

The effects of exclusion of dietary egg and milk in the management of asthmatic children: a pilot study

Authors

Noor Aini Mohd Yusoff,

Department of Nutrition and Dietetics, Faculty of Allied Health Sciences, Universiti Kebangsaan Malaysia, Jalan Raja Muda Abdul Aziz, 50300 Kuala Lumpur, Malaysia

Shelagh M Hampton,

School of Biomedical and Molecular Sciences, University of Surrey, Guildford, Surrey GU2 7XH, England

J W T Dickerson,

School of Biomedical and Molecular Sciences, as above

Jane B Morgan,

School of Biomedical and Molecular Sciences, as above

Corresponding author:

Jane B Morgan

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Abstract

Current understanding of the use of exclusion diets in the management of asthma in children is limited and controversial.

The aim of this study was to examine the effects of excluding eggs and milk on the occurrence of symptoms in children with asthma and involved 22 children aged between three and 14 years clinically diagnosed as having mild to moderate disease. The investigation was single blind and prospective, and parents were given the option of volunteering to join the 'experiment' group, avoiding eggs, milk and their products for eight weeks, or the 'control' group, who consumed their customary food.

Thirteen children were recruited to the experimental group and nine to the control group. A trained paediatrician at the beginning and end of the study period assessed the children. A seven-day assessment of food intake was made before, during and immediately after the period of dietary intervention in both groups. A blood sample was taken from each child for determination of food specific antibodies and in those children who could do so, the peak expiratory flow rate (PEFR) was measured.

Based on the recommended nutrient intake (RNI), the mean percentage energy intake of the children in the experimental group was significantly lower ($p < 0.05$) in the experimental group. After the eight-week study period and compared with baseline values, the mean serum anti-ovalbumin IgG and anti-beta lactoglobulin IgG concentrations were statistically significantly reduced ($p < 0.05$) for both in the experimental group. In contrast, the values for anti-ovalbumin IgG in the control group were significantly increased and those for anti-beta lactoglobulin IgG were practically unchanged. The total IgE values were unchanged in both groups.

Over the study period, the PEFR in those children in the experimental group able to perform the test was significantly increased, but no such change was noted in the children in the control group who could do the test.

These results suggest that even over the short time period of eight weeks, an egg- and milk-free diet can reduce atopic symptoms and improve lung function in asthmatic children.

INTRODUCTION

In the UK there are over three million people with asthma.^{1,2} In adults and children a clinical response can be triggered by a wide variety of agents. These include dietary and environmental allergens, viral infections, exercise, exposure to fumes and other irritants, certain drugs, food, drink and food additives.³

In asthmatic children aged less than two years, an adverse reaction to cows' milk is reported to be the most common 'allergic reaction' followed by an adverse reaction to eggs.⁴ Anderson⁵ and Weeke⁴ reported that amongst the factors that determine asthma prognosis the following were important:

age, immune status, sex, mother's age at child-birth, infections, other allergic diseases, and signs and symptoms of food allergy. Anderson⁶ commented that up to the early 1990s little interest and investigative effort had been directed towards a possible role for foods in the provocation of atopic asthma. Perhaps the general feeling was that inhaled allergens, rather than those consumed in food, were more likely to be the main causes and immediate sensitivity reactions to foods were reported to be less frequent in children with asthma than in those with eczema. The results of only a few clinical trials seem to have been published and priority has been

on the effectiveness of dietary intervention during pregnancy,⁷⁻¹⁰ during pregnancy and lactation,^{11, 12} in infants,^{13, 14} and in children,¹⁵ on the prevention of atopy development.

No reports have been found in which the value of eliminating food allergens has been assessed in the management of asthma in children. The present study was undertaken with the defined objective of determining the potential benefits of dietary avoidance of egg, and egg products, and milk and milk products, in reducing the symptoms of asthma in children.

Allergic reactions are usually mediated by IgE antibodies to specific antigens. However, IgE has been found not to be suitable for general risk screening in neonates¹⁶ and in older individuals can give falsely negative and falsely positive results.¹⁷ Pastorello¹⁸ suggested that positive skin prick testing (SPT) and specific IgE levels may be unrelated to clinical symptoms and may simply be due to cross-reaction between allergens present in commercial materials. These reports, together with an increased recognition of the value of IgG measurement¹⁹ led us to measure both total IgE levels, as a check on previous observations, and food specific IgG levels in our children.

METHOD

The study design was of a single blind prospective nature. Parents, children and the investigator (NMY) were aware of the study groups to which the children had been allocated. However, the paediatricians who saw the children were 'blind' in relation to the study groups during the pre-study and the post-study assessments of the children.

Duration of the study

The half-life of IgG antibody is 23 days and the residual time of mast cells is two to three months.²⁰ Therefore, to enable any change to occur during the study, eight weeks abstinence from egg and milk was considered reasonable. For children, it was anticipated that compliance with the diet would be difficult if the study lasted longer than this.

Subject recruitment

Seventy-one asthmatic children aged three to 14 years were recruited from the 111 asthmatic children attending the

Outpatient Department in the Royal County Hospital and the Frimley Children's Centre. These subjects were screened for selection into the study, based on food specific IgG antibody levels. The baseline values against which these levels were assessed were obtained in 19 non-atopic non-asthmatic children (no personal and family history of atopy or asthma) chosen from a total of 45 children approached.

Of the 71 asthmatic children tested, 43 (61%) were identified as possible candidates for dietary intervention as their anti-ovalbumin IgG concentrations were above the mean concentrations found in the non-atopic non-asthmatic children (>500 ug/ml), an arbitrary cut-off point for selection. Of the 43 possible subjects, 22 agreed to participate in the study. Parents were given the option of allocating their children into the experimental (diet intervention) or control (no diet restriction) groups respectively. As a result, 13 children were included in the group on the diet with nine in the control group. The children in the experimental group were advised to adhere to a diet devoid of egg and egg products and milk and milk products. Children in the control group were asked to continue to eat their customary diet during the eight weeks of the study.

Anthropometric measurements

The investigator measured the weights and heights of all the children before the study began and after it was completed. Weights (in light clothing) were measured with calibrated Seca weighing scales and were recorded to the nearest 0.1 kg. Heights (standing, no shoes) were measured with an upright stadiometer and recorded to the nearest 0.1 cm.

Guidance on egg and milk avoidance

The investigator for the families in the experimental group produced a booklet on egg- and milk-free food products. This booklet was compiled from two British Dietetic Association publications, *Egg Free Booklet*,²¹ and *Cows' Milk Free Booklet*. *Cows' Milk/Egg Free Booklet*.²² These booklets provided lists for various commercial food items that could be consumed by the children in the experimental group. In addition, verbal advice was given to families when the

investigator (who is a qualified dietician) met them (see below). Since the timing of the study coincided with Easter, children in the experimental group were given a dairy- and egg-free 'Chocolate Bunny' (D & D London, UK). No dietary advice was offered to the control families, and if advice was sought, only that of a general nature was given.

Dietary supplements

The experimental children were provided with a hypoallergenic milk supplement (Pepti-Junior, Cow & Gate, Nutricia, Trowbridge, Wiltshire, UK) to replace all milk drinks. A recipe booklet (Cooking with Pepti-Junior, published by Cow & Gate, Nutricia) provided parents with advice on the more versatile use of the milk supplement. Parents were contacted regularly for replenishment of the milk supplements. The children in the experimental group were also given a calcium supplement in the form of a tablet (Calcichew, 500 mg calcium tablet, Shire Pharmaceuticals Ltd, Andover, Hants, UK), which was taken on alternate days to ensure that calcium requirements were met. In addition, children were advised to consume a daily helping (4 g) of a yeast extract (Marmite) in order to obtain the recommended amount of riboflavin.

Assessment of non-compliance

Monitoring non-compliance was essential in the experimental children. If a dietary accident occurred, the parents were asked to record on a form designed for the purpose the date and type of eggs and/or milk products consumed. The investigator kept regular contact with the parents by telephone and home visits. This ensured that the morale of the parents and their children, especially those in the experimental group, was maintained throughout the study.

Recording of energy and nutrient intake

All parents were asked to record their children's daily food intake for the first, fourth and eighth week in a seven-day estimated 'food diary', developed and validated by the Dunn Clinical Nutrition Centre, Cambridge, UK. The food diary was validated by the UK European Prospective Investigation of Cancer and Nutrition studies comparing various dietary assessment methods in nutritional

epidemiology.^{23, 24} The food diary contained colour photographs of small, medium and large portions of 17 foods pictured on a ten-inch dinner plate. Parents could choose one of the amounts shown in the photograph or indicate that their children consumed less than the smallest or more than the largest amount shown. Parents were encouraged to weigh foods using their home kitchen scale (not validated) if any food consumed was not available, or no similar food was available in the pictures. Parents were given stamped addressed envelopes to mail completed food diaries to the investigator.

The food diary was also used to monitor non-compliance in the experimental group for the food intake records were checked as soon as the diaries were received and any queries were clarified immediately with parents. The amount of food consumed and recorded in the food diaries was either computed directly with portion sizes or converted into weight (g) using Food Portion Sizes²⁵ on the computer programme, Comp-Eat 4.0 (Lifeline Ltd, London, UK). Nutrient analysis was undertaken using this programme and compared with the Dietary Reference Values for Food Energy and Nutrients for the United Kingdom.²⁶ Intakes of calcium and minerals and vitamins derived from supplements were included in the computed nutrient analysis. Because of the fact that the children varied in age between three and 14 years of age and were of both sexes, the results of the dietary assessments were expressed as a percentage of the recommended nutrient intakes (RNI).²²

Clinical assessment

All the children who participated in the study were invited to Frimley Park

Hospital or Frimley Children’s Centre for clinical assessment carried out by a paediatrician or a trained registrar responsible for running the Out-Patient Paediatric Asthma Clinic at the Frimley Children’s Centre. The paediatrician and registrar were both involved in the design of the study and the pre- and post-dietary clinical assessments. They agreed to use the same methods and criteria to reduce any bias in their assessment. On both occasions, one of the two clinicians, without knowledge of the children’s study group, evaluated the children using a standard form for current signs and symptoms of asthma including the presence of coughing, nocturnal coughing, wheezing, the number of asthmatic episodes during the past eight weeks and current medication including the type, dose and frequency of medication.

Peak expiratory flow rate

All the children were assessed for their ability to perform the measurement of the PEFr. Those children who were able to perform this measurement correctly were given a Mini-Wright Peak Flow Meter (Clement Clarke International Ltd, UK) if they did not already own one. Children who were able to make the PEFr measurement were asked to record the best of three measurements taken twice daily (first thing in the morning and just before going to bed) on a fortnightly chart. These charts were mailed to the researcher (stamped addressed envelope provided) together with the food diary after the first, fourth and eighth week of the dietary intervention period.

Blood sampling and analysis

A 2 ml non-fasting venous blood sample

was taken from the children at the start and at the end of the intervention period by one of the doctors or a nurse. The blood sample was allowed to clot at room temperature, centrifuged and the serum aliquoted and frozen at -20°C until the completion of the intervention period.

The sera taken at the beginning and at the end of the intervention period were analysed in the same batch for the measurement of anti-ovalbumin IgG and anti-beta lactoglobulin using indirect ELISA methods.²⁷ Total IgE was measured with the CAP system of Pharmacia (Uppsala, Sweden).

Statistical analysis

The data were analysed using the Statistical Package for Social Science (SPSS). Paired Student’s t-test was used to test the significance of the difference in the anthropometric and dietary data before and after exposure to dietary intervention in the two groups of children. As the data for the specific food IgG, IgE and total IgE antibodies were not normally distributed despite being logarithmically transformed, statistical analyses were performed using the non-parametric, Mann-Whitney U tests and Wilcoxon signed rank sum tests.

Ethical approval

Ethical approval for the study was obtained from the South West Surrey Regional Health Authority Ethics Committee in March 1995 and from the North West Surrey Local Research Ethics Committee in August 1995.

RESULTS

Subjects

The mean age and gender of the 22 children in the experimental and control groups are given in Table 1. The range of ages of the children in each group was rather wide and each group contained children of both sexes and more boys than girls. There was no significant difference between the changes in the mean heights of the children in the two groups at the end of the study compared with those at the beginning. However the control children gained a significant amount of weight during the study period whereas those on the special diet showed a mean loss in weight (Table 1). It is to be noted that some individual children in both

Table 1		
Gender, height and weight of asthmatic children in the study during the eight-week dietary intervention		
	Experimental	Control
Number of children	13 (8 male, 5 female)	9 (7 male, 2 female)
Mean age (range), years	6.5 (4-14)	5.0 (3-8)
Mean height change (range), cm	0.6 (0-1.65)	0.5 (0-1.2)
Mean weight change (range), kg	-0.16 (-1.2-1.15)	+0.34* (-0.6-1.2)
*Mean weight gain in the control group was significantly higher in the experimental group (p<0.05)		

groups lost weight during the study.

Dietary supplements

None of the control children received or consumed vitamin or mineral supplements. All the children on the egg- and milk-free diets received and consumed 500 mg calcium on alternate days and two of the children took multi-vitamin supplements daily containing vitamins A, D, E, C, thiamin, riboflavin, niacin, pyridoxine and pantothenic acid. Two children in this group consumed soya milk as their main drink. The hypoallergenic formula (Pepti-Junior) was not popular as a milk alternative eaten with cereals with ten of the children. It was said to be 'unpalatable' when eaten in this way. One child complained of being sick after consuming it, and another refused to drink it after tasting it for the first time despite the mother masking it with flavourings. Alongside this response, three children requested additional supplies after the first consignment and tolerated it for the first few weeks before

rejecting it. Mothers utilised the formula in cooking with the help of the recipes provided.

Compliance with the egg- and milk-free diet

Of the 13 children who were on the diet, six appeared to have inadvertently consumed small amounts of egg and milk products during the study period. These foods were in the form of cakes consumed once or twice in family gatherings. The remaining seven children strictly followed the diet for the whole of the eight weeks. No significant differences were observed in the levels of food-specific IgG antibodies in those children who complied fully with the diet compared with those who complied partially.

Energy and nutrient intake

The results of the 21-day food records from the two groups of asthmatic children are summarised in terms of the percentages of the RNI in Table 2. The children on the experimental diet

consumed a significantly lower percentage of energy than the controls. The protein intake of both groups of children was high, with some children in both groups having more than 300% of the RNI. It is to be noted that the mean percentages of the RNI for most nutrients consumed by the children on the experimental diet were lower than those of the controls and this was particularly true for the amounts of iodine and vitamin A. Although the value for calcium intake exceeded 100% of the RNI in the children on the experimental diet, there were some children who, in spite of taking the supplement, consumed only 61% of the RNI. At least one of the control children also consumed a similar amount of calcium. The amount of zinc consumed was inclined to be low in children in both groups. In spite of being told to take a supplement containing riboflavin, at least one child in the experimental group consumed only 49% of the RNI for this vitamin. Some children in both groups, and particularly those on the restricted diet, had low intakes of

Table 2

Percentage of RNI consumed by the experimental and control asthmatic children derived from 21-day food record data. Values include the contribution from supplements (see text for detail)

	Experimental		Control	
	Mean % $\pm$ SD	Range	Mean % $\pm$ SD	Range
Energy	84 $\pm$ 14*	55-105	100 $\pm$ 11	84-113
Carbohydrate	116 $\pm$ 9	103-131	106 $\pm$ 4	99-111
Protein	182 $\pm$ 60	106-319	251 $\pm$ 52	197-356
Fat	102 $\pm$ 9	88-115	116 $\pm$ 7	108-125
Calcium	109 $\pm$ 30	61-149	155 $\pm$ 63	60-275
Iron	125 $\pm$ 57	60-249	133 $\pm$ 18	113-165
Zinc	77 $\pm$ 32	31-138	95 $\pm$ 20	68-119
Selenium	135 $\pm$ 45	60-195	168 $\pm$ 56	106-277
Iodine	47 $\pm$ 22	10-84	122 $\pm$ 89	55-330
Thiamine	227 $\pm$ 86	134-345	172 $\pm$ 36	130-240
Riboflavin	155 $\pm$ 89	49-287	189 $\pm$ 55	129-279
Nicotinic acid	213 $\pm$ 41	125-266	189 $\pm$ 28	150-230
Pyridoxine	238 $\pm$ 82	145-421	193 $\pm$ 43	134-260
Vitamin B ₁₂	188 $\pm$ 49	90-255	339 $\pm$ 97	180-456
Folate	137 $\pm$ 66	73-298	171 $\pm$ 53	115-263
Vitamin C	274 $\pm$ 153	117-517	241 $\pm$ 91	157-376
Vitamin A**	75 $\pm$ 39	10-147	171 $\pm$ 114	93-435
Vitamin E	113 $\pm$ 50	43-213	116 $\pm$ 33	76-168

* Mean value in children in the experimental group was significantly ($p < 0.05$) lower than in the control group

** Vitamin A equivalent

vitamin E. By contrast, the amounts of nicotinic acid, pyridoxine and vitamin C consumed by the children on the restricted diet exceeded those of the control children.

Immunoglobulin concentrations

Results for the analysis of the immunological data are given in Table 3. In the children that had been in the experimental group, the mean serum anti-ovalbumin IgG concentration was significantly ($p<0.01$) lower at the end of the diet period than it was at the beginning of the study. This contrasted with the values in the control group, which increased ($p<0.05$) during the study period. Similarly, the post-study anti-beta lactoglobulin IgG concentrations for the experimental group were also significantly ($p<0.01$) lower at the end of the study than at the beginning. The post-study values for this immunoglobulin for the control group were not significantly different from their baseline values. The post intervention values for the total IgE concentrations were not significantly different from the baseline values in either group.

Peak expiratory flow rate

Of the 22 asthmatic children participating in the study, 11 (50%) were able to carry out the PEFR measurement correctly (six from the experimental group and five controls). Figure 1 shows the mean values for the two groups of children before and after the eight-week study period. After completing

the eight weeks on the exclusion diet the mean value for the PEFR had risen by 22% ($p<0.05$) whereas the value for the controls had decreased by 0.6%. The value for one child in this group had actually decreased by 25%, which may have indicated a forthcoming asthma attack.

Other outcomes

One experimental child was able to sleep undisturbed throughout the remainder of the study after one week on the diet and another experimental child's eczema improved. Neither of these children claimed an improvement in their asthma. It was noted that after the trial was completed and the experimental children reverted to their usual diet, several mothers reported one of the following: one child had an asthma attack after consuming a piece of cake, two children frequently required a beta 2 agonist when engaged in sports activities, the eczema of three children got worse and the child whose sleep had become undisturbed while on the trial reverted to her earlier sleep pattern after the trial.

One child from the restricted diet group and one of the controls had reduced their intake of a beta 2 agonist over the course of the study. Both children showed an improvement in their PEFR value and had reduced concentrations of anti-ovalbumin IgG, anti-betalactoglobulin and total IgE values. The child on the restricted diet reported improved 'well-being' when engaged in sports activities.

DISCUSSION

In 1968 Rowe and Rowe²⁸ conducted a survey on 1,491 asthmatic patients. They reported that 40% of children under five, 25% of children between five to 15 years, 29% of adults 15 to 55 years, and 40% of adults over 55 years, had asthmatic episodes with foods. These results were based on case histories, skin tests, and response to the Rowe 1-2-3 elimination diets. They were convinced that if physicians were more concerned, they would find that half the cases of allergic asthma and psychogenic asthma in adults were caused by an adverse response to foods.

Van Metre *et al*²⁹ evaluated the Rowe cereal-free 1-2-3 diet along with a high allergenic foods diet in a double-blind crossover study on 18 randomly selected asthmatic adults with no history of diagnosed food allergy. No difference in the frequency or severity of asthmatic symptoms was observed in these subjects after a three-week period following the Rowe cereal-free diet. However, Rowe and Rowe²⁸ commented that the duration of Van Metre's trial was too short and noted that the body requires a longer period of time to adapt before any improvement in a subject's respiratory symptoms could be expected.

The present study involved 22 children in a single-blind diet intervention study of eight weeks. Their parents allocated the children to either the experimental group or the control group. The resulting groups contained 13 and nine children respectively,

Table 3

Food specific IgG and total IgE concentrations in the serum of asthmatic children before and after the eight-week dietary intervention

		Experimental		Control	
		Mean (SD)	Range	Mean (SD)	Range
Anti-ovalbumin IgG (mg/ml)	Baseline	2483 (935)	999-3939	1447 (956)	28-2981
	Post diet	1876 (805)*	652-3147	1659 (1033)**	34-3609
Anti-betalactoglobulin IgG (mg/ml)	Baseline	223 (182)	13-567	399 (600)	31-1886
	Post diet	149 (108)***	8-343	415 (686)	53-2198
Total IgE (kU/ml)	Baseline	1603 (2469)	4-4096	851 (1547)	13-4794
	Post diet	1610 (2387)	8-7258	694 (1149)	7-3545

* Mean value significantly lower in the post diet period compared with the baseline value ($p<0.01$)

** Mean value significantly higher in the post diet period compared with the baseline value ($p<0.05$)

*** Mean value significantly lower in the post diet period compared with the baseline value ($p<0.01$)

with the experimental group containing children up to 14 years of age and the control group up to eight years of age.

The study cannot be considered as more than a pilot because of the small number of children involved. Of the 111 children attending the collaborating hospitals, 43 were identified as possible subjects for the study. After being acquainted with the requirements of the investigation and the degree of commitment required by both parents and children, only 22 agreed to participate. Those who did were dedicated to the investigation and problems with the diet were minimal; rather more parents (13) agreed to the inclusion of their children in the diet group than in the control (9). Ethical considerations precluded the inclusion of a control group of non-asthmatic children.

The eight-week study period was used on the basis that the half-life of IgG is 23 days and the residual time of IgG on the mast cells is two to three months.²⁰ Although a period on a diet devoid of eggs and milk of 12 weeks would have been preferred, compliance would have been even more difficult. Over the eight-week study period, the mean weights of the children in the experimental group decreased by 0.16 kg whereas those of the control group rose by 0.34 kg. The reason for the loss in weight of the experimental group was probably that the food consumption of the experimental group did not achieve the RNI for energy (84%) whereas that of the controls did (100%). The amount of protein consumed by the experimental group was also lower (182% RNI compared with 251% for the controls). It is to be noted that in spite of being asked to take appropriate supplements, the intakes of many of the micronutrients by the experimental group were below those of the controls. This may suggest that not all the children on the restricted diet actually consumed the supplements. The biggest differences were for iodine (47% RNI in experimental children and 122% RNI in controls) and for vitamin A equivalents (75% RNI in experimental children and 171% RNI for controls). This is evidently a matter that should be given special attention in future trials of restricted diets in asthmatic children.

When considering the dietary intake of the two groups of children it should be

noted that the foods in the experimental diet were different in taste, texture and variety, especially those likely to have been favourite foods such as desserts and snacks which included cheese, ice cream and yoghurt. Milk and eggs not only enhance flavour, but also enhance the texture of most commercial and home-prepared foods. A longer study period might have given time for the children to adapt to the new foods and hence to increase their food consumption.

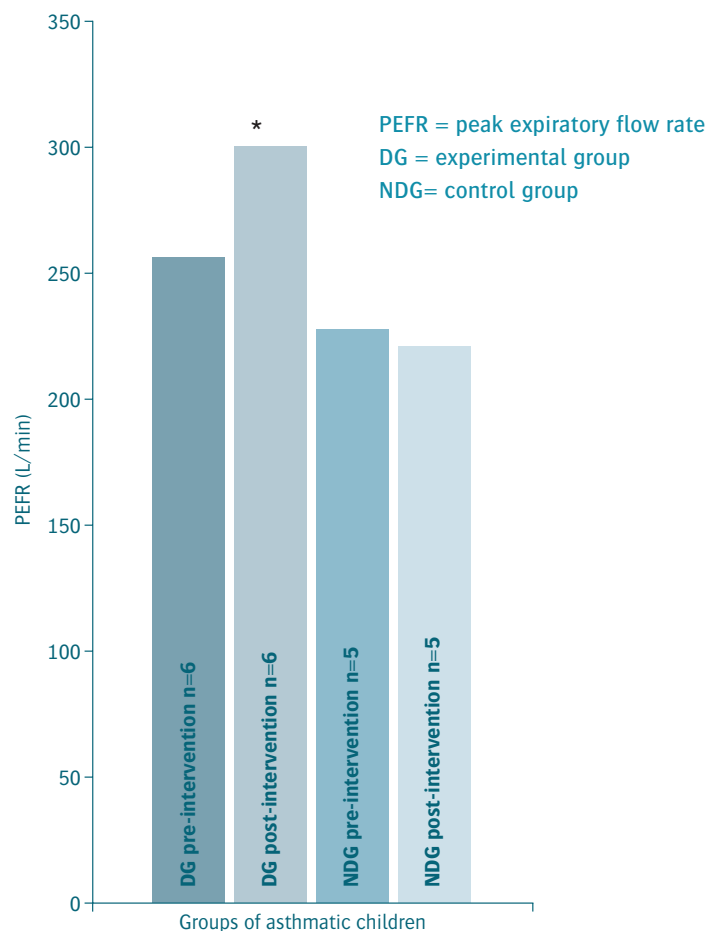
Immunological effect of egg- and milk-free diet

All the children on the experimental diet had significantly reduced concentrations of specific food IgG antibody to

ovalbumin and beta lactoglobulin after eight weeks on a diet devoid of eggs and milk. This finding seems to confirm that antibody measurements can be used to test for compliance in food exclusion studies. The changes in IgG were associated with functional improvement in the five children on the experimental diet who were able to perform the PEFR test, which is a measure of lung function. Admittedly, these numbers are small, but for each individual child the effect on well-being should not be under-estimated. For two of the children the paediatrician confirmed an improvement in well-being. The same children claimed that they were 'less chesty' when engaged in sports activities and thus required less treatment with a

Figure 1

Mean peak expiratory flow rate for the experimental group and the control group of asthmatic children before and after eight-weeks dietary intervention



beta agonist. One child reported an improvement in eczema. None of the children had a change of grading in their total IgE results. The finding of no change in the total IgE levels in children, but clinical improvement correlated with a decrease in food specific IgG levels, in

children receiving a milk-free, egg-free diet seems to confirm the greater reliability of food specific IgG measurements in the children.

CONCLUSION

An egg-free, milk-free diet caused a

decrease in the concentrations of the corresponding IgG components in the blood that was associated with functional and clinical improvements in asthmatic children. These beneficial changes tended to be lost when the diet was stopped.

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RSPH Fish & Chip Supper

Harry Ramsden's, Brighton, Sunday 18 April 2004 – 12th Annual Public Health Forum

To kick off the four-day Annual Public Health Forum, organised by the UKPHA and the World Federation of Public Health Associations, The Society is holding a Fish & Chip Supper on Sunday 18 April at the world-famous Harry Ramsden's restaurant. The supper offers an opportunity to put aside the pressing health issues that will dominate the week and break the ice with colleagues from around the globe with a traditional British three-course meal. All Society members living in Brighton or attending the conference are welcome to join us.

To book, send credit card details or a cheque for £19 per person, to

The Royal Society for the Promotion of Health, 38A St George's Drive, London SW1V 4BH

Or email: events@rspgh.org

Please mark your correspondence, 'Fish & Chip Supper'.