Outcome of Maternal Modification Intervention and the Role of Breastfeeding in Allergy Prevention in Children

A major project submitted in partial fulfilment for the award of the degree of Master of Science, University of Wollongong

Hayley Gilbert

Department of Biomedical Science
University of Wollongong

Contents

Acknowledgments

Supervisors; Anne Swain, Velencia Soutter & Robert Loblay.

Ting (Chloe) Liang who helped in data collection and analysis.

The staff at the Royal Prince Alfred Hospital, Allergy Unit and the families of subjects who have helped in this study.

Funded by Royal Prince Alfred Hospital Allergy Unit.

Abstract

Introduction

Food allergy in children is a major health risk with the possibility of life threatening anaphylaxis. To lessen this burden, the causes of allergy and possible means for allergy prevention need to be assessed. This study aimed to evaluate the effectiveness of maternal avoidance of highly allergenic foods and assess the benefit of breastfeeding for allergy prevention in high risk children.

Methods

Subjects were selected from an initial cohort of 2114 patients between 0 and 18 years who were seen by Dr. Velencia Soutter at the Royal Prince Alfred Hospital Allergy Consulting Rooms from 1992 to 2005. Information on breastfeeding duration, any maternal modification, Skin Prick Tests (SPT), eczema and asthma were acquired from patient family records.

Results

Siblings to a child with a food allergy whose mother had followed a modified diet (Modified group) showed less eczema ($p < .005$) and asthma ($p < .001$) than siblings whose mother had not (Non modified group). Differences in food sensitisation were not significant between groups. Breastfeeding duration had no effect on asthma or eczema. There was a significant increase in subjects with any food sensitisation before the age of one for both Modified ($p < .05$) and Non modified groups ($p < .05$) breastfed for 6 months or longer but not after this age. Breastfeeding for 6 months or longer did not significantly increase the mean number of sensitisations to food before the age of one in the Modified group ($p > .05$) as it did in the Non modified group ($p < .005$).

Conclusion

A maternal modified diet can be recommended in the second half of pregnancy and during lactation to help prevent a child developing eczema and asthma. Extended breastfeeding cannot be recommended as a means to prevent allergy. An extended breastfeeding duration of 6 months and longer may be a risk factor for food sensitisation before the age of one in high risk children, especially when no dietary avoidance measures are taken.

Outcome of Maternal Modification Intervention and the Role of Breastfeeding in Allergy Prevention in Children

Introduction

There has been a widespread increase in the incidence of atopic disease around the world in the last decade (Hill et al., 1997). The incidence of food allergy had been reported to be 4- 6% in children (Zeiger, 2003) with the most common food allergies being egg, milk and peanut (Hill et al., 1997). Food allergy in children is a major heath risk with the possibility of life threatening anaphylaxis (Clark & Ewan, 2003). To lessen this burden, the causes of allergy and possible means for allergy prevention in children need to be assessed.

Hereditary factors have been shown to be a major influence in the incidence of atopic disease. A positive family history of allergy has been shown to be a significant risk factor in the development of eczema, asthma, allergic rhinitis and for a positive Skin Prick Test (SPT) result (Arshad, Stevens & Hide, 1993). A twin study demonstrated hereditary factors to be a major influence in the incidence of peanut allergy where 64.3% of monozygotic twin pairs showed concordance compared to 6.8% of dizygotic twin pairs (Sicherer, 2000). Allergy still occurs, however, in high proportions of children born to non atopic parents (Arshad et al., 1993).

Food allergy is most often begins within the first two years of life (Wood, 2003). It is acquired through the process of sensitisation whereby the immune system produces allergen specific immunoglobulin E antibodies in response to specific food proteins (Wood, 2003). Children may be vulnerable to sensitisation due to the immaturity of the immune system at this age (Wood, 2003). It has also been suggested that abnormal permeability of the intestine wall to larger molecules may be a causative factor to sensitisation and is typical of atopic individuals (Jackson et al., 1981). Childhood, therefore, may be a critical time of increased risk of sensitisation in those possessing a genetically programmed predisposition.

Environmental exposure to food protein in early life increases the chance of sensitisation (Arshad, Bateman, & Matthews, 2003). Maternal elimination diets during pregnancy, and also lactation, age of solid food introduction (Fergusson, Horwood, & Shannon, 1990) and breastfeeding have all been found to influence the development of atopy.

Evidence suggests that allergens can pass from a mothers' diet to her child through breast milk and also across the placenta. In a study by Szepfalusi et al. (2000), allergen injections in vitro to the maternal side of the placenta were transferred to the fetal side of the placenta. Infants who were exclusively breast fed have showed cutaneous hypersensitivity to foods (Cant, Marsden & Kilshaw, 1985). Allergens such as peanut and egg proteins have also been detected in breast milk (Cant et al., 1985, Vadas, Wai, Burks, Perelman, 2002).

Maternal dietary interventions for allergy prevention during pregnancy and lactation have had conflicting results. A randomized controlled study by Hide, Matthews, Tariq & Arshad (1996) found that breastfeeding mothers excluding highly antigenic foods from their diet showed significantly less total allergy sensitisation, asthma and eczema at age 1. After follow up at 2 and 4 years, total allergy continued to be higher in the control group. A similar modification intervention has also been found to be successful in preventing allergy (Arshad, Matthews, Gant & Hide, 1992). In this study, mothers eliminated dairy products, eggs, fish and nuts from their diets and also took measures to avoid airborne allergy exposure. The intervention group was four time less likely to develop sensitisation or asthma than the control group.

In a study by Hattevig, Kjellman, Sigurs, Bjorksten & Kjellman, (1989), an intervention group followed a modified maternal diet in the first 3 months postpartum free from eggs, cow's milk and fish. It showed significantly lower rates of atopic dermatitis at 6 months compared to a control but not after this age (Hattevig et al., 1989). Similarly, Lilja et al.(1991) found that maternal egg and cows milk reduction in atopic mothers in the third trimester of pregnancy or in pregnancy and lactation did not influence the immune response in infants.

Clinical guidelines have recommended exclusive breastfeeding for the first 4 – 6 months of life to prevent atopic disease (Prescott & Tang, 2005), however the role of breastfeeding in allergy prevention is still unclear in the scientific literature. Protective factors and allergy inducing factors have both been identified in breast milk (Friedman & Zeiger, 2005). Differences in methodology such as length and exclusiveness of breastfeeding, atopic outcome measured and ages of follow up have also made past studies difficult to compare.

Breastfeeding in those with an atopic history has been found to reduce the risk of asthma and food allergy at age 7 however the risk reversed for asthma at age 14 (Matheson et al., In Press). A non randomized cohort study of 1037 children in New Zealand found any duration of breastfeeding longer than 3 weeks increased the risk of asthma and atopy at age 13 (Sears et al., 2002).

A randomised trial of 13 889 mother-infant pairs found that an increase in breast feeding length and exclusivity in the intervention group had no effect on risk of developing allergic symptoms of asthma, hay fever and eczema or positive SPTs at a follow up of 6 years (Kramer et al., 2007).

Some studies have found a preventative effect of breast feeding on allergy occurrence. Breastfeeding has been found to prevent infantile eczema (Matheson et al., In Press). A Swedish study assessed duration of exclusive and partial breast feeding separately in a birth cohort of 4089 infants (Kull, Wickman**,** Lilja**,** Nordvall **&** Pershagen, 2002). There was a positive effect for breast feeding which was much more profound with extended exclusive breast feeding than partial breast feeding (Kull et al., 2002). A preventative effect of breastfeeding was also found in a 17 year non randomized study (Saarinen & Kajosaari, 1995). Breast feeding for 6 months or longer was associated with less eczema and food allergy at age 1 and 3 compared to breast feeding for less than one month or from 1 up to 6 months (Saarinen & Kajosaari, 1995).

A maternal elimination diet during lactation has been suggested to possibly enhance the beneficial effects of breastfeeding (Kajosaari, 1994). Maternal diet, however, has not been controlled as a confounding variable in studies analysing the role of breastfeeding. Sensitisation through breastfeeding may have influenced past results, contributing to the conflicting findings.

This study aimed to evaluate the effectiveness of a maternal dietary intervention aimed at modifying the risk of atopic symptoms and allergy of siblings of a child with food allergy. It aimed to assess the role of breastfeeding duration for allergy prevention and also to determine if dietary modification influences the effects of breastfeeding on atopic disease.

It was hypothesised that infants whose mother followed the modification program suggested by Royal Prince Alfred Hospital Allergy Unit would be sensitised to fewer food allergens, have lower number of subjects sensitised to any food allergen and a reduced incidence of eczema and asthma than siblings whose mother did not. It was hypothesised that breastfeeding for 6 months or longer would have no protective effect on food sensitization and the incidence of eczema or asthma when compared to those breastfed for a shorter time. It was also hypothesized that the benefits of breastfeeding would be more profound when maternal allergen avoidance was undertaken.

Method

Ethics

This study was approved by the ethics committee of the Central Sydney Area Heath Service.

Subjects

Subjects were selected from an initial total cohort of 2114 patients with eczema and possible food related symptoms who were seen by Dr. Velencia Soutter at the Royal Prince Alfred Hospital Allergy Consulting Rooms from 1992 to 2005. Any additional siblings of these patients not previously recorded, born before October 2007, were included. Subjects included were children aged 0-18 years old with family record

including at least one sibling with a food allergy. Subjects without any Skin Prick Test (SPT) result or modification status were excluded. A Total of 1580 subjects were included in analysis.

Subjects in the modified group were advised by The Royal Prince Alfred Hospital Allergy Unit, after already having an allergic child, to avoid binging on any food in the second half of pregnancy and during breast feeding (Soutter, Swain, & Loblay, 2002). They were advised to avoid egg, all nuts, seeds, cheese and chocolate (Soutter et al, 2002). In this diet, some dairy, fish and lean meat was permitted. Avoiding possible trace amounts of allergen was not prescribed due to the potential of impaired weight gain. Environmental measures were also suggested. These were total cigarette smoke avoidance, a well ventilated household and dust mite precautions.

Atopic disease markers

To assess allergen sensitisation, patients' positive SPT results were used. In a SPT, a drop of protein extract was placed on the forearm and a small prick was made through the drop. A positive skin prick test was defined as a 3mm x 3mm or greater wheal on the skin after 10-15 minutes in the presence of a 3mm x 3mm or greater response to 1% histamine dilution and no response to a 0.9% saline control. The presence or absence of eczema and the presence or absence of asthma at any time during a patient's history were also used as a marker of atopic disease.

Procedure

Information was obtained from patient consultations with Dr Velencia Soutter and patient family records. SPT results for milk, soy, wheat, egg, fish, shellfish, sesame, peanut, other nuts, meat and other food allergies, age when SPT was taken, duration of breast feeding, if maternal modification measures were used during pregnancy and breast feeding, and the presence of eczema and asthma were entered into excel 2000 for each subject. SPT results were sorted into four age categories for each group for SPT sensitisation comparisons;

- SPT taken less than 1year,
- 1 year to less than 2 years,
- 2 years to less than 5 years,
- 5 years and above.

Subjects were also divided into length breastfed for each age group; less than one month, one month up to 6 months and greater than 6 months (Saarinen, Kajosaari, 1995).

Statistical Analysis

Data were analysed using SPSS (SPSS for Windows Version 12.0, September 2003, SPSS Inc. Chicago, Illinois USA). Two tailed analysis were used with a *p*-value of $< .05$ considered statistically significant. Data were analysed for normality using the Shapiro-Wilk test and Levene's test of homogeneity of variance. Non parametric tests were used on data which was not distributed normally. Sibling data were used in between-group analysis. Pearson's Chi-squared test, the computed Odds Ratios (OR) and corresponding 95% Confidence Intervals (CI) were used to compare eczema and asthma and the presence of a positive SPT for each age group. Mann-Whitney U was used to compare the number of positive SPTs between-groups for each age.

Within-group analysis of the effect of breast feeding length on number of positive SPT's was made using Mann-Whitney U test. Within-group comparisons of breastfeeding length and the presence of a positive SPT, eczema or asthma were done using Pearson's Chi-squared test, the computed OR and corresponding 95% CI. All children whose mother had not modified their diet were included in the within-group analysis.

Results

Two hundred and seventy five subjects who were a sibling to a child with food allergy had mothers followed dietary modification guidelines (Modified group). There were 1305 subjects those whose mothers did not follow these guidelines (Non modified group) of which 271 were siblings to a child with a food allergy.

The Number of subjects with a history of eczema or asthma for the Modified and Non modified group are shown in Table 1.

Table 1.

Number of Subjects with a History of Asthma or Eczema

	Modified[a]	Non modified[b]	OR (95% CI)
Eczema	143(52%)	178(66%)	0.57 (0.40-0.80)*
Asthma	37(13%)	93(34%)	0.30 (0.19-0.46)**

Note. n[a] = 275 for modified group. n[b] = 271 for non modified group

*$p < .005$. **$p < .001$.

Siblings in the Modified group showed less eczema (OR, 0.57; CI, 0.40-0.80, $p = .002$) and asthma (OR, 0.30; CI, 0.19-0.46, $p = .0001$) than siblings in the Non modified group.

Comparisons between the Modified and Non modified group of sensitisation to any food and the mean number of food sensitisations are summarised in Figure 1 and Figure 2 respectively.

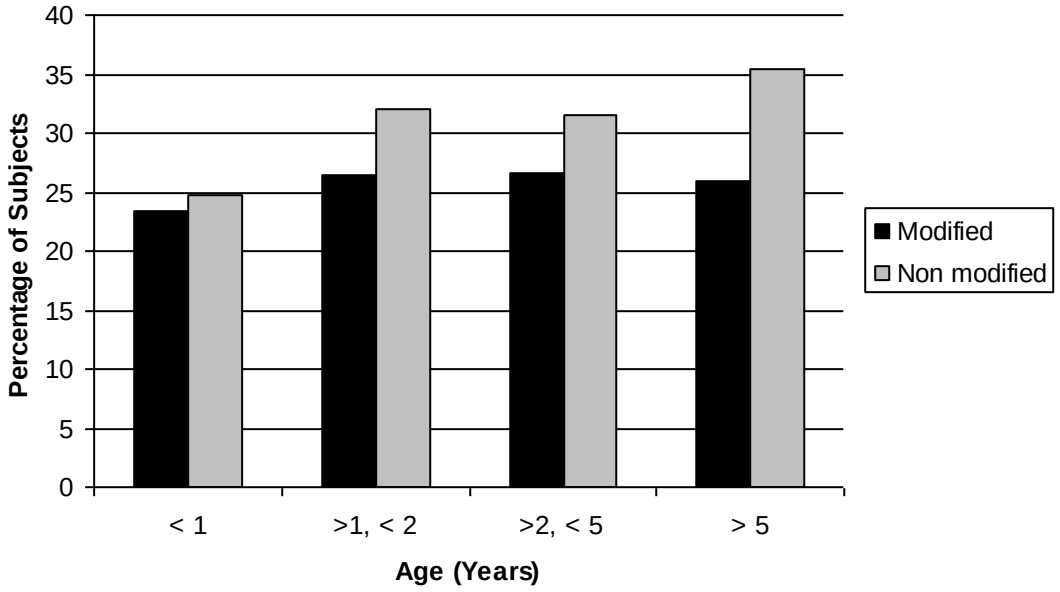

Figure 1. Percentage of subjects with any food allergy as shown as a positive SPT result.

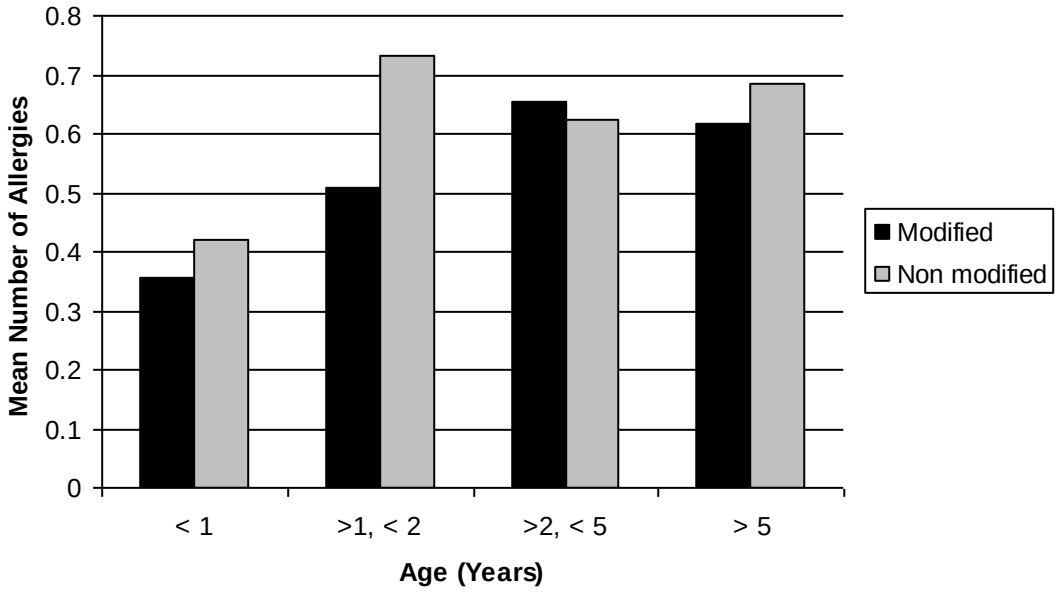

Figure 2. Mean number of sensitisations to foods shown as a positive SPT result.

There were no significant differences in food sensitisation between the Modified and Non modified group for any age. A trend was evident, however, for the Modified group to be

sensitised to less foods and have less subjects who were sensitised to any food than the Non modified group.

Breastfeeding for 6 months or longer was compared to less than one month and from 1 to 6 months in both groups for any influence of the outcome of asthma and eczema. Breastfeeding duration had no effect on asthma or eczema in either group as can be seen in Table 2.

Table 2

Number of Subjects with a History of Eczema and Asthma for Breastfeeding length

	Length of Breastfeeding			
	<1 Month	≥1 Month, <6 Months	≥6 Months	χ^2
No modification				
Eczema	96 (90%)	416 (85%)	583 (82%)	4.65
Asthma	38 (36%)	164 (34%)	261 (37%)	1.36
Modification				
Eczema	7 (53%)	45 (52%)	91 (52%)	0.02
Asthma	2 (15%)	9 (10%)	26 (15%)	1.06

There were no significant differences between outcome measures between a breastfeeding duration of less than one month or from 1 up to 6 months in both groups. To overcome the small sample sizes in the less than one month group, these two groups were pooled together for analysis of food sensitisation.

There was a significant effect for breastfeeding duration on food sensitisation before the age of one. An increase in sensitisation was seen for both the modified and nonmodified group with extended breastfeeding for 6 months or longer. The effect of breastfeeding on the number and presence of sensitisation to foods is shown in Table 3 and Table 4 respectivly for the Non modified group.

Table 3

Mean Number of Food Allergies in the Non Modified Group

	Length of Breastfeeding				
Age (Years)	< 6 Months M	< 6 Months SD	≥ 6 Months M	≥ 6 Months SD	Mann-Whitney U
< 1	1.72	1.52	2.67	1.59	8950*
≥1, < 2	2.56	1.72	2.30	1.76	22124.5
≥ 2, < 5	1.82	1.67	1.94	1.70	76503.5
≥ 5	1.86	1.85	1.84	1.71	61616.5

Note. *$p < .005$

Table 4

Presence of any Food Allergy in the Non Modified Group

Age (Years)	Length of Breastfeeding		
	< 6 months	≥ 6 months	OR (95% CI)
< 1	94 (72%)	141 (82%)	0.56 (0.32-0.96)*
≥ 1, < 2	174 (85%)	185 (85%)	1.00 (0.59-1.705)
≥ 2, < 5	233 (74%)	386 (77%)	0.86 (0.62-1.19)
≥ 5	232 (76%)	302 (74%)	1.12 (0.79-1.57)

Note. *$p < .05$

Those Breastfed for 6 months or longer had sensitisation to more foods in the Non modified group (M=2.38, SD=1.80) than those breastfed for less than 6 months (M=1.72, SD=1.52), U= 8950, p= .002. In this group, there were also more subjects with any

sensitisation to food (82%) when compared to those breastfed for less than 6 months (72%), (OR, 0.56; CI, 0.32-0.96, *p*= .048).

The effect of breastfeeding on the number and presence of sensitisation to foods is shown in Table 5 and Table 6 respectivly for the Modified group.

Table 5

Mean Number of Food Allergies in the Modified Group

	Length of Breastfeeding				
Age (Years)	< 6 Months		≥ 6 Months		
	M	SD	M	SD	Mann-Whitney U
< 1	0.18	0.49	0.45	0.89	1312
≥1, < 2	0.93	1.46	0.94	1.34	1278
≥ 2, < 5	1.55	1.73	0.94	1.48	742.5
≥ 5	1.33	1.59	1.78	2.04	218

Table 6

Presence of any Food Allergy in the Modified Group

Age (Years)	Length of Breastfeeding		
	< 6 months	≥ 6 months	OR (95% CI)
< 1	6 (13%)	17 (26%)	0.32 (0.12-0.84)*
≥ 1, < 2	18 (44%)	21 (32%)	0.82 (0.40-1.67)
≥ 2, < 5	19 (23%)	21 (25%)	0.94 (0.46-1.92)
≥ 5	9 (24%)	12 (32%)	0.67 (0.24-1.9)

Note. *p< .05.

Those Breastfed for longer than 6 months had more subjects in the modified group (26%) than those breastfed for a shorter time (13%) showing sensitisation to any food allergy (OR, 0.32; CI, 0.12-0.84, $p = .028$). There was no effect of breastfeeding on SPT results after this age.

Discussion

This study aimed to evaluate the effectiveness of a maternal dietary intervention. It also aimed to assess the role of breastfeeding duration for allergy prevention and to determine if dietary modification influences the effects of breastfeeding on atopic disease. Modification appeared to reduce the development of eczema and asthma with a trend for less food sensitisation. Breastfeeding had no effect on allergy markers after age 1. In those less than 1, a breastfeeding duration for 6 months or longer increased food sensitization rates. This effect was more evident in the Non modified group.

The results of this study are in support of the original hypothesis where modification guidelines suggested by Royal Prince Alfred Hospital Allergy Unit were beneficial in reducing the incidence of eczema and asthma. Modification also appeared to reduce food sensitization, however these findings were not significant.

These results are similar to those of Hide et al (1996) and Arshad et al., (1992) whereby excluding highly antigenic foods from the diet while breastfeeding prevented infantile eczema and asthma. In contrary to Hide et al (1996) and Arshad et al., (1992), this study failed to show significantly less food sensitisation in early childhood with modification. This may be due to the nature of the intervention. For practical reasons, trace amounts of food allergen were allowed within the modification recommendations which may have caused some sensitisation. The severity of food allergy was not considered in these studies which could potentially be reduced with maternal modification.

Some past studies have found no effect of maternal modification on any allergy markers. This can be explained by their study design. Hattevig et al., (1989) used a modification intervention duration of 3 months, after which a child could be sensitised through breast milk when their mothers' diet returned to normal. The intervention group had a small

sample size (n=65) which may have also prevented any significant findings. Lilja et al.(1991) found no effect with maternal egg and cows milk reduction. A more stringent dietary guideline may be necessary in order to prevent allergenic proteins being transferred to a child causing sensitisation.

The results of this study do not support the original hypothesis of a protective effect of breastfeeding. Breastfeeding duration had no impact on eczema or asthma. These findings were similar to Kramer et al., (2007). Evidence has been contradictory on these markers mainly due to age at follow up. The effects of breastfeeding may potentially change during childhood from a protective effect to one of increased allergy risk in adolescence (Matheson et al., In Press & Sears et al., 2002). Due to the nature of the data, age comparisons of eczema and asthma were not able to be made.

In cotradiction to the original hypothesis, breastfeeding was a risk factor for sensitisation before the age of one with no effect after this age. This finding was inconsistent with past studies which found a preventative effect of extended breastfeeding duration on food sensitisation (Matheson et al., In Press, Kull, et al., 2002, Saarinen & Kajosaari, 1995). Since it is not possible to truly randomise a study on breastfeeding length due to ethical considerations, there may be some characteristics of women who choose to breastfeed for a longer period which impacted on allergy outcomes. Those mothers following suggested breastfeeding guidelines may be more heath conscious and more aware of atopic risk factors.

The findings of the present study suggest that allergens in breast milk may be sensitising infants. In those breastfed for a longer duration, there was an increased time period for potential senstisation through breast milk, however, after this age breastfeeding duration did not affect allergy outcomes.

The Hygiene hypothesis may also provide some explanation for the increased risk of sensitisation among those breastfed for 6 months or longer. Breast milk may provide antiviral antibodies and other factors which reduce the incidence of infections. Those

who are breastfed are also more likely to be at home with their parent, away from childcare centres, lowering the risk of infection (Friedman & Zeiger,2005). Frequent infections in early childhood may be protective against allergy development, stimulating a T_H1 immune pathway (Strachan, 2000). A T_H2 immune pathway may increase the risk of allergy in those not exposed to infections. Extended breastfeeding, therefore, may prevent an allergy prone child to develop the normal T_H1 immune pathway which increases the risk of allergy.

It was also hypothesised that an extended breastfeeding duration for 6 months or longer would be more beneficial when maternal allergen avoidance was undertaken. Breastfeeding still remained a risk factor for sensitisation before age 1, however, the risk was not as profound in the modified group. Modification prevented the increased number of sensitisations to food allergens that accompanied longer breastfeeding in the non modified group. This suggests that sensitising allergens in breast milk play role in increasing allergy outcomes in children.

Future research examining the interaction between modification and breastfeeding for allergy outcomes could use age marked asthma and eczema to provide insight on any age related changes. A more strict maternal diet may provide additional sensitisation protection. The benefits of such a diet and the feasibility of the option for application would need to be assessed. Future research could also look at the severity of food allergy as a dependant variable of modification and breastfeeding.

Conclusion

A maternal modified diet in the second half of pregnancy and during lactation can be recommended to families at high risk as it may help prevent eczema and asthma. Extended breastfeeding can not be recommended as a means to prevent allergy. Breastfeeding for 6 months and longer may be a risk factor for food sensitisation before the age of one in high risk children, especially when no dietary avoidance measures are taken. Breastfeeding however still has many health benefits to an infant for neural development and chronic disease (Kemp & Kakakios, 2004) and its avoidance is not warranted by these findings.

References

Arshad, S. H., Matthews, S., Gant, C. & Hide, D. W. (1992) Effect of allergen avoidance on development of allergic disorders in infancy. *The Lancet*, *339*(8808), 1493-1497.

Arshad, S. H., Stevens, M., Hide, D. W. (1993). The effect of genetic and environmental factors on the prevalence of allergic disorders at the age of two years. *Clinical & Experimental Allergy*, *23*(6), 504–511.

Cant, A., Marsden, R. A., & Kilshaw, P. J. (1985). Egg and cows' milk hypersensitivity in exclusively breast fed infants with eczema, and detection of egg protein in breast milk. *British Medical Journal*, *291*(6500), 932–935.

Clark, A.T., & Ewan, P.W. (2003). Food allergy in childhood: have the dangers been underestimated? *Archives of Disease in Childhood*, *88*(1), 79-81.

Hattevig, G., Kjellman, B., Sigurs, N., Bjorksten, B., & Kjellman, N. I. M. (1989). Effect of maternal avoidance of eggs, cow's milk and fish during lactation upon allergic manifestations in infants. *Clinical & Experimental Allergy*, *19*(1), 27–32.

Fergusson, D. M., Horwood, L. J., & Shannon, F. T. (1990). Early solid feeding and recurrent childhood eczema: A 10-year longitudinal study. *Pediatrics*, *86*(4), 541-546.

Freidman, N. J. & Zeiger, R. S. (2005). The role of breast-feeding in the development of allergies and asthma. *Journal of Allergy and Clinical Immunology*, *115*(6), 1238-1248.

Hide, D. W., Matthews, S., Tariq, S., Arshad S. H. (1996). Allergen avoidance in infancy and allergy at 4 years of age. *Allergy*, *51*(2), 89–93.

Hill, D. J., Hosking, C. S., Zhie, C.Y., Leung, R., Baratwidjaja, K., Iikura, Y., Iyngkaran, N., Gonzalez-Andaya, A., Wah, L. B., Hsieh, K. H. (1997). The frequency of food allergy in Australia and Asia. *Environmental Toxicology and Pharmacology*, *4*, 101–110.

Jackson, P. G., Lessof, M. H., Baker, R. W., Ferrett, J., MacDonald, D. M. (1981). Intestinal permeability in patients with eczema and food allergy. *The Lancet*, *13*(1), 1285-6.

Kajosaari, M. (1994). Atopy prevention in childhood: the role of diet. Prospective 5-year follow-up of high-risk infants with six months exclusive breastfeeding and solid food elimination. *Pediatric Allergy and Immunology, 5* (Suppl 1), 26-28.

Kemp, A. & Kakakios, A. (2004). *Journal of Pediatrics and Child Health, 40*(7), 337-339.

Kramer, M. S., Matush, L., Vanilovich, I., Platt, R., Bogdanovich, N., Sevkovskaya, Z., Dzikovich, I., Shishko, G., & Mazer, B. (2007). Effect of prolonged and exclusive breast feeding on risk of allergy and asthma: Cluster randomised trial. *BMJ online, 11 September 2007*, available; http://www.bmj.com/cgi/content/full/bmj.39304.464016.AEv1

Kull, I., Wickman, M., Lilja, G., Nordvall, S. L., Pershagen, G. (2002). Breast feeding and allergic diseases in infants—a prospective birth cohort study. *Archives of Disease in Childhood, 87*, 478-481.

Lilja, G., Dannaeus, A., Foucard, T., Graff-Lonnevig, V., Johansson, S. G. O., Öman H. (1991). Effects of maternal diet during late pregnancy and lactation on the development of IgE and egg and milk specific IgE and IgG antibodies in infants. *Clinical & Experimental Allergy, 21*(2), 195–202.

Matherson, M.C., Erbas, B., Balasuriya, A., Jenkins, M. A., Whaarton, C. L., Tang, M. L., Abramson, MJ., Walters, E. H., Hopper, J. L. & Dharmage, S. C. (In Press) Breastfeeding and atopic disease: A cohort study from childhood to middle age. Journal of Clinical Immunology.

Prescott, S. L., Tang, M. L. K. (2005). The Australasian Society of Clinical Immunology and Allergy position statement: summary of allergy prevention in children. *Medical Journal of Australia, 182*, 464-467.

Saarinen, U. M., Kajosaari, M., (1995). Breastfeeding as prophylaxis against atopic disease: prospective follow-up study until 17 years old. *The Lancet, 46*(8982):1065-9.

Sears, M. R., Greene, J. M., Willan, A. R., Taylor, D. R., Flannery, E. M., Cowan, J. O., Herbison, G. P., & Poulton, R. (2002). Long-term relation between breastfeeding and development of atopy and asthma in children and young adults: a longitudinal study. *The Lancet, 360*(9337), 901.

Sicherer, S. H., Furlong, T. J., Maes, H. H., Desnick, R. J., Sampson, H. A. &. Gelb, B. D. (2000). Genetics of peanut allergy: A twin study. *Journal of Allergy and Clinical Immunology, 106(1),* 53-56.

Soutter, V., Swain, A., & Loblay, R. (2002) *Food Allergy Prevention,* Royal Prince Alfred Hospital Allergy Unit, Camperdown.

Strachan, D. P. (2000). Family size, infection and atopy: the first decade of the "hygiene hypothesis". *Thorax, 55*(Supp 1), 2-10.

Szepfalusi, Z., Loibichler, C., Pichler, J., Reisenberger, K., Ebner, C., Urbanek, R. (2000). Direct evidence for transplacental allergen transfer. Pediatric Research, 48(3), 404-407.

Vadas, P., Wai, Y., Burks, W., Perelman, B., (2001). Detection of peanut allergens in breast milk of lactating women. *Journal of the American Medical Association, 285*, 1746-1748.

Wood, R. A. (2003). The Natural History of Food Allergy. *Pediatrics, 111*(6), 1631-1637.

Zeiger, R. S. (2003). Food Allergen Avoidance in the Prevention of Food Allergy in Infants and Children. *Pediatrics, 111*(6), 1662-1671.