ACUTE SENSITIZATION IN AN INFANT TO COW'S MILK PROTEIN.

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It has long been known that certain diseases such as asthma, eczema, urticaria and intestinal disturbances are often the result of an acute sensitization of the individual to certain foods, especially the protein part of the food. The majority of infants who are sensitive to proteins of various kinds have a family history of eczema, asthma or some similar disturbance and the case to be described, has a family history of these conditions and herself has eczema.

Even mild cases of hypersensitiveness to cow's milk are uncommon, but such an extreme example as the one reported here must be very rare and there are but few reports of such cases. Many are sensitive to cow's milk only, but the present case was equally sensitive to a large number of foods, including fresh and dried cow's milk, goat's milk, egg albumen, etc. Two such extreme cases are very clearly described by Tisdall and Erb¹.

By anaphylaxis is meant the development under certain conditions of a hypersensitiveness to foreign proteins, which may not be toxic in themselves. The term is applied to states of increased susceptibility to substances introduced into the body. If a minute dose of a foreign protein, such as horse serum, is given a patient and after an interval of not less than ten days a second larger dose is administered, grave symptoms of collapse associated with vomiting and diarrhoea may develop, and even death may occur in a small percentage of cases. It appears that the anaphylactic shock does not occur before the 10th day following sensitization, but once established it may last through life.

The nature of sensitization is not definitely known, but it is closely related to anaphylaxis. The chief difference is that to produce the latter condition experimentally in animals, it is necessary to give a preliminary injection of the foreign protein. The majority of cases who are sensitive to protein, show the typical reaction directly after the first injection of the offending protein, as happened in the case to be recorded². It is likely that these cases simply inherit the tendency to become sensitized easily, and that some time before the comparatively large dose of protein is taken, minute sensitizing doses have been given. If so, the condition is identical with anaphylaxis.

Shannon³ has shown that it is possible for minute quantities of protein to be absorbed and secreted essentially unchanged in the mother's milk, without producing any reaction in the mother, but when the mother's milk is ingested a definite reaction is produced due to the foreign protein.

Colic, vomiting, diarrhoea, repeated respiratory infections, and eczema in breast-fed babies are often the result of allergic reactions to food coming to the infant through the breast milk. Sensitization is often multiple and may be due to a majority of the foods in the mother's dietary. The repeated exacerbations

of eczema may be due to newly acquired sensitization to foods the mother eats. The manifestations of exudative diatheses are the result of anaphylactic reactions to food proteins in the mother's dietary, and not the result of fat intolerance in the majority of cases.

The case to be described developed eczema at the age of $3\frac{1}{2}$ months, possibly due to the foreign protein of the milk taken by the mother passing through into the human milk. It is curious to note that the baby gave a mild positive skin reaction to the mother's milk.

Symptoms. The symptoms of extreme hypersensitiveness are generally first noticed when an attempt is made to wean the infant and cow's milk is given. The symptoms arise directly the infant is given the cow's milk and they are most alarming and even dangerous. Within a few minutes of the infant taking the milk, he starts to cry and refuses to take the bottle. A minute or two later all the parts touched by the milk begin to swell, including the lips, tongue, mucous membrane of the mouth and oesophagus. If milk is spilt on the face the skin becomes red and swollen. The swelling in the mouth and pharynx causes difficulty in breathing and so endangers life from asphyxia. At the same time the infant becomes much shocked and in the event of recovery, he recovers in a short time though he is left much exhausted and upset for some hours.

Diagnosis. The diagnosis is unmistakable as the symptoms come on immediately after taking cow's milk in some form. The diagnosis is later confirmed by performing the skin test for cow's milk and other foods. A skin test is done by scarifying a small area of skin with a needle and placing on this area the milk or other food which is to be tested. If the test is positive, a red wheal will cover the site if the reaction is strong, while if the reaction is mild a redness only will appear. No change will take place with a negative reaction. By using the skin test, we can find which foods will cause trouble when given, and all foods should be tested carefully in this way, before they are given. Thus serious trouble is prevented before the infant is desensitized.

Treatment. The treatment of these cases consists in gradually desensitizing the patient to the peculiar kinds of foods to which he has an idiosyncrasy. It is a most difficult task and one that takes many months to bring about a cure in an extreme case.

Directly the condition is recognized it is essential that every effort should be made to continue the breast milk for a time, even though only a little is available. A wet nurse may be obtained, if the mother's milk has quite gone, to tide the infant over a few weeks.

The feeding of an infant, who cannot take cow's milk in any form, is most difficult, and it is hard to find an adequate diet to supply sufficient protein for the needs of a growing infant. Most of these infants, especially the severe cases, react to goat's milk in the same way as to cow's milk. If goat's milk is found to be suitable, it is most useful, though it is difficult to obtain in a hurry. Failing goat's milk, starchy foods such as groats or Benger's Food made with water, may be used and will supply the carbohydrate part of the food. Cod-liver oil emulsion can be used to supply the fat. It must be remembered

that cream will not do, as it comes from milk and will contain some protein, though some of the milder cases take it without harm. Banana and orange juice supply the fresh part of the food necessary. Fish made up in various ways is useful, and in the case to be described was a most useful form of diet, as the infant did not react to it.

The process of desensitization consists in giving minute doses of cow's milk at the start and gradually increasing the dose day by day. The increase of dose is governed by the ability of the infant to take the quantity of milk without developing any reaction. If a reaction such as urticaria, irritability, etc., is noticed, the dose must be kept the same for a time or even reduced for a day or two. In an extreme case it is wise to go slowly and not to hurry, as a setback is serious and prolongs the desensitizing time. Later on the rate of increase of the milk can be made more quickly. For the immediate treatment and relief of the acute symptoms a hypodermic injection of adrenalin (1-1,000) should be given. Brandy is also useful.

CASE REPORT.

Baby, female, born 9th January, 1928.

Family History. On the paternal side, no history of eczema, asthma or food or drug idiosyncrasy. Mother had eczema as a child until the age of 10 years; uncle had eczema and hay fever; grandmother had asthma and was also very sensitive to strong sunlight.

Pregnancy was uneventful. Birth weight, 7 lb., and she was well developed and healthy. Breast feeding started at once and continued without event up to 9 months. Baby gained weight steadily though rather slowly. Vaccinated at the age of 3 weeks and a week later became cross and rather more upset than is usual.

At the age of 3½ months started with eczema on the scalp which spread to the face and body. The usual treatment was adopted and the eczema improved only to return again after a few days and persist. At the age of a few weeks old, the baby had one small feed of diluted cow's milk without any ill effects. Apart from this she had no food other than breast milk, except a little orange juice and Virol at times, until weaning was attempted at the age of 9 months.

Weight at 9 months was 13 lb. 1 oz. For the description of the immediate subsequent events after the infant was given cow's milk, I am indebted to the father, who is a medical man. At the age of 9 months it was decided to wean the baby and a milk and water mixture was given with a spoon. Almost immediately the upper lip began to swell and it was thought that she had bitten her lip. The feed was continued although the baby cried vigorously and resented the feed strongly. A bottle was then tried. In all little over 1 oz. of the mixture was given in 10-15 minutes. Acute illness set in almost at once. The baby was then noticed to have marked oedema of the face, especially of the lips, which were more than twice their normal size and completely everted. There seemed to be much difficulty in swallowing due to swelling of the tongue and possibly also of the oesophagus. The skin became red where the milk had been spilt on the face in the endeavour to feed the baby at the start. She could not vomit at this time because of the swelling in the mouth and pharynx. She then appeared very distressed, pale, and cyanosed. Dyspnoea with rapid breathing was marked. As soon as the swelling subsided about 4 hours later, she vomited curdled milk mixed with mucus and also spat up some blood. Brandy was given during the acute attack and helped to revive her. Only boiled water was given for the rest of the day and during the night. By the next morning the oedema of the face and

lips had quite disappeared, but she appeared pale and somewhat distressed. Small feeds from the breast were started again and by the evening she appeared quite normal. During the day she passed a motion containing much curd, mucus and clots of black blood.

As the result of what had taken place it was evident that the baby was extremely sensitive to cow's milk, and that she had had a severe anaphylactic shock. The baby was 9 months old and it was imperative to start with food to supplement the breast milk which could not be expected to last long or at any rate to be sufficient. Since cow's milk is such a staple article of food during infancy and childhood, it was evident that she could not go through life without it and that it was necessary to desensitize her as soon as possible. It was then decided to try a weak dried milk mixture (Cow & Gate) very gradually in small doses. A teaspoonful of this mixture was given and in 5 minutes a second teaspoonful. The lips then began to swell and the face to be oedematous. The feed was stopped at once and she appeared to be only slightly distressed. Two hours later she began to wheeze, and passed a curdy motion as before. Accurate daily records were then kept and the exact diet recorded. It was evident that the correct line of treatment was to try to desensitize her to cow's milk, as she could not possibly grow up without it. Various skin tests were then done at intervals with different foods, and no food was ever given unless the skin test was negative. Cow's milk gave the following reaction—after 5 minutes there appeared an urticarial blotch larger than a penny and the swelling extended over the area of skin where the milk had been placed. The swelling over the scarified area remained until the evening. Cumming⁴ describes such a case.

White of egg gave an even more marked reaction than the cow's milk and an urticarial rash came on the abdomen and groins and thighs. The rash lasted half an hour and then faded.

It became evident that she was no ordinary case of cow's milk hypersensitization but that she was sensitive to other foods as well.

The desensitization to milk was then started in the following manner. One drop of milk measured with a hypodermic syringe, in 4 ozs. of water was used as the stock solution and one teaspoonful of this mixture was given 3 times a day, making .03 min. of milk to a feed or .09 min. per day. Even after this small dose of cow's milk it was noticed that a slight urticarial rash appeared on the neck and under the chin 20 minutes after giving the milk mixture. This rash disappeared in 10 minutes. She also became irritable. There were no general symptoms. From this it was clear that the infant reacted to the minutest quantity of cow's milk and that desensitization must go on very slowly at any rate at the beginning.

The diet, then, consisted of 3 breast feeds, with two of groats made with water, together with the milk mixture. She also had a small teaspoonful of cod-liver oil emulsion 3 times a day, and orange juice. The milk mixture was gradually increased by adding an extra drop of milk to the 4 oz. of water each day. Any attempt to strengthen the milk mixture too quickly gave rise to an increase of the eczema, irritability, asthma and vomiting of mucus. By the end of the first month just over 13 min. of actual milk was being taken without reaction. She weighed 13 lb. 15 oz., an increase of 14 oz. in the month, showing that she was getting enough food. Further skin tests were then done, so as to add to the dietary. The following articles gave no reaction.

(1) Yolk of Egg.	(5) Chocolate.
(2) Banana and stewed apple.	(6) Potato.
(3) Fish.	(7) Biscuit.
(4) Farola.	(8) Butter.

The following, in addition to the milk, gave a positive reaction.

- (1) White of egg (very marked)
- (2) Soup made from beef, tomato and carrot.
- (3) Whey.
- (4) Malt.
- (5) Virol.
- (6) Breast milk gave a slight reaction. It is probable that the eczema, which started at 4½ months was caused by the breast milk.

The diet was then increased by those foods which gave negative reactions. The yolk of egg was obtained by hard boiling the egg so as to 'set' the white. The eczema still continued to trouble her, showing that she was having a reaction to the food. She was also inclined to wheeze and cough a good deal at times. By the end of the second month she was having nearly a teaspoonful of milk a day and it was possible to increase the milk by $2\frac{1}{2}$ min. a day. Fish was a great help in the dietary as she took it well. By the end of the third month she was having just over two teaspoonsful of milk daily.

At this time she had a marked setback probably due to very cold weather and to the fact that the cows were fed in a different manner. Dried milk was then substituted for the fresh milk and all went well again. By the end of the fourth month 1 oz. of milk a day was taken. By the end of the fifth month she was having 2 oz. of milk a day, with an increase of a teaspoonful daily. By the end of the sixth month, age $15\frac{1}{2}$ months, she was having 10 oz. of milk a day. Her weight was then 16 lb. There was no eczema and she had cut ten teeth. From the various skin tests it is obvious that the child will have to be desensitized to malt, etc. This should be an easier and quicker task than the cow's milk. It is also clear that as she grows up a careful watch will have to be kept on her diet, especially when new foods are tried, and the skin tests will be most helpful.

Great precautions will have to be taken also before she is given any serum or antitoxin and a small preliminary dose must be tried before the necessary quantity is injected.

Adrenalin should be available at all times.

During the time that the mother was breast feeding this baby, she was taking Ovaltine regularly. Ovaltine contains malt, egg and milk, all of which give a marked positive skin test on this baby. It is likely that the baby's eczema was at least aggravated by the Ovaltine, which was secreted in the breast milk.

The baby, who is now eighteen months old and is well in every way, except that she is under weight ($17\frac{1}{2}$ lb.) and rather thin. She has 16 teeth and is bright and active. She is having 20 oz. of whole milk a day and a good varied diet, which she takes well.

The skin test for milk is still mildly positive, but gives a far less marked reaction than it did at the beginning. Egg white gives a fairly strong reaction still and she is now being desensitized to this food in the same way as was done with milk.

TABLE SHOWING SUMMARY OF SKIN TESTS.

<i>Positive.</i>	<i>Negative.</i>
Cow's milk + + + +	Benger's Food.
Dried Milk + + + +	Robinson's Groats. Farola.
Goat's Milk + + + +	Cod liver oil ; Scott's Emulsion.
White of Egg + + + +	Barley.
Whey + + +	Butter.
Ostelin + +	Banana.
Osteomalt + +	Fish (plaice, halibut, etc.)
Soup + +	Potato.
Virol + +	Apple juice, orange, pear, prunes.
Malt + + +	Honey.
Tomato + +	Carrot, sprouts, etc.
Breast Milk +	Chicken.
Mutton Broth +	Bacon "dip."
Veal „ +	Biscuits.
Marmite + +	Yolk of egg.
Golden Syrup +	Chocolate.

CHART SHOWING RATE OF INCREASE IN THE AMOUNT OF MILK GIVEN DAILY.

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