

# Serum proteins and zinc as parameters to monitor the health of children in a rural Tanzanian community

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## **Serum proteins and zinc as parameters to monitor the health of children in a rural Tanzanian community**

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### **Summary**

Total protein concentration, zinc, prealbumin, albumin, alpha-1-, alpha-2-, beta- and gammaglobulin concentrations were measured in serum samples collected in three successive years (1982, 1983 and 1984) from children (1 month–15 years) of Kikwawila village, Tanzania. The analysis of a total of 1590 serum samples provided the baseline data for children living in a rural Tanzanian community.

The total protein values and the concentrations of betaglobulin were within the range described for Caucasians. Albumin, prealbumin, alpha-1- and alpha-2-globulin concentrations were below these standard values. On the other hand the gammaglobulin concentration was twice as high. The concentrations of total protein, gammaglobulin and prealbumin correlated with age. From 1982 to 1983 a significant decrease of most of the serum components (incl. zinc) was observed, although in children older than 2 years the alpha-1-globulins increased. All values increased again from 1983 to 1984, except for the zinc concentration, which decreased further.

The individual fluctuations were analysed by comparing paired values for the children participating in the period 1982–1983, or 1983–1984. The proportion of children showing large fluctuations, sometimes exceeding the selected limits of tolerance, was larger in the period 1982–1983 than 1983–1984. This was consistent with the overall pattern found for all children.

The prealbumin level, which has been postulated to be an indicator for malnutrition or borderline malnutrition, was analysed in detail. The values were far below normal values (200–300 mg/l), reaching a plateau with 130 mg/l among 4–6-year-old children. The individual fluctuations indicated a decrease

from 1982 to 1983, which was considerable both in terms of the proportion of children showing a decrease (55%) and in the magnitude of the decrease. There was an increase from 1983 to 1984 but this increase did not compensate for the loss in 1983. Prealbumin concentrations showed a slight trend towards decreased values with stunting and wasting. No direct correlation was found between the other biochemical parameters and the parasite or anthropometric data collected at the same time. It was difficult to establish direct relationships between the biochemical parameters, which mainly indicate the health status of the child at the time-point of the survey, and anthropometric parameters which reflect the history of the individual over a long period.

No direct correlation could be established between the biochemical parameters and the parasitological data. It is suggested that the decrease of the concentration of the serum protein components seen from 1982–1983 was most probably the result of factors not monitored in the surveys, such as variations in food availability and/or communicable diseases.

**Key words:** serum protein; prealbumin; zinc; child health; nutrition; parasites.

## Introduction

The interactions between nutrition, infection, immunity and environment are manifold and complex. The health of children has to be regarded as the result of all these factors (Tanner and de Savigny, 1987). A coordinated interdisciplinary analysis, which includes the social and economic background and an appropriate control group, is necessary to unravel the major mechanisms influencing community health. The main restriction on such studies is the lack of an appropriate control group. This problem could be overcome by the monitoring of a variety of parameters over several years.

Anthropometric, parasitological (Tanner et al., 1987b) and clinical data (Degrémont et al., 1987) provide important information about the health of a population. They can be complemented by data obtained from serum protein analysis. Electrophoretic fractionation of serum proteins combined with densitometric evaluation allows the definition of a variety of disease patterns (Sunderman, 1964). The absolute concentrations of the individual serum protein fractions can be compared with results from other population groups.

The concentrations of serum proteins in children of different African countries have been reported by several authors (e.g. Edozien, 1960; da Rocha-Afodu, 1978), but no information was available for children in Tanzania. The longitudinal, community-based study, initiated in 1982 in Kikwawila village, to investigate the effect of the complex interactions between disease and nutrition on health (Tanner et al., 1987b; Degrémont et al., 1987), provided the setting for gathering baseline information about serum protein concentrations in rural

Tanzanian children. Repeated cross-sectional studies were carried out to investigate the predictive power of biochemical parameters for the health of these children, which was monitored in parallel by anthropometric, parasitological and clinical parameters. The biochemical data about the serum protein concentrations were used to search for effects of parasitic infections and/or nutritional limitations on public health. In particular, prealbumin was evaluated as a possible parameter to detect borderline protein-energy-malnutrition in this rural community.

The present paper summarizes the baseline data on the serum protein concentrations found after cellulose acetate electrophoresis, and on prealbumin and zinc concentrations. The major fluctuations of the serum protein concentrations in 1982, 1983 and 1984 are compared with the results of the nutritional and clinical data.

## Material and Methods

The serum samples were collected in the Kapolo and Kikwawila sectors of Kikwawila village (Kilombero District), Tanzania, each year in October. The present study was part of the comprehensive surveys on the health status of children in 1982, 1983 and 1984 (Tanner et al., 1987a). Details of the study design, the population surveyed and the health interventions undertaken are described in this volume by Tanner et al. (1987a).

Blood samples could only be taken from fingerpricks, which yielded less than 100  $\mu$ l of serum for all serological and biochemical assays. *Total serum protein* was estimated using the Bradford reagent (Bio-Rad Laboratories). A volume of 3  $\mu$ l serum was dispensed with a Helena Microdispenser and made up to 300  $\mu$ l with water. Two samples of the diluted serum, 100  $\mu$ l each, were pipetted into clean glass tubes and 5 ml of the diluted Bio-Rad dye reagent was added. The standard curves were prepared in 1982 and 1983 with Bio-Rad bovine serum albumin and in 1984 with standard stabilized human serum (No. ORDT 07, Behring Diagnostika, Hoechst-Pharma AG, Zürich). The protein concentrations in the serum samples were calculated by taking the mean of the duplicate determinations.

*Serum protein electrophoresis* was carried out in the Field Laboratory of the Swiss Tropical Institute in Ifakara on cellulose acetate foils. 3  $\mu$ l of sera was used to fill the sample wells in the Super Z application system (Helena Laboratories, Texas, USA). The serum samples were applied onto the Titan III cellulose acetate foils according to the manufacturer's instructions, together with a serum control (serum electrophoresis control from Helena Laboratories). After staining, the cleared foils were analysed in Basel using a Quick Scan Jr. Plus densitometer (Helena Laboratories). The relative percentage of the individual fractions was recorded and used to compute absolute values (g/l) of serum protein components.

*Prealbumin* was measured with M-Partigen immunodiffusion plates (Behring-Institute, Hoechst-Pharma AG, Zürich). The standard curve was established with a human control serum (ORDT, Behring Diagnostika, Hoechst-Pharma AG, Zürich), undiluted and at dilutions 1:2 and 1:4. The serum zinc concentration was determined by atomic absorption spectroscopy (Varian AAS 875). 10  $\mu$ l serum samples and the standards were directly aspirated into the flame using microsampling equipment (Stürchler et al., 1987).



## Results

The widely-used Biuret assay to determine protein concentrations in serum samples could not be used for this study owing to the small volume of serum available. Consequently, the Bio-Rad method was used for the assay of total serum protein, because it requires a much smaller volume. To check the validity of comparing results obtained in different years, two tests were carried out by thawing a small sample of the stored sera from all three surveys and assaying them all at the same time (Table 1). In one test, sera from ten children who participated in all three surveys showed the same changes as observed in the cohort. In another test thirteen samples were chosen at random from each year, and the values from the parallel test showed no significant deviations from the results obtained from the independent determinations as reflected by the ratio of the original over repeated values, which was always close to 1.

The concentration of a variety of different serum components was analysed in children from 1 month to 15 years of age. The values for total protein, albumin, prealbumin and zinc concentrations represent the status at the time of blood collection in October 1982, 1983 and 1984. The study population was not broken down into age and sex (Tanner et al., 1987a) in the overall description (Fig. 1). The Caucasian reference values were taken from published data (Geigy Scientific Tables, 1968 and 1979). Samples from more than 500 children from 1 month to 15 years of age were assayed each year for total protein concentrations. Samples from 51–127 children (1 m–5 years) were also assayed for prealbumin and zinc concentrations. Protein and zinc concentrations were equal to or only slightly lower than the reference values, whereas albumin and prealbumin concentrations were distinctly lower (Fig. 1). All four parameters showed decreased concentrations in 1983 (unpaired t-test  $P < 0.001$ ). The mean concentrations of the four serum components were compared with the median concentrations. The values were symmetrically distributed (sign test,  $P < 0.05$ ). From 1983 to 1984 the concentrations of total protein, albumin and prealbumin increased again significantly ( $P < 0.001$ ). Zinc concentrations showed a slight decrease, which was not significant ( $P > 0.3$ ). All four parameters correlated with age (data not shown). When the data were broken down into age groups (0–2, 3–5 years, and, where possible, 6–10 and 11–15 years) each age group showed a drop in the concentrations from 1982 to 1983.

In a next step, the mean concentrations of the various protein fractions determined by serum protein electrophoresis were recorded (Fig. 2). Children of the age groups 0–1, 1–2, 4–5 and 9–10 years (number of samples see Table 2) were chosen from all three surveys. The total protein and beta-globulin concentrations paralleled the caucasian reference values. Albumin, alpha-1- and alpha-2-globulin concentrations were distinctly lower than the reference concentrations. All gammaglobulin concentrations were about 70% higher than the reference caucasian values. The mean concentrations of total protein, albumin,

Table 1. Reproducibility of the protein determinations (Bio-Rad assay) made in 1982, 1983 and 1984

Survey	1982		1983		1984	
	cohort (N 10) <sup>a</sup>	sample (N 13) <sup>b</sup>	cohort	sample	cohort	sample
Original mean conc. ....	63 ± 6	65 ± 10	62 ± 8	63 ± 7	67 ± 7	68 ± 4
Repeated mean conc. <sup>c</sup> .....	71 ± 5	66 ± 3	70 ± 7	69 ± 8	72 ± 8	73 ± 5
Ratio original/repeated .....	0.88	0.99	0.89	0.91	0.93	0.93

<sup>a</sup> For the cohort the samples were taken from the same 10 children for all three years.

<sup>b</sup> Simple random sample of sera collected in 1982, 1983 and 1984, respectively.

<sup>c</sup> The repeated assays for the cohort and the random samples were carried out on separate occasions.

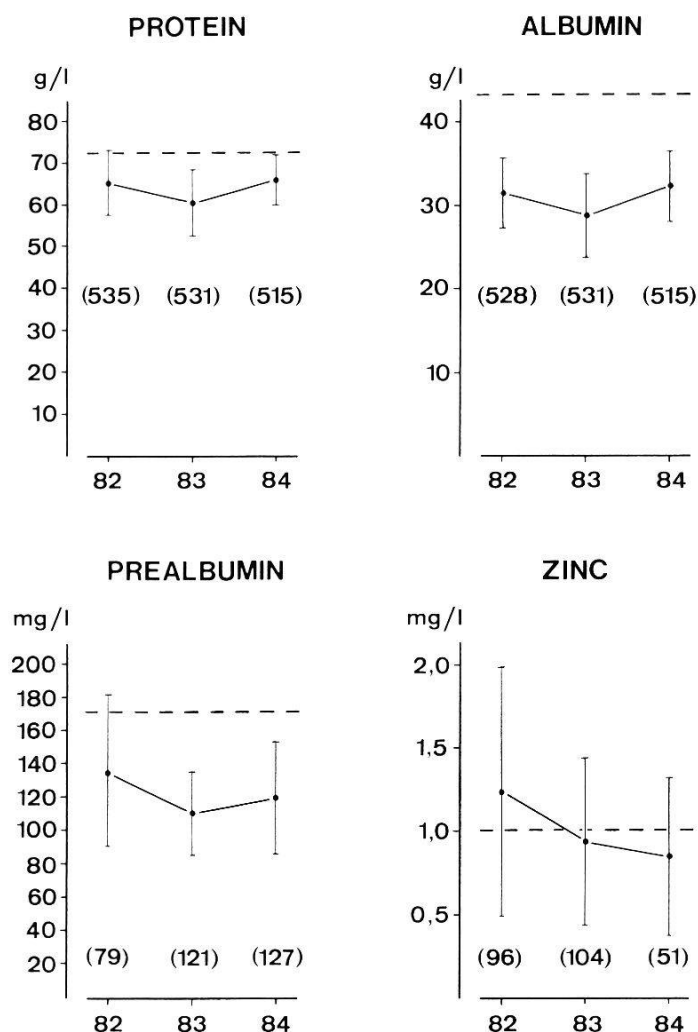


Fig. 1. Mean serum concentrations ( $\pm$  standard deviation) of total protein, albumin (children 1 month to 15 years), prealbumin and zinc (children 1 month to 5 years) in Kikwawila village in 1982, 1983 and 1984. Dotted lines represent Caucasian reference values (Geigy, 1979). Number of samples assayed per year in brackets.

alpha-2-, beta- and gamma-globulin decreased in all age groups in 1983. In contrast, the alpha-1-globulin concentrations increased in 1983, except in the group of one year old children.

The depression of the serum protein concentrations in 1983 was not caused by a changing composition of the study population. This point was tested by selecting children who participated in both surveys 1982 and 1983 and/or 1983 and 1984. From more than 500 children studied in each survey, 270 (54%) participated in the surveys 1982 and 1983; 179 (36%) children participated in 1983 and 1984. The protein concentrations for each child from the two surveys were paired and the necessary age corrections were made for the children  $\leq 2$  years, to compensate for rapid changes owing to the normal growth during the first two years. The children were then grouped according to age (0–5, 6–15 years). The fluctuations were monitored for each individual child for each

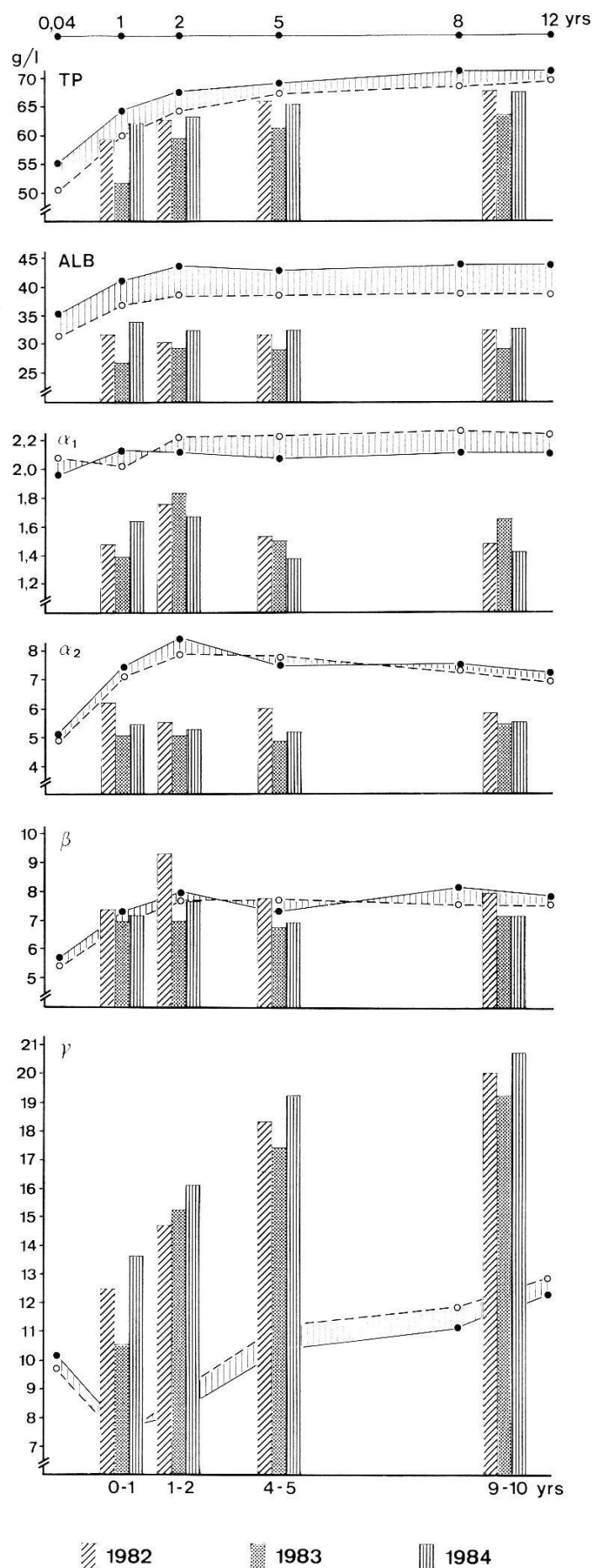


Fig. 2. Mean concentrations (g/l) of the serum protein fractions of children of Kikwawila village (age groups <1, 1-2, 4-5, 9-10 years) determined in 1982, 1983 and 1984 by cellulose acetate electrophoresis. Caucasian reference values (Geigy, 1968 and 1979) (●—●; ○—○) are given for comparison. TP = total protein, ALB = albumin,  $\alpha_1$  = alpha-1-globulin,  $\alpha_2$  = alpha-2-globulin,  $\beta$  = betaglobulin,  $\gamma$  = gammaglobulin.

Table 2. Number of samples used in each age group to calculate the mean values of the individual serum protein fractions (see Fig. 2)

Survey	Age groups (years)				Total number assayed	% of total number surveyed
	<1	1-2	4-5	9-10		
1982 .....	54	26	91	68	239	(45)
1983 .....	27	34	87	64	212	(40)
1984 .....	31	10	64	67	172	(33)
Total	112	70	242	199	623	(40)

serum protein fraction. The analysis also revealed that mass treatment offered to the population in May 1983 (Kapolo sector: ornidazole, Kikwawila sector: ornidazole and albendazole; Tanner et al., 1987a, b) did not substantially influence the different serum components measured. There was neither a difference in the mean concentration between treated or untreated children, nor in the patterns of fluctuation in the two periods 1982-1983 and 1983-1984 (data not shown). The further analysis therefore no longer compared groups of treated versus untreated children.

To describe the fluctuations between the different surveys more clearly, limits of tolerance (2S) independent of distribution were established. In our case limits were set which comprised between 75 and 95% of the values of one or the other serum protein component with a probability of 95%. Fig. 3 summarizes the fluctuations between the two periods 1982-1983 and 1983-1984. The paired values for each child for all biochemical parameters assayed were subdivided into those showing an increase or a decrease larger than  $\frac{1}{2}$  S, or a fluctuation less than  $\frac{1}{2}$  S of the whole heterogeneous group (meaning that differences below  $\frac{1}{2}$  S are not real physiological deviations). In both periods the percentage of children showing fluctuations which were smaller than  $\frac{1}{2}$  S was similar. Between 20 and 35% of the children showed an increase of more than  $\frac{1}{2}$  S in the period 1982-1983, whereas a larger number of children (28-58%) showed such an increase in the period 1983-1984. The opposite was true for the group of children with a decrease. In the period 1982-1983, 38-48% showed a decrease in serum protein concentration, whereas only 20-38% showed a decrease in the period 1983-1984. This general trend in the fluctuations was best seen in the analysis of the changes in the total protein, albumin and gammaglobulin fractions. The alpha-1-globulin fraction differed from the other parameters in that 40% of the children showed an increase in the period 1982-1983, whereas a smaller number of children (34%) showed such an increase in the period 1983-1984 (Fig. 3).

The children whose protein values showed fluctuations larger than 2 S were

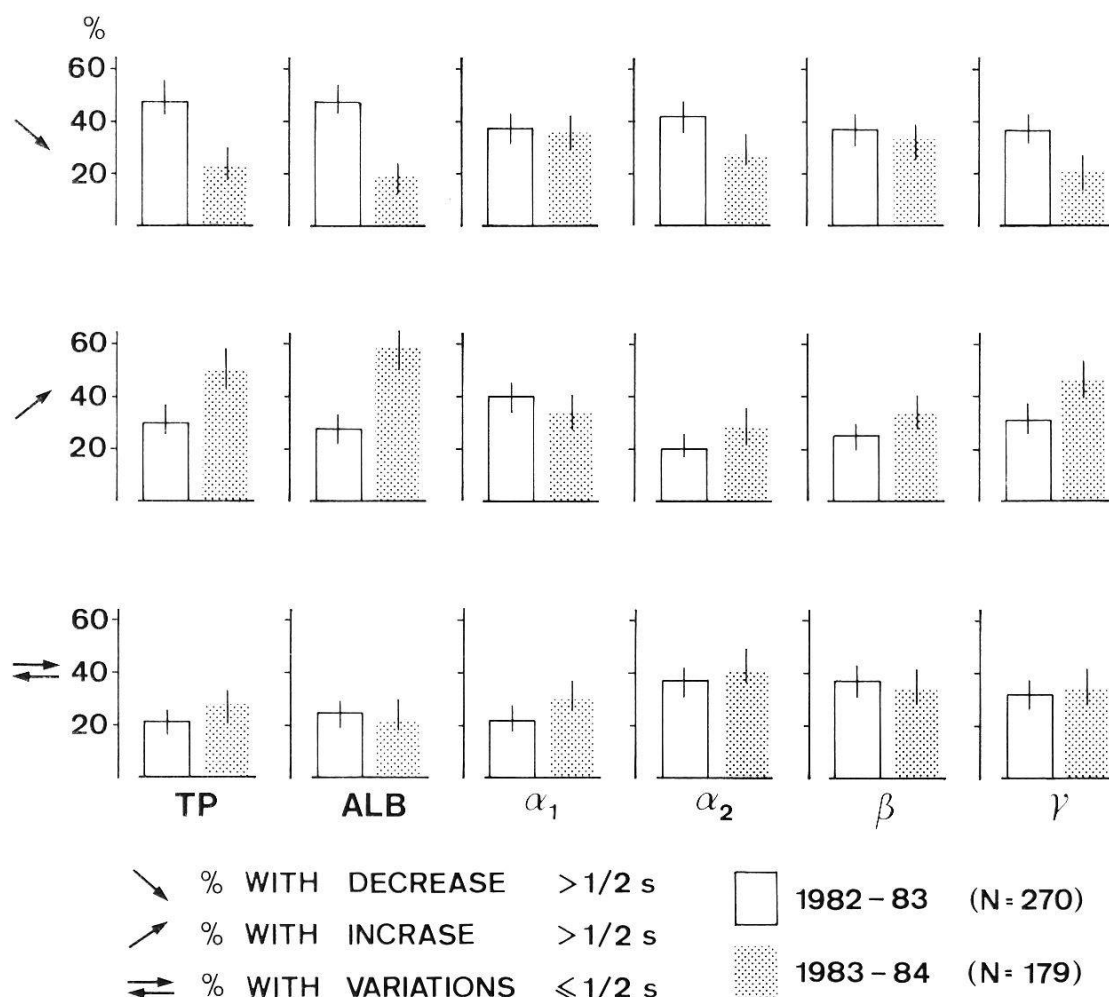


Fig. 3. Frequencies (%) with 95% confidence interval of fluctuations in the concentration of serum protein fractions in children of Kikwawila village observed for the periods 1982–1983 and 1983–1984. The children were grouped into those with increased or decreased values greater or within  $\frac{1}{2} S$  = limits of tolerance, i.e. including between 75–95% of all values with a probability of 95%).

grouped into those showing an increase and those showing a decrease, to obtain information about the extent of the fluctuations (Fig. 4). In the period 1982–1983, only 3–8% of the children showed an increase in concentration larger than 2 S, compared with 5–19% children in the period 1983–1984. The percentage with a decrease larger than 2 S was bigger in the period 1982–1983 (4–15%) than 1983–1984 (1–7%). An exception was again the alpha-1-globulin concentration, with a higher percentage of increases in the period 1982–1983 compared to the period 1983–1984 (Fig. 4).

The estimated limit of tolerance was used to find the number of children whose protein concentrations crossed this limit from one year to the other. The children were grouped into those whose values moved out of the selected normal range and those whose values returned to it (Fig. 5). Two age groups (0–5 and 5–15 years) were made.



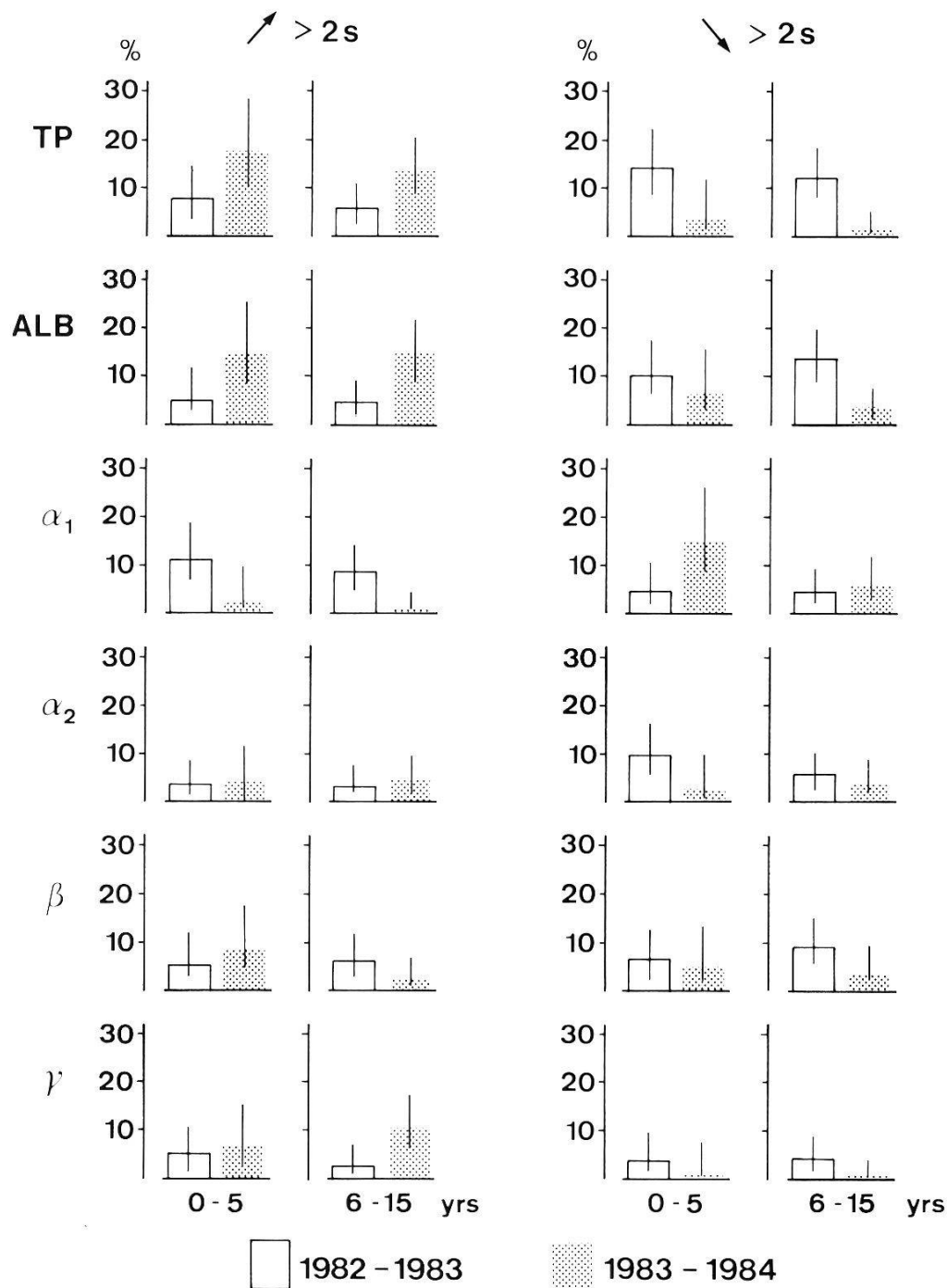


Fig. 4. Frequencies (5) with the 95% confidence interval of fluctuations in the concentration of serum protein fractions in children observed for the periods 1982–1983 and 1983–1984. Children (two age groups:  $\leq 5$  and 6–15 years) were grouped according to increased or decreased values greater than the limits of tolerance (2 S).

In the periods 1982–1983 and 1983–1984 between 0.4 and 12% of the children had protein, albumin, beta- and gammaglobulin values which returned into the limits. An almost identical percentage of children had some protein values which moved outside the limits. A striking difference was found in the proportion of the fluctuations of the alpha-1- and alpha-2-globulins. In the

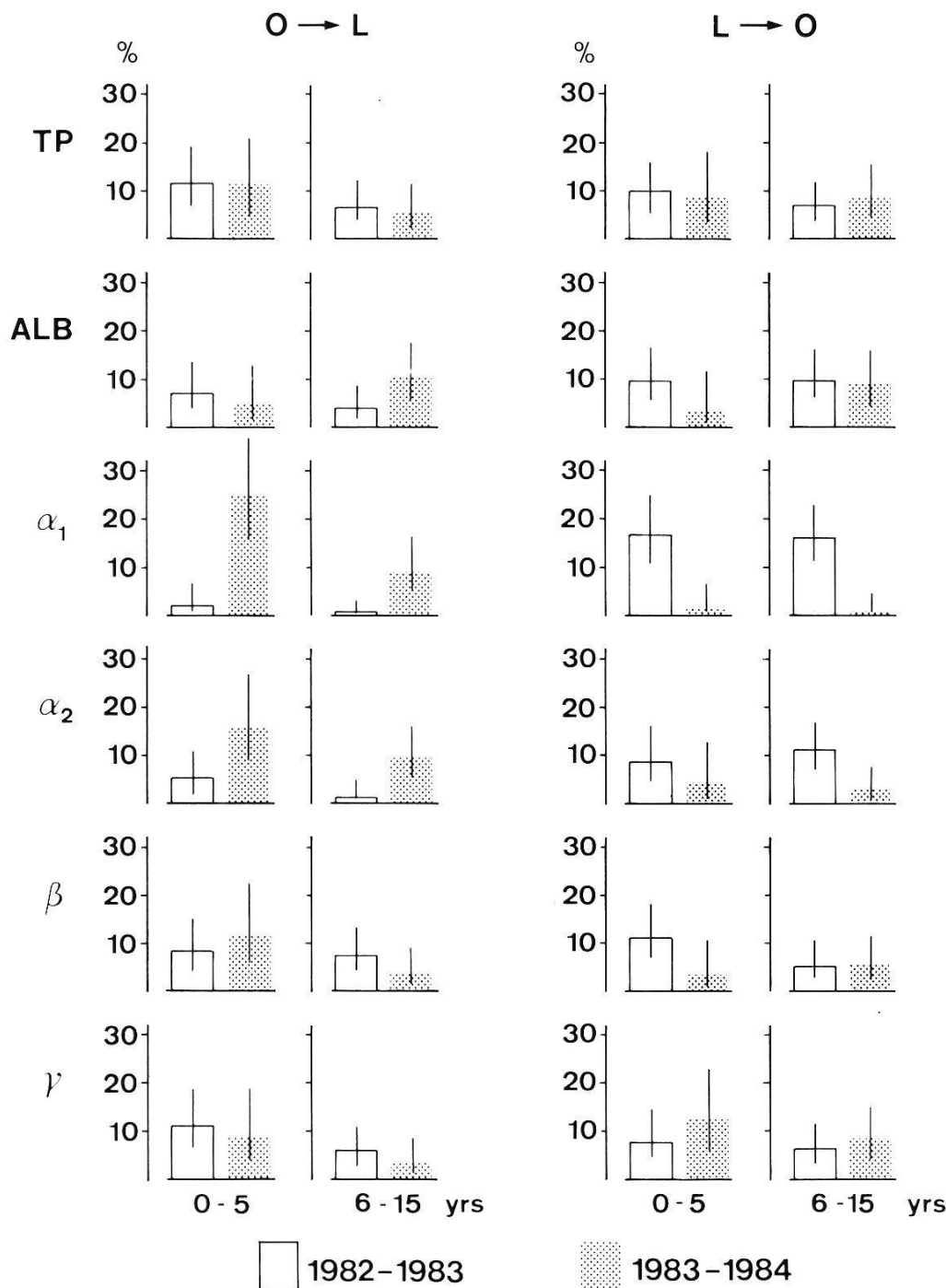


Fig. 5. Frequencies (%) with the 95% confidence interval of children showing fluctuations in the concentrations of serum protein fractions crossing the limits of tolerance, i. e. outwards ( $L \rightarrow O$ ) or inwards ( $O \rightarrow L$ ).

period 1982-1983, 16% ( $N = 42$ ) of the children of both age groups showed alpha-1-globulin values which moved outside the limits of tolerance. Only two children younger than 5 years returned to the normal range. A similar fluctuation was detected in the alpha-2-globulin fraction where 10% of the children moved out of the range. Five percent of children younger than 5 years returned to the normal range, compared to only one out of 148 in the older age group. In

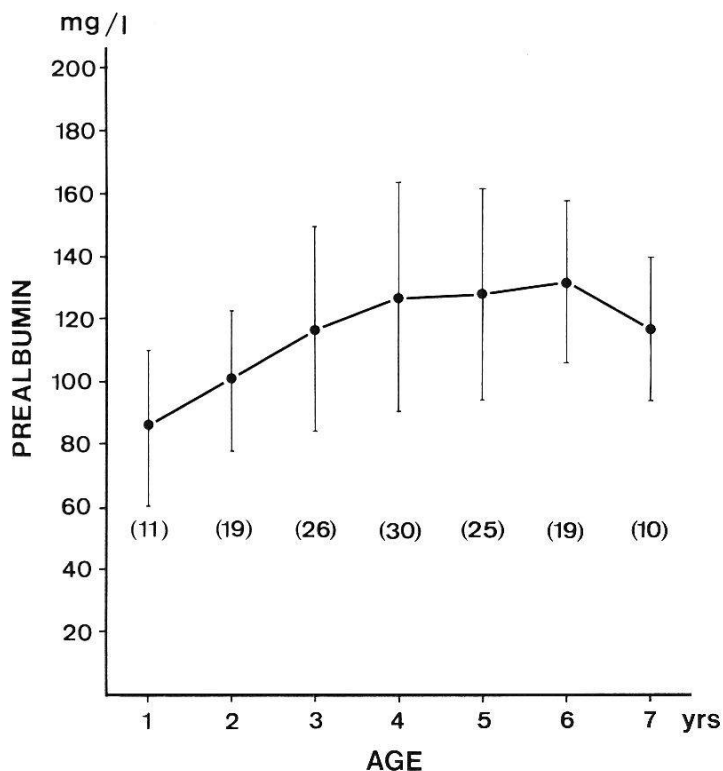


Fig. 6. Age dependent increase in the prealbumin concentrations (mean  $\pm$  SD) of the children  $\leq 7$  years. Pooled values from 1982, 1983 and 1984. Number of samples analyzed in brackets.

the period 1983–1984 the two fractions “normalized” again, especially among the group of children from 0–5 years age, where 24% of the values in the alpha-1-globulin and 15% in the alpha-2-globulin fraction returned. The percentage in the older group of children was somewhat lower (9%) for both serum protein fractions. No child was found whose alpha-1-globulin values moved out of the selected range in the period 1983–1984 and only around 4% where the alpha-2-globulin fraction did so. Most of the children whose alpha-1-globulin values were out of the normal range in 1983 showed values which returned in 1984, as revealed by the analysis of the data of individual children who participated in all three surveys (data not shown).

A cohort of 170 children could be followed during the three consecutive years (Tanner et al., 1987b). All serum parameters measured in this cohort showed the same tendency as described for the total population (data not shown). Since prealbumin is postulated as a parameter to monitor protein-energy malnutrition (Ogushina et al., 1980) the prealbumin concentrations were analysed in detail. Prealbumin determinations were made with all sera from children  $< 5$  years in 1982 and  $< 7$  years in 1983 and 1984. All the prealbumin concentrations from the children studied in the three surveys (1982  $N = 79$ ; 1983  $N = 121$ ; 1984  $N = 127$ ) were used to evaluate age-dependent changes (Fig. 6). The mean prealbumin concentrations reached a plateau at the age of 5 years with 130 mg/l. The individual fluctuations in the prealbumin concentrations of

Table 3. Fluctuations in the concentrations of prealbumin in a cohort of 45 children (0–5 years old) followed for three consecutive years (1982, 1983 and 1984)

Observation periods	Frequency (%) of children with:				
	Decreased prealbumin conc.		Increased prealbumin conc.		Net change in prealbumin mg
	% (N)	mg	% (N)	mg	
1982–1983 .....	51 (23)	–942	40 (18)	+415	–527 (45)
1983–1984 .....	40 (18)	–378	55 (25)	+630	+252 (45)
Overall <sup>b</sup> .....		–1320		+1045	–275 (45)

<sup>a</sup> Four children (1982–1983) and two children (1983–1984) showed no change in prealbumin concentrations.

<sup>b</sup> Corresponds to overall difference in the changes of prealbumin concentrations from 1982–1984.

a cohort of 45 children surveyed in all three years showed the same decrease in 1983 as was found for the whole group of children (Fig. 1 and Table 3): 51% of the children had decreased values from 1982 to 1983 compared with 40% from 1983 to 1984 and 13% had decreased values in all three surveys. This resulted in a total deficiency of 527 mg prealbumin in the total group of 45 children. From 1983 to 1984 a partial recovery was found, with a net increase of 252 mg per 45 children. From 1982 to 1984 the group of children therefore still showed a loss of 275 mg in spite of an expected age-dependent increase.

Parasitological as well as anthropometric parameters were compared with the biochemical parameters to test for any possible relationship. Protein and prealbumin concentrations, and the concentrations of the various serum fractions, did not show any correlation with either the prevalence or the intensity of *Schistosoma haematobium* infection, hookworm infection or *Strongyloides* spp. infection, nor with the malariometric parameters. No change in the serum protein concentrations could be related to the increased incidence of hookworm infections in the period 1983–1984.

Stunting and wasting were compared with the biochemical parameters and again no significant correlations could be found.

The children with a high alpha-1-globulin value in 1983 were analysed on an individual basis. Each child's parameters were compiled and common characteristics searched for. Each child showed a distinct picture; there were no common characteristics except the high alpha-1-globulin values. Prealbumin concentrations were compared with the corresponding anthropometric parameters (Table 4). In most cases where the children showed clear signs of stunting and/or wasting (N = 10) the corresponding prealbumin concentrations had not been determined owing to the lack of sufficient serum (N = 8). No significant differences were detected in the prealbumin concentrations between children with stunting and/or wasting and the normal group. A trend towards lower prealbumin concentrations was found in children with stunting stage 3 and wasting stages 2 and 3 (Table 4).

## Discussion

The present study provided biochemical information, in addition to the clinical, parasitological and anthropometric data (Degrémont et al., 1987; Tanner et al., 1987b), about the health status of the population in Kikwawila. The study is a further approach to a better understanding of the complex relationships between nutrition-infection-immunity and environment (Tanner and de Savigny, 1987). The quasi-experimental design of the study only allowed an exploratory analysis of the data (Tanner et al., 1987b), which could highlight basic trends.

The biochemical data allowed us to establish mean reference values for

Table 4. Relationship of mean (arithmetic) prealbumin concentrations (mg/l) with the anthropometric parameters of stunting and wasting in children 1 month to 7 years

	Stunting (Weight for age)			Wasting (Height for age)		
	4 years			4-7 years		
	mean $\pm$ SD	(N)		mean $\pm$ SD	(N)	mean $\pm$ SD (N)
Stages 0 and 1 .....	115 $\pm$ 40	(27)		133 $\pm$ 32	(31)	122 $\pm$ 34 (91)
Stage 2 .....	118 $\pm$ 40	(27)		129 $\pm$ 35	(12)	116 $\pm$ 37 (40)
Stage 3 .....	105 $\pm$ 22	(28)		116 $\pm$ 33	(12)	97 $\pm$ 10 (5)

Table 5. Comparison of mean serum protein concentrations from Nigerian children, newborns from Zaire, and children of Kikawwila village, Tanzania; Caucasian standard values added for comparison

Age groups	Place	N	Mean concentrations (g/l)					Methods <sup>a</sup>	Reference	
			Total protein	Albumin	Alpha-1-globulin	Alpha-2-globulin	Beta-globulin			Gamma-globulin
Newborns	Zaire	42	53,8	32,4	1,7	3,9	5,0	10,8	CAE	Mwanba et al., 1984
1-6½ years	Nigeria	249	66,4	29,0	3,6	8,3	8,3	17,1	PE	Edozien, 1960
1-5½ years	Nigeria	75	71,3	37,1	5,3	8,9	8,9	10,1	PE	de Rocha-Afodu, 1978
5½-10 years	Nigeria	23	67,5	37,1	3,7	7,3	8,7	11,6	PE	de Rocha-Afodu, 1978
0.1-5 years	Tanzania	420	63,8	32,0	1,5	5,5	7,6	17,1	CAE	present study
5-10 years	Tanzania	371	66,8	32,1	1,5	5,6	7,6	19,8	CAE	present study
1-3 years	Caucasian	20	70,2	43,6	2,0	8,3	7,7	10,3	CAE	Liappis, 1972
7-10 years	Caucasian	59	72,5	43,6	2,1	7,4	8,1	11,1	CAE	Liappis, 1972

<sup>a</sup> PE = paper electrophoresis; CAE = cellulose acetate electrophoresis



different serum protein components in children in rural Tanzania. This information made it possible to compare the serum protein concentrations of the children of Kikwawila with the values reported for similar groups elsewhere (Table 5).

The mean total serum protein concentration (65 g/l) (as determined by the Bio-Rad protein assay), measured for a group of approximately 530 children per year for three years, was slightly lower than the Caucasian reference values (Table 5). It compared well with the values reported for Nigerian village children near Ibadan (Edozien, 1960), but was lower than the value reported for a group of children in Lagos (71.3 g/l; da Rocha-Afodu, 1978). A direct comparison of the concentrations of serum components reported by different authors is difficult, since the absolute values obtained may vary according to whether paper electrophoresis or electrophoresis on cellulose acetate foils was used (Liappis, 1972). However, all concentrations of the serum protein components except the beta- and gammaglobulins were clearly lower than the Caucasian values (Table 5). Betaglobulin concentrations were similar to the Caucasian ones, and there was a large increase of 70% in the gammaglobulin concentrations.

The protein concentrations of the different fractions were compared with those found for other children in Africa. The albumin concentrations were between two values reported for Nigerian children (2.9 g/l; 3.71 g/l); the gammaglobulin concentrations were identical with those reported by Edozien (1960) from a rural Nigerian community. A high gammaglobulin concentration is regarded as a response to infection and is commonly found in tropical areas (Chandra and Newberne, 1977; Cohen and Warren, 1982). In the case of the children of Kikwawila, one may suggest that the high IgG levels reflect a response to the extremely high level of parasite infections, such as malaria, which was found in 85% of the children below 2 years of age (Tanner et al., 1987b). Not a single child was parasite-free for 3 years. Thus, no real control data are available.

Reduced concentrations of albumin, alpha-1- and alpha-2-globulins, and elevated gammaglobulins is a pattern frequently found in hepatopathies, especially those involving hepatocellular damage (Sunderman, 1964). No direct correlation of this pattern with the degree of hepatopathy could be made, since the appropriate parameters could not be assayed during these community-based surveys. A hospital-based study in nearby Ifakara (14 km south of Kikwawila) in 1982 and 1983 stressed the importance of hepatic disorders in rural southeastern Tanzania and indicated the etiologic pattern. For example, more than 75% of children below the age of 15 years had serum markers for hepatitis B (Stahel et al., 1984; Robyn, 1986). It is therefore tempting to suggest that the altered serum pattern found among children in Kikwawila was also partially related to the high endemicity of hepatitis B.

The reduced concentrations of alpha-1-globulin found in this study were

not detected in the Nigerian children (Table 5). Reduced levels of alpha-1-globulins are normally attributed to an alpha-1-antitrypsin deficiency (Fisher et al., 1976) associated with an inborn error (ZZ phenotype) accompanied by pulmonary emphysema and neonatal liver disease (Sharp and Freier, 1972). Such deficiencies are relatively rare and no report of their occurrence in Tanzania was found. The possibility cannot be excluded, that the generally low values found for alpha-1- and alpha-2-globulins, were related to a peculiarity inherent in the method, whereas the relatively higher values found using the paper electrophoretic technique might be due to the known "albumin trailing" on paper fibers. Determination of the concentrations of alpha-1-globulin and antitrypsin, which are normally present only in low concentrations, for example by radial immunodiffusion or automated immunoprecipitation techniques, would help to clarify this question.

Prealbumin and zinc concentrations were only determined in children who were below the age of 5 years in 1982. Whereas the prealbumin concentrations were below the Caucasian reference values (Weeke and Krasilnikoff, 1972), the zinc concentrations were within reference ranges (Williams, 1981). Albumin and prealbumin concentrations are often used to assess protein-energy-malnutrition (PEM) (Ingenbleek et al., 1972). However, when the data for albumin and prealbumin were compared with the anthropometric parameters no clear-cut relation could be established. The concentrations of the two proteins in the groups of children showing wasting (stages 2 and 3) or stunting (stages 2 and 3) were similar to those in a group with no obvious sign of nutritional deficiencies (Table 4). The prealbumin concentrations increased with age to a plateau of 130 mg/l at 4 years. Ingenbleek et al. (1975) reported on a study in which a control group of children from Senegal (up to the age of 2½ years) had prealbumin concentrations between 157 and 296 mg/l, and a group of children with PEM showed prealbumin concentrations in the range from 34 to 115 mg/l. Ogunshina et al. (1980) described concentrations  $\geq 200$  mg/l in Nigerian schoolchildren as normal, and mean concentrations of 136 mg/l as a sign of malnutrition. Anthropometric and biochemical parameters were combined and applied to detect moderate protein-energy malnutrition in preschool children in southern Cameroon (Delpeuch et al., 1980). The group of children regarded as controls had mean prealbumin concentrations of 132 mg/l. This value compares well with the values found in our study.

Whether the relatively low concentrations of prealbumin are indicative of borderline PEM in the Kikwawila population cannot be decided. Firstly there were no clear parallel findings with the anthropometric data and in addition no controls were available which could be used for comparison. It has been reported that low levels of prealbumin are frequently associated with cirrhosis (Agostoni et al., 1968; Inada and Sterling, 1967). The low prealbumin concentrations could therefore also be a reflection of liver disturbances (see above). There was a decrease of the prealbumin concentrations in the period 1982–1983

followed by a certain recovery in the period 1983–1984. The loss of prealbumin in the period 1982–1983 was not reflected in an increase of malnutrition which could be detected at the anthropometric or clinical level.

In February and August 1983 a food consumption survey was made in Kikwawila (Lukmanji and Tanner, 1985). The diets of all age groups were highly deficient in energy and protein in February, and though the protein standards were met in August, energy deficiency still existed. An agricultural survey in 1984 (Zehnder et al., 1986, 1987) confirmed the restricted availability of food. Thus, the results of the surveys of food-consumption and agricultural production may explain the decreased prealbumin concentrations in October 1983, which could have been a reflection of seasonal food shortages. The direct correlation of prealbumin and retinol concentrations (Stürchler et al., 1987) shows that both could serve as nutritional indicators.

All the biochemical parameters assayed, except alpha-1-globulin, showed decreased concentrations in the period from 1982–1983, both in the cross-sectional analysis and in the cohort study. This decrease was found in the concentrations of total protein, prealbumin, retinol and zinc, which were assayed independently in different laboratories. The biochemical data thus suggest a substantial impairment of the health of the children in 1983. However, this biochemical impairment was not paralleled by any indication on the clinical, parasitological or anthropometric level. In contrast, anthropometric parameters improved from 1982 to 1983 and the prevalence of *Giardia lamblia* and hookworm decreased substantially (Tanner et al., 1987b).

The individual serum protein fluctuations during the three years of the survey are described in detail in the Results section. The limits of tolerance were used to define better the observed fluctuations in the concentrations of the serum proteins. It remains to be shown, whether these limits could also be used as indicators to detect pathological situations. The trend towards an increase in alpha-1-globulin concentration and a decrease in albumin, prealbumin and alpha-2-globulin in 1983 as compared to 1982 and 1984 is indicative of an increase in the incidence of acute inflammatory reactions (Alper, 1974). This could have been due to increased bacterial and viral infections, which were not recorded in the three surveys. It is also possible that the children showed increased inflammatory reactions caused by the migratory larvae of fresh hookworm infections. This hypothesis is supported by the high prevalence of hookworm infections in 1984, and also by the higher incidence found in the period 1983–1984 (Tanner et al., 1987b). No direct correlation could be established with hookworm infection, probably because of the low intensity of the infections. The very low intensity of infection observed in Kikwawila does not cause a major gastrointestinal blood loss (Roche and Layrisse, 1966) which would lead to a change in serum protein concentrations (Gupta et al., 1974). The intensity of *S. haematobium* infection was highest in 1983, but there was no correlation between the presence of the parasite in individuals and changed

biochemical parameters. Data on *G. lamblia* infection were difficult to interpret, because the diagnostic method used predominantly detected cysts, but not vegetative forms which are shed at irregular intervals. Thus, no information was available about those who were actually sick (Tanner et al., 1987b).

It was impossible to sort out any effect of a single parasite on the biochemical parameters, because only 30% of children had a monospecific parasite infection in any one survey, whereas 60% had two or more species (Tanner et al., 1987b). Not a single child was found to be parasite-free for more than one survey. Thus no adequate control group could be formed for this study. Multi-parasitism exerts a synergistic effect, which can change the health status of a child drastically from one year to another. The different serum protein concentrations measured are a composite resulting from a variety of influences, which can hardly be analysed individually in such a population.

The clinical and anthropometric data indicated an improvement of the nutritional status in 1983 and a reversal in 1984, where 65% of the younger children (0–5 years) showed stunting and or wasting, whereas only a moderate increase in frequency of stunting was seen in children from 6–10 years of age. This is in direct contrast to the biochemical data. The difference can probably be explained by the fact that the biochemical parameters can only indicate the situation at the time when the blood sample was taken and they do not reflect the history of a child's metabolism. For example, low prealbumin levels may increase to normal within a few weeks following nutritional rehabilitation (Atinmo et al., 1983). There is a lag before any changes in biochemical parameters are reflected at the clinical or anthropometric level, because a sustained modification of the metabolism is necessary for such changes to occur. The types of parasite infections frequently alter in this population. Thus no single infection lasts long enough to assure a sustained biochemical change.

The decreased concentrations of almost all serum components in 1983 could have been an early indication of a subsequent impairment in health, which was reflected in the increased frequency of clinical signs of malnutrition, and of stunting and wasting, a year later in 1984 (Degrémont et al., 1987; Tanner et al., 1987b). The evaluation of the results of the 1985 survey will show whether the increase in the biochemical parameters observed in the period 1983–1984 was followed by a reduction in the signs of clinical malnutrition and an improvement of anthropometric parameters.

The biochemical analysis of a total of 1590 serum samples has provided baseline data for a number of parameters for children living in a rural Tanzanian community. It seems likely that the values found here could serve as reference for children living in an environment with similar epidemiological and nutritional features. The present data show that many factors may affect the level of biochemical parameters. Finally, this study has demonstrated that before any single serum parameter, such as e.g. prealbumin or zinc, can be promoted as a tool to monitor child health, the relevant limits and its predictive



power have to be carefully assessed in the epidemiological setting concerned; especially in areas with different types and levels of infectious diseases.

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