

Food antibodies in malnutrition

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Chandra, R. K. (1975). *Archives of Disease in Childhood*, 50, 532. **Food antibodies in malnutrition.** Antibodies to several food proteins were detected in the serum of 13 out of 20 malnourished children. Antibody activity was found mainly in the IgG and IgA classes. On ingestion of food items to which antibodies were demonstrated, no untoward symptom occurred nor was complement activation observed *in vivo*. It is suggested that food antibodies in malnourished children result from atrophied gut mucosa and reduced secretory immune response, which permit passage of intact or incompletely digested protein molecules, and impaired phagocytic function of hepatic reticuloendothelial system. Such antibodies do not appear to play any immediate immunopathological role.

Antibodies to common food antigens have been seen in the serum of healthy infants and of patients with a variety of gastrointestinal and other systemic disorders (Heiner, Sears, and Kniker, 1962; Holland *et al.*, 1962; Gold and Adelson, 1964; Nelson, 1964; Taylor, Truelove, and Wright, 1964; Buckley and Dees, 1969; Drucker *et al.*, 1969; Ferguson and Carswell, 1972; Freier, 1973; Triger and Wright, 1973; Davies *et al.*, 1974). One of the pathogenetic mechanisms for the formation of food antibodies is the penetration of unaltered or incompletely digested dietary proteins across the gut mucosa. In protein-calorie malnutrition, the mucous membrane of the intestine is thin with a marked villous atrophy (Amin, Walia, and Ghai, 1969), pancreatic and intestinal digestive functions are reduced (Hansen, 1968), and the secretory antibody response is impaired (Chandra, 1975b). All these factors are likely to facilitate freer absorption of large molecular weight proteins which would then have an access to the systemic lymphoid tissues. In this paper the frequent presence of blood antibodies to food antigens, the titre and immunoglobulin class of these antibodies, and their immunopathological significance are reported.

Material and methods

Patients. 20 infants, aged 6 to 30 months, were diagnosed to be malnourished on the basis of reduced dietary intake, loss of subcutaneous tissue, and hair

changes. Weight and height were between 50 and 70% of the 50th centile of Harvard growth charts. None of the children had gastroenteritis at the time of blood sampling. Tests were done on admission and after 7-10 days of hospital stay during which period the children received a diet containing milk, wheat, rice, egg, meat, vegetables, and legumes. 20 age-sex matched healthy children served as controls.

Antibody tests. Sera were tested against milk proteins, gluten, egg proteins, and sheep serum by microdouble immunodiffusion (Ouchterlony, 1962) and tanned sheep erythrocyte haemagglutination method (Boyden, 1951). Test proteins were obtained from Sigma. In positive samples, the immunoglobulin class of antibodies to β -lactoglobulin was determined by the red cell linked antigen-antiglobulin reaction (Coombs *et al.*, 1965). Complement activation after ingestion of milk was studied by the method of Mathews and Soothill (1970).

Results

Antibodies to multiple dietary proteins were present in the serum of 13 malnourished children. In many, antibodies to more than one food were present (Table I). After intake of hospital diet for 7-10 days, the incidence of blood antibodies increased, especially to sheep serum and egg proteins, which were rare constituents of food consumed at home. No untoward symptom was observed after the intake of food items to which antibodies had been shown.

Antibody activity was detected mainly in the IgG and IgA classes (Table II). The serum content of IgG antibody was usually higher than that of IgA, except in 3 patients. Low titres of

TABLE I
Incidence of food antibodies

| Protein | Malnourished (20) | | Healthy (20) |
|------------------------|-------------------|-------------------------------|--------------|
| | On admission | After receiving hospital diet | |
| Casein | 4 | 5 | 0 |
| Lactalbumin | 5 | 5 | 0 |
| β -lactoglobulin | 10 | 12 | 2 |
| Gluten | 7 | 9 | 0 |
| Sheep serum | 1 | 5 | 0 |
| Egg white | 1 | 8 | 1 |
| Egg yolk | 0 | 4 | 0 |

TABLE II
Immunoglobulin class and titre of antibodies to β -lactoglobulin

| Group and case no. | Reciprocal antibody titre | | |
|---------------------|---------------------------|--------|-----|
| | IgG | IgA | IgM |
| <i>Malnourished</i> | | | |
| 1 | 64 | 0 | 0 |
| 2 | 64 | 8 | 0 |
| 3 | 128 | 8 | 0 |
| 4 | 256 | 0 | 0 |
| 5 | 256 | 32 | 0 |
| 6 | 1024 | 128 | 0 |
| 7 | 1024 | 4096 | 8 |
| 8 | 4096 | > 8000 | 128 |
| 9 | > 8000 | 256 | 32 |
| 10 | > 8000 | 1024 | 128 |
| <i>Healthy</i> | | | |
| 11 | 64 | 0 | 0 |
| 12 | 32 | 0 | 0 |

IgM antibody were found in 4 samples. In the two apparently healthy children with milk precipitins antibody to β -lactoglobulin was detected in the IgG class only. None of the children showed evidence of complement activation *in vivo* after ingestion of milk.

Discussion

Several causative factors may contribute to the frequent occurrence of food antibodies in malnourished children. Nutritional deficiency produces structural and functional alterations of intestinal mucosa (Amin *et al.*, 1969). The villous height is markedly reduced, the epithelial cells are cuboidal and atypical, and the lamina propria is infiltrated with inflammatory cells. The mucosal changes vary in severity and may be indistinguishable from typical coeliac histology. Similar findings can be reproduced in experimental animals (Ramalingaswami and Deo, 1968). The lesions are reversible on nutritional rehabilitation. The thin atrophic gut may be more permeable to large molecular weight proteins which could be absorbed

intact without prior digestion, and stimulate immunologically competent lymphoid tissues to form antibodies.

Increased permeability of the intestine is a physiological phenomenon in the first few weeks of life. Using a complement fixation method, Lippard, Schloss, and Johnson (1936) detected lactalbumin in the blood of the majority of infants from 4 to 20 days old. It was not found after the age of 5 months. Peak titre of antibodies to milk proteins are seen at the age of 3 months (Kletter, *et al.*, 1971) and decline rapidly subsequently. Infants who are initially breast fed have a much reduced antibody response when they ultimately receive bovine milk, compared to infants given cow's milk from birth (unpublished data). In infants who are small for gestational age, indicating fetal malnutrition, there is a high frequency of food antibodies (Chandra, 1974, 1975a). Gruskay and Cooke (1955) observed increased intestinal permeability to egg albumin during convalescence from gastroenteritis. In Wiskott-Aldrich syndrome, in which diarrhoea is a prominent symptom, a high titre of IgA antibody to casein was found (Hunter, Feinstein, and Coombs, 1968).

Malnutrition impairs digestive processes in the small intestine. There is atrophy of the pancreas with corresponding reduction in the output of tryptic and lipolytic enzymes. The flat intestinal mucous membrane has low levels of disaccharidases and possibly of other enzymes. Impaired digestion permits the continued presence of potentially antigenic protein molecules which may then be absorbed intact through the mucosa.

Secretory antibodies are important for exclusion of antigens at the mucosal level (Soothill, 1973). In malnutrition, the thymus and gut-associated lymphoid structures are shrunken (Vint, 1937; Smythe *et al.*, 1971; Chandra, 1972; Chandra, Sharma, and Bhujwala, 1973) and the secretory antibody response to viral vaccines is reduced (Chandra, 1975b). Impaired local immunity in malnourished individuals may permit the passage of antigens more freely than in those with intact secretory antibodies.

The 'scavenger' function of the phagocytic system may also play a role in development of antibodies to antigens absorbed from the gut. In patients with liver disease, in whom portalsystemic shunts permit bypass of the hepatic reticulo-endothelial system, there is a high incidence of antibodies to enterobacterial antigens (Triger and Wright, 1973). Nutritional deprivation is associated with impaired function of circulating microphages (Seth and Chandra, 1972; Selvaraj and

Bhat, 1972) and tissue macrophages (Saba and Di Luzio, 1968; Ratnakar *et al.*, 1972; Passwell, Steward, and Soothill, 1974).

The immunopathogenetic significance of food antibodies is debatable. Most antibody activity was confined to the IgG and IgA classes of immunoglobulins; IgG antibody titre exceeded that of IgA in most of the samples. We did not employ the radioallergosorbent test to detect specific IgE antibodies. The absence of untoward symptoms and the lack of complement activation *in vivo* after ingestion of milk in malnourished children with circulating antibodies to β -lactoglobulin point against any allergic attributes of these antibodies.

In conclusion, food antibodies in the serum of malnourished children are probably the result of structural, functional, and immunological changes in the intestine which permit absorption of dietary proteins and of reduced phagocytic function of hepatic reticuloendothelial system. Both these factors allow antigen access to the systemic lymphoid tissue which is stimulated to form antibodies.

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