

## Secretory IgA in protein-calorie malnutrition

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**Reddy, V., Raghuramulu, N., and Bhaskaram, C. (1976).** *Archives of Disease in Childhood*, **51**, 871. **Secretory IgA in protein-calorie malnutrition.** The secretory IgA system was investigated in children with protein-calorie malnutrition (PCM). The results of the study indicated that in children suffering from kwashiorkor and marasmus the concentration of IgA in duodenal fluid, saliva, nasal secretions, and tears was significantly reduced on admission and returned to normal 4 weeks after treatment. However, the concentration of secretory IgA in children with mild to moderate PCM was similar to that of normal children. Secretory IgA deficiency may be an important factor in promoting bacterial growth and this may account for the increased incidence and severity of mucosal infections in children with severe PCM.

Gastroenteritis and respiratory infections are common among malnourished children. It has been shown that phagocytic activity of leucocytes (Selveraj and Seetharam Bhat, 1972) and cell-mediated immunity (Bhaskaram and Reddy, 1974) are impaired in severe protein-calorie malnutrition (PCM). Levels of circulating immunoglobulins, however, have been reported to be either normal or raised in this condition (Keet and Thom, 1969). Secretory antibodies of the IgA class play an important role in the protection of mucosal surfaces against certain infectious agents. Recent evidence suggests that this local immunity is independent of systemic immunity (Tomasi, 1972). A study was therefore undertaken to investigate the secretory IgA system in children with PCM.

### Subjects and methods

Thirty-eight children aged between 1 and 6 years were investigated. They were classified into 3 groups based on deficit in weight for age. 12 children whose weights were above 80% of the standard (Indian Council of Medical Research, 1972) were considered normal, while 10 children whose values were between 60–80% of the standard but who had no clinical signs of malnutrition were classified as mild-moderate PCM. 16 children with weights below 60% of the standard were considered as suffering from severe PCM. 10 of these children had signs of kwashiorkor and the other 6 were marasmic. 3 normal children, 4 children with mild-moderate PCM, and 9 with severe PCM had diarrhoea,

i.e. more than three loose stools per day. Only those with moderate diarrhoea who could withstand the investigation were selected.

Children in the first 2 groups were mostly sibs of patients admitted to hospital. Consent of the parents was given before the investigations were done.\*

**Collection of samples.** Blood samples were obtained from all the subjects for estimation of serum immunoglobulins and albumin. Duodenal fluid, saliva, tears, and nasal secretions were collected within 2 or 4 days of admission.

To obtain the duodenal fluid intubation was carried out after an overnight fast and mild sedation. After the

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\*The Editors asked the authors of this paper about the ethics of the investigations done on the control children, and the authors replied as follows. 'Consent of the parents was obtained before the investigations were done. Normal children were sibs of the patients with severe malnutrition admitted to hospital. Investigations were first done in the patients and it was explained to the parents that similar investigations would be done in their sibs and that they were not necessary but would help us in getting more information about the disease. There was no problem with regard to the collection of blood samples, saliva, or tears, but some parents did not agree to duodenal intubation as it causes some discomfort to the child. Investigations were done only in those cases where consent was given by the parents.'

'In India, 1–2% of the children in poor communities suffer from severe forms of protein-calorie malnutrition like kwashiorkor and marasmus, while a majority suffer from mild-moderate PCM which manifests as varying grades of growth retardation. We have carried out a series of investigations, including the present study, to determine the functional significance of growth retardation. It is important to know the level of weight deficit which is associated with altered functional capacity, particularly the immunocompetence. These studies will not only help us in identifying the malnourished children who are at increased risk, but also to suggest guidelines for action. These are the circumstances which prompted us to do investigations in normal children and it must be pointed out that they do not involve any risk.'

rubber tube was passed into the stomach, the child was placed in the right lateral position. Bile-stained fluid was aspirated within 30–60 minutes, pH of the fluid was checked, and any sample with a value below 6 was rejected. The fluid was immediately placed in a water bath at 56°C for 30 minutes.

To obtain nasal secretions the child was placed on one side with the head tilted downward. 5 ml normal saline was slowly instilled through the upper nostril and the fluid aspirated through the lower nostril with a rubber catheter. Blood-stained specimens were discarded. Saliva and tears were collected directly into test tubes. All samples were preserved in a frozen condition until analysis which was carried out within a week.

Children with kwashiorkor and marasmus were treated with a diet providing 4 g/kg protein and 200 cal/kg per day. The investigations were repeated in 9 children 4 weeks after treatment when there was obvious clinical improvement.

Serum immunoglobulins (IgG, IgM, IgA) and IgA levels in the secretions were determined by the radial immunodiffusion technique (Fahey and McKelvey, 1965). Specific antiserum to secretory IgA and purified colostral IgA were used for the quantitation of secretory IgA. The lower limit of sensitivity of the immunodiffusion technique in our laboratory is 1 mg/100 ml. The concentration of protein in the secretions was determined by Lowry's method (Lowry *et al.*, 1951), and serum albumin by the Biuret method (Gornall, Bardawill, and David, 1949).

### Results

Serum albumin concentration was significantly low in children with severe PCM. However, there

was no significant difference between normal children and those with mild-moderate PCM. Serum levels of IgG, IgM, and IgA were similar in all 3 groups (Table I).

On admission, children with severe PCM had significantly lower IgA concentrations in duodenal fluid, saliva, nasal washings, and tears compared with normals. The differences were significant whether the values of IgA were expressed as g/l of secretion or mg/g protein (Tables II and III). There were no differences between kwashiorkor and marasmus. Although protein concentration of the secretions was slightly lowered in malnourished children, the differences were not significant. 4 weeks after treatment there was a significant increase in the IgA levels in all 9 malnourished children studied.

The concentration of protein and the levels of IgA in the secretions of children with mild-moderate PCM were similar to those of normal subjects (Tables II and III). There was no correlation between serum IgA levels on the one hand and secretory IgA levels on the other. Individual values of secretory IgA did not seem to be related to the presence or absence of diarrhoea.

### Discussion

The results show that there is no deficiency of serum immunoglobulins in protein-calorie malnutrition. Although malnourished children with infection had slightly higher levels of IgG, there was no

TABLE I  
*Serum immunoglobulins in children*

Group	Weight (% of standard)	No. of subjects	Serum albumin (g/l)	Serum immunoglobulins (g/l)		
				IgA	IgG	IgM
Normal	> 80	12	39 ± 1.9	1.07 ± 0.22	14.33 ± 1.09	1.57 ± 0.12
Mild-moderate PCM	60–80	10	34 ± 6.0	0.87 ± 0.15	16.18 ± 2.06	1.69 ± 0.11
Severe PCM	< 60	16	19 ± 2.0*	1.25 ± 0.18	13.64 ± 1.24	1.53 ± 0.09

Values are mean ± SE. \*P < 0.001 compared to normal.

TABLE II  
*Secretory IgA levels in children (g/l)*

Group	No. of subjects	Duodenal fluid	Saliva	Tears
Normal	12	0.42 ± 0.04	0.24 ± 0.07	0.31 ± 0.14
Mild-moderate PCM	10	0.33 ± 0.052	0.16 ± 0.052	0.18 ± 0.054
Severe PCM				
Before treatment	16	0.07 ± 0.022*	0.04 ± 0.022†	0.1 ± 0.019‡
After treatment	9	0.26 ± 0.044§	0.12 ± 0.025	0.15 ± 0.01

Values are mean ± SE.

\*P < 0.001; †P < 0.01; ‡P < 0.05 compared to normal; §P < 0.001; ||P < 0.05 compared to values before treatment.

TABLE III  
Secretory IgA levels in children (mg/g protein)

Group	No. of subjects	Duodenal fluid	Saliva	Nasal secretions	Tears
Normal	12	120.7 ± 16.75	59.9 ± 13.99	91.1 ± 14.87	43.8 ± 27.57
Mild-moderate PCM	10	123.2 ± 17.07	65.6 ± 13.53	84.1 ± 10.01	50.3 ± 11.02
Severe PCM					
Before treatment	16	25.1 ± 8.99*	12.8 ± 7.58†	25.7 ± 9.47†	31.7 ± 7.59‡
After treatment	9	69.3 ± 14.16§	39.3 ± 9.11	84.5 ± 14.50§	27.9 ± 2.54

Values are mean ± SE.

\*P < 0.001; †P < 0.01; ‡P < 0.05 compared to normal; §P < 0.01; ||P < 0.05 compared to values before treatment.

significant difference in the mean levels between the three groups. These findings are similar to those reported earlier (Keet and Thom, 1969).

The most important observation made here is that in children with kwashiorkor and marasmus there was a significant deficiency of secretory IgA on admission and that the values returned to normal after treatment. However, the concentration of IgA in the mucosal secretions was not altered in those with mild-moderate PCM. This is in line with our earlier studies where it was found that antibody response to typhoid antigen was impaired in children with kwashiorkor but not in those with mild-moderate PCM (Reddy *et al.*, 1976). These results suggest that the immunological functions may not be affected until the child develops a severe degree of malnutrition.

The concentration of IgA in the duodenal fluid, saliva, nasal secretions, and tears was reduced in children with severe PCM without exception. Since the total protein concentration of these secretions was not much altered, a low level of secretory IgA may be considered as a selective deficiency.

Infection may be considered as the most important cause of diarrhoea and it may occur both in well-nourished and malnourished children. However, diarrhoea is often more severe and persists for a longer period in children with kwashiorkor. Bacterial overgrowth in the small intestine has been consistently reported in children with malnutrition (Mata *et al.*, 1972). This may be related to secretory IgA deficiency. The bacterial pathogens or even the organisms which are normal inhabitants of upper respiratory tract and lower intestinal tract may spread to the small intestine, undergo proliferation, and cause diarrhoea. Similarly, the organisms can spread to the lower respiratory tract causing respiratory disease. A decrease in IgA concentration in nasal secretions of malnourished children has also been reported by Sirisinh *et al.* (1975). Low secretory IgA may thus play an important

role in the pathogenesis of mucosal infections in children with severe PCM.

Secretory IgA levels were not altered in children with mild-moderate PCM. This finding is of considerable practical importance since a majority of the children in poor communities suffer from milder grades of malnutrition. It has generally been held that the increased incidence of infections seen in undernourished children is due to their impaired immunological status and on this basis it has been suggested that improvement in their nutritional status is one way of reducing infective episodes in malnourished children. Data presented here indicate that improvement in the nutritional status alone may not have an impact on the problem unless efforts are made simultaneously to improve the home environment which favours frequent infections.

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