

Milk Allergy: Clinical Picture and Familial Incidence

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THE clinical manifestations of a sensitivity to cow's milk have already been well documented,¹⁻⁶ and well recognized by allergists. However, many of their colleagues in pediatric and general practice are unaware of the importance of this sensitivity as a cause of recurrent gastrointestinal and respiratory disease in infants and children. In studying such patients we noted that four features were commonly present: (1) the disorder usually had its onset soon after the initial feeding of cow's milk or of a formula derived from cow's milk; (2) the child who is sensitive to cow's milk is also often sensitive to foods other than milk; (3) a parent or grandparent of such a child is often reluctant to drink milk, and (4) other relatives are frequently known to be sensitive to milk.

To determine whether the above impressions were valid, it was decided to analyze the pertinent data of a consecutive series of 150 milk-sensitive subjects. The analysis forms the basis of this paper.

MATERIALS AND METHODS

The material is based on data derived from 150 infants and children seen in consultative practice over a 10-year period. The children usually presented with vomiting, diarrhea, recurrent respiratory infections, asthma, eczema, or some combination of these. The symptoms subsided completely with the elimination of milk and dairy products from the diet, and returned when the patient was again given cow's milk. In many instances other foods also caused respiratory and gastrointestinal symptoms. When this was the case, these foods also had to be excluded from the diet before the child was symptom-free. Once a suitable formula had been found for the baby, the original symptoms could always be made to recur by giving the baby cow's milk. This challenge was always carried out with unboiled homogenized milk and not

with a prepared formula. Most prepared formulas have been heat-treated so that the proteins are modified; they may also contain various additives not present in cow's milk. Thus an infant may be insensitive to the prepared formula and yet sensitive to unmodified cow's milk; the converse also obtains. Studies by skin tests and tests for passive transfer and precipitins,⁷ and more recently for passive cutaneous anaphylaxis, were carried out in some of the children, but as these studies were not found reliable in establishing or excluding the diagnosis of sensitivity to cow's milk they were discontinued. These findings are in keeping with the studies of others.^{8,9} The biological test, i.e. the reaction of the child to the feeding of whole cow's milk, was therefore the sole basis on which the diagnosis of milk-sensitivity was established. The challenge with milk was carried out when the child had fully recovered from his initial illness; in cases of doubt it was repeated. Repeated challenges with cow's milk were not carried out routinely, for the child had often been ill for a considerable time and had not responded to any other form of treatment. When taken off milk, he was symptom-free for the first time. In many instances the challenge was repeated by parents at their own volition because they doubted that cow's milk could make a child ill. Later the challenge was repeated at our instigation to determine whether the child was still sensitive to milk.

The symptoms with which these children presented may be caused by various non-allergic diseases, and studies were carried out to exclude such disorders. No child, for example, had an infectious gastroenteritis, none had celiac disease or fibrocystic disease of the pancreas, and none had agammaglobulinemia. None, as far as we could determine, had intolerance to lactose. The clinical features of the latter disorder resemble those found in diarrhea due to cow's milk sensitivity. For this reason all infants with diarrhea seen in the early part of the study were offered breast milk and/or lactose; all remained symptom-free on such formulas. It was therefore assumed that some factor in milk other than lactose was responsible for the diarrhea. In the latter part of the study lactose deficiency was excluded in many of the babies by a study of the disaccharidase activity of the small bowel mucosa.¹⁰

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The material was analyzed and the following information extracted: (1) the presenting symptoms; (2) the time between the first introduction to cow's milk, either in the form of a formula or as ordinary cow's milk, and the onset of symptoms; (3) the time between establishing the diagnosis of sensitivity to milk and recovery, i.e. the development of tolerance to milk; (4) evidence of sensitivity to other foods with particular reference to soya bean products; (5) the incidence of milk sensitivity in parents and siblings; (6) the attitudes to milk of the parents of the milk-sensitive child; and (7) the attitudes of the parents toward milk as well as the incidence of sensitivity to milk in parents and children, as compared with similar findings in 100 families seen consecutively in the outpatient department. The children in these latter families presented with diseases such as mongolism, mental retardation and congenital anomalies which are considered to be unrelated to sensitivity to milk. Although the latter patients are referred to as controls, they are not strictly control subjects; they are used simply for comparison. When sensitivity to milk was suspected in these "control" subjects, it was confirmed by first demonstrating the relief of symptoms when milk and dairy products were excluded from the diet, and their recurrence when these products were re-introduced. Milk sensitivity in these patients was always an incidental finding and was not the cause of the child's main disability.

RESULTS

Modes of Presentation

Most children presented with more than one symptom; for example, vomiting was often associated with diarrhea, or recurrent pneumonia with gastroenteritis. In Table I it will be noted that there are twice as many presenting symptoms as there are cases. In all instances the symptoms were precipitated by milk, they subsided when milk was discontinued and they returned when the child was once more challenged with milk. It cannot be assumed from these data that eczema is a less common manifestation of sensitivity to milk than, for example, recurrent bronchitis, since children with eczema may often be referred directly to the derma-

TABLE I.—PRESENTING SYMPTOMS IN
150 MILK-SENSITIVE SUBJECTS

Diarrhea	50
Diarrhea with obvious blood	20
Vomiting	51
Recurrent bronchitis	79
Rhinorrhea	43
Colic and abdominal pain	28
Asthma	26
Eczema	20

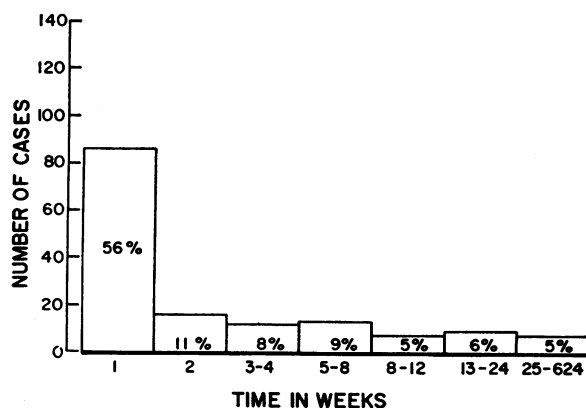


Fig. 1.—Time between first exposure to milk and onset of symptoms.

tologist. Anemia, though on occasion due to sensitivity to cow's milk, was not considered a presenting symptom.

Relationship Between Introduction of Formula and Onset of Symptoms

The presenting symptoms in 56% of the children followed either immediately after the first feeding or within a week of the introduction of formula (Fig. 1). Some children were symptom-free on a prepared formula and developed symptoms only after the introduction of ordinary cow's milk. One baby, the sibling of four other known milk-sensitive children, was watched and followed carefully when offered her first feeding of formula at the age of 24 hours. She took it readily, but immediately coughed and sneezed. During the course of the next three days she developed a bronchiolitis. Her symptoms disappeared only after the exclusion of milk from her diet. Not all children develop their symptoms immediately; in some there is a latent period. The longest latent period noted in the families studied was that of a grandmother who had been able to take milk and remain symptom-free until she was 42 years of age, when she developed asthma which only cleared after milk and dairy products had been excluded from her diet.

Time from Onset of Symptoms to Loss of Sensitivity to Milk (Fig. 2)

A few of the children recovered spontaneously in the course of a few months. These children had only to be taken off milk for this period after which they were able to tolerate it in abundance and remain symptom-free. One of the most sensitive infants made a spontaneous recovery in this way. Many children, however, did not make such rapid and complete recoveries, and only during the course of several years, possibly by a process of hyposensitization,

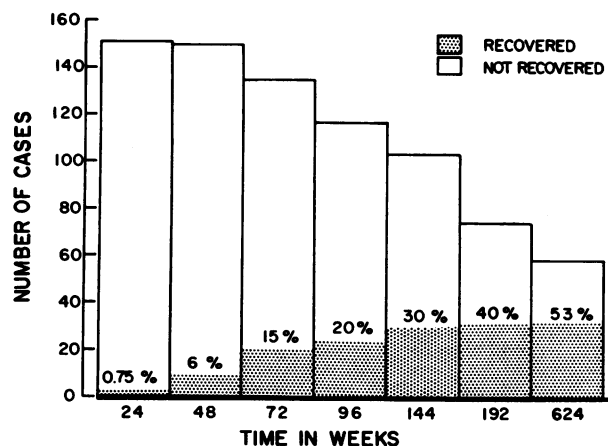


Fig. 2.—Time from onset of symptoms to recovery.

became tolerant to milk. Thirty (40%) of 75 children followed through to the age of 3 $\frac{3}{4}$ years and 53% of the children followed through to the age of 12 years had lost their sensitivity to milk. Some children may never lose their sensitivity to milk, and in this respect may resemble some of the parents in this study who are still sensitive to milk.

Sensitivity to Other Foods

As mentioned previously, milk-sensitive children are frequently sensitive to other foods. Table II illustrates a few of the foods to which some children in this study were sensitive. Data are available only for the foods listed; these foods were selected as ones to which hypersensitivity is relatively common. Not every child was challenged with these foods, but when they

TABLE II.—COMMON FOODS TO WHICH A SENSITIVITY WAS OBSERVED IN MILK-SENSITIVE CHILDREN

Soya-bean preparations	27
Egg	11
Wheat	10
Rice	8
Oats	8
Beef	7
Chicken	4

were and an allergic reaction occurred, this was noted together with the reaction. Soya-bean preparations were included because earlier experience had indicated that sensitivity to them was not uncommon. From the table it might appear that soya preparations are less well tolerated than other foods, but this is not necessarily the case, for if any other single food had been given repeatedly and in large quantities, as soya preparations were, a greater incidence of sensitivity to them would most likely have been observed.

Soya preparations are, however, far from innocuous. Of 75 babies to whom these prepara-

tions were given, 27 were sensitive either to them or to other substances incorporated in the formula. The clinical reactions of the 27 babies to soya are listed in Table III.

TABLE III.—REACTIONS OF 27 MILK-SENSITIVE INFANTS TO SOYA BEAN FORMULAS

Diarrhea	20
Vomiting	14
Asthma	9
Eczema	6
Bronchitis	3

In all of these cases the symptoms were precipitated when the child was given the soya preparation and subsided when the preparation was discontinued. In some instances the child reacted in the same way, for example with diarrhea, bronchitis or asthma, to both cow's milk and to soya; in other instances the child reacted differently to both, for example developing vomiting and diarrhea while on cow's milk and eczema when on a soya formula.

Attitudes of Parents to Milk

Many parents of the milk-sensitive children were reluctant to drink milk; some quite frankly hated it. The attitudes of the parents and those of the controls are listed in Fig. 3. The parents were not asked whether they drank milk but whether they liked it; in some instances this question was posed when it was already known that the child was sensitive to milk; in other instances the question was asked when the nature of the child's disease was not known. Some parents who did not like milk, had milk on cereals or in coffee; others avoided it com-

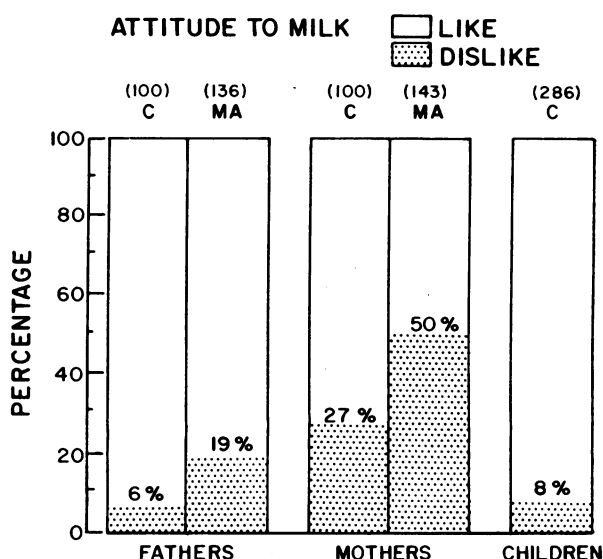


Fig. 3.—Attitudes toward milk of the parents of control children (C), of the parents of milk-sensitive children (MA) and of the control children (C).

pletely. Not all who liked milk drank it; some avoided it because they considered it to be fattening. Some parents indicated that they liked milk, but were only prepared to drink it if it was ice-cold; such parents often found warm milk nauseating. These parents are included among those who like milk. Six per cent of the fathers of the so-called "control" children did not like milk and 19% of the fathers of children allergic to milk disliked it; 27% of the mothers of "control" children did not like milk, whereas 50% of the mothers of the milk-sensitive children disliked it. In the control families the proportions of fathers and sons who disliked milk are the same; the proportions of mothers and daughters are not. From these figures it seems probable that approximately 20% of the girls who like milk will, when they reach adulthood, dislike it. Why this should be so is not clear.

Incidence of Milk Sensitivity in the Parents and Controls (Fig. 4)

It was not possible to study mothers and fathers of four of the milk-sensitive children because the children were adopted; in addition three mothers and 10 fathers were inaccessible. One mother, a physician, when first seen was aware that she was sensitive to milk, because drinking cow's milk had caused a persistent urticaria. The remainder of the parents did not know that they were in fact sensitive to milk. It was not therefore possible, when interviewing parents, to ask simply "Are either of you sensitive to milk?" and to take their answer at its face value. An enquiry had to be made into the health of the parents. Those who appeared to have symptoms, for example a recurrent rhinorrhea, that might be referable to milk were asked to discontinue taking milk and dairy products for a trial period of a month, to make a note of any change in symptomatology, and then, a month later, to start drinking milk again in abundance. Those who were sensitive to milk were surprised to discover that what they had believed to be, for example, a smoker's cough, cleared completely in the course of two to three weeks on a milk-free regimen, and returned promptly when milk was taken again. Unexpected changes also occurred in bowel habits. For example, a father who thought that he had an "irritable" colon and who had had to visit the toilet three to five times a day and who experienced indigestion and pruritus ani, found that on a milk-free regimen his stools became formed and were passed only once daily and that his pruritus ani subsided. The studies on parents were time-consuming but rewarding. The

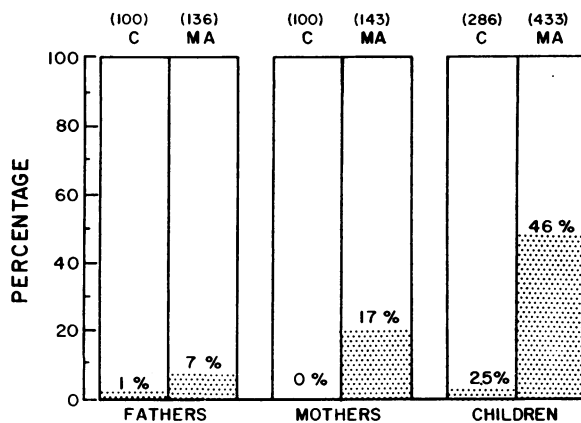


Fig. 4.—Incidence of milk sensitivity in the parents and children of the control (C) and of the milk-sensitive (MA) families.

incidence of these sensitivities may be higher than the data indicate, for only those parents suspected of being sensitive to milk were taken off milk and later challenged. Only one of the control fathers was sensitive to milk, whereas 7% of the fathers of milk-allergic children were sensitive to it; none of the control mothers were sensitive to milk, whereas 17% of the mothers of milk-sensitive children were.

Incidence of Milk Sensitivity in Siblings (Table IV)

A number of the children under study had been adopted and a number were referred from the far north, so we had no details of the reactions of their siblings. Complete data were, however, available in 140 of the 150 families. In these we found that of 225 older siblings 34 were still sensitive to milk, though from histories obtained from the parents others might have been sensitive in infancy and early childhood but had lost their sensitivity by the time they were seen by us. The ratio of normal to allergic children in this group was 100 to 18. Of 68 children born after the proband, 44 were not sensitive to milk and 24 were; the ratio of unaffected to affected was approximately 2:1. Our data suggest that when parents of a milk-sensitive child have a second child, the chances that it will also be sensitive to milk are one to two.

TABLE IV.—INCIDENCE OF MILK SENSITIVITY IN SIBLINGS. THE INDEX CASE IS THE FIRST CHILD STUDIED IN EACH FAMILY

	Normal	Allergic	Ratio N:A
Index cases.....	—	140	—
Older sibs.....	191	34	100:18
Younger sibs.....	44	24	100:54
Total.....	235	198	100:84

Are Children Ever Sensitive to Breast Milk?

An analysis of the 150 children under study revealed that three developed their first symptoms while still "on the breast", before they had been offered any form of cow's milk. Two of these children vomited breast milk. When they were taken off breast milk and were placed on cow's milk, they continued to vomit the latter. The third child developed vomiting, rhinorrhea, asthma and eczema while still on breast milk. This was the only child seen by us at this early age. The mother herself had a rhinorrhea. We asked her to stop drinking cow's milk; her own rhinorrhea subsided and so did the baby's symptoms. We subsequently found that adding no more milk to her diet than would colour her coffee was enough to precipitate eczema and wheezing in the baby. Babies certainly can be upset by factors in breast milk. We have encountered several similar examples—the ingestion of strawberries, tomatoes and oranges by the mother has produced eczema in the infant; crab has caused urticaria; and radishes have caused diarrhea. To confuse the picture even more it must be added that we have encountered one infant, not included in this analysis, who thrived on cow's milk, but was sensitive to many other foods, and did not thrive on breast milk.

DISCUSSION

Milk sensitivity can cause eczema, recurrent diarrhea and vomiting, persistent rhinorrhea and recurrent attacks of bronchiolitis and pneumonia in infants and children. However, it is only when the relationship between milk and the presenting symptom is recognized that the correct treatment can be initiated. In our experience and in the experience of others¹¹ the degree of sensitivity to milk varies from child to child; some children can tolerate a little milk on cereals, while others cannot tolerate even the small amount of milk commonly found in a slice of bread or in most margarines. The degree to which milk must be excluded therefore varies from patient to patient. In addition, when treating children, it must always be borne in mind that the child who is sensitive to milk is often sensitive to other foods. It is therefore not always easy to find a suitable substitute for cow's milk, and when this is the case the physician may be tempted to conclude that his patient has some basic underlying problem, such as cystic fibrosis of the pancreas. Such a possibility should have been excluded in the initial studies. When there is difficulty in finding a suitable substitute for cow's milk, the food most likely to be tolerated in our experience is breast

milk; a supply of the latter is essential for the proper study and treatment of some of these children. Rarely a child may be sensitive to constituents in breast milk. When a baby is receiving all his nourishment from breast milk and has evidence of allergic disease not due to such extrinsic factors as inhalants or contactants, the diet of the mother has to be modified. Our experience in this respect has been confirmed by the studies of others.¹² During the last 10 years we have encountered only two children, not included in this series, who could not tolerate breast milk. One child had had an infectious gastroenteritis and could not even tolerate glucose orally until three months had elapsed after the initial illness. It was assumed that in this instance the intestinal lining had been so damaged by the enteritis that a long period of complete rest of the alimentary canal was required before it was again able to function normally, at which time all foods were tolerated. The second child, already alluded to, had multiple food sensitivities, refused breast feedings and did not thrive when offered breast milk, but tolerated cow's milk well; in fact this was the only food which she was able to tolerate over a period of many months. The jejunal mucosa of this child had normal lactase, maltase and invertase activity.

The early recognition of cow's milk sensitivity is important. Once it has been recognized, cow's milk and dairy products will be avoided and only those foods which the child tolerates will be allowed. He will then be able to grow up relatively free from repeated gastrointestinal and respiratory illnesses. The parents are also relieved of much unnecessary expenditure on antibiotics and hospital care, while the physician will be spared the frustration of helping the patient to get better, only to see him relapse. The parents and the physician having been made aware that the child is sensitive to one food and knowing that he may well be sensitive to others, offer him only one new food at a time; by this means other food sensitivities will be the more easily detected. This early detection of factors to which the child is allergic also obviates the much more tedious investigation of suspected food allergies in the child when he is older and on a full diet. It often assists in the recognition, treatment and relief of symptoms in siblings and parents, for food sensitivities in the child are not infrequently present in close relatives.¹³ Finally, as the disease so commonly occurs in siblings, the parents may be advised that children born to them subsequently may also be sensitive to milk. From our data it appears that there is a 33% chance of this occur-

ring. Armed with this knowledge, the parents of children under study have been able to recognize and even manage food sensitivities in children born to them after the child that brought them to our attention.

Why is cow's milk singled out as the antigen for so many children and adults? There are, we think, two reasons. First, all babies and children are given milk repeatedly and in large quantities, so that even those who are only minimally sensitive to it develop symptoms. Secondly, cow's milk contains many ingredients; it provides almost all the nutrients necessary for normal growth and development, and it seems likely that, if someone is sensitive to an ingredient in any food, he could easily be sensitive to one in cow's milk. Cow's milk, however, may contain not only substances made by the cow but others derived from food and still others, such as penicillin, introduced by man. The child may be sensitive to any of these. It is possible that on rare occasions alfalfa, clover, brome grass and other substances which the cow is ingesting in large quantities, may appear in the milk and be the sensitizing agents. This is analogous to the situation which arises when a breast-fed baby, sensitive to oranges, develops eczema, the latter subsiding only when the mother herself stops eating oranges. People may, in fact, be sensitive to milk from one cow and not from another. For this reason it is unwise to assume that because a child and his parents or siblings are all sensitive to milk, that they are necessarily sensitive to the same factor in milk.

Closely allied to a sensitivity to milk is an antipathy to it. This antipathy is an interesting phenomenon and warrants further study. It may be present at birth—we have seen it in newborns and even in a premature. Our data (Fig. 3) suggest that it is present in approximately one child in 20. It is as common in boys as in girls. Between infancy and parenthood, however, a significant proportion of girls (between one in four and one in five) develop a dislike or even a hatred of milk, so that among adults the antipathy is much more common among women than among men. This may be one of the reasons why osteoporosis is relatively common in elderly women, with or without an intestinal lactase deficiency.¹⁴⁻¹⁶ The antipathy to milk is more common in milk-sensitive than in milk-insensitive families, but it cannot be equated with milk sensitivity, for we have been unable to demonstrate that those who dislike milk are necessarily sensitive to it. Nor can we say that the converse applies, namely that those who are fond of milk are never sensitive to it, for some milk-sensitive subjects are among those who are

most addicted to it. Nevertheless the antipathy to milk sometimes appears to be a protective mechanism; some children with a persistent rhinorrhea and bronchitis who have always disliked milk, but who have been made to drink it by well-intentioned parents, remain free from respiratory problems when they are at last allowed to avoid the milk and dairy products they have previously tried to avoid.

Summary An analysis of 150 milk-sensitive children and their families has indicated the following:

Milk and other food sensitivities are a common cause of recurrent gastrointestinal and respiratory disorders in infants and children.

The initial onset of symptoms in the child often dates from the original introduction of cow's milk into the diet.

Children sensitive to milk are frequently sensitive to other foods.

The parents of milk-sensitive children have an increased incidence either of an overt milk sensitivity, or of a reluctance to drink milk.

The early recognition and treatment of cow's milk and allied sensitivities make it possible to spare such children frequent and unnecessary illness and their parents unnecessary expense.

Résumé L'observation clinique de 150 enfants allergiques au lait a mis en évidence les faits suivants:

La sensibilité au lait et à d'autres aliments est une cause fréquente de troubles digestifs et respiratoires chez le nourrisson et l'enfant.

Les symptômes débutent souvent chez l'enfant au moment où le lait de vache est introduit pour la première fois dans son alimentation.

Les enfants allergiques au lait sont souvent allergiques à d'autres aliments.

Leurs parents avaient une tendance plus marquée, soit à une nette allergie au lait, soit à une répugnance pour cet aliment.

La découverte et le traitement précoces de la sensibilité au lait et des allergies connexes permettra d'épargner à ces enfants d'inutiles et fréquents malaises et à leurs parents des dépenses inutiles.

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