term 'familial' does not seem to apply to such a situation.

While Tandler's faulty recanalization concept may be of lesser importance in explaining atresias beyond the duodenum (where no 'solid stage' has been satisfactorily demonstrated), it may well apply to duodenal atresias. This is supported by the observation that it may be accompanied by other errors of growth, notably Down's syndrome (Bodian *et al.*, 1952). This prompted us to search for a chromosomal aberration, but the karyotype studied was normal.

The occurrence in three consecutive sibs of an uncommon condition such as duodenal atresia strongly suggests genetic determination. The parents being first cousins, it is possible that we are dealing with an autosomal recessive gene.

Summary

Three sibs born consecutively with atresia of the third part of the duodenum are described. No additional disease was found, and chromosomal studies from one case were normal. The parents are first cousins, and it is assumed that the anomaly in this kindred is determined by an autosomal recessive gene.

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Immunoglobulins in Protein-Calorie Malnutrition

It is well established that deficiency of immunoglobulins predisposes to infection. We set out to ascertain whether such a deficiency exists in patients with protein-calorie malnutrition, which might in part account for the common clinical observation of an association between malnutrition and infection. Brown and Katz (1965) reported a significant decrease in the serum IgG levels of 20 children with kwashiorker compared with 5 normal children. In 7 marasmic infants, Najjar, Stephan, and Asfour (1969) found the mean serum levels of IgG, IgM, and IgA to be higher than in healthy children. In a comparison between 11 children with kwashiorkor and 11 well-fed children suffering from similar infections, Keet and Thom (1969) found no significant difference in the serum levels of IgG and IgM. IgA levels were much increased in the kwashiorkor group.

Patients and Methods

Serial estimations of serum IgG, IgA, and IgM were made on admission, during recovery, and during convalescence in 24 patients with protein-calorie malnutrition suffering from a variety of infections. Almost all had gastro-enteritis, and upper respiratory tract infections; pneumonia and viral infections (including 4 cases of chicken-pox and one of measles) were also common. The children were between 7 and 34 months old (mean age 20 months) and the majority were obvious cases of kwashiorkor. Four patients died, all in the first week.

During the same period we were studying another group of patients who had recurrent or persistent infections. For comparative purposes we have tabled the immunoglobulin levels of 12 of them who showed no evidence of malnutrition, and were of similar ages to the 24 subjects. The nature of the infections in this control group was different. Otorrhoea, pneumonia, meningitis and upper respiratory tract infections were commonest. Only one child had gastro-enteritis, and one had chicken-pox. The age range was 7–31 months (mean 19 months).

Immunoglobulins were measured by the radial diffusion method, using commercially available antibody-agar plates (Hyland laboratories, Los Angeles). Serum total proteins and albumin were measured by the biuret method, using 28·3% sodium sulphate to precipitate globulins.

Results

These are shown in the Table. The means, standard deviations, and Student's t test for small samples were done on the logarithms of the observed values. The 2 SD range about the geometric means recorded is thus exponential, and in most cases exceeds the observed range.

TABLE

Serum Total Proteins, Albumin, and Immunoglobulins in 24 Malnourished and 12 Well-fed Children with Infection

Malnourished Patients	No.*	Serum Protein Concentrations (mean ± 2SD)				
		Total Protein (g./100 ml.)	Albumin (g./100 ml.)	IgG. (mg./100 ml.)	IgA. (mg./100 ml.)	IgM. (mg./100 ml.)
Day 1–4	22	3·9	1·6	1106	154	93
	Range	2·6–5·9	0·9–3·1	492–2479	77–308	27–324
Day 5–18	23	5·9	2·9	1214	169	150
	Range	4·3–8·3	1·7–4·7	648–2273	76–380	58–387
Day 19–42	16	7·4	3·7	1486	116	143
	Range	6·5–8·4	3·3–4·3	852–2593	57–239	51–403
Well-fed patients (controls)	12	7·1	3·6	1476	99	120
	Range	4·9–10·2	2·4–5·4	661–3302	28–357	34–430

*There were 4 deaths in the malnourished group. Sera were not obtained before day 4 or during convalescence in every case.

The serum total protein and albumin were low in the malnourished children on admission, showed a rise during recovery, and were similar to the control group in convalescence, reflecting repair of the nutritional state. The mean serum IgG increased from 1106 mg./100 ml. to 1486 mg./100 ml., and the difference is significant ($t = 2 \cdot 5$, $p < 0 \cdot 02$). Mean IgM serum levels behaved similarly. The difference between the admission level of 93 mg./100 ml. and the convalescent level of 143 mg./100 ml. is significant ($t = 2 \cdot 2$; $p < 0 \cdot 05$). There was a significant decrease in the IgA level from 154 mg./100 ml. to 116 mg./100 ml. ($t = 2 \cdot 3$, $p < 0 \cdot 05$). Both IgM and IgA reached their highest levels during the 5–18-day period.

The serum levels of all 3 immunoglobulins in the malnourished group during convalescence were similar to those of the well-fed patients, most of whom were in the post-acute phase of their infections. The differences between these two sets of figures are not statistically significant.

Comparison can be made with data on healthy children of similar ages from at least two published series. Allansmith *et al.* (1968) used assay materials of the same manufacture as ours, and Buckley, Dees, and O'Fallon (1968) checked some of their sera with the commercial plates. In both these large series, the statistical evaluation was also done on logarithms of the observed values.

The mean levels of IgG at different ages found by these two groups of authors are in close agreement, and are represented by a single curve in the Fig. The 2 SD range is delimited by thinner lines. A logarithmic scale is used for the ordinate and the 2 SD range is therefore symmetrical about the mean. Against this background have been plotted the serum IgG levels of our malnourished patients on admission (crosses) and during convalescence (circles). The levels are mostly high initially, and reach or exceed the upper 2 SD level at 3 to 6 weeks. It should be noted that paired sera were not always available. However, in only one patient's convalescent serum was the IgG level lower.

Figures of our IgA and IgM data are not shown. The agreement between the two quoted series here is not as close. Using the higher values reported by Allansmith *et al.* (1968) (e.g. IgM 84 mg./100 ml. at 18 months), the over-all pattern of our IgM levels is similar to that shown for IgG. The increase to convalescent levels in the individual cases is, however, less consistent.

The initial serum levels of IgA in all our malnourished patients exceed the means for healthy children in the same age-groups in the reports

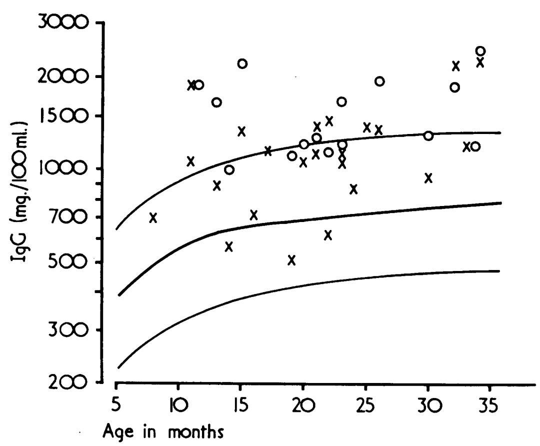

FIG.—*Serum levels of IgG in malnourished children. X On admission; O during convalescence. Curve of mean ± 2SD for healthy children drawn after data from Allansmith* et al. (*1968*) *and Buckley* et al. (*1968*).

quoted. Most are in the high normal range or exceed it. The values in convalescence, though lower, still show an unequal distribution, the majority being above the means.

Discussion

It is clear that synthesis of IgG, IgA, and IgM is not quantitatively impaired in these malnourished patients. Our results confirm and extend the findings of Keet and Thom (1969) in a very similar group of patients, and the conclusion appears to be true also of the marasmic form of malnutrition (Najjar *et al.*, 1969). The high initial levels which we report suggest that the response to infection may already be under way when these patients are first seen. The further rise in IgG and IgM in convalescence to levels of the same order as those in well-nourished controls with infection suggests that the response is adequate.

The high levels of IgA during the first 18 days are interesting. Keet and Thom (1969) also comment on this point, and their sera were presumably collected early in the disease. The high incidence of gastro-enteritis in our malnourished group, compared with the controls, leads us to speculate whether the gut was the first site of antigenic exposure, with early synthesis of IgA by plasma cells in the lamina propria.

Summary

Serial derminations of IgG, IgA, and IgM in sera of 24 children with protein-calorie malnutrition, who had a variety of infections, showed that there was a significant increase in the IgG levels in convalescent compared with admission sera. IgA showed a significant decrease. Initial levels of all 3 immunoglobulins were high compared with reported values for healthy children. The levels reached during convalescence were similar to those in 12 well-nourished children, also with infection.

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