

FOOD INTOLERANCE IN CHILDREN WITH ECZEMA

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ABSTRACT

Introduction: There is little known about the relationship between eczema and food intolerance. Food intolerance is defined as a pharmacological adverse reaction to food. It is diagnosed by a positive reaction to a food challenge after the systemic elimination of all natural and added chemicals, also called the Elimination Diet. The primary aim of this project was to investigate in children with eczema; food intolerance, associated symptoms, most common chemicals not tolerated, clinical reactions to chemicals and coexisting food intolerance and food allergy. The secondary aim was to investigate outcomes of the elimination diet and current dietary restrictions. *Methods:* Data was collected from medical and dietetic notes of 418 children with eczema ages up to twelve years seen at the RPAH Allergy Unit between 1995 and 1997. Parents and carers were sent a questionnaire to obtain information about the child's symptoms, reactions to food challenges, and dietary restrictions. All information was entered into a confidential database for analysis. Children were grouped based on this information as food intolerant; food sensitised/allergic; and food intolerant & sensitised. *Results:* Approximately half of those children with food intolerance, also had a food allergy. Salicylates, amines and milk were the most common substances responsible for food intolerance reactions and eczema symptoms. Children with food intolerance alone experienced more behaviour-related symptoms than children with both intolerance and allergy. Children who did not attempt the diet commonly avoided additives and dairy. Post elimination diet restrictions included salicylates, amines, milk and additives. *Discussion:* Results indicate that food intolerance in children with eczema is common. Formal dietary investigation should be advised if there is any indication that the child's eczema might be food related. Food intolerance in children, and the coexistence of food intolerance and food allergy need to be further researched.

1 INTRODUCTION

It is known some individuals in the population, both adults and children suffer from adverse reactions to food. Adverse food reactions are the abnormal response exhibited in certain individuals after eating foods that are otherwise tolerated by the majority of people in the community (Esteban 1992). They encompass a wide range of mechanisms and symptoms. Adverse reactions to foods should be categorised as food allergy (immunological) or food intolerance (non-immunological). It is the misuse of both these terms to diagnose all sorts of symptoms and diseases that has led to the controversy surrounding unpleasant reactions to food (Wuthrich 1996).

The area of adverse reactions to food is one of ongoing research, popular public attention, and of strong interest to the media. In 1984 the American Academy of Allergy and Clinical Immunology established a number of definitions of terms used for food reactions. It is the lack of universal acceptance of these definitions by lay and media persons that has resulted in the confusion over the prevalence of true food allergy and intolerance in the community (Clarke, McQueen, Samild & Swain 1996, Guarnaccia 1995).

It is essential that food reactions be diagnosed and classified correctly. Firstly for better management and support, and secondly to increase understanding of the epidemiology, true prevalence, etiology, pathogenesis, genetics and natural history of the condition (Schwartz 1992). There are conflicting reports and research concerning the prevalence of adverse food reactions. Contrary to public perception food intolerance occurs more

commonly than food allergy, and is estimated to effect up to 10 percent of the population. Food intolerance is far less researched than food allergy and is often under-reported due to its difficult diagnosis (Clarke et al 1996).

Researchers have shown the incidence of eczema is increasing (Ferguson 1992). A study proceeding this one, conducted at the Royal Prince Alfred Hospital showed that a large percentage of children with eczema have food related problems. It is widely recognised that eczema is an atopic disease often caused by food allergies, however little is known about the role food intolerance has in exacerbating eczema (Personal Communication 1997). In those children with eczema, asthma and rhinitis, food allergy and food intolerance may coexist in the same individual (Clarke et al 1996).

DEFINITIONS

Food Intolerance

Food intolerance is a term describing an abnormal response to an ingested food or food additive. It is non-immunological and has a number of reactive mechanisms. For the purposes of this study the pharmacological or chemical responses to food will be addressed (Royal College of Physicians and the British Nutrition foundation 1984).

Food intolerance occurs in children and adults. Symptoms may involve the skin, gastrointestinal tract, upper respiratory tract or the central nervous system and can be provoked by a wide range of chemical substances. Natural chemicals such as salicylates, amines and glutamates, and additives such as preservatives, colours and flavours commonly cause adverse responses. Recently the public has become very

concerned about the affects of food additives and are linking their use to many chronic diseases (Lessof 1985). The response to chemicals is dose-related and often cumulative. Diagnosis is made difficult because reaction time is variable and the offending chemical(s) are often contained in many foods (Loblay & Swain, 1986).

The most effective method of diagnosing food intolerance is by systematic elimination and blind challenge. Blood and skin tests are not useful in the diagnosis unless a food allergy is also suspected. Under strict guidance from the dietitian, the patient undergoes a diet which eliminates all foods likely to cause symptoms. Specific food chemicals are then reintroduced into the diet as capsules or in food form. The challenge results are carefully assessed and a modified diet based on the response to challenges is prescribed. The patient is constantly reassessed and gradual liberalisation of foods is encouraged as tolerated (Clarke et al 1996, Loblay & Swain 1986).

Food Allergy

Food allergy or "food hypersensitivity" is the term used to describe an immune reaction resulting in of the production of IgE (immunoglobulin E) antibodies after ingestion of proteins in commonly eaten foods such as egg, peanut, milk, fish, soy and wheat and other nuts (Schwartz 1992, Esteban 1992). The prevalence of food allergy has been estimated by different researchers at between 1 and 10 per cent depending on the age of the child (Clarke et al 1996, Moneret-Vautrin 1994, Zeiger 1990).

In contrast to food intolerance an allergic reaction is immediate and is characterised by itching, burning and swelling around the mouth, nausea, vomiting and abdominal

cramps, urticaria, and asthma. In rare cases anaphylaxis may occur. The severity of the response is dependent on the sensitisation of the individual (Clarke et al 1996, Loblay & Swain 1992).

The Skin Prick Test (SPT) or radioallergosorbent test (RAST) are used to diagnose allergy in combination with clinical examination and dietary modification. A negative SPT has a predictive accuracy of 95 per cent therefore is a useful test for excluding food allergy (Moneret-Vautrin 1994). Food sensitisation is determined by a positive SPT result, which indicates the involvement of specific IgE. A positive SPT is considered significant if the wheal diameter on the skin is greater than 3 mm. 50 percent of patients with a positive SPT will display clinical symptoms of food allergy. This test is useful in warning those patients sensitised to certain foods of a possible allergic reaction prior to that food being introduced into the diet (Sampson 1983).

The double blind placebo controlled food challenge (DBPCFC) is the scientific "gold standard" used to confirm true food allergies. This procedure is time-consuming, expensive, and demands skill and as a result few studies have used DBPCFC as a means of diagnosing food allergy. These studies provide the most accurate data on the prevalence of true allergy (Esteban 1992, Schwartz 1992, Walker 1992).

Management of food allergy involves complete avoidance of the food allergen. In extreme cases this involves even minimal contact with the offending food. Regular consultation with the dietitian ensures allergic reactions are avoided without compromising the nutritional adequacy of the diet (Clarke et al 1996, Loblay & Swain

1992). As children frequently grow out of their allergies an attempt should be made every 6-12 months to skin prick test for the offending food. When the SPT becomes negative the food may be cautiously reintroduced.

1.2 LITERATURE REVIEW

Eczema and Food Intolerance

Eczema (atopic dermatitis) is a multifaceted disease affecting 5-6 percent of children. Onset is usually in the first twelve months and resolution of symptoms is usually partial (Moneret-Vautrin 1994). Recent studies show the incidence of eczema is increasing and estimate its prevalence to be 10 per cent in children under five years of age (Personal Communication 1997, Ferguson 1992). It is characterised by itchy lesions on the face and body that when scratched weep serous fluid and blood. Excessive scratching of the dry, rough skin leads to tissue damage (Atherton 1981).

It has been widely shown that food is implicated in the pathogenesis of eczema. Ferguson describes one double-blind, controlled trial in which 60 percent of children with atopic eczema had positive responses to specific food challenges after appropriate elimination (Ferguson 1992). This finding is supported by a recent study conducted at the Royal Prince Alfred Hospital (RPAH) which showed that 65 percent of 111 children with eczema studied, had a known response to diet and challenges (Personal Communication 1997).

The relationship between eczema in children and food allergy has been thoroughly researched and documented. It is believed that a proportion of patients with atopic

diseases such as asthma, rhinitis, eczema and urticaria will have food allergy as a primary cause of their disease (Edwards 1995). It has been postulated that 35 percent of eczema cases are due to food allergy. It is also agreed that food allergy is common in children with eczema, and that certain foodstuffs aggravate the condition. In one study 81 percent of children diagnosed with food allergy had eczema or a previous history of eczema (Moneret-Vautrin 1994).

The pathological events that occur in the skin are largely unknown. In atopic children with eczema it is assumed the skin releases histamine in response to the excessive production of IgE antibodies after exposure to an antigen. This may explain the mechanisms involved in those children with allergies, however many children with clinically typical eczema do not have elevated IgE levels when tested (Atherton 1981). In these children with eczema and food intolerance, little is known about the mechanisms involved, etiology and prevalence. A study by the RPAH alone, showed that 24 percent of children with eczema had an intolerance to cow's milk that was non-IgE mediated (Personal Communication 1997).

Food intolerance or food sensitivity is used to describe " an abnormal physiologic response to an ingested food or food component" (Clarke et al 1996, Guarnaccia 1995). The reaction is non-immunological and can include pharmacological, metabolic, toxic or idiosyncratic responses to food or food components (Guarnaccia 1995).

Pharmacological food intolerance effects children and adults, with women being effected more commonly than men (Clarke et al 1996, Loblay & Swain 1986, Young

1994). Symptoms can involve the skin, gastrointestinal tract, respiratory tract or central nervous system, either individually or in any combination. Symptoms can be provoked by a variety of naturally occurring and added chemicals that are present in a wide range of foods. The most recognised symptoms are urticaria and/or angiodema, migraine and irritable bowel syndrome (including symptoms of nausea, bloating, abdominal pain, constipation and diarrhoea) (Lessof 1985, Loblay & Swain 1986). This is supported by the claim that less than 3 percent of cases of chronic urticaria have food allergy, with a proportion of the remainder due to food intolerances (Lessof 1985).

Symptomatology

Common skin symptoms include urticaria (hives), angiodema (swelling) and eczema. Gastrointestinal symptoms frequently seen include nausea, vomiting, recurrent abdominal pain, flatulence and diarrhoea. Respiratory tract responses are characterised by nasal congestion and rhinitis. In those children susceptible to breathing difficulties, asthma may be provoked. Food components adversely effecting the central nervous system can cause headaches, lethargy, reduced concentration, depression and hyperactivity to name a few (Clarke et al 1996). In children headaches, recurrent abdominal cramps and limb aches are common, with parents frequently reporting sleep and behaviour disturbances (Loblay & Swain 1986).

Prevalence

There is limited literature on the prevalence of food intolerance in the community, and an urgent need for population studies with large numbers of people. The lack of knowledge of the incidence of food intolerance may be attributed to I. Difficulty of

diagnosis due to the dose-related and cumulative nature of the disease II. Cost and time involved in controlled testing III. Lack of distinction between food allergy and food intolerance and, IV. Difficulty in obtaining large numbers of subjects for population studies especially children (Wuthrich 1996).

Studies have shown a significant discrepancy between patients' perceived adverse food reactions and actual diagnosis (Ferguson 1992, Moneret-Vautrin 1994)). A study by Young and associates showed that of the 20 percent of a random UK population, who complained of adverse food reactions, 1-2 percent had a positive result to controlled challenges (Young 1994). Sampson indicates that less than half perceived food reactions are confirmed by double-blind, placebo-controlled challenges (Sampson 1988). To obtain accurate data on the incidence of adverse food reactions, stringent screening and scientific testing must be conducted as part of the study protocol to negate the bias of over-perception of the population. Bock concluded that the best way to establish an adverse food reaction is dietary exclusion and controlled challenges repeated several times (Bock 1988).

Double-blind challenge procedures have revealed high rates of responses to placebo. This placebo effect is rare in children, but the significance of this in relation to the prevalence of adverse food reactions in children is limited as there have been no population studies conducted with infants using double-blind challenges (Ferguson 1992). Double-blind, placebo-controlled food challenges are also limited by the identical nature of clinical signs of food allergy and food intolerance (symptoms of the skin, gastrointestinal tract and respiratory system). A distinction between food allergy

and food intolerance can only be made if tests are carried out determining immunological involvement. Due to the large variability in diagnostic sensitivity of immunological tests (SPT and RAST) it is suggested that some cases of food allergy may go undetected and as a result be misdiagnosed as food intolerance (Bindslev-Jensen, Skov, Madsen & Poulsen 1994). Many prevalence studies fail to distinguish food allergy and food intolerance, two separated diseases, because this involves more extensive testing. Studies that attempt this will obtain reliable data on the coexistence of food allergy and food intolerance.

A paper by Clarke et al reports that food intolerance occurs more commonly than food allergy, with an estimated prevalence of 10 percent of the population (Clarke et al 1996). A Dutch study investigating food intolerance in 5-6 year old children found that based on parents' perception of "probable" food intolerance prevalence was 4 percent. The validity of this finding must be questioned because of the absence of double-blind challenges in the study protocol. The study also showed that parents often associated food intolerance with eczema, hives, chronic diarrhoea and hyperactive behaviour which is commensurate with literature on symptomology (Aardoom, Hirasing, Rona, Sanavro, van den Heuvel & Leeuwenburg 1997, Clarke et al 1996).

Chemicals Involved In Food Intolerance

Symptoms can be provoked by a variety of chemical substances, both natural and artificial. Both may cause adverse reactions in sensitive people if sufficiently large amounts are ingested. Recently, there has been a lot of emphasis placed on the adverse effects of food additives, which will be discussed in more detail later, however

reactions to naturally occurring chemicals in foods are far more frequent. Natural chemicals are found in nearly all plant and animal foods (Loblay & Swain, 1986).

The effects of these compounds are dose-related and the reactions are often delayed, from one to two hours up to 2 days. For each chemical the dose threshold for triggering symptoms varies depending on the individual's recent intake of food, so a particular food may provoke a different reaction on different occasions. These characteristics of food intolerance often confuse patients as to what foods are causing symptoms, and in many cases lead to misconceptions about, and the unnecessary avoidance of some foods (Clarke et al 1996, Loblay & Swain 1986). In a study by Rona & Chinn it was found that between 20-30 percent of children with perceived food intolerance were currently or had previously avoided some types of food (Rona & Chinn 1987).

Salicylates

The most widely distributed of the natural chemicals precipitating symptoms is the salicylates, which includes aspirin (Settipane 1983). It is estimated that an average Australian diet contains enough natural salicylate to provoke symptoms in sensitive individuals when consumed on a daily basis (Loblay & Swain 1986). In 1985 Swain and colleagues embarked on a study to analyse commonly eaten food and drinks for salicylate content (Swain, Dutton & Truswell 1985). They were found naturally in many fruits, vegetables, nuts, herbs and spices, tea and coffee, and beer and wines. They are also contained in peppermint flavouring and perfumes (Swain, Soutter & Loblay 1991). In a study investigating food intolerance in 2000 patients, salicylates were shown to have the highest frequency of positive challenge reactions, implying that

the salicylate family is the most common cause of diagnosed food intolerance. Almost all patients reacted to one or more substances. Symptoms of eczema were provoked by salicylates in 52 percent of patients (Loblay & Swain 1986).

Amines

Another naturally occurring chemical known to cause adverse food reactions is the biogenic amines. Amines in food, provoke a non-immunological reaction that can behave in a physiologically manner similar to histamine, which is released as a result of an immunological reaction. This may explain why there is a similarity in symptoms between food allergy and intolerance (Lessof 1985) Amines are derived from protein breakdown and fermentation. They are naturally contained in many foods such as bananas, avocados and tomatoes, but can also develop during cooking and storage. High levels are found in cheese, alcoholic drinks, chocolate, yeast extracts and fish products (Lessof 1985, Maga 1978). In the above study, the most common reactions induced by amine challenges were systemic symptoms such as headache, lethargy and gastrointestinal complaints. Eczema occurs to a much lesser extent (Loblay & Swain 1986).

Glutamate

Glutamate is a naturally occurring compound often found in foods high in flavour such as tomatoes, cheese, meat and yeast extracts, and stock cubes. Pure monosodium glutamate (MSG) may be added to foods like soups and Asian cooking to enhance flavour (Loblay & Swain 1986, Swain et al 1991). Current misconceptions regarding MSG have resulted in its often unnecessary exclusion from individuals' diets. The

RPAH study found 72 percent of cases of MSG reactions induced irritable bowel syndrome. Eczema was provoked in 35 percent of patients (Loblay & Swain 1986).

Food Additives

Recently there has been much public concern that food additives cause adverse reactions. There is sufficient literature to state that the incidence of intolerance to food additives is low (Cater 1995, Lessof 1985, Wilson & Scott 1989). The community are making associations between the increasing incidence of food intolerance and the widespread use of chemicals into foodstuffs based on media reports and claims by "alternate" therapy persons (Mansfield 1988). A study in the UK found that although 7 percent of a population sample claimed to react to food additives, fewer than 0.5 percent of the population were actually affected when given double-blind challenge tests (Lessof 1985, Carter 1995). This is commensurate with Wilson and Scott's study which showed less than 5 percent of children with an alleged food additive intolerance had a scientifically diagnosed intolerance (Wilson & Scott 1989). People who respond adversely to food additives are frequently sensitive to natural chemicals, and their effect appears to exacerbate a pre-existing condition rather than induce it. The most common additives provoking symptoms are preservatives, colourings, flavours and MSG regardless of whether they are derived naturally or artificially (Lessof 1985, Loblay & Swain, 1986). The mechanism behind reactions to additives is largely unknown, but in patients with urticaria, food colours are released due to a pharmacological effect as opposed to an allergic mechanism (Lessof 1985).

Cow's Milk Intolerance

Cow's milk and cow's milk-based formulas are known to cause a high incidence of adverse reaction in the first year of life. The two main types are cow's milk allergy and cow's milk intolerance, both involving different mechanisms. Symptoms of cow's milk intolerance are dose-related and are triggered by large amounts of cow's milk antigen (Schwartz 1992). Symptoms include vomiting, reflux, diarrhoea, eczema and asthma. The Gut Foundation reports that infants with isolated cow's milk intolerance rarely have a history of eczema, and that skin reactions may be caused by allergies to other foods or intolerances to other chemicals (The Gut Foundation 1995). Symptoms occur up to 72 hours after ingestion of normal amounts of cow's milk, which is in contrast to the immediate onset of symptoms with milk allergy (Clarke et al 1996).

A study investigating cow's milk reaction in children with eczema, found that the percentage sensitised to cow's milk (determined by positive SPT) was similar to those exhibiting non-allergic reactions to milk (approximately 24 percent). This finding suggests cow's milk intolerance is equally as prevalent as cow's milk allergy in children with eczema. The remaining 35 percent were tolerant to cow's milk (Personal Communication 1997).

An interesting study by Schwartz, attempted to group children based on SPT results, and the time of onset of symptoms after ingestion of cow's milk. He found a group of children with both I. Symptoms and reaction times to that of clinical cow's milk intolerance, and II. Positive SPT to milk (Schwartz 1992). It has been suggested that in

children with eczema where food allergy and food intolerance coexist, cow's milk may trigger symptoms through both mechanisms (Clarke et al 1996).

Management of Food Intolerance

Patients with suspected adverse reactions to food are assessed by careful history and if required physical examination. Dietary investigation is warranted if chronic symptoms appear to be precipitated by food or drink and/or there is a history of recurrent hives, irritable bowel syndrome or mouth ulceration (Loblay & Swain 1986).

It is important that patients who have made dietary changes based on misconceptions about food, and those who request to investigate the possibilities of dietary treatment, be given the opportunity to explore the role of diet under the supervision of an experienced physician or dietitian. An unsympathetic approach or hasty apportioning of symptoms to psychological factors may lead to self-imposed diets or self-referral to unqualified practitioners (Carter 1995, Clarke et al 1996). It is of particular concern that exclusion diets for children are nutritionally adequate and that misdiagnosis, as a result of delayed treatment is minimised (Cant 1985, Kay & Lessof 1985).

The Elimination Diet

The first step in the diagnosis and management of suspected food intolerance is to determine whether diet is involved. The elimination diet which includes systematic elimination of natural and added chemicals, followed by blind challenge, is a diagnostic tool used to identify patients whose symptoms are diet-related and also the substances provoking adverse symptoms (Loblay & Swain 1986). The diet is based on the

principle that the removal of certain foods from the diet results in an improvement of the disease and re-introduction results in a worsening (Edwards 1995). Allergy testing is only conducted in those individuals with a suspected coexistence of allergy and intolerance.

Researchers from the Allergy Unit, RPAH have designed a Simplified Elimination Diet based on the distribution of natural and added chemicals in food. Symptoms are assessed as diet-related according to the patient's response to the strict elimination of food chemicals for a minimum of two weeks. If there is no improvement from symptoms after 6-8 weeks, the diet is abandoned and food is not considered an important factor. Patients who experience significant improvement from symptoms remain on the diet and are administered food challenges. Open challenges with wheat and milk are performed first, followed by double-blind capsule challenges with salicylates, amines, MSG, artificial colours and some preservatives. Children are more commonly challenged with specific foods as opposed to capsules. This is because information bias is not usually a factor and there is less requirement for a blind procedure, and also it allows children variation in an otherwise bland diet. If a reaction occurs to a food challenge the patient must wait until symptoms have cleared completely before attempting another challenge. Capsule challenges that produce uncertain results are repeated as open food challenges. At the completion of the testing schedule the capsules are decoded and an individualised diet prescribed avoiding only those substances which caused a reaction (Clarke et al 1996, Loblay & Swain 1986).

Patients are encouraged to liberalise their diet by including small amounts of the suspected foods grouped by chemical composition. Sensitivity varies between individuals and some may build up tolerance by regular exposure to small amounts of the chemicals to which they had a reaction. The aim of effective dietary management is to broaden the diet as much as possible without provoking symptoms (Loblay & Swain, Carter 1995). The dietitians' role in the management and liberalisation of the diet is an important one, so it is essential that patients remain in contact throughout this time period. Over-restrictive and severely socially-debilitating diets provide the potential for frustration and consequently total abandonment of the diet. A study looking into the compliance problems in the dietary management of eczema found that even with highly motivated parents, 46 percent of children over 3 years of age gave up diets (Hathaway 1983). Future research into the dietary management of patients who have previously been investigated for food intolerance would provide useful information into the relationship between level of dietary restriction and severity of symptoms.

Anaphylaxis and Food Intolerance

Anaphylaxis refers to a systemic allergic reaction involving multiple body systems. It affects mostly children with highly atopic dispositions, one study reporting that all six patients with severe anaphylactic reactions had asthma, rhinitis and eczema (Sampson, Mendelson & Rosen 1992). Clinical signs occur within minutes with the itching of lips and may progress in some acutely sensitive individuals to shortness of breath and shock (Moneret-Vautrin 1994).

It has been suggested that the incidence of food-induced anaphylaxis has increased over the last few years (Sampson et al 1992). As discussed previously, an aim of this study is to investigate the coexistence of food allergy and food intolerance. It is hoped that by examining the incidence of anaphylaxis in children with food intolerance it will provide more insight into this relationship between food allergy and intolerance.

1.3 AIMS

The purpose of this study is to investigate the role of food intolerance in children with eczema. The study is in parallel with another study by Natalie Saunders using the same eczema population with an emphasis on the role of food allergy. Preliminary studies have shown a strong relationship between eczema and food allergy in children, however fewer studies have focused on the relationship between eczema and food intolerance. This study aims firstly to investigate eczema and food intolerance, and secondly to examine the less researched area of coexisting food intolerance and food allergy.

Areas of Investigation

1. Associated symptoms of those children with eczema
2. Most common food intolerances experienced in children with eczema obtained from results of food challenges
3. Symptoms provoked by food challenges with particular reference to challenges which commonly cause eczema reactions
4. The effectiveness of dietary modification
5. Frequency of anaphylactic reactions to food in children with food intolerance

2 METHODS

2.1 Setting

The setting for the study was the Allergy Consulting Rooms at the Royal Prince Alfred Hospital Medical Centre, Newtown, NSW.

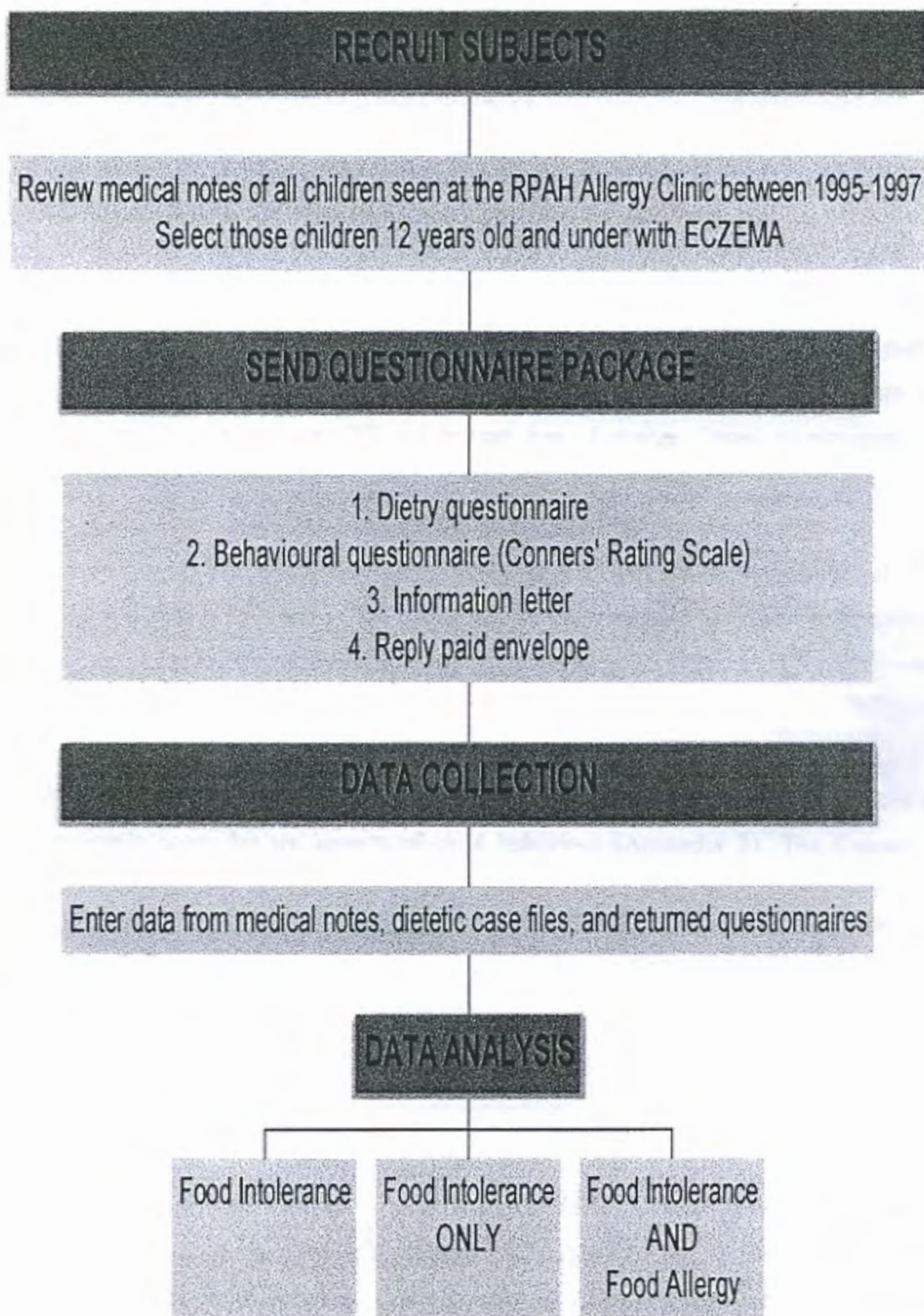
2.2 Study Design

The study involved selecting children with eczema who have been seen at the Allergy Consulting Rooms and collating data obtained from their medical records, dietetic files, and returned questionnaires. The information on the total population was gathered by research students Narelle Greenlees and Natalie Saunders. The students later divided the sample into food intolerant and food allergy subgroups respectively for separate statistical analysis. Figure 1 illustrates the methodology in a flow diagram.

2.3 Population

Children 12 years and under who had been seen by Dr. Velencia Soutter (Paediatrician) between 1995 and 1997 and who presented with eczema or had a past history of eczema were eligible for inclusion in the study. The children were selected from a total cohort of 1200 patients.

Figure 1 : Flow diagram of methodology



2.4 Procedure

Preliminary information was gathered from medical records and dietetics files of the children seen by Dr Soutter between 1995 and 1997.

Parents and carers of those subjects meeting the selection criteria (n=418) were sent a questionnaire package containing:

1. An information letter detailing the purpose of the research, what was involved from the participants, and names and contact numbers of the people conducting the study. The letter included an invitation for those children with food allergies to return to the clinic for a follow-up SPT and consult free of charge. Travel reimbursement was offered (Appendix 1)
2. A questionnaire developed by Dr Velencia Soutter and Dr Robert Loblay of the Allergy Consulting Rooms. The questionnaire was designed to collect information on past and present symptoms, diet, food challenges, medication, and food reactions (Appendix 2)
3. A Connor's Questionnaire for subjects 3 years and older. The Connors provides a percentile score for six aspects of child behaviour (Appendix 3). The Connor's questionnaire was including to provide further information to another researcher and was not used for the current study.
4. Reply paid envelope

2.5 Analysis

Data gained from the medical records, dietetic files, returned questionnaires and follow-up SPTs were recorded in a confidential database on Access (Microsoft Office 97). All statistics were calculated using Excel 6.0. A Chi test was used to determine gender differences in the sample.

The total population was divided into three groups so that a parallel study by Natalie Saunders focusing on food allergies could be carried out. This study focuses on food intolerance, so any data relating to food allergies which has been included in this study has been used with the permission of Natalie Saunders.

Group 1 Food Sensitization: Subjects with a positive SPT

Group 2 Food Intolerance: Subjects with positive food challenge reactions and a negative SPT or not tested (by physicians assessment)

Group 3 Food Sensitization and Food Intolerance: Subjects with a positive challenge reaction and a positive SPT

2.6 Ethical Approval

Ethical approval was obtained from the Ethics Review committee of the Central Area Health service. Consent for the questionnaire sent to subjects was implied from completion and return of the questionnaire.

2.7 Funding

The funding for the study came from the Lady Askin Trust RPAH, which was established for allergy research.

RESULTS

GENDER

In the total sample population of 418 children with eczema, there were significantly more males 58.4% (n=244) than females 41.6% (n=174), [$p < 0.05$, $p = 0.01$, $df = 1$]

AGE OF PRESENTATION

Table 1: Age of presentation of children with eczema at the RPAH Allergy Clinic between 1995 and 1997

Age in Months	Total (n=418)	Males (n=244)	Females (n=174)
0-6	24	9	15
6.1-12	58	34	24
21.1-1.8	49	26	23
18.1-24	32	19	13
24.1-36	46	22	24
36.1-60	87	55	32
>60	122	79	43

RESPONSE TO QUESTIONNAIRE

Of the 418 questionnaire packages sent, 146 were returned either by mail or personally giving a response rate of 35%. Data from the questionnaire was combined with information from the medical and dietetic case files, to give complete dietary information for 244 children (58% of total sample).

AGE OF ONSET OF ECZEMA

The age of onset of eczema was documented for n=69. Mean age of onset was 8.35 months (SD 11.1), range 1-72 months (0.08-6 years).

SYMPTOMS ASSOCIATED WITH ECZEMA

On presentation to the allergy clinic, childrens' symptoms were recorded by Dr Soutter as part of standard medical procedure. The occurrence of eczema or a history of eczema was 100%. The most common symptoms associated with eczema were found to be rhinitis (42%) and wheeze/asthma (37%). A summary of associated symptoms is presented in Table 2.

Table 2: Symptoms associated with eczema in total study population

Associate Symptoms	No. of Children	% of Population
	n = 418	
Eczema	418	100
Rhinitis	174	42
Asthma/wheeze	153	37
Diarrhoea/loose stools	81	19
Urticaria	68	16
Irritable behaviour	41	10
Sleep disturbance	36	9
Angiodema	28	7
Anaphylaxis	23	6

"FOOD INTOLERANCE ONLY" SAMPLE (FI only)

42 children from the total sample population had a positive reaction to a food challenge on the Elimination Diet *and* had a negative Skin Prick Test or were not skin prick tested (because there was no indication of food allergy based on the medical assessment).

The food challenge information was obtained from returned questionnaires and/or dietetic files. In 34 cases food challenge information was gained from the questionnaire (Questionnaire Sample), and 29 cases gained from dietetic files (Dietetic Sample). 19 children had information from both sources. A comparison was made between the two samples to validate the dietetic files as a reliable source of data. Table 3 shows the comparison for age and sex, and Table 4 details challenge results for the two samples.

Table 3: Comparison of "Food Intolerance Only" samples for age and sex.

	Questionnaire Sample n=34	Dietetic Sample n=29
Mean Age	3.36 (SD 0.43)	3.31 (SD 0.46)
Sex Distribution		
Males	60%	48%
Females	41%	52%

Table 4: Comparison of positive challenge reactions for "Food Intolerance Only" samples.

Challenges	CHALLENGE RESPONSE	
	(%)	
	Questionnaire Sample n=34	Dietetic Sample n=29
Salicylate	24	28
Amines	19	20
Milk	13	9
Preservatives	10	4
Antioxidants	8	5
Colours	5	6
Wheat	4	6

The two samples are comparable for age, sex and challenge results thereby validating both sources of information as accurate and reliable. The data was combined to give n=42 in the Food Intolerance Only group.

FOOD ALLERGY (FOOD SENSITISATION) SAMPLE

In 418 children with eczema, 202 children (48%) were sensitised to one or more food allergens. 166 children had a significant positive SPT that was greater than 3 mm in wheal diameter.

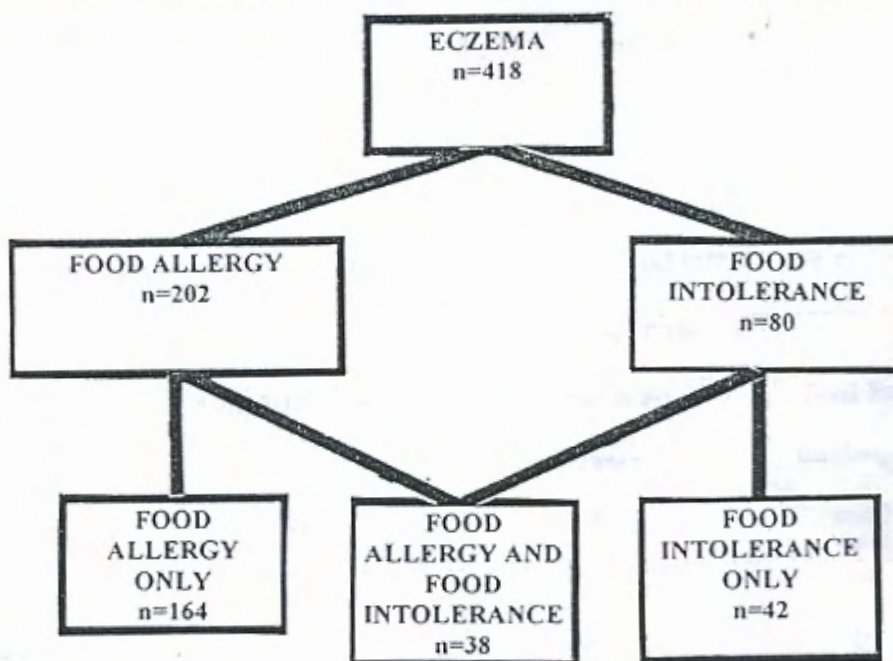
FOOD INTOLERANCE & FOOD ALLERGY SAMPLE (FI/FA)

38 children were found to have a positive reaction to a food challenge *and* a positive SPT.

TOTAL FOOD INTOLERANCE SAMPLE

The "Total Food Intolerance" sample (n=80) comprised of those children with food intolerance regardless of allergic status. It was attained by adding the FI only group (n=42) and the FI/FA group (n=38). Figure 2 shows the diagrammatic representation of the number of children in each sample.

Figure 2: Diagrammatic representation of samples within the eczema population.



DEMOGRAPHIC DATA

Table 5: Age and sex distribution for the different sample populations.

	Food Intolerance Only n=42	Food Allergy & Food Intolerance n=38	Total Food Intolerance n=80
Mean Age (years)	3.41 (SD 0.39)	2.62 (SD 0.46)	3.04 (SD 0.30)
Males (%)	60	48	54
Females (%)	40	55	46

SYMPTOMS ASSOCIATED WITH ECZEMA IN FOOD INTOLERANCE

42 children in the FI only sample reported a total of 205 symptoms (past and present) on attendance to the clinic, whilst 38 children in the FI/FA sample reported 148 symptoms. The symptoms were grouped according to the target organ (see footnotes this page). Percentage of presenting symptoms was calculated and presented in Table 6 for all groups and Figure 3 overpage for all children with food intolerance. A comparison of the results for the FI only and the FI/FA samples can be seen in Figure 1, Appendix 4.

Table 6: Presenting symptoms in a child population with food intolerance and eczema.

PRESENTING SYMPTOMS (%)			
Symptoms	Food Intolerance Only n=42	Food Allergy & Food Intolerance n=38	Total Food Intolerance n=80
Skin ¹	31	40	34
Respiratory ²	23	30	26
GIT ³	22	19	21
CNS ⁴	24	11	19
Total	100	100	100

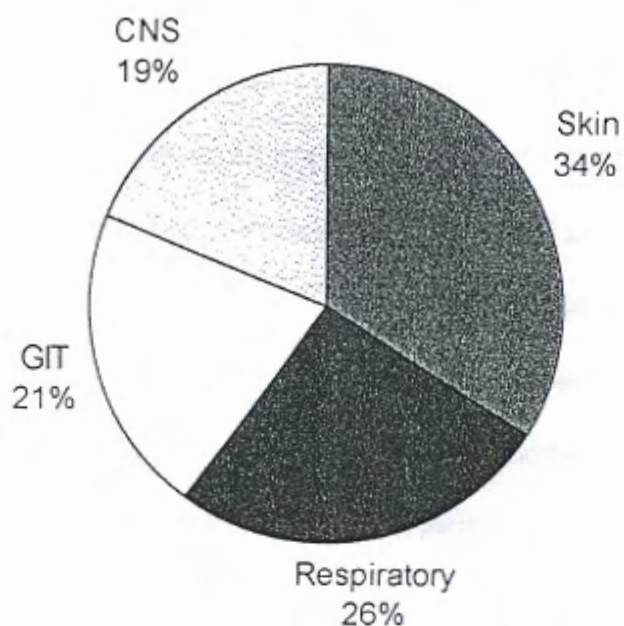
¹eczema, hives/angiodema, nappy rash, perianal and vaginal irritation, and other rash

²rhinitis, asthma/wheeze, cough, anaphylaxis, ear infection, grommets, sinus irritation, and other respiratory symptoms

³diarrhoea/loose stools, pain/cramp/colic, wind/gas/bloating, constipation reflux, vomiting, nausea, mouth ulcers, IBS, other GIT

⁴hyperactive, irritable, mood swings, screaming, aggressive, anxious, depression, violence, concentration, diagnosed ADD, learning difficulties, headache, growing pains/muscle pain, sleep disturbance

Figure 3: Presenting symptoms in children with eczema and food intolerance (n=80)



SKIN SYMPTOMS

Symptoms effecting the skin were noted in 31% and 40% for the FI only and FI/FA samples respectively. Individual skin symptoms attributing are presented in Table 7

Table 7: Specific skin symptoms as a percentage of total the symptoms

	SKIN SYMPTOMS (%)	
	Food Intolerance Only	Food Intolerance & Food Allergy
Eczema	21	27
Hives/angiodema	3	7
Nappy rash	3	3
Other ¹	4	4
	31	40

¹ perianal and vaginal irritation, and other rash

RESPIRATORY SYMPTOMS

Respiratory symptoms accounted for 23% of symptoms in the FI only group, and 30% in the FI/FA group. These symptoms were further grouped according to physiological response (see footnotes next page). Percentage contribution of all respiratory symptoms is presented in Table 8. For the FI group rhinitis, asthma, and ear infections equally contributed to respiratory symptoms. For the FI/FA group, rhinitis and asthma were the most common respiratory symptoms, with very few reports of grommets and ear infections. Anaphalaxis, as expected occurred in no patients in the FI only group.

Table 8: Specific respiratory symptoms as a percentage of total symptoms

	RESPIRATORY SYMPTOMS	
	(%)	
	Food Intolerance Only	Food Intolerance & Food Allergy
Nose ¹	9	13
Ears ²	7	3
Chest ³	7	10
Anaphylaxis	0	4
	23	30

¹ rhinitis, sinus irritation

² grommets, ear infection

³ asthma/wheeze, cough

GASTROINTESTINAL SYMPTOMS

GIT symptoms accounted for 22% and 19% of total symptoms in the FI only and the FI/FA groups respectively. Individual symptoms are shown in Table 9. Symptoms characteristic of irritable bowel syndrome were the most common symptoms for the two samples. Children were more likely to suffer from vomiting related symptoms in the FI/FA group than the FI only group.

Table 9: Specific GIT symptoms as a percentage of total symptoms

	GIT SYMPTOMS (%)	
	Food Intolerance Only	Food Intolerance & Food Allergy
IBS ¹	18	12
Vomiting ²	1	6
Mouth Ulcers	3	<1
	22	19

¹ diarrhoea/loose stools, pain/colic, wind/gas/bloating, constipation

² vomiting, nausea, reflux

CENTRAL NERVOUS SYSTEM SYMPTOMS

CNS symptoms were implicated in 24% of total symptoms in the FI only group, and 11% of total symptoms in the FI/FA group.

Table 10: Specific CNS symptoms as a percentage of total symptoms

	CNS SYMPTOMS (%)	
	Food Intolerance	Food Intolerance & Food Allergy
Behaviour ¹	14	8
Leg Aches ²	4	<1
Sleep disturbance	2	2
Headache	4	<1
	24	11

¹ hyperactive, irritable, mood swings, screaming, aggressive, anxious, depression, violence, diagnosed ADD, learning difficulties

² leg/growing pains, muscle/joint pain

CHALLENGE RESULTS

Patients were asked to report the challenges they attempted, and the type and severity of symptoms experienced (see Appendix 2, Question 11). The most common challenge reactions in eczema children with food intolerance were found to be salicylates (23%), amines (22%) and milk (13%). Frequency of positive reactions for all groups is shown in Table 11. Figure 2, Appendix 4 demonstrates the percentage of positive challenge reaction for the Total Food Intolerance group in descending order.

Table 11: Percentage of eczema populations with positive reactions to challenges

Challenge	TOTAL CHALLENGE RESPONSE		
	(%)		
	Food Intolerance Only n=42	Food Intolerance & Food Allergy n=38	Total Food Intolerance n=80
Salicylate	24	22	23
Amines	20	23	22
Milk	11	14	13
Preservatives	8	8	8
Glutamate	5	10	7
Colours	5	9	7
Antioxidants	7	3	5
Propionate	6	3	5
Wheat	5	6	6
Nitrate	1	3	2
Other*	7	0	4

* Includes wheat, soy, rice, potato, lamb, gluten

CHALLENGES AND ECZEMA

A major focus of the study was to investigate the chemicals involved in the onset of eczema in food intolerance. Results were calculated using the Total Food Intolerance sample (n=80). The percentages of food intolerant children who had eczema reactions to food challenges are presented in Table 12. The highest incidence of eczema was found for salicylates (7%) and amines (5%). Milk and colours elicited eczema in 3% of the food intolerant sample. For those challenges where the total number of positive reactions are low (for example nitrate, propionate and antioxidants) there is a possibility for inaccuracy in the calculation of these results.

Table 12: Percentage of food intolerant children (n=80) with eczema reactions to challenges.

Challenges	No. of Positive Reactions ALL SYMPTOMS	% with positive reactions (n=80)
		ECZEMA ONLY
Salicylates	77	7
Amines	70	5
Milk	40	3
Colours ^a	23	3
Glutamate	24	2
Propionate	15	3
Antioxidants ^b	16	1.5
Preservatives ^c	28	<1
Wheat	17	1.5
Nitrate	6	1
Other ^d	10	<1

^a erythrosine/tartrazine

^b BHA/BHT

^c sorbate/benzoate/monosodium-bisulphite

^d included soy, rice, potato, lamb, gluten

SYMPTOMS PROVOKED BY CHALLENGES

Patients administered challenges were required to keep a diary recording the type, onset and severity of symptoms experienced after taking a challenge. Chemicals to which there was no reaction, were considered to be tolerated. Symptoms were grouped according to their target organ (see footnotes next page). Results were calculated for the chemicals that provoked the most reactions and are presented in Table 13 for the FI only group and Table 14 for the FI/FA group. Unknown symptoms to positive challenges were also included. This was frequently the case when patients reported a positive reaction to a particular challenge on the questionnaire but did not provide detail of the symptom/s experienced.

When the two groups were compared for salicylates, the FI/FA group experienced 50 percent more eczema reactions than those in the FI Only group. This is in contrast to the behaviour symptoms, which were much higher for the FI Only group (32%) than for the FI/FA group (3%). Amines elicited a high percentage of behaviour symptoms (42%) in the FI Only sample. For both groups, the percentage of IBS reactions to milk was high (37-43%). For the FI Only sample, 16 percent of symptoms provoked by milk were behavioural, however this was not experienced in the FI/FA sample. Preservatives induced 31 percent eczema and skin symptoms in the FI/FA group. No eczema was seen in the FI Only group for preservatives, however the occurrence of behaviour symptoms was very high (57%).

Figures 4, 5 and 6 enables a clear comparison to be made between the FI only and the FI/FA groups.

Table 13: Percentage frequency of symptoms for common food intolerances in children with eczema and food intolerance.

Challenge	CHALLENGE RESPONSE - FOOD INTOLERANCE ONLY (%)					
	Eczema	Other Skin ¹	IBS ²	Behaviour ³	Respiratory ⁴	Unknown
Salicylate	20	12	15	32	2	19
Amines	18	12	15	42	0	12
Milk	21	5	37	16	5	16
Preservative	0	0	7	57	0	36

¹ hives, other rash, itch only, vaginal irritation

² diarrhoea/loose stools, pain/colic, vomiting/reflux, wind/bloating, mouth ulcers

³ hyperactive, irritable, aggressive, anxious, sleep disturbance, headache, growing/leg pains

⁴ asthma/wheeze, rhinitis

Table 14: Percentage frequency of symptoms for common food intolerances in children with eczema and food intolerance & food allergy.

Challenge	CHALLENGE RESPONSE - FOOD ALLERGY & FOOD INTOLERANCE (%)					
	Eczema	Other Skin ¹	IBS ²	Behaviour ³	Respiratory ⁴	Unknown
Salicylate	40	26	9	3	3	20.0
Amines	28	14	22	3	6	27.8
Milk	24	10	43	5	14	4.8
Preservative	23	8	15	8	8	38.5

¹ hives, other rash, itch only, vaginal irritation

² diarrhoea/loose stools, pain/colic, vomiting/reflux, wind/bloating, mouth ulcers

³ hyperactive, irritable, aggressive, anxious, sleep disturbance, headache, growing/leg pains

⁴ asthma/wheeze, rhinitis

Figure 4: Percentage challenge response for ECZEMA

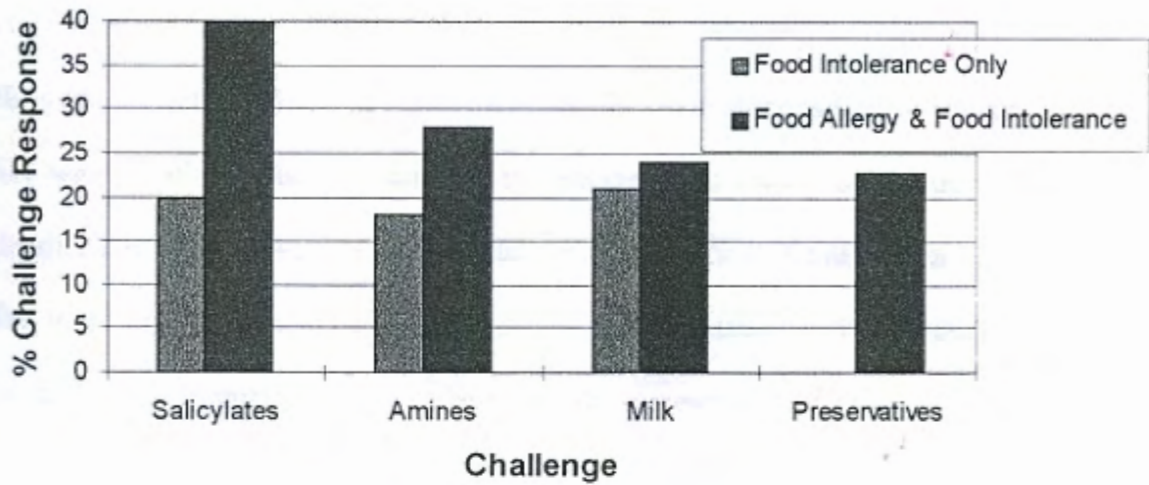


Figure 5: Percentage challenge response for IBS SYMPTOMS

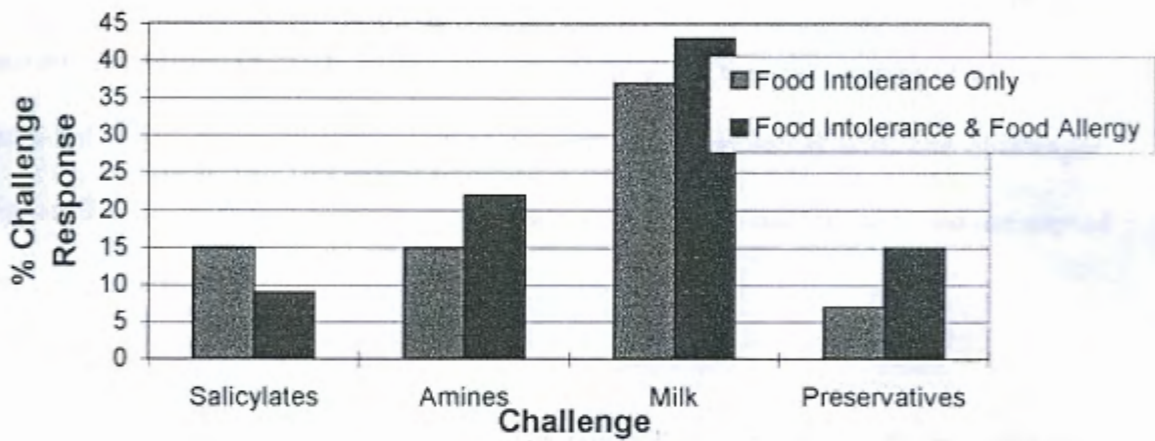
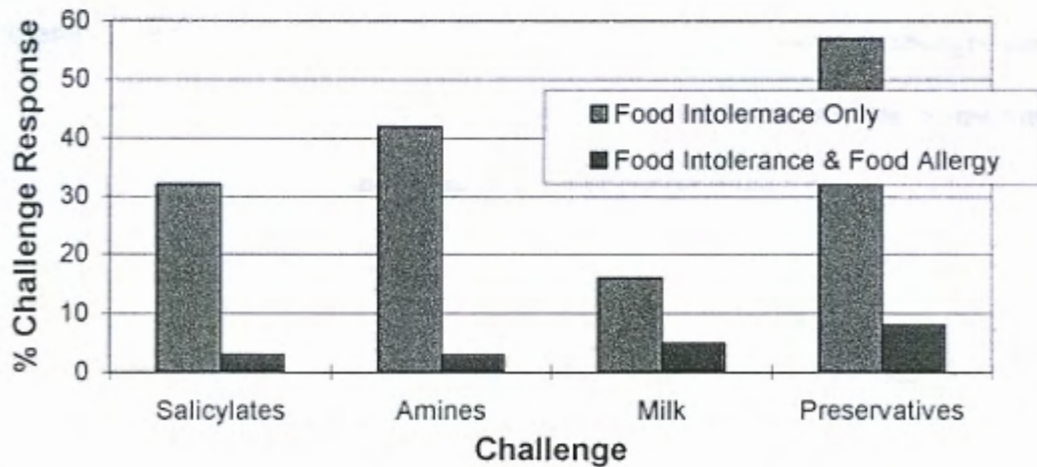


Figure 6: Percentage challenge response for BEHAVIOUR SYMPTOMS



ELIMINATION DIET

Of 191 patients whose dietary information was complete n=133 (70%) went on the Elimination Diet. n=60 (30%) did not start the diet. Explanations for not attempting the diet were available for 49 patients. 16 reported that they just avoided allergens identified by the positive SPT, 14 claimed the diet was too difficult, and in 11 cases the diet was not recommended by the clinic. Other reasons included child refusal, resolution of symptoms, and advice being sought somewhere else.

Improvement in symptoms on the diet were reported in 77% of children, with the average time taken for symptoms to start to subside being seventeen days (range = immediate-120 days). In less than 1% of children on the diet, symptoms were not recorded. Of those who showed improvement 82% proceeded with the challenges. Figure 3 summarises the number of patients who went on the diet and attempted challenges.

44 children out of 58, who did not start the elimination diet, reported they were on a modified diet. Information about the self-imposed dietary changes made were available for 26 children. More than half the parents reported avoiding or limiting additives such as preservatives, colours, and highly processed foods. Other common changes were to eliminate or reduce dairy, and limit foods high in salicylates and amines. Some omitted specific foods from the diet such as chocolate and orange juice.

Figure 7: Patients who attempted the elimination diet and challenges

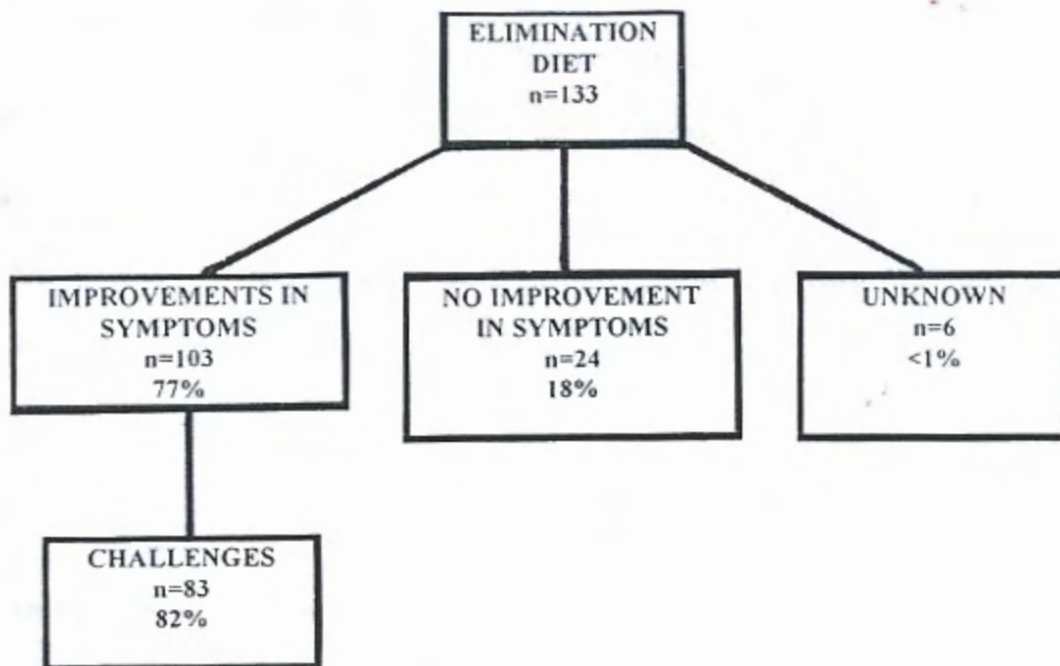


Table 15 outlines the type of challenges administered. 60% of children tested with foods only, and 30% tested with capsules and food. Rarely patients tested with capsules only.

Table 15: Capsule and food challenges undertaken by 83 children on the elimination diet

Type of Challenge	Number of patients	%
Food	51	61
Double-blind capsule	6	<1
Both	32	32
Unknown	6	6

DIETARY RESTRICTION

The questionnaire asked parents to indicate their child's current dietary restrictions for six different foods and chemicals (see Appendix 2, Question 15). Dietary restrictions were known for n=154 patients, as reliable data was also obtained from the dietetic case files. Results showed that salicylates, amines, additives, MSG and dairy were the most restricted. Wheat was restricted the least.

Table 16: Present dietary restrictions for n=154 children

Food/Chemical	Current Diet	
	Total number of restrictions*	% 'highly restricted'
Additives	90	49
Amines	83	39
Salicylates	80	35
MSG	72	81
Dairy	69	64
Wheat	29	34

* included 'somewhat restricted', 'quite restricted' and 'highly restricted'

FOOD INTOLERANCE AND ANAPHYLAXIS

In the total sample of eczema children, 23 (6%) had experienced food induced anaphylaxis, with an equal ratio of boys to girls. 22 (96%) had multiple food allergies. Food challenge information was available for 7 patients. 6 children had a positive reaction to challenges, accounting for 26% of those with anaphylaxis. It was calculated that between 1-2% of the total sample population (n=418) were highly atopic which predisposed them to anaphylaxis.

OUTCOME OF TREATMENT

Question 2 in the dietary questionnaire (see Appendix 2) asked carers to report how their child was compared to when they first presented to the clinic. 140 answers were received for the question, a response rate of 33% for the total study population (n=418). 56% reported their child was much better, 24% a little better, 12% the same, and 8% claimed their child was completely well since coming to the clinic. From the responses received 80% reported some improvement.

DISCUSSION

Eczema

The prevalence of allergic disease in the population has been shown to be increasing (Edwards 1995). The present study revealed that children with a past or present history are highly atopic, and 40 percent also have rhinitis and asthma. The association between atopic disease such as eczema, asthma and rhinitis, and food allergy is so strong that it is advised that children exhibiting any of these symptoms be investigated for food allergy (Carter 1995).

Researchers and physicians agree that the age of onset of eczema is usually before one year of age (Moneret-Vautrin 1994). This study found the average onset of eczema was between eight and nine months, which is similar to other studies in this area.

Eczema population

In this study, the total eczema population was categorised according to those with allergies or intolerance. Children with a positive Skin Prick Test (SPT) were diagnosed with food sensitisation. Children with positive food challenges and a negative SPT were considered food intolerant. It was assumed that patients not skin prick tested were negative based on the physician's assessment that there was no indication of food allergy.

The questionnaire response rate was 35 percent, thereby limiting the number of patients with complete dietary information. Information was also recorded in the dietetic case

file from follow-up phone consultations and visits to the clinic. Data from the questionnaire and diet records were found to be similar.

The prevalence of food intolerance and food allergy in the general population is beyond the scope of this study. However results have shown that in those presenting to the Allergy Clinic with eczema, almost 20 percent of children with eczema have one or more food intolerances. This figure may underestimate the actual incidence of food intolerance in the sample because dietary information was not complete for all subjects and only those with complete information was included. Food allergy/sensitisation was demonstrated in 48 percent of the eczema population. This figure more closely represents true prevalence, as the diagnostic measure was complete for all subjects.

The coexistence of food intolerance and food allergy was seen in 9 percent of the eczema population, however the accuracy of this figure is limited by the potential for under-calculation of food intolerance in the sample. It was shown that in a sample of eighty food intolerant children, 50 percent also had a food allergy/sensitisation. These results emphasise the multifaceted nature of adverse food reactions in eczema, and imply that successful investigation of dietary factors in a patient with eczema requires recognition of the possibility of concurrent food allergies and intolerances.

In children, the prevalence of eczema has been estimated at between 5-10% (Moneret-Vautrin 1994, Soutter 1996) and 4-10% for food intolerance (Aardoom et al 1997, Clarke et al) respectively, but to date there are no studies investigating the relationship between childhood food intolerance and eczema. Considering the findings of this study,

intolerant/food allergy subjects. Anaphylaxis was present in the food allergy/intolerant group but not present in the food intolerance only group.

CNS symptoms

CNS symptoms were reported in 24 percent of cases with food intolerance, twice as frequently as those with concurrent food intolerance and food allergy. The majority of these were attributable to behaviour-orientated symptoms such as hyperactivity, irritability and ADD, and to a lesser extent leg aches and headaches. It is expected that children with food intolerance will experience more behaviour-related problems when compared with children with food sensitisation. However there has been no speculation to date about the extent of behavioural symptoms in children with both intolerance and allergy (Clarke et al 1996, Loblay & Swain 1986). It appears, from the results of this study that children with food allergy as well as food intolerance will experience less adverse behavioural responses to food chemicals, than those with exclusive food intolerance.

GIT symptoms

Irritable bowel related symptoms were reported more frequently in the food intolerance group (18%) than in the food intolerance/food allergy group (12%), which supports literature reporting the high incidence of abdominal pains and colic in children with food intolerance (Loblay & Swain 1986). It was also found that in a sample of food intolerant children, those with food allergy were six times more likely to suffer from nausea, vomiting, and reflux. This is explained by the immediate response of IgE

it is likely that the importance of this relationship is greatly underestimated. Formal studies focusing on eczema as a consequence of food intolerance and not solely as an allergic disease need to be conducted, making information regarding coexistence of the two types of food reactions much clearer.

Age at presentation

The difference between age at presentation to the clinic and age of onset of eczema for children with food intolerance compared with allergy should be recognised. Results found that whilst average onset of eczema was eight to nine months, children on average did not attend the clinic until three years of age. A reason for this may be that symptoms were not severe enough to warrant medical treatment until the child was older. Another explanation may be that due to the nature of food intolerance and the difficulty in making associations between foods and symptoms, parents did not suspect dietary factors.

Symptoms

In this group of food intolerant children with eczema the most common symptoms experienced were skin related. This is expected given the study population were children with eczema. The next most frequently reported symptoms were respiratory related, followed by gastrointestinal (GIT) and symptoms of the central nervous system (CNS). These findings are comparable to the symptoms for the total eczema population, where rhinitis, asthma and diarrhoea/loose stools were most frequently associated with eczema (See Table 2, Results).

It has been estimated that between 33 and 62 percent of children with eczema will suffer from food allergy (Sampson & McCaskill 1985). It is not surprising then that common symptoms relating to eczema were found to be rhinitis and asthma. What is interesting though is that these typically atopic symptoms were also exhibited in many children with food intolerance and no food allergy. The mechanisms involved in triggering food intolerance reactions are largely unknown and are not addressed in this study. However, these results accentuate the difficulty experienced by patients and physicians in understanding the etiology and pathogenesis of adverse reactions to food.

Skin Symptoms

Eczema, as a percentage of total symptoms was higher for children with both food allergy and food intolerance (27%), than for infants with intolerance alone (20%). With this in mind, it is believed that a proportion of patients with atopic disease such as eczema will have food allergy as a primary cause of their disease (Edwards 1995). The association between food intolerance and eczema is much less recognised, so it is not surprising that results showed a higher incidence of eczema in a sample that included children with allergies.

Respiratory symptoms

Respiratory symptoms most commonly associated with food allergy are rhinitis and asthma (Lessof 1985). This is supported by the results of the current study, which found rhinitis and asthma to be more common in a group of food intolerant and food allergic children, as opposed to children with food intolerance alone. Ear infections typically associated with chemically sensitive individuals were low in the food

mediated reactions, as compared to the often delayed response involved in food intolerance reactions.

Chemicals involved in food intolerance

The systematic elimination of chemicals from the diet followed by blind challenge is the most accurate diagnostic tool to date for the diagnosis of food intolerance (Ferguson 1992). Patients reported type and severity of symptoms (if any) for each challenge attempted, in the questionnaire. This information was also obtained from dietetic case files.

The first challenge recommended after an improvement in symptoms, is the salicylates, hence the most common food challenge attempted. This means that the percentage of positive challenge reactions for salicylates will be calculated using a sample that will be large enough to be representative of the study population. The questionnaire investigated how many chemicals each patient tested and reported that out of 78 responses, 72 percent of subjects did not finish all the challenges. The consequences of this are that a smaller number of subjects attempted the additive challenges such as colours and nitrites. A guide to the order of food challenges can be seen in Table 1, Appendix 5, however this may vary from patient to patient.

The findings of the challenge results were commensurate with recent research into the frequency of salicylate intolerance (Swain 1988). Salicylates were found to be the most common substance implicated in positive challenge reactions for a given food intolerant sample (n=80), affecting 23 percent. An interesting result for the amines

revealed that they are equally as common as intolerances to salicylates, affecting 22 percent. Results were similar between children with food intolerance and children with food intolerance/food allergy.

Milk was the third most common food to cause positive reactions, with 13 percent of food intolerant children being effected. There was a 3 percent variance between the result for those with food intolerance and those with coexisting allergy and intolerance, the higher value in the later group being expected because milk may act as an intolerant and/or allergic substance. The results for milk may compared to another study conducted at the RPAH, which found 24 percent of a sample of eczema children exhibited non-allergic reactions to milk (Soutter 1996). Another source has stated that children with exclusive milk intolerance rarely have a history of eczema (Bolin et al 1995). In the current study it was shown that children found to be milk intolerant, had other food intolerances resulting in eczema. Further studies that may be useful could look at investigating all challenge results and symptoms for those children who tested positive to milk.

Recent literature has indicated that the perception of food additive intolerance far outweighs the actual occurrence of reactions to added food chemicals (Carter 1995, Lessof 1985, Wilson & Scott 1989). The results of this study confirmed that the incidence of reactions to food additives such as colours, preservatives and MSG, were low, especially when compared to the involvement of salicylates and amines in food intolerance. The elimination of additives from so many people's diet may lead to some improvement and may be benefit from a nutrition aspect because the foods generally

avoided as a consequence of reducing additives are heavily processed 'junk' foods. This is of much importance for growing children.

Chemicals provoking eczema

In the eczema literature there is little published about the role of intolerance to natural and artificial chemicals. The most common chemicals found to be involved in food intolerance reactions were shown to be the same chemicals inducing the most eczema symptoms. Salicylates and amines provoked eczema symptoms in 7 percent and 5 percent of children with food intolerance respectively. It was also revealed that around one third of all positive reactions to salicylates involved an eczema response. Comparing the eczema response to salicylates for children with food intolerance only and children with food intolerance/food allergy further investigated this. We found that the intolerance/allergy children experienced twice as much salicylate-induced eczema than those with only food intolerance. This is in support of literature that states in some allergic individuals with eczema, asthma or rhinitis, food chemicals may aggravate their pre-existing symptoms (Clarke et al 1996). From this it can be implied that salicylates further exacerbate eczema in children with a coexistent food allergy and intolerance.

Milk was found to cause eczema in 3 percent of children with food intolerance. This finding refutes the claim that infants with cow's milk intolerance rarely suffer from eczema, and that this eczema displayed in an individual with cow's milk intolerance is due to another chemical response (Bolin et al 1995).

Eczema reactions to antioxidants, wheat and nitrites contributed to less than 2 percent of children with food intolerance. Preservatives are involved in less than 1 percent of eczema reactions. The implications of this may be applied to the elimination diet procedure. A child presenting for the investigation of food intolerance with exclusively eczema symptoms may be advised to keep wheat in the diet and challenge those chemicals which have been commonly shown to aggravate eczema (for example salicylates and amines). Leaving wheat in the diet has many advantages to parents of children on the elimination diet, which express difficulty in preparing meals because the diet is so restrictive.

Chemicals provoking other symptoms

Salicylates and amines

Symptoms of behaviour have been strongly associated with salicylate intolerance (Loblay & Swain 1986, Swain 1988). Children with food intolerance only were found to be ten times more like to suffer adverse behaviour from a salicylate challenge than children with both allergy and intolerance. This is often the experience of many dietitians who report that children being investigated for allergy have a quiet temperament and bad skin, whereas those suspected of food intolerance are bouncing off the walls with an abundance of energy. Considering this, it may be suggested that non-atopic eczema patients experience a greater number of other symptoms in response to salicylate intolerance. This trend was also seen for amines, but is supported in the literature to a lesser extent. Whereas other research has found salicylates to be the major cause of behaviour symptoms in food intolerance (Loblay & Swain 1986, Swain

1988). The current study showed amines to induce the most behaviour-related symptoms in eczema patients.

Cow's milk

The public often confuses cow's milk allergy with cow's milk intolerance although the mechanisms involved are different (Schwartz 1992). This study showed that 37 percent of children with food intolerance exclusively had gastrointestinal responses to milk which highlights the already well known association between milk and GIT symptoms (Lessof 1985, Schwartz 1992). This figure was even higher for the infants with food intolerance and food allergy, which was expected considering this group included both intolerance and allergic reactions to milk. A notable difference between the two samples was that the intolerance only children experienced 16 percent behaviour symptoms that were not seen in the food intolerance/allergy children. This may also be explained by the suggestion that a different reactive mechanism is involved based on whether the patient is atopic.

Preservatives

Preservatives attributed to around 30 percent of eczema and skin symptoms for the children with concurrent food allergy and intolerance. There was no incidence of preservative-induced eczema in the children with food intolerance only.

The Elimination Diet

The systematic elimination of food chemicals followed by challenging is the preferred diagnostic tool used at the Allergy Unit, RPAH to investigate possible food intolerance.

In the present study 133 children reported attempting the Simplified Elimination Diet recommended by the dietitian. The main reason for not attempting the diet was that they just avoided allergens identified by the positive SPT. The difficulty of the diet is emphasised by the number of cases that reported not attempting the diet because it was too hard. The dietitian must recognise this and provide all the information and support needed to the patient, so that the diet may be carried out as easily as possible.

A large proportion of the children who did not attempt the diet for one reason or another, were on a modified diet at the time of the study. The most common changes reported were the avoidance of additives. This information supports other recent studies, which have shown people to be very concerned about the use of added chemicals in our food (Wilson & Scott 1995, Mansfield 1988). This study also showed that of those who attempted the diet, additives, amines, salicylates and MSG were the most common foods restricted. It is also of nutritional importance that many patients are choosing to eliminate or reduce dairy foods. Dietitians must ensure that parents are educated about dietary requirements of children, so that if they do impose their own diet restrictions, then the diet they follow is nutritionally adequate.

Food challenges were the most frequently used method to test challenges. Food challenges are open to subjective interpretation and bias. The most accurate results are seen in those cases where food challenges and double blind capsule challenges are attempted (Lessof 1995).

In extreme cases, contact with food can lead to anaphylaxis. It is believed that anaphylactic responses to food are increasing (Sampson et al 1992). 11 percent of children with eczema and food allergy/sensitisation had a history of anaphylaxis. It appears that these reactions are occurring in a very sensitive group of individuals with multiple food allergies.

In this study, 26 percent of those with a history of anaphylaxis had concurrent food intolerance. It appears that the children with food intolerance and food allergy are exquisitely sensitive so that only a minute amount of food allergen causes a severe reaction. The dietary management of both the food intolerance and the food allergy is indicated.

Eighty percent of the responses received, indicated an improvement in symptoms since visiting the clinic. While this information may be used to assess the effectiveness of treatment at the clinic, it must be remembered that those who found improvements in their child since attending the allergy unit, are more likely to respond to a questionnaire than those that had no success. It is therefore important to obtain responses from all patients regardless of effectiveness of treatment so that an accurate assessment can be made on the testing, dietary modification, and education of patients who visit the clinic.

CONCLUSIONS

- Food intolerance is common in children with eczema. Dietary information was incomplete for the entire sample so the true prevalence of food intolerance in the sample is unknown.
- Children with eczema and food intolerance suffer from a range of skin, respiratory, gastrointestinal and central nervous system symptoms.
- Salicylates, amines and milk are the most common substances responsible for food intolerance and eczema symptoms in a sample of children with eczema and food intolerance.
- 50 percent of children with food intolerance and eczema have a coexisting food allergy.
- Children with food intolerance alone experience more behaviour-related symptoms in response to food chemicals than children with food intolerance and food allergy.
- Many children who do not attempt the elimination diet are on a modified diet low in additives and dairy foods.
- The chemicals most commonly restricted in the diet corresponds with the most common chemicals causing reactions, with the exception of additives and MSG.
- Food intolerance is common in highly sensitive individuals with a history of anaphylaxis

RECOMMENDATIONS

The management of food intolerance and the appropriate diet for the food intolerant child should be discussed with a specialist dietitian and regular follow up is recommended. This ensures that the child is obtaining adequate nutrition, and that foods are not unnecessarily eliminated if the chemical becomes tolerated.

There is an obvious lack of knowledge of both the incidence and prevalence intolerance. There is an urgent need for population studies on children to be carried out. This would provide much more insight into the epidemiology, etiology, pathogenesis and genetics of an otherwise little known condition.

Food intolerance is not preventable. The avoidance of the chemicals such as salicylates, amines, glutamates, colours or preservatives does not prevent infants from developing symptoms of food intolerance on exposure. Formal dietary testing is the only way food intolerance can be diagnosed, and this may change with time and environmental factors. The natural history of food intolerance is an area that must be investigated.

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APPENDIX 1



*Allergy Unit
Royal Prince Alfred Hospital*

Suite 210 RPAH Medical Centre, 100 Carillon Ave, Newtown 2042

August, 1997

Dear Parent,

Re: _____

You and your child are invited to participate in a study of the role of adverse reactions to food (allergy and/or intolerance) in children. The research is being conducted by Drs Robert Loblay, Velencia Soutter, and Anne Swain, together with Natalie Saunders Narelle Greenlees and Brett Churnin (Master of Nutrition and Dietetics students), at the Royal Prince Alfred Hospital (RPAH) Allergy Unit.

If you agree to participate, we would be grateful if you could complete the enclosed questionnaires (as best you can) and return them as soon as possible. A pre-paid return addressed envelope is included for your convenience.

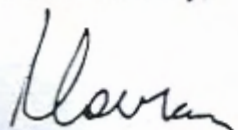
Once the questionnaires are returned, those children with food *allergies* will be offered a follow up appointment on a Monday for skin prick testing and review by the doctor and dietitian. You will recall that skin testing is an accurate way to identify food allergies and that children often grow out of these by school age.

Children who have food *intolerances* will be offered the opportunity to come back to the Allergy Unit for a review by the doctor and dietitian.

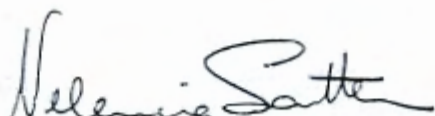
Please note, all travel expenses will be reimbursed on request. There will be no charge for the review appointment.

All questionnaires and skin prick test results will become a part of your child's medical record. Any information obtained during this study will be treated confidentially. If you decide to participate and then change your mind, you and your child may freely withdraw without being disadvantaged in any way. Whatever you decide, your child's treatment or your relationship with medical or dietetic staff at the clinic will not be affected.

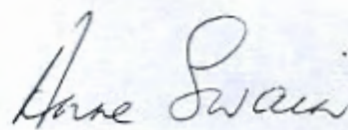
Yours sincerely,



Robert Loblay



Velencia Soutter

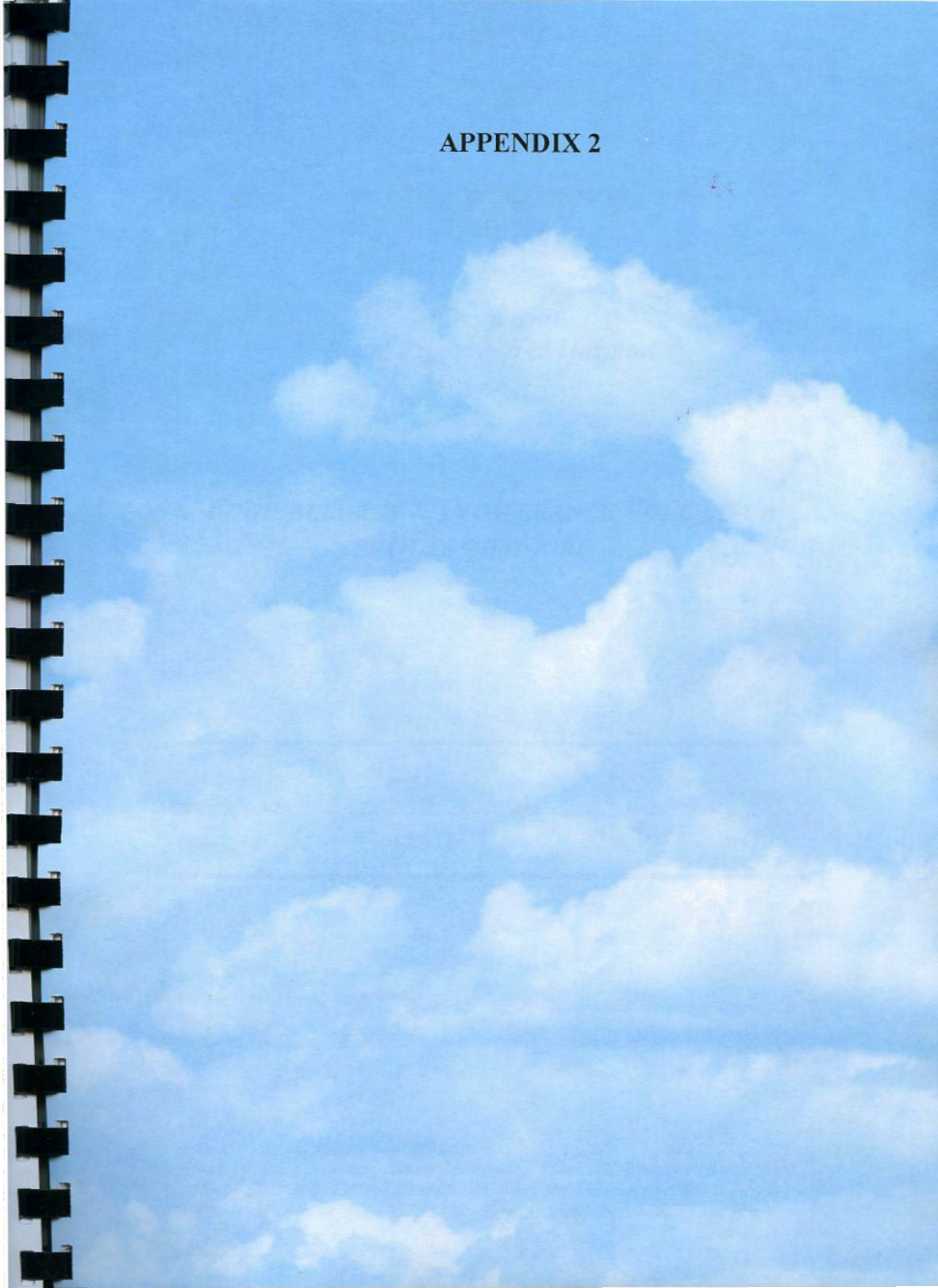


Anne Swain

This study has been approved by the Ethics Review Committee (RPAH Zone) of the Central Sydney Area Health Service. Any person with concerns or complaints about the conduct of the research study can contact the Secretary of the Committee on (02) 9515 6766.

Phone: 9515 8244 Fax: 9550 1029 E-mail: anne@immu.rpa.cs.nsw.gov.au

APPENDIX 2



*Allergy Unit
Royal Prince Alfred Hospital*

*FOOD ALLERGY & INTOLERANCE FOLLOW-UP
QUESTIONNAIRE*

CHILD'S NAME: AGE: DATE:/...../.....

*If you have any questions, contact Anne Swain, Velencia Soutter or Robert Loblay
Allergy Unit, Suite 210, RPAH Medical Centre, 100 Carillon Ave. Newtown 2042
Phone: 9515 8244 Fax: 9550 1029 E-mail: anne@immu.rpa.cs.nsw.gov.au*

FOOD ALLERGY & INTOLERANCE QUESTIONNAIRE

Please tick the boxes and answer the questions to the best of your recollection. Put a question mark if you're uncertain or can't remember.

1. Did you start your child on the *Elimination Diet* after coming to the Allergy Clinic? Yes No
If No, skip to Question 13.
If Yes:
2. When did you start? /
month year
3. Did you notice any improvement in symptoms? Yes No
If No, skip to Question 12.
If Yes:
4. How long before you noticed any improvement?
5. Was there a "withdrawal" effect (temporary flare-up)? Yes No
If Yes: When? (days after starting)
How long did it last? (days)
6. How long did it take altogether for your child's symptoms to settle on the *Elimination Diet*?
..... (days / weeks)
7. Did you do any Challenges? Yes No
If No, skip to Question 14.
If Yes:
8. Were they food or capsule challenges, or both? food capsule both
9. How long did you take doing the challenges? (wks / mths)
10. Did you finish all the challenges? Yes No

FOOD ALLERGY & INTOLERANCE QUESTIONNAIRE

11. Please list the reactions your child had to challenges:

- Describe the main symptoms you recall after each challenge. If you're not sure, or can't remember, put a question mark (?). For those challenges not done, write "N/D".
- Indicate the severity of reactions by circling the relevant numbers.

CHALLENGE	Type	SYMPTOMS	None	Mild	Mod.	Severe
Milk / dairy	Food		0	1	2	3
Wheat	Food		0	1	2	3
Colourings (102-155)	Capsule		0	1	2	3
Preservatives *	Food		0	1	2	3
	Capsule		0	1	2	3
Antioxidants (310-321)	Food		0	1	2	3
	Capsule		0	1	2	3
Nitrates (249-252)	Food		0	1	2	3
	Capsule		0	1	2	3
Propionates (280-283)	Food		0	1	2	3
	Capsule		0	1	2	3
Salicylates	Food		0	1	2	3
	Capsule		0	1	2	3
Amines	Food		0	1	2	3
	Capsule		0	1	2	3
MSG (621)	Food		0	1	2	3
	Capsule		0	1	2	3

* benzoates (210-213), sorbates (200-203), sulphites (220-228)

12. If your child's symptoms did not improve, how long did you persist with the *Elimination Diet* before deciding it wasn't helping?

..... (days / weeks / months)

Did your child go back to his/her normal diet?

Yes No

13. If your child didn't start the *Elimination Diet*, please explain the reasons (eg. too difficult, child refused, symptoms got better, sought advice elsewhere, etc.)

Even if you didn't do the strict *Elimination Diet*, did you modify your child's diet based on the information you were given at the clinic?

Yes No

If Yes, what changes did you make?

.....

FOOD ALLERGY & INTOLERANCE QUESTIONNAIRE

14. What symptoms did your child have:

- (a) *before* coming to the Clinic,
- (b) at his/her best *on the Elimination Diet*, and
- (c) how are those symptoms *now*?

Indicate their severity at each stage by circling the relevant numbers:

SYMPTOMS		NONE	MILD	MOD	SEVERE
Eczema	Before	0	1	2	3
	On diet	0	1	2	3
	Now	0	1	2	3
Hives, swellings	Before	0	1	2	3
	On diet	0	1	2	3
	Now	0	1	2	3
Blocked / runny nose, etc	Before	0	1	2	3
	On diet	0	1	2	3
	Now	0	1	2	3
Ear infections, glue ears	Before	0	1	2	3
	On diet	0	1	2	3
	Now	0	1	2	3
Reflux, vomiting	Before	0	1	2	3
	On diet	0	1	2	3
	Now	0	1	2	3
Colic, wind, tummy pain	Before	0	1	2	3
	On diet	0	1	2	3
	Now	0	1	2	3
Loose stools, diarrhoea	Before	0	1	2	3
	On diet	0	1	2	3
	Now	0	1	2	3
Headaches	Before	0	1	2	3
	On diet	0	1	2	3
	Now	0	1	2	3
Sleep disturbance	Before	0	1	2	3
	On diet	0	1	2	3
	Now	0	1	2	3
Behaviour problems	Before	0	1	2	3
	On diet	0	1	2	3
	Now	0	1	2	3
Learning difficulties	Before	0	1	2	3
	On diet	0	1	2	3
	Now	0	1	2	3
Limb aches & pains	Before	0	1	2	3
	On diet	0	1	2	3
	Now	0	1	2	3
Mouth ulcers	Before	0	1	2	3
	On diet	0	1	2	3
	Now	0	1	2	3
Other (specify)	Before	0	1	2	3
	On diet	0	1	2	3
	Now	0	1	2	3

FOOD ALLERGY & INTOLERANCE QUESTIONNAIRE

15. Do you still have your child on a modified diet at present? Yes No

If *Yes*, circle the numbers below to indicate how much your child's intake is restricted for each class of foods or chemicals.

[If you restrict your child's intake of natural salicylates and/or amines, indicate approximately how many serves per day he/she usually tolerates.]

Foods / chemicals	Not restricted	Somewhat restricted	Quite restricted	Highly restricted
Additives	0	1	2	3
Milk / dairy	0	1	2	3
Wheat	0	1	2	3
Salicylates	0	1	2	3
Amines	0	1	2	3
MSG	0	1	2	3
	Any amount tolerated	3 or more "moderate" serves / day	Tolerates 1-3 "moderate" serves / day	Less than 1 "moderate" serve / day

16. How often does your child experience food *intolerance* reactions now?

	Never	Occasionally	Fairly often	Frequently
Accidentally	0	1	2	3
Knowingly	0	1	2	3
		Less than once a month	1-3 times per month	Once a week or more

17. *Overall*, how is your child now compared with when you first brought him/her to the Clinic?

worse
 the same
 a little better
 much better
 completely well

18. Has your child continued to need medications? Yes No

If *Yes*, please indicate which ones:

Steroid creams	<input type="checkbox"/>	Ritalin / dexamphetamine	<input type="checkbox"/>
Antihistamines	<input type="checkbox"/>	Antibiotics	<input type="checkbox"/>
Nasal sprays	<input type="checkbox"/>	Other	<input type="checkbox"/>
Asthma drugs	<input type="checkbox"/>	<input type="checkbox"/>

ALLERGY REACTIONS

19. Did your child have any *allergies* to food proteins when tested at the clinic?
(Diagnosed by skin prick testing.)

Yes No Not tested

20. If Yes, please circle which foods were positive (+), negative (-), or not tested (0), and indicate whether or not your child can tolerate the food now:

FOOD (PROTEIN) ALLERGEN	WHEN FIRST TESTED AT CLINIC (Age:)			WHEN LAST RE-TESTED (Age:)			IS THE FOOD TOLERATED NOW? (Age:)		
	pos	Neg	not done	pos	neg	not done	yes	no	don't know
Egg	+	-	0	+	-	0	Y	N	?
Milk	+	-	0	+	-	0	Y	N	?
Peanut	+	-	0	+	-	0	Y	N	?
Other nuts	+	-	0	+	-	0	Y	N	?
Sesame	+	-	0	+	-	0	Y	N	?
Soy	+	-	0	+	-	0	Y	N	?
Wheat	+	-	0	+	-	0	Y	N	?
OTHER (specify):									
1.	+	-	0	+	-	0	Y	N	?
2.	+	-	0	+	-	0	Y	N	?
3.	+	-	0	+	-	0	Y	N	?

21. Has your child had any serious reactions (eg. anaphylaxis, asthma, blocked throat) to a food *allergen* since being tested at the Clinic?

Yes No

If Yes, how many times?

Please give details:

.....

22. Has your child required further treatment elsewhere? If so, what was done?

.....

ADDITIONAL COMMENTS

Please make any additional comments you think may be relevant concerning your child's progress since first attending the Clinic.

Which aspects of the advice you received at the Clinic did you find most helpful?

Which aspects do you feel could be improved?

Thank you for taking the time to answer this questionnaire.

Within the next year or two, we hope to begin producing a newsletter for people with an interest in adverse food reactions. If you would like to be on the mailing list for further information please tick the "Yes" box and fill in your address details.

- Yes, I would like to be on the mailing list for further information.*
- Do not send me any further information.*

PREFERRED MAILING ADDRESS:

.....
.....
.....

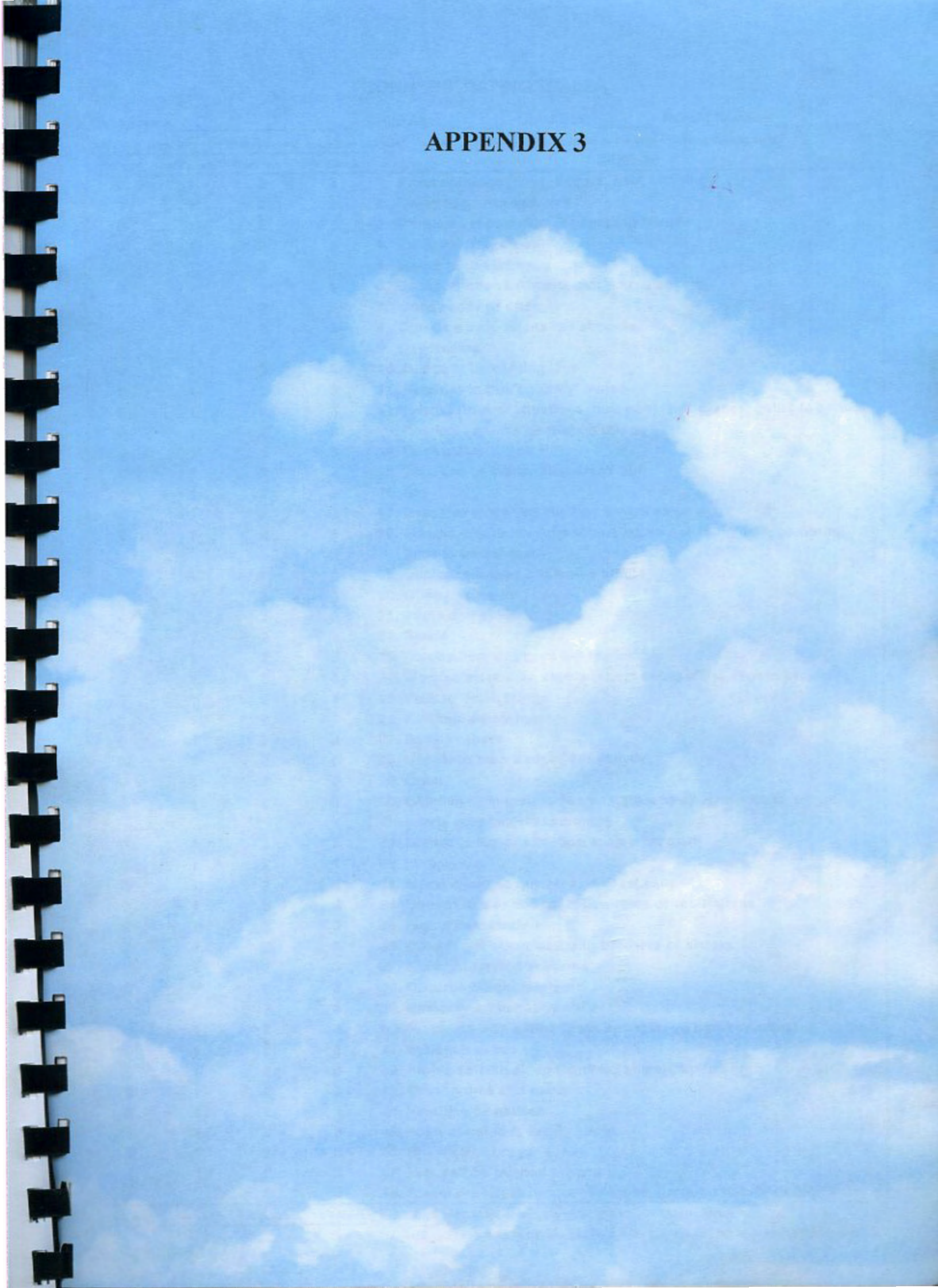
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TELEPHONE:

Home:

Work:

APPENDIX 3



CONNERS' RATING SCALES

Child Name: _____ Child Age: _____ Child Sex: _____ Parent Name: _____

Instructions: Read each item below carefully, and decide how much you think your child has been bothered by this problem during the past month.

				CPRS-48
Not at All	Just a Little	Pretty Much	Very Much	
0	1	2	3	1. Picks at things (nails, fingers, hair, clothing)
0	1	2	3	2. Sassy to grown-ups
0	1	2	3	3. Problems with making or keeping friends
0	1	2	3	4. Excitable, impulsive
0	1	2	3	5. Wants to run things
0	1	2	3	6. Sucks or chews (thumb, clothing, blankets)
0	1	2	3	7. Cries easily or often
0	1	2	3	8. Carries a chip on his/her shoulder
0	1	2	3	9. Daydreams
0	1	2	3	10. Difficulty in learning
0	1	2	3	11. Restless in the "squirmy" sense
0	1	2	3	12. Fearful (of new situations, new people or places, going to school)
0	1	2	3	13. Restless, always up and on the go
0	1	2	3	14. Destructive
0	1	2	3	15. Tells lies or stories that aren't true
0	1	2	3	16. Shy
0	1	2	3	17. Gets into more trouble than others same age
0	1	2	3	18. Speaks differently from others same age (baby talk, stuttering, hard to understand)
0	1	2	3	19. Denies mistakes or blames others
0	1	2	3	20. Quarrelsome
0	1	2	3	21. Pouts and sulks
0	1	2	3	22. Steals
0	1	2	3	23. Disobedient or obeys but resentfully
0	1	2	3	24. Worries more than others (about being alone, illness or death)
0	1	2	3	25. Fails to finish things
0	1	2	3	26. Feelings easily hurt
0	1	2	3	27. Bullies others
0	1	2	3	28. Unable to stop a repetitive activity
0	1	2	3	29. Cruel
0	1	2	3	30. Childish or immature (wants help s/he shouldn't need, clings, needs constant reassurance)
0	1	2	3	31. Distractibility or attention span a problem
0	1	2	3	32. Headaches
0	1	2	3	33. Mood changes quickly and drastically
0	1	2	3	34. Doesn't like or doesn't follow rules or restrictions
0	1	2	3	35. Fights constantly
0	1	2	3	36. Doesn't get along well with brothers or sisters
0	1	2	3	37. Easily frustrated in efforts
0	1	2	3	38. Disturbs other children
0	1	2	3	39. Basically an unhappy child
0	1	2	3	40. Problems with eating (poor appetite, up between bites)
0	1	2	3	41. Stomach aches
0	1	2	3	42. Problems with sleep (can't fall asleep, up too early, up in the night)
0	1	2	3	43. Other aches and pains
0	1	2	3	44. Vomiting or nausea
0	1	2	3	45. Feels cheated in family circle
0	1	2	3	46. Boasts and brags
0	1	2	3	47. Lets self be pushed around
0	1	2	3	48. Bowel problems (frequently loose, irregular habits, constipation)

CONNERS' RATING SCALES

Child Name: _____

Child Age: _____

Parent's Name: _____

T	A. Conduct Problem					B. Learning Problem					C. Psychosomatic					D. Impulsive-Hyperactive					E. Anxiety					F. Hyperactivity Index					T
	3/5	6/8	9/11	12/14	15/17	3/5	6/8	9/11	12/14	15/17	3/5	6/8	9/11	12/14	15/17	3/5	6/8	9/11	12/14	15/17	3/5	6/8	9/11	12/14	15/17	3/5	6/8	9/11	12/14	15/17	
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34																					0 0							45			

Child Name: _____

Child Age: _____

Parent's Name: _____

T	A. Conduct Problem					B. Learning Problem					C. Psychosomatic					D. Impulsive-Hyperactive					E. Anxiety					F. Hyperactivity Index					T	
	3/5	6/8	9/11	12/14	15/17	3/5	6/8	9/11	12/14	15/17	3/5	6/8	9/11	12/14	15/17	3/5	6/8	9/11	12/14	15/17	3/5	6/8	9/11	12/14	15/17	3/5	6/8	9/11	12/14	15/17		
100+	18+		19+					11+	9+		4+		6+														22+		100+			
99				16+							6+																23+	22+	21+	99		
98		14+	17+					9+				6+																		98		
97	17			18				9+																				21		97		
96				15					10																		12			96		
95													6+																	95		
94			16																									20	20	19	94	
93	16	13		17					8																			21			93	
92					14			12						5																	92	
91			15					8	8																				11	11		91
90	15		16						9																				30	20		90
89		12											5	5															18		89	
88			14	13							3																	29	18	17	88	
87				15				11		7																		19			87	
86	14												5															12	11		86	
85								7	8																				18	17	16	85
84		11	13	14	12			7																								84
83								10																								83
82	13																															82
81			12	13																												81
80		10			11					6			4	4																15		80
79	12							9		7																						79
78				12				6	6					4																		78
77			11		10																											77
76	9																															76
75	11			11																												75
74			10					8		6	5		2																			74
73					9																											73
72	10			10					5					3																		72
71		8						5					3	3																		71
70			9					7																								70
69					8																											69
68	9			9						5																						68
67		7	8								4																					67
66																																66
65	8			8	7			6		4																						65
64								4																								64
63			7																													63
62		6		7	6					4																						62
61	7							5			3			2		2																61
60			6																													60
59				6								1		2																		59
58		5			5					3	3																					58
57	6							4			3																					57
56			5	5																												56
55																																55
54	5				4						2																					54
53		4	4	4																												53
52								3		2																						52
51									2	2																						51
50	4			3	3																											50
49		3	3																													49
48								2																								48
47	3				2																											47
46			2		2						1																					46
45								1	1																							45
44		2						1																								44
43	2				1	1																										43
42			1																													42
41											0																					41
40	1	1								0																						40
39			0	0	0			0	0																							39
38								0																								38
37																																37
36	0																															36
35		0																														35
34																																34

APPENDIX 4

Figure 1: Symptoms associated with eczema in children with food intolerance

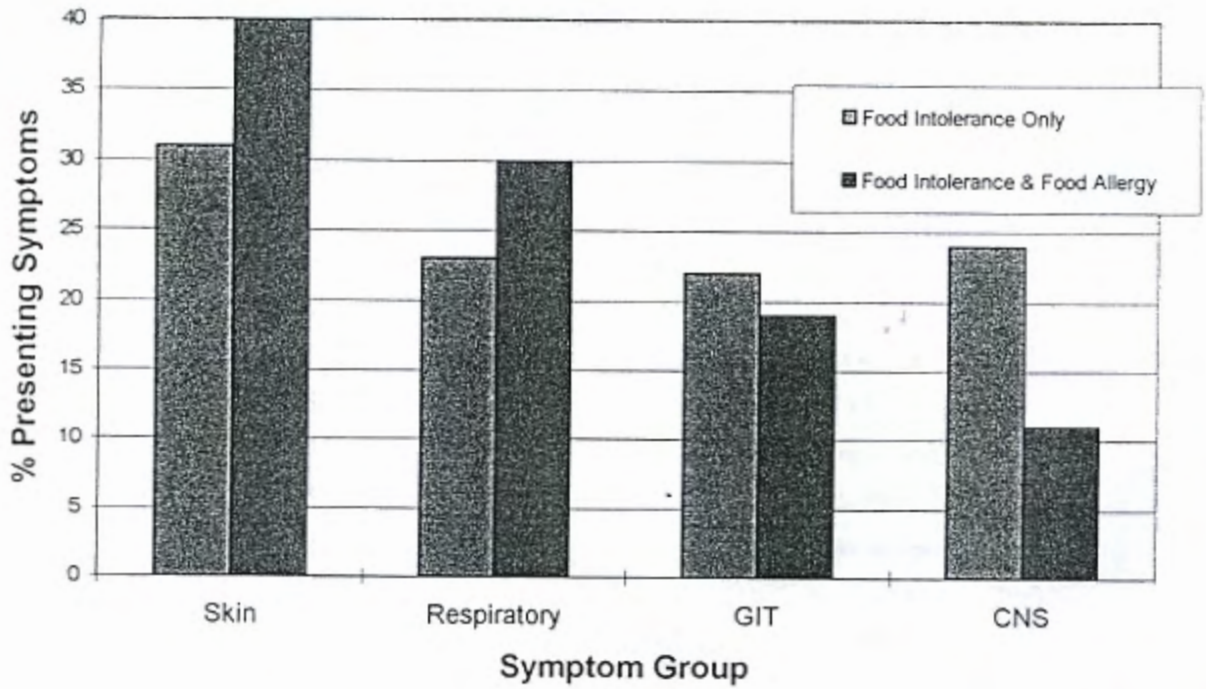
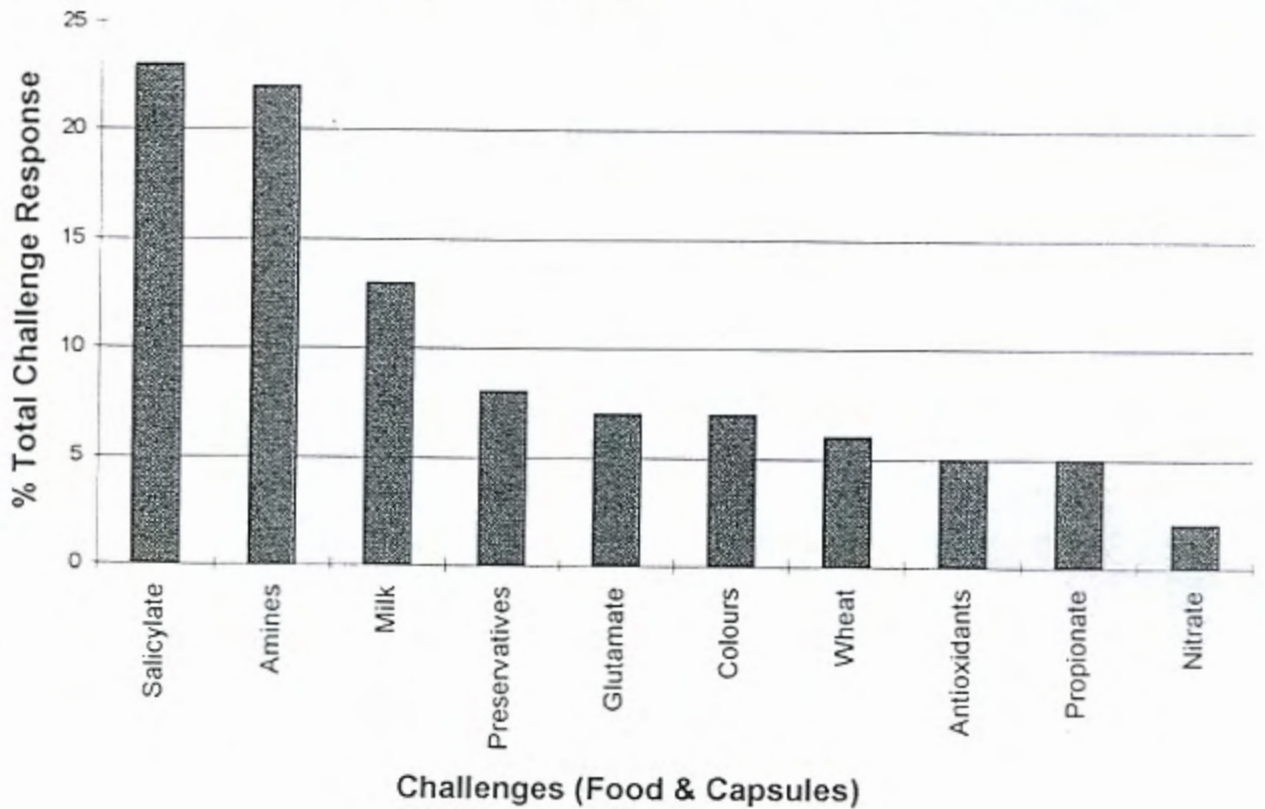


Figure 2: Positive Challenge Reactions for Total Intolerance Sample with Eczema



APPENDIX 5

Table 1: Suggested order of food challenges on the elimination diet

Order	Challenge
1*	Milk
2*	Wheat flour
3*	Bread
4	Salicylates
5	Amines
6	MSG
7	Propionates
8	Sorbates
9	Benzoates
10	Antioxidants
11	Colours
12	Nitrites
13	Sulphites

*Provided these have been eliminated from the diet

(Swain, Loblay & Soutter 1997)