

Persistent nausea and food aversions in pregnancy

A possible association with cow's milk allergy in infants

JUDITH M. BAYLIS, A. R. LEEDS *and* D. N. CHALLACOMBE

Department of Nutrition, Queen Elizabeth College, London, and Somerset Children's Research Unit, Musgrove Park Hospital, Taunton, Somerset

(Received 22 March 1982; accepted for publication 18 May 1982)

Summary

In a retrospective study the mothers of twenty-one children with well-defined cow's milk allergy and an equal number of matched controls were asked about their health and diet in pregnancy and the pattern of feeding of their children in infancy. Corroborative evidence was obtained from the medical notes. Nausea in pregnancy was found to be more persistent and atopic disease more common among the mothers of the milk allergic children; in this group food aversions during pregnancy were also more common particularly to dairy produce. The milk-allergic infants had been breast-fed for longer and had cow's milk introduced into feeds later than the control group. It is suggested that nausea in pregnancy may be a physiological response to foetal sensitization by dietary antigens such as cow's milk protein, due to impaired placental permeability in atopic pregnant women. A larger prospective study is indicated to substantiate this hypothesis.

Introduction

Feeding problems in infancy have, for many years, been recognized as being associated with intolerance to cow's milk which may be due to an allergic reaction to one or more of the proteins in the milk. Allergic reactions to food are very diverse and variable in severity. In cow's milk allergy, projectile vomiting or regurgitation of feeds may be accompanied by chronic diarrhoea, colic, a reluctance to feed, periods of prolonged screaming and a poor sleep pattern. A degree of eczema, urticaria, severe nappy rash and excessive pallor may be apparent. A history of recurrent respiratory infections and a degree of malnutrition may be prominent.

The mechanism of the allergic reaction has been the subject of much research and interest has been shown in the permeability of the intestinal mucosa. It has recently been shown that intestinal permeability in eczematous patients, with or without food allergy, could be impaired (Jackson *et al.*, 1981). It seems reasonable to suggest that placental permeability may be similarly impaired in some women allowing large

Correspondence: Dr A. R. Leeds, Department of Nutrition, Queen Elizabeth College, London W8 7AH.

molecules, such as milk protein, to reach the foetus. It has been shown that placental transmission of dietary antigens occurs in rats and rabbits (Hemmings & Kulangara, 1978).

Evidence for intra-uterine sensitization has been put forward in a study which showed high agglutination antibody titres to some dietary antigens in amniotic fluid (Matsumura *et al.*, 1975). It is known that maternal IgG antibodies can be transferred across the placenta to provide the infant with a passive immunity in the neonatal period. Measurement of IgG antibodies to β -lactoglobulin in cow's milk in atopic maternal and cord sera indicates transport across the placenta and 50% of the infants studied developed atopy by the age of 2 years (Dannaeus, Johansson & Foucard, 1978). If impaired placental permeability in atopic pregnant women exists and allows dietary antigens and antibodies to reach the foetus, a reaction could be set up to form abnormal immune complexes.

Vomiting by the mother in pregnancy could be regarded as a physiological response to foetal sensitization by dietary antigens. Severe vomiting in pregnancy has been associated with raised levels of human chorionic gonadotrophin (HCG) and it is suggested that vomiting commences when a threshold level of the hormone is produced by the placenta (Kauppila, Huhtaniemi & Ylikerkala, 1979). HCG may influence reduced lymphocyte responsiveness to antigens and may have a role in foetal protection (Stern, 1976). After birth a sensitized infant could develop clinical symptoms of milk allergy on further exposure to the antigen present in cow's milk formula feeds or possibly to antigens in the mother's breast milk (Jakobsson & Lindberg, 1978).

The hypothesis would be supported if those mothers with a personal or family history of atopy suffered vomiting in pregnancy and their infants developed the feeding problems associated with cow's milk allergy.

Patients and methods

The twenty-one subjects for the study were selected from the medical records of children with well-defined cow's milk allergy. The diagnosis, made at Musgrove Park Hospital, Taunton, was based on a convincing clinical history, a positive radioallergo-sorbent (RAST) test to cow's milk and a good response to dietary treatment. Small intestinal biopsy in ten cases revealed histological changes compatible with cow's milk allergy. All children had IgE levels higher than the normal level for age but levels of other immunoglobulins, where measured, showed no characteristic pattern. At the time of the study, the children (sixteen males, five females) ranged in age from 1 year 5 months to 5 years 5 months.

Twenty-one children were selected from the register of immunizations and vaccinations for the Health District to act as controls. Each control was drawn from the same general practice as the subject and matched for age, sex and parity (13 para 1, 7 para 2, 1 para 3).

The mothers were interviewed concerning their diet and health during pregnancy, in particular the frequency, daily pattern and duration of nausea and vomiting. Maternal age during pregnancy ranged from 21–35 years (median 26 years) in the subject group and 17–43 years (median 26 years) in the controls. Birth weights ranged from 2.25–4.18 kg (median 3.35 kg) in the subject group and 2.35–3.8 kg (median 3.4 kg) in the control group. The pattern of feeding and the development of the clinical signs associated with allergy in the children were included in the interview.

The information given at the interview was substantiated with data from the medical notes and information given by the family practitioner and health visitor. Non-parametric statistics were used to analyse the results: Wilcoxon matched-pairs, signed-ranks test and χ^2 test (Siegel, 1956).

Results

Eighteen subject and eighteen control infants were breast-fed. The duration in the subject group was from 2 days to 18 months (median 16 weeks) and in the control group from 3 days to 8 months (median 11 weeks). All the children were given cow's milk before breast-feeding ceased. Two subjects and one control were complemented with a formula feed from birth. The subjects were exclusively breast fed for longer (median 16 weeks, range 1–20 weeks), than the controls (median 6 weeks, range 1–14 weeks) ($P < 0.005$, Wilcoxon matched-pairs, signed-ranks test) (Fig. 1). Also, cow's milk was introduced into the feed of the subject group later than the controls ($P = < 0.05$ Wilcoxon matched-pairs, signed-ranks test) (Fig. 2), however there were two clusters in the subject group, one at 16 weeks and the other at zero.

The presence of a family history of atopy was found in all subjects and twelve controls and atopic disease was more common in the mothers of the subjects ($\chi^2 = 4.05$ $P = < 0.05$).

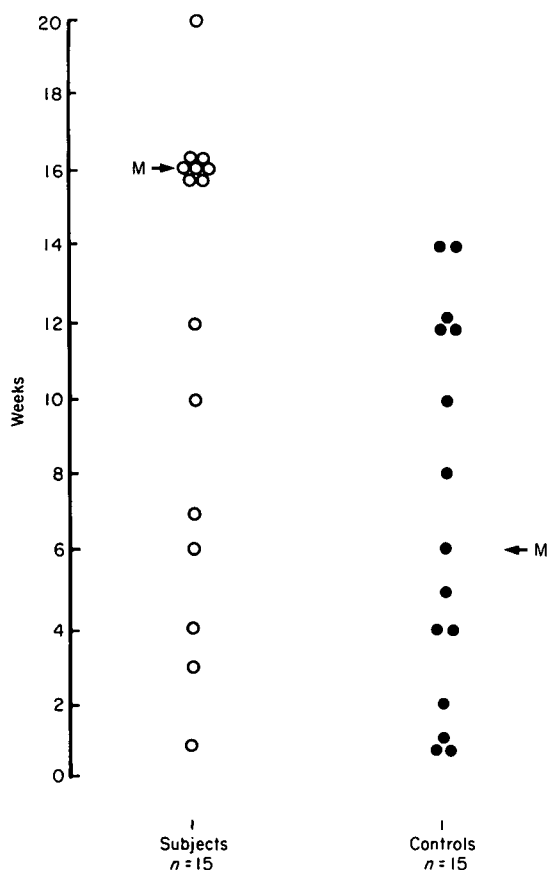


Fig. 1. Duration of exclusive breast-feeding in the breast fed infants (weeks). M, median value.

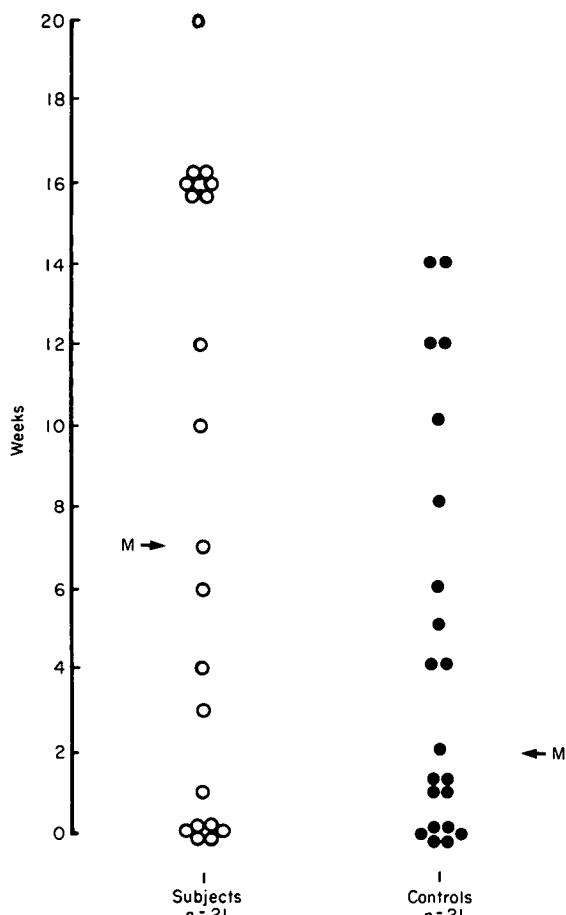


Fig. 2. Age of introduction to cows milk (weeks). M, median value.

The mothers of seventeen subjects and sixteen controls complained of nausea at some time during their pregnancy. There was no difference in the incidence and frequency of vomiting between the two groups but nausea was more persistent throughout the day in the subject group ($\chi^2=9.33$, $P<0.01$) (Fig. 3).

The types of food for which mothers developed an aversion during pregnancy are shown in Fig. 4. Food aversions developed in eighteen mothers in the subject group and nine in the control group. Thirteen in each group declared that they had made a conscious effort to increase their intake of cow's milk during pregnancy. A normal dislike of milk and dairy produce was stated by seven mothers in the subject group who estimated their milk intake to be less than $\frac{1}{4}$ pint a day. All the mothers in the control group said they regularly consumed more than this amount together with other dairy produce.

Discussion

The clinical signs were found to be more prevalent and specific in the subject group as was to be expected. Severity of a symptom is difficult to quantify. Measurement could

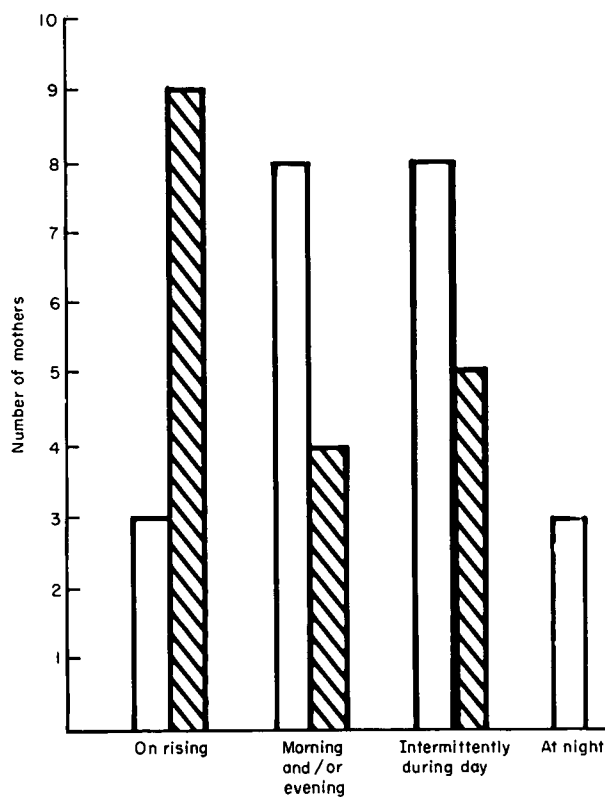


Fig. 3. Occurrence of nausea during 24-hr period. □, Subjects; ▨, controls.

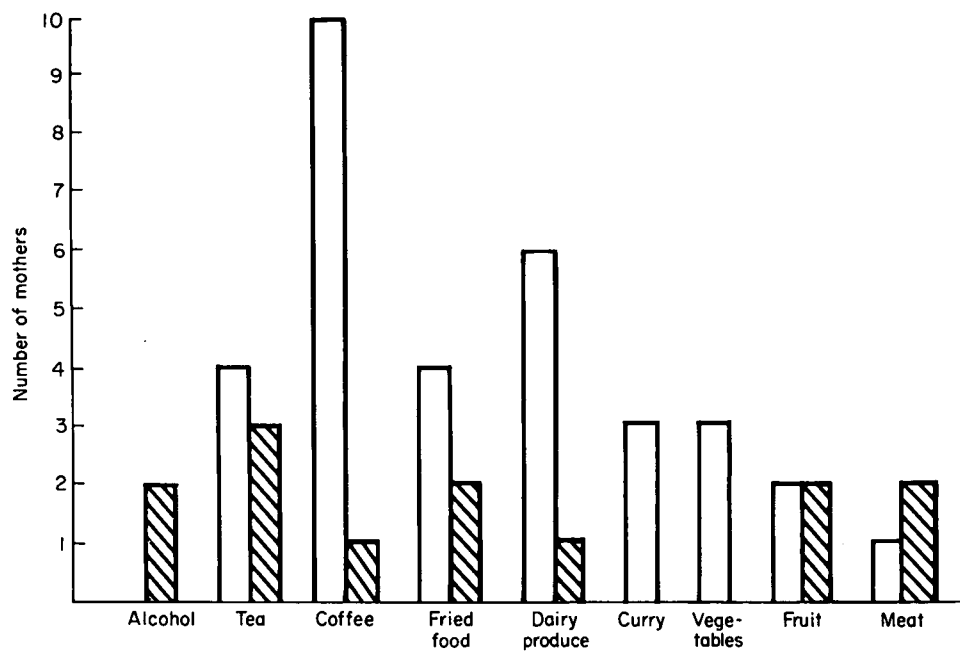


Fig. 4. Aversion to food in pregnancy. □, Subjects; ▨, controls.

be based on the duration of symptoms but the difficulty in obtaining accurate information and the natural history of some signs, such as eczema, make this an imprecise criterion to use. Early age of onset does not necessarily imply severity. Vomiting from birth could be projectile with resultant dehydration and failure to thrive, or slight regurgitation of feeds causing no such problems.

Prolonged breast-feeding has been shown to delay the onset of atopic disease, particularly for those with a family history of atopy (Saarinen *et al.*, 1979). In our study the allergic infants had been exclusively breast-fed for longer and had cow's milk introduced later than the non-allergic group, however, in Fig. 2 the values for the subjects cluster at 0 and 16 weeks, suggesting two distinct groups. Without the 16-week cluster the distribution of values is very like that of the control values, and it is possible that the 16-week cluster reflects the knowledge of some mothers of allergic children about the possible value of prolonged breast-feeding and later introduction to cow's milk. The results do however seem to suggest that potentially allergic infants will develop clinical allergy at whatever age cow's milk is introduced. Every effort was made to determine accurately the age of introduction to cow's milk for it has been known for breast-fed infants to be given an unrecorded formula feed during the first 10 days of life. Some infants whose onset of symptoms cannot be related to the introduction of cow's milk may have been sensitized by milk allergens present in the mothers breast milk.

This study shows that children with cow's milk allergy are more likely to have mothers with a personal history of atopy and are more likely to have other relatives with atopic disease. This finding has also been observed in a prospective study in which it was concluded that a negative family history was the best assurance against acquiring allergic disease (Hide & Guyer, 1981).

Although there was no difference between the incidences of vomiting in the two groups nausea was more persistent throughout the day in the subject group. Though vomiting is inextricably linked with nausea many people seem to develop a resistance to vomiting even when very nauseated, and this may account for inconsistency between the findings for nausea and vomiting.

Food aversions were significantly more common among mothers of the subjects. The marked aversion to coffee has been reported elsewhere (Hook, 1978) although aversion to dairy produce was not mentioned by any of 250 women in that study; however 4% said they had decreased their intake of milk during pregnancy. In our study six of twenty-one mothers in the subject group and only one of twenty-one in the control group developed an aversion to dairy produce. Since tea and coffee are vehicles for milk in some individuals the aversion to tea and coffee may also reflect aversion to milk. Unfortunately in this study no record was kept of whether tea and coffee were taken with, or without milk. It is interesting to speculate that an aversion to some foods may develop as a physiological response to provide foetal protection against dietary antigens. A specific study to measure the dietary intake of dairy produce in atopic pregnant women may provide useful data or further clues.

The limitations of this study are well recognized. Some mothers were asked to recall details of at least 5 years previously and may have confused these with subsequent pregnancies. However, it was surprising how closely the information given by the mothers agreed with information which had been recorded at the time in the medical notes. A larger prospective study to follow mothers through pregnancy and their offspring through infancy would provide accurate and interesting evidence towards

establishing whether or not a relationship between nausea and vomiting in pregnant, atopic women and food allergy in their infants does exist.

Acknowledgments

We are grateful to Farley Health Products Ltd, Plymouth for their support of this work, and to Mrs J. Glass, Ms Susan Elliott and Mike Etherington for preparing the typescript, figures and plates respectively. Professor A.E. Bender and Dr Patricia A. Judd gave helpful advice.

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