To Our Readers

We are very happy to note the interest with which all of you are reading the quarterly issues of the Nutrition in Disease Management - Update Series. The current issue consists of two articles: The first is on 'Diagnosis and Management of Food Intolerance by Diet" which focuses on "food allergy", an area in the field of Clinical Nutrition which is currently arousing considerable interest. The second is a review article which aims at updating existing information on the nutritional role of probiotics.

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Diagnosis And Management Of Food Intolerance By Diet

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INTRODUCTION

Food intolerance is any reproducible adverse reaction to a food that is not psychologically based. It is a term including all organic reactions to food, including allergies, enzyme defects, toxic and pharmacological reactions. Food allergy is defined as an abnormal immunological reaction to food. The symptoms attributed to food intolerance and allergy are wide and include anaphylaxis, angioedema, urticaria, vomiting, rhinitis, diarrhoea, post gastroenteritis enteropathy, eczema and migraine. The true incidence of food intolerance is unknown, but it is generally agreed that food intolerance is most common in infants and young children. The most common foods leading to reports of intolerance in childhood in the UK are cow's milk, eggs and nuts.

Diet is the cornerstone of diagnosis and treatment of food intolerance. Used in combination with food challenges, diet is the only dependable method able to identify offending foods. Food(s) or food constituents that are suspected of causing symptoms are removed from the diet for a specified period to see if symptoms improve. This is followed by a series of open and double blind placebo-controlled food challenges (DBPCFC) in an attempt to reproduce the original reactions and prove the diagnosis. This

may be used in combination with laboratory tests such as skin prick tests or radioallergosorbent tests (RAST) to identify suspect foods. However, these have their limitations, as they can show that an IgE reaction has occurred but not that the reaction has been enough to cause symptoms or need treatment.

The diagnosis of food intolerance often involves five stages:

* History and clinical assessment
* Clinical and laboratory tests
*Diagnostic exclusion diet
*Open food challenges
*Double blind placebo-controlled food challenges.

HISTORY AND CLINICAL ASSESSMENT

This includes a full assessment of the symptoms, their frequency, dietary history, past and present treatments and family history of atopic disease. A detailed diary of food intake, symptoms, their severity, and any medication should be recorded for at least seven days. This may give vital clues as to which foods are precipitating symptoms, but often the relationship between diet and symptoms is unclear. It is important that data is collected on baseline anthropometric measurements, nutritional intake, biochemical and nutritional parameters.

DIAGNOSTIC DIETS

There are five types of diagnostic diet; the type chosen will depend upon the history and severity of symptoms. Most diagnostic diets are difficult; and it is better if other conventional treatments are tried first. All potential dietary hazards should be discussed with patients or their carriers at the outset. Unless a relationship with food appears likely from the history, other diseases should be excluded before trying exclusion diets, particularly in infants and young children with severe symptoms. However, severe symptoms should not exclude a diagnosis of food allergy and intolerance.

EXCLUSION DIET

This is the commonest and simplest diagnostic diet. It usually involves excluding one or two foods, which appear likely from history to be responsible for symptoms, for example, milk ingestion causes immediate vomiting; strawberries provoke an urticaria reaction. Dietary intervention necessitates complete exclusion of the identified food(s) or else intolerance may be missed. If symptoms disappear, it is likely that food is responsible. However, it should also be recognised that symptom improvement might be coincidental or even due to a placebo effect15.

Some exclusion diets are difficult to adhere to, as the excluded food may be a major component of the diet, for example, milk and wheat. It may also be hidden in the form of many food derivatives in manufactured foods. Dietetic advice is essential to ensure that:

- Excluded foods are substituted for alternative palatable, accessible and affordable substitutes; l the diet is nutritionally adequate;
- Practical information is given on shopping, food preparation and cooking; and
- Accurate, comprehensive but understandable information is given on interpreting food labels.

A diagnostic diet should always be accompanied by plans to reintroduce the omitted foods after a defined period. The duration required before a food challenge is attempted varies. It partly depends upon the type of food excluded, the diagnosis, severity of symptoms and the age of the patient. For example, milk intolerance in young children is only temporary and 85 per cent have acquired tolerance by the age of three years31. However, due to the severity of symptoms in young infants the initial food challenge may be delayed until after the age of one year, although many young children may accidentally expose themselves first. If the presenting symptoms are life threatening, food challenge is rarely attempted. Allergy to peanuts is usually severe and, often lifelong, so peanut challenges are uncommon.

EMPIRICAL DIET

An empirical diet involves excluding common food allergens associated with a specific condition when a dietary cause is suspected but cannot be identified. In adults the common foods and additives excluded include milk, eggs, wheat, peanuts, citrus fruits, fish, nuts, preservatives and dyes27,38,43,50,63. Similar foods are excluded in childhood, but chicken and soya are also commonly avoided, particularly in food sensitive enteropathy61.

The duration of use of empirical diets before the food challenge is variable. In many conditions they are continued for at least six to 12 weeks. In migraine and urticaria, the duration will depend upon the frequency of the attacks. If symptoms occur only every week or two, it may take a few months to be certain of success or failure15. In atopic eczema, a minimum of six weeks is needed owing to the natural fluctuation in disease state, the time taken for severe eczema to improve and the possibility of chance improvement or placebo response15.

FEW-FOOD DIET

This is a strict diet, allowing a small selection of low allergen food to be given for a short period of usually two to three weeks. It is generally only used when the symptoms are severe, the history is complex and there is some suggestion from the history that foods may be contributing to some of the symptoms. The idea of a few-food diet is not new. Rowe first described this type of diet53. The diet usually includes one meat, one cereal, two fruits and vegetables, a milk substitute and cooking oil or fat source. Few-food diets have successfully been used in the diagnosis of food intolerance in atopic eczema20,47, hyperkinetic syndrome23, migraine22,40.

Examples of alternative few-food diets are given in Table I. The foods permitted in the basic diet can be adapted according to individual food preferences, age of the patient and clinical symptoms. The duration of the basic few-food diet should not exceed three weeks. More prolonged use may result in an inadequate intake of energy and other nutritional deficiencies39. However, in some conditions such as eczema and hyperactivity, it may take full three weeks before there is an improvement in symptoms and in eczema, some advocate the basic diet for longer20. In general, if symptoms do not improve within three weeks, it is probable that foods are not the cause of the symptoms, alternatively that the patient has failed to comply or that the diet still contains a food to which the patient is intolerant.

Food reintroduction in few-food diets should be conducted carefully, slowly and systematically. Food reintroduction varies from one new food every one to two days to one food every seven days. The latter approach is better in conditions such as eczema, migraine and hyperactivity when delayed reactions may occur. Initially, only small portions of a new food should be given and at least one accompanying adult should be present in case of anaphylaxis.

The order in which foods are reintroduced is flexible, and is influenced by food preferences, food allergenicity, nutritional and culinary properties, for example, it is more useful to introduce foods such as wheat early rather than fruits. Some advise introduction of foods by families. However, this is probably illogical, as cross-reactivity between different foods in a family is unusual15.

Throughout the reintroduction phase, accurate records of foods introduced and symptoms should be documented. Few-food diets are particularly difficult to follow and reports of non-compliance or diet abandonment are common. Nevertheless, for some, a few-food diet can lead to identification of hidden food allergens and their subsequent avoidance can result in a dramatic improvement in symptoms which far outweighs the trials and tribulations of this difficult diet.

Table I: Examples of few-food diets

	Diet 1	Diet 2
One meat	Lamb	Chicken
One vegetable	Carrots	Cabbage
One carbohydrate food		Rice Potatoes
One fruit	Pears	Apples

Plus milk substitute (or vitamin and mineral supplement), salt, sugar, water and fruit juice.

ELEMEMTAL DIET

An elemental diet is a chemically defined diet whose protein source is derived from aminoacids, with added oligosaccharides, fat, minerals and vitamins. Elemental diets are generally only used when symptoms are severe and have provided a diagnostic tool for food intolerance since the mid 1970s25,33. All food is usually withdrawn and is replaced with a low allergen aminoacid based elemental formula for a specific time period. This regimen is then used to provide nutritional support whilst foods are formally reintroduced into the diet. Elemental diets have had success in the management of severe atopic eczema in children but not in adults14,44, in chronic gastrointestinal symptoms in infancy, and in paediatric and adult Crohn's disease49. In paediatric Crohn's disease, an elemental diet aids healing of the mucosa, down-regulation of inflammation62, improves nutritional state and is as effective as high doses of steroids in inducing remission40.

Elemental diets commonly need to be administered by a nasogastric tube but on improved palatability some patients can drink sufficient volumes orally. Elemental diets are hyperosmolar so should be well diluted or taken with extra water. They are best taken as chilled drinks, but for an adult, drinking a volume of 2.5 to 3 litres daily for a few weeks can be tedious and demanding. Daily dietary intake charts should be kept and weekly anthropometric measurements made and monitored.

ROTATION DIETS

This is a modification of the oligoantigenic or few-food diet. It is rarely used by dieticians in the UK, but is popular in the USA46. These complicated diets involve rotating a food or family of foods in the diet, so a food or its family is eaten only once in anything from three to 30 days. The aim is to give the body a rest from each food family. Foods are excluded if known or suspected of causing symptoms or commonly associated with food intolerant reactions58. There are no controlled studies documenting the effectiveness of such diets.

FOOD CHALLENGES

The aim of a food challenge is to study the consequences of food or food additive ingestion15. They are necessary

* to confirm or refute a diagnosis, and

*to investigate the development of food tolerance. The food challenge should, ideally, replicate normal food consumption in terms of dose, route and food type15.

OPEN CHALLENGES

Initially, in severe cases, minute quantities of challenge food are introduced, and incrementally increased over hours until average portion sizes are eaten. In clinical paediatric practice, the majority of food challenges are open. Open challenges are simple and practical but are disadvantaged by observer bias. The parents, patient and hospital staff knows what food is being given and this may influence the response and the interpretation of any observations made. The challenge may be continued for several days in cases of reported delayed reactions.

Doubleblind Placebo-controlled Food Challenge (DBPCFC) Tests

This is the only definitive procedure for the diagnosis of food intolerance. DBPCFC are difficult to do successfully and are time consuming, and as a result are not commonly used in clinical practice. However, they are necessary when there is a doubt about diagnosis as well as for research. They have helped establish that the population as a whole65 and parents21 mistakenly perceive food or food additives to be responsible for more symptoms than they are. This test should not be used if there is a clear history of major allergic symptoms following ingestion of a specific food.

In a DBPCFC, the patient remains unaware of whether a specific food or placebo is being given. A 'neutral' observer such as a doctor or nurse is also unaware of what is being administered and this has the advantage of objectivity. The patient, parent and medical observer score results. During challenge procedures, the patient should remain on a limited diet, eating foods known not to cause symptoms. Suspect food allergens can either be disguised by mixing with another food, added to opaque capsules, or given in a liquid medium. The placebo should always be indistinguishable from the test food.

There are several practical problems with blind challenges:

- Ideally the test food should be given in the same form which provoked symptoms, but it is difficult to mask the smell, texture and flavour of certain foods. The challenge mixture should always be palatable and acceptable if given orally.
- Encapsulated food for challenges is commonly recommended. However, standard capsules only contain up to 500 mg of food. They therefore can only contain a limited quantity of challenge material, and if it is given in a dried format, it will probably reduce its allergenicity. Furthermore, patients need to be able to swallow whole capsules so this type of DBPCFC is unsuitable for young children.
- Subjects may require different quantities of allergen in order to provoke a reaction. Hill, Ball and Hoskins28 demonstrated that 8 to 10 g of cow's milk powder caused a reaction in some patients, whereas others required up to 10 times the weight of milk powder before symptoms developed. A negative reaction to the allergen in a blind challenge does not always signify that food intolerance does not exist, as the quantity or length of challenge may have been inadequate. Ideally, the

quantity of food needed to cause symptoms should be established during an open food challenge first.

- A reaction may not occur during DBPCFC if the challenge is given during a dormant phase of disease. For example, in urticaria, salicylate intolerance may only occur in subjects with active disease. Equally, if symptoms are induced by a combination of food and exercise, which is sometimes reported45, exact conditions may be difficult to reproduce with a DBPCFC.

COMMON EXCLUSION DIETS

Milk-free Diets

A milk-free diet involves the exclusion of not only cow's milk or cow's milk infant formulae, but also a wide range of food which contains cow's milk or cow's milk containing components or derivatives (Table II). Cow's milk is found in foods such as yoghurt, ice cream, chocolate, butter and margarine but is also hidden in manufactured foods such as biscuits, sweets, and tinned and processed meats.

Milk Substitutes

Milk is a cheap, popular and valuable source of nutrition in a young child's diet and its contribution should not be underestimated. Half a litre of cow's milk each day provides 26 per cent of the estimated average requirement for energy, 70 per cent of the vitamin A, and 100 per cent of the calcium and riboflavin dietary reference value for a one- to three-year-old boy (Department of Health, 1991). In the absence of milk it is important that young children are provided with a nutritionally adequate low allergenic formula to provide a source of calories as well as other nutrients. Several factors influence the choice of milk substitute including nutritional composition, evidence of satisfactory nutritional status, palatability, ease of preparation, cost, availability and allergenicity.

Table II: Milk derivatives and possible milk containing derivatives found on food labels

* Skimmed milk powder
* Milk solids
* Milk protein
* Non fat milk solids
* Whey
* Whey protein, hydrolysed whey protein
* Margarine
* Shortening
* Animal fat
* Whey syrup sweetener
* Casein
* Caseinates
* Hydrolysed casein
* Sodium caseinate
* Butter
* Cream
* Buttermilk
* Butter fat
* Artificial cream
* Cheese
* Cheese powder
* Lactose
* Flavourings
* Yoghurt

There are several choices of milk substitute including:

- soya milks,
- protein hydrolysates,
- aminoacid formula,
- meat-based formula,
- alternative animal milks.

Soya milks:

Soya beans are predominantly produced in the USA and belong to the leguminosae family along with lentils and peas. The globulin fraction of soya bean is the major protein component (90 per cent) and is principally composed of the glycoprotein ß-conglycin and glycine. Soya milk was first used to feed babies with cow's milk intolerance as early as 1909. The modern generation of soya bean formulas is based on soya-protein isolate supplemented with L-methionine,taurine and carnitine.

Due to the possibility of secondary soya intolerance, some do not recommend this as the first choice of milk in cow's milk protein intolerance (CMPI). There is particular concern that soya protein can induce enteropathy in young infants with and without CMPI, with atrophy of the villi similar to that caused by CMPI. However, the allergenicity of soya has probably been overestimated and some suggest that soya protein should be the preferred choice for children with CMPI which is IgE mediated, or associated with skin or lung symptoms.

Protein hydrolysates:

There are a number of extensively hydrolysed protein hydrolysate formulas available internationally. Protein hydrolysates are the result of heat treatment and/or enzymatic cleavage, which is used in order to produce peptides of minor antigenic activity54. It has been suggested that protein hydrolysates should contain peptides with a molecular weight of less than 1,200 daltons, as allergic responses, including anaphylaxis, have been provoked in animals by peptides with molecular weights of 1,300 daltons or greater.

Casein hydrolysates:

Two casein hydrolysate formulas have been available since the early 1940s - Nutramigen and Pregestimil (Mead Johnson). The preparations contains free aminoacids and short chain peptides with over 97 per cent of the latter having a molecular weight of less than 1,000 daltons32.

Although there is considerable clinical experience with these formulas, most reports of severe reactions to casein hydrolysates52,55 including anaphylactic reactions are relatively new.

Whey hydrolysates:

There are extensively hydrolysed whey nutritionally complete formulas available internationally. Although they have been shown to be clinically effective, severe reactions to extensively hydrolysed whey formula have been reported42. It is hypothesised that whey protein trypsin hydrolysates may have epitopes in common with cow's milk protein, including beta lactoglobulin, inducing an immunogenic cross-reactivity between hydrolysate and cow's milk proteins.

Aminoacid formula:

With increasing reports of reactions to protein hydrolysate formulae, international use of aminoacid-based infant formulas is growing30,34.

Meat-based formula:

There are increasing reports of homemade meat-based modular feeds being successfully used as an alternative to protein hydrolysate formulas64. In one study, in three infants given a homemade meat-based formula, increased levels of creatinine, blood urea nitrogen and metabolic acidosis were noted, but these returned to normal after the protein content was lowered64. In the UK, a modular feed based on commercially available chicken meat is occasionally used for infants with chronic diarrhoea caused by intolerance to cow's milk, soya or protein hydrolysate. The feed is expensive, unpalatable and allergic reactions to chicken have been noted60. The use of such feeds requires close supervision by a paediatric dietician. The use of meat-based modular feeds has not been evaluated in the management of CMPI.

Animal milk:

Goat's, sheep's and ass's milk have all been used in the management of CMPI24,37. They are all nutritionally unsuitable if given in unmodified form to infants under one year and they contain lactose. There is evidence to demonstrate a strong cross-reactivity between cow's, goat's and sheep's milk24,26 and they should not be used in the management of cow's milk intolerance.

NUTRITIONAL HAZARDS OF DIET THERAPY

There have been several reports in the literature of poor growth and nutritional deficiencies in children on allergy diets but the diets have usually been self-selected or have been recommended and supervised by workers with little expertise in the field of nutrition36,51. Roesler, et al described nine children who were failing to thrive on limited diets because their parents believed they had allergic reactions to multiple foods. Only two patients reacted during a DBPCFC. David described a 10-month-old child with eczema who had been diagnosed by a non-medical allergist as having an allergy to 57 foods. The child was placed on a diet consisting of mashed potato, pure orange juice and pineapple juice only. Not surprisingly, weight loss and failure to thrive accompanied this. In a survey of children between five and 11 years, those who were perceived to have food intolerance by their parents and were avoiding three or more foods, were on average 4.2 cm shorter than children on a normal diet48.

Even simple milk-free exclusion diets have been shown to adversely affect nutritional status. Two separate studies have reported young children on milk-free diets to have a lower height-for-age59 and a lower weight-for-length index35, when compared to healthy age-matched control children. Calcium intake has been shown to be significantly lower for both adults41 and children5 on a milk-free diet. There have been at least two reports identifying children on milk-free diets who developed rickets, probably as a result of calcium deficiency13,16.

It is essential that all diet therapy is supervised by a dietician to ensure that the prescribed diet is nutritionally adequate and contains sufficient energy to support normal growth and weight gain. Growth, weight gain and nutritional intake should be regularly monitored throughout dietary trials. Appropriate vitamin and mineral supplementation should be prescribed as necessary.

CONCLUSION

Although the dietary management of food allergy and intolerance is very important, there is ample evidence that over diagnosis and unsupervised dietary restriction can not only cause physical harm, but can also be socially isolating and very stressful to both parents and child.

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Probiotics - A Possible Role In Nutrition And Health Promotion

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With the adoption of vigorous 'child survival strategies', including oral rehy dration, infant and child mortality in India has significantly declined even among the poorest undernourished segments of the population. Most of the surviving children, however, continue to remain stunted and undernourished and

fail to thrive. As a result of this expanding pool of substandard survivors, as high as 52 per cent of India's under-fives are presently stunted1.

Among the components likely to be used in functional foods, prebiotics and probiotics are already used as food ingredients. Probiotics are foods that contain live bacteria, which are beneficial to health. A prebiotic is a non-digestible food ingredient that beneficially affects the host by selectively stimulating the growth and/or activity of one or limited number of bacteria in the colon that have the potential to improve host health2.

The bacterial genera most often used as probiotics are lactobacilli and bifidobacteria. They can be given in the form of fermented foods such as curd or yoghurt that may briefly establish in the gut. A number of health-related effects of probiotics are documented such as alleviation of lactose intolerance, decreasing the duration of rotavirus diarrhoea, and prevention of recurrence of superficial bladder cancer. Each effect has been shown in at least two human clinical studies by different research groups. Colonic fermentation has been shown to be altered following probiotic intake, either as fermented milks or freeze dried cultures3,4,5. Lactobacillus acidophilus therapy in the prevention and adjuvant therapy of certain infectious diseases especially gastrointestinal disorders in children and adults is advocated in many parts of the world. The recent emphasis on feeding lactobacilli is attributed to the side effects of antibiotics6.

Some of the "health benefits" claimed for probiotics, are listed below:

* Nutritional enhancement: Yoghurt contains a significantly higher concentration of folic acid, niacin and riboflavin than milk.

* Control of intestinal disorders: Rotavirus diarrhoea; Colitis; Lactose intolerance; Salmonella and shigella infection

* Control of other disorders: Ethanol induced liver disease; Cancer of the colon; Hypercholesterolaemia

* Other uses: Treatment of food allergies; Adjuvant for vaccines; Increased weight gain during development

Acute infections of the gut are usually self-limiting, characterised by diarrhoea and often vomiting. Acute diarrhoea is responsible for 3 to 4 million deaths annually worldwide, many of which are children. It accounts for 20 to 30 per cent of all mortality7,8. Several studies by different groups in developed9 and developing countries10,11 have shown that some probiotic lactobacilli significantly shorten the duration of rotavirus diarrhoea.

A number of probiotics have been added to animal feeds to increase the weight of domestic animals. The increase in weight gain presumably results from infection control and from increased digestibility of nutrients. Animal feeding studies in young rats12,13 fed a liquid diet consisting either of milk, yoghurt, or fermented milk have shown a significantly higher weight gain for the animals on the fermented products. In four weeks the animals fed milk gained 116 g, 136.3 g when fed yoghurt and 131.3 g when maintained on a fermented milk diet. A similar study has been conducted in humans14. From a number of different types of observations, evidence has emerged that probiotics are beneficial in promoting growth in young animals and humans.

The use of lactic acid producing bacteria in foods, especially members of the genus lactobacillus, in foods has a long history and most strains are considered commensal microorganisms with little or no pathogenic potential. Their ubiquitous presence in intestinal epithelium and the human gastrointestinal tract and their traditional use in fermented foods and dairy products attest to their safety, and they are generally recognised as safe15,16. Most probiotics have been designated as 'generally recognised as safe' (GRAS). From the evidence available till date, it appears that Lactobacillus GG is the most potent among the lactobacilli in decreasing the incidence of diarrhoeal morbidity. Unfortunately, a major

limitation in using Lactobacillus GG in the developing countries is the cost factor. Lactobacillus acidophilus is readily available in the developing countries and activated cultures of the same can be used as probiotic food supplements. The acidophilus strain is more feasible from the economic standpoint in the developing world but does not appear to be as potent as Lactobacillus GG in its beneficial effect on diarrhoeal morbidity. Insufficient viability and survival of Lactobacillus acidophilus in commercial food products remains a problem17.

It has been shown that probiotics may change the gut mucosal barrier by stabilising the intestinal mucosa, normalising intestinal permeability and improving gut immunology. Another consequence of intake of probiotics is the prevention of overgrowth of pathogenic bacteria and viruses. The human consumption of probiotics appears to be safe.

The composition of the intestinal microflora, together with the gut immune system allows resident bacteria to exert a protective function. Certain probiotic species have been shown to shorten the duration of rotavirus diarrhoea in children but more work is needed. Prospective studies are needed to arrive at definite conclusions and make long-term recommendations.

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Centre now on the World Wide Web

The Centre for Research on Nutrition Support Systems is now easily accessible from any corner of the globe, at all times. The CRNSS's Website (www.crnssindia.org) provides comprehensive information about the Centre, its objectives, activities, publications and research programmes. The site also provides an electronic version of the Nutrition in Disease Management - Update Series

VII ISPEN Annual Conference

The VII Annual Conference of the Indian Society for Parenteral and Enteral Nutrition (ISPEN) is being organized by the Gujrat Chapter from 16th- 18th February 2001. The proposed symposia includes:

¨ Micro and macro nutrient requirements.
¨ Surgical stress and nutrition.
¨ Hypoalbumin
¨ Trace elements
¨ Lipids as a source of energy.
¨ Perioperative nutrition in GI diseases.
¨ Parenteral Nutrition in low birth weight infants.
¨ Dietetic value of Indian foods.
¨ Enteral nutrition in neurological problems.
¨ Role of elemental diets

One specific highlight of the scientific program is the pre-conference workshops.

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