics sensitive to at least one chemical. Diagnosis can frequently be made by an aware physician from history alone; however, confirmation by dietary withdrawal of likely chemicals and subsequent oral challenge is usually required.

Dietary management of urticaria and angio-oedema

(For a discussion of urticaria and angio-oedema, see the article by Roberts-Thomson et al., this Supplement.)

Following confirmation of a diagnosis of chronic idiopathic urticaria and/or angio-oedema, it is our usual practice, within the RPAH Allergy Clinic, to offer patients a diet designed to eliminate several food additives and natural constituents (Appendix 5). The test substances are encapsulated in clear gelatin. The challenges are administered second daily in a random order in the doses shown in Appendix 6. A positive result is recorded if urticaria and/or angio-oedema appears within 24–48 hours of administration of the test substance. In the event of a positive result, further challenge is delayed until 48 hours after lesions have subsided. Approximately 90% of the urticaria/angio-oedema sufferers have lesions appear following one or more of the challenges. The frequency of reactions to these challenges is depicted in Table 3.

TABLE 3: Urticaria/angio-oedema challenge results

Test substance	Frequency of reactions
Placebo (beta-carotene, starch)	zero*
Tartrazine	30%*
Na-benzoate	35%*
4-OH benzoic acid	17%*
Brewers' yeast	27%*
Acetylsalicylic acid	61%*
Na-salicylate	32%†
Na-metabisulphite	33%†

*n = 168; †n = 117.

Following completion of the challenge protocol, long-term dietary modification based on individual oral provocation results is advised. In our patient group, follow-up studies have demonstrated that complete remission is sustained in the majority (77%), while a further 20% suffer only occasional episodes of (less intense) symptoms of urticaria/angio-oedema. A small proportion (3%) will relapse, despite adherence to a modified diet.

Systemic reactions to food

As outlined above, systemic symptoms provoked by a pharmacological idiosyncrasy to food components can affect the skin, gastrointestinal tract, respiratory tract and central nervous system. There is a very wide clinical spectrum, and in individual patients any combination of symptoms may be experienced, either simultaneously or at different times throughout life. Table 4 shows the incidence of symptoms in 74 patients seen at the RPAH immunology/allergy service (those whose presenting complaint was urticaria were not included). It is evident that there is a higher incidence of CNS than GI symptoms, although this would almost certainly be the reverse if patients were selected from a gastroenterology clinic. A careful history often reveals past urticaria (frequently in childhood), and this can be a valuable clue to the diagnosis. Common GI symptoms include nausea, vomiting, recurrent abdominal pain, flatulence and bouts of diarrhoea. Recurrent aphthous ulceration, though

TABLE 4: Symptoms of systemic reactions to foods

Symptoms	Frequency of reactions
Headache	98%
Myalgia	96%
Lethargy	98%
Visual	75%
Cognitive	90%
Peripheral	60%
GI symptoms	70%
Urticaria (past or present)	50%
Nasal/sinus	40%
Asthma	17%

infrequent, is characteristically found in salicylate-sensitive patients. Respiratory symptoms generally involve the upper respiratory tract, with nasal congestion, excess mucus production, recurrent pharyngitis or sinusitis. Food components may also precipitate asthma in patients with bronchial hyperreactivity (see above).

Neurological symptoms are often the most bizarre, and may lead to the patient's being diagnosed as "neurotic". Headaches (often migrainous), generalized lethargy and myalgia are the commonest, and may be accompanied by cognitive and perceptual abnormalities (impaired memory and concentration, confusion, mental agitation or depression, blurred vision, dizziness, tinnitus, dysphasia, dysgraphia, tremor, etc) suggestive of an organic brain syndrome. Patients often describe a sensation of being "drugged" or "hung-over". Concrete neurological signs of organic pathology are not found, and investigations of the CNS generally produce normal results. In some individuals, peripheral manifestations are prominent, with paraesthesia, dysaesthesia, limb pains and dysautonomic symptoms (sweating, palpitations, flushing, pallor, etc). When such symptoms are accompanied by dizziness, patients may be inappropriately labelled as suffering from hypoglycaemia.

Investigations are performed as indicated by the history and examination, to exclude other diseases. In the typical patient, tests of immunological, haematological, biochemical and endocrine function produce uniformly normal results. An elevated ESR points towards some other inflammatory or infective cause for the symptoms, and can be a helpful screening test.

Dietary evaluation involves a modification of the approach used in recurrent urticaria (see above). A similar elimination diet is employed, with the additional exclusion of milk and wheat products, for a period of 2–6 weeks, followed (when symptoms have settled) by double-blind challenge with a full range of food components (see Appendix 6). In our experience, compliance is excellent (> 80%), particularly when relapse occurs after minor indiscretions. Partial or complete response to dietary elimination is achieved in

TABLE 5: Systemic reactions to challenges

Challenge substance	Frequency of reactions
Salicylates	78%
Nitrates	70%
Preservatives	68%
Tartrazine	56%
Brewers' yeast	56%
MSG	53%
Amines	47%
Bakers' yeast	36%
Gluten	33%
Annatto	33%
Lactose	33%
Placebo (starch, sucrose)	10%

50–65% of patients, depending on selection criteria, and of these over 90% react to several challenges with a recurrence of symptoms (Table 5). A definitive diet is then prescribed, depending on the results, avoiding only those foods which contain incriminated compounds. Over the next few months, gradual liberalization of foods by chemical grouping is encouraged, in an attempt to induce tachyphylaxis and raise the threshold for triggering of symptoms. In patients with a mild degree of sensitivity, it is sometimes possible to return to a virtually normal diet without relapse. In more severe cases the diet may need to be very stringent, and food intolerance may be aggravated by other factors, such as environmental chemicals, hormonal changes or emotional stress, each of which may require separate attention.

Acknowledgements

Our thanks are due to Ms Gabrielle Boyd, Department of Dietetics, RPAH, for expert dietetic advice to our patients; and to Marilyn Stack, Lyn Scott and Karen Barnes for manuscript preparation.

References

1. Hipprocrates. The Hippocratic collection. London: Encyclopedia Britannica, Vol. 11. 1957: 584.
2. Rowe AH. Elimination diets and the patient's allergies. Philadelphia: Lea & Febiger, 1944.
3. May CD, Bock SA. A modern clinical approach to food hypersensitivity. *Allergy* 1978; 33: 166.
4. Denman AM. Food Allergy. *Br Med J* 1983; 286: 1164-1166.
5. Swain AR, Dutton S, Truswell AS. Salicylates in food. *J Am Diet Assoc* 1984 (in press).
6. Bock SA, Buckley J, Holst A, May CD. Proper use of skin tests with food extracts in diagnosis of hypersensivity to food in children. *Clin Allergy* 1977; 7: 375-383.
7. Reisman RE. American Academy of Allergy position statements — controversial techniques. *J Allergy Clin Immunol* 1981; 67: 333-338.
8. Baker GJ, Collett P, Allen DH. Bronchospasm induced by metabisulphite-containing foods and drugs. *Med J Aust* 1981; 2: 614-616.
9. Stevenson DD, Simon RA. Sensitivity to ingested metabisulfites in asthmatic subjects. *J Allergy Clin Immunol* 1981; 68: 26-32.
10. Freedman BJ. Asthma induced by sulphur dioxide, benzoate and tartrazine contained in orange drinks. *Clin Allergy* 1977; 7: 407-415.
11. Freedman BJ. Sulphur dioxide in foods and beverages: its use as a preservative and its effect on asthma. *Br J Dis Chest* 1980; 74: 128-134.
12. Towns SJ, Mellis CM. The role of acetyl salicylic acid and sodium metabisulfite in chronic childhood asthma. *Pediatrics* 1984; 73: 631-637.
13. Allen DH, Baker GJ. Chinese-restaurant asthma. *N Engl J Med* 1981; 305: 1154-1155.

Appendix 1: Chemical content of various foods

Compound	Common foods
Natural	
Salicylate* (and benzoate)	Citrus and most other fruits (*except:* banana, mango, pawpaw, peeled pears) Most vegetables, herbs and spices (*except:* potato, peas, beans, cauliflower, cabbage, brussell sprouts, lettuce, celery, onion, asparagus, garlic) Honey, licorice, almonds, mint flavours Tea, some coffees, fruit juices, most alcoholic beverages (*except:* whisky, gin, vodka)
Amines	Cheese, chocolate, avocado, banana, tomato, sauerkraut, broad beans, canned figs, soy sauce Meat extracts, yeast extracts, fish (smoked, pickled or dried), liver Alcoholic beverages (*except:* whisky, gin, vodka)
Glutamate (MSG)	Tomato, mushroom, soy sauce, yeast extracts, meat extracts, wine Cheeses (parmesan, camembert, blue vein) (*NB:* MSG is also added to enhance the flavour of Chinese/Asian foods and commercial savoury foods)
Brewers' yeast	Vegemite and other yeast extracts, some wines, some beers
Additives	
Benzoic acid, Na-metabisulphite*,†	Fruit juices, cordials, soft drinks, syrups, etc
Sorbic acid	Fruit juices, cordials, soft drinks, dried fruits, dried vegetables, etc
Nitrates	Processed meats
Anti-oxidants	Oils, food cooked in oil, margarine
Colourings (azodyes)	Cordials, soft drinks, jams, jellies, cakes, biscuits, pastry, confectionery

* See Ref. 5; † See also Appendix 3.

Appendix 2: Ingested chemical challenge schedule for asthma

Chemical dose	Clinical asthma severity: Mild	Moderate	Severe	V. severe
(i) Metabisulphite (capsules)				
Dose 1	50 mg	25 mg	10 mg	5 mg
Dose 2	100 mg	50 mg	50 mg	25 mg
Dose 3	–	100 mg	100 mg	50 mg
Dose 4	–	–	–	100 mg
(ii) Metabisulphite in 0.5% citric acid solution (30 mL)				
Dose 1	25 mg	10 mg	5 mg	5 mg
Dose 2	50 mg	25 mg	25 mg	25 mg
Dose 3	–	50 mg	50 mg	50 mg
(iii) Tartrazine				
Dose 1	1 mg	1 mg	1 mg	1 mg
Dose 2	10 mg	10 mg	10 mg	10 mg
Dose 3	50 mg	50 mg	50 mg	50 mg
(iv) Acetylsalicylic acid				
Dose 1	300 mg*	30 mg	30 mg	30 mg
Dose 2	600 mg	180 mg	60 mg	60 mg
Dose 3	–	300 mg	180 mg	180 mg
Dose 4	–	600 mg	300 mg	300 mg
Dose 5	–	–	600 mg	600 mg
(v) MSG				
Dose 1	2.5 g	2.5 g	0.5 g	0.5 g
Dose 2	5.0 g	5.0 g	1.5 g	1.5 g
Dose 3	–	–	2.5 g	2.5 g
Dose 4	–	–	5.0 g	5.0 g

* Has taken aspirin without developing asthma.

Note: Only one drug or food additive challenge to be performed per day; one dose per day of MSG.

Appendix 3: Approximate sulphite (expressed in terms of sulphur dioxide) in average servings of selected foods

Food	Amount of serving	Total sulphite (mg/serve)
Some chilled fruit juices, soft drinks, cordials*	250 g	15–25
Wine/cider*	100 ml	15–30
Sausages (and sausage meat)*	110 g	40–45
Pickles (eg. pickled onions)*	15–30 g	10–25
Cheese mixture, paste	30 g	5–10
Dehydrated fruit*	30 g	45–90
Dehydrated vegetables	50 g	25–75
Potatoes (french fries)*	150 g	NA
"Fresh" fruit salad*,†	250–500 g	NA
Potato crisps*	25–100 g	NA

* Indicates sulphite-containing foods which commonly provoke asthma.
† Refers to commercially prepared "fresh" fruit salad (illegal, but occurs).
NA = not available.

Appendix 4: Questionnaire for drugs, foods and food additives likely to provoke asthma

Questions	Likely provoking substance
1. Do any foods, beverages or medications provoke your asthma?	
2. Beverages	
(a) Does wine or beer provoke asthma or hayfever?	Metabisulphite Salicylates ?Alcohol ?Moulds
(b) Do commercially prepared fruit juices provoke asthma within minutes of ingestion?	Metabisulphite Benzoic acid Tartrazine
(c) Do dairy products provoke respiratory symptoms?	(Some cheese pastes, metabisulphite) Milk protein
3. Foods	
(a) Do nuts, eggs or seafood provoke your asthma?	Food allergens Metabisulphite
(b) Do dried fruit or dried vegetables cause asthma? (either ingestion of or during preparation of same)	Metabisulphite
(c) Do pickled onions provoke asthma as soon as they are eaten?	Metabisulphite
(d) Does ingestion of potato chips or french fries cause asthma at times?	Metabisulphite
(e) Can sausages or frankfurts provoke wheeze or cough?	Metabisulphite

Appendix 4 continued overleaf.

Appendix 4 (continued)

(f) Does commercially prepared "fresh" fruit salad cause asthma?	Metabisulphite
(g) Has severe asthma occurred following a Chinese meal?	Monosodium glutamate
(h) Does fresh citrus fruit provoke asthma?	Salicylates
4. Drugs	
(a) Do you take any coloured medications, especially yellow, green or orange?	Tartrazine
(b) Do you take any aspirin-containing medication or other analgesics?	Acetylsalicylic acid
(c) Does the patient take any non-steroidal anti-inflammatory agent, such as Indomethacin?	"Cross-reactivity" with salicylate sensitivity

Appendix 5: Elimination diet

Lamb, beef, chicken, turkey, veal
Potatoes,* lettuce, parsley
Pears* (fresh or sugar-and-water preserved)
Unpreserved bread, rice, plain flour, additive-free spaghetti/plain biscuits, semolina, gelatine, salt
Coffee,† mineral water, milk, eggs
Safflower/sunflower oil (cold-pressed)
Sugar, golden syrup

*Without skin; †Specified brands (salicylate-free)

Appendix 6: Challenges used at RPAH

Challenge compounds	Dose
*Group 1**	
Acetylsalicylic acid†	300 mg
Sodium Benzoate	500 mg }
4-OH-benzoic acid	200 mg }
Sodium metabisulphite†	500 mg }
Tartrazine	30 mg
Brewers' yeast	600 mg
Starch (placebo)	2 × 600 mg
Group 2	
Acetylsalicylic acid†	2 × 600 mg
Sorbic acid	200 mg
Sodium nitrite	100 mg }
Sodium nitrate	100 mg }
BHA (antioxidant)	50 mg }
BHT (antioxidant)	50 mg }
Tyramine	140 mg
Phenylethylamine	4 mg
MSG†	2 × 2.8 g
Gluten	1.5 g
Lactose	700 mg
Sucrose (placebo)	2 × 700 mg

Brackets indicate challenge compounds that are taken together.
*Group 1 challenges are used for patients with urticaria alone. If patients have experienced systemic symptoms, both challenge groups are administered.
†In asthmatic patients these compounds should only be taken under medical supervision. One quarter of the dose is taken every hour, provided there is no reaction. Patients should be kept under observation for at least 2 hours after the last dose.

AUSTRALASIAN MEDICAL PUBLISHING COMPANY LIMITED
71-79 Arundel Street, Glebe, N.S.W. 2037