SERUM VITAMIN B₁₂ AND FOLIC ACID (P.G.A.) LEVELS IN HYPOPROTEINAEMIA AND MARASMUS IN INDIAN CHILDREN

BY

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The syndrome of kwashiorkor is seen predominantly in countries where children suffer from nutritional deficiencies, particularly of protein. In countries like India, where the diet is often deficient in animal protein, an associated vitamin B₁₂ deficiency also occurs, and vitamin B₁₂ and folic acid play an important role in the amino acid metabolism. Clinical trials have been undertaken to study the growth promoting effect of vitamin B₁₂ in infants and children; since very little is known about the initial levels of serum vitamin B₁₂ and folic acid (P.G.A.) in these cases, it is difficult to judge whether or not there were, in fact, deficiencies. The results of such trials are conflicting (Rascoff, Dunewitz and Norton, 1951; Benjamin and Pirrie, 1952; Finberg and Chow, 1952; Wilde, 1952; Campbell and McLaughlan, 1955).

In a previous study in healthy Indian medical students, vegetarians tended to have significantly lower serum vitamin B₁₂ and folic acid levels than meat eaters from the same group (Dhopeswarkar, Trivedi, Kulkarni, Satoskar and Lewis, 1956; Satoskar, Kulkarni and Rege, 1961b). These vegetarians had no clinical or other haematological evidence of vitamin B₁₂ or folic acid deficiency and the serum protein patterns revealed no evidence of hypoproteinaemia (Satoskar and Lewis, 1954). In contrast to this, significantly higher serum vitamin B₁₂ values were observed in Indian mothers belonging to low socio-economic groups and their infants. The mean serum albumin and A/G ratios in these mothers were lower than the normal standards, indicating some degree of hypoproteinaemia (Kulkarni, Satoskar, Parikh and Chitre, 1959; Satoskar, Kulkarni, Mehta and Parikh, 1961a).

High serum vitamin B₁₂ levels have been reported in various liver disorders (Rachmilewitz, Aronovitch and Grossowicz, 1956; Jones, Mills and Capps, 1957; Mackay, Cowling and Gray, 1957; Rachmile-

witz, Stein, Aronovitch and Grossowicz, 1958; Nelson and Doctor, 1960). Earlier studies indicated that some of the cases of protein malnutrition also had significantly raised serum vitamin B₁₂ (Dhopeswarkar *et al.*, 1956; Macdougall and Ross, 1960; Satoskar, 1960; Satoskar *et al.*, 1961a). We have therefore studied the serum levels of vitamin B₁₂ and folic acid in proven cases of protein malnutrition and marasmus.

Material and Methods

Children aged between 1 and 8 years with a clinical diagnosis of protein malnutrition or marasmus, according to the criteria described elsewhere (Gopalan and Ramalingaswami, 1955), were included in this study. Patients with associated major illnesses such as tuberculosis or liver disorders were excluded. Since many of the cases studied had fever or some respiratory infection at the time of admission, similar cases without clinical evidence of protein malnutrition or marasmus were also studied for comparison, together with healthy normal children from a similar age group.

Serum proteins were analysed by paper electrophoresis (Kulkarni, 1957). Haemoglobin levels were measured by Sahli's method, and packed cell volume and other routine haematological determinations by standard techniques (Wintrobe, 1956).

Serum vitamin B₁₂ assays were carried out with *Euglena gracilis* (Hutner, Bach and Ross, 1956). The folic acid levels were assayed with *Streptococcus faecalis* (Mitbender and Sreenivasan, 1954). All the estimations were done twice.

Liver biopsies were obtained in all the cases of protein malnutrition and marasmus. The grading of the slides was done without any previous knowledge of the clinical severity or the biochemical data.

Results

Serum Vitamin B₁₂ and P.G.A. Levels in Healthy Children. Table 1 shows the serum protein patterns, vitamin B₁₂ and folic acid levels in newborn Indian

TABLE 1

MEAN SERUM PROTEINS WITH STANDARD ERROR, VITAMIN B₁₂, AND P.G.A. LEVELS IN NEWBORN INDIAN INFANTS, HEALTHY CHILDREN AND CHILDREN WITH RESPIRATORY INFECTIONS IN LOW SOCIO-ECONOMIC GROUPS

Group	No.	Age Range (years)	Total Proteins (g. %)	Albumin (g. %)	Gamma Globulin (g. %)	Total Globulins (g. %)	A/G Ratio	A/γ-G Ratio	Serum Vitamin B ₁₂ (μg./ml.)	Serum P.G.A. (mμg./ml.)
Newborn infants with weights over 5 lb. ...	40	—	5.69 0.09	3.66 0.07	1.20 0.03	2.03 0.05	1.86 0.04	3.05 0.08	1,585* (240-4,800)	69.4* (11-148)
Apparently healthy children ...	17	3-10	6.58 0.08	4.02 0.11	1.33 0.06	2.55 0.08	1.62 0.09	3.18 0.25	365† (50-900)	13.9† (3-37)
Children with respiratory infections ...	10	4-10	6.71 0.15	3.17 0.10	1.90 0.09	3.54 0.13	0.91 0.05	1.71 0.09	428‡ (50-1,080)	18.9 (4-40)

* Mean of 20 infants; † Mean of 15 children; ‡ Mean of eight children.

Figures in parenthesis denote the range.

infants, in 17 apparently healthy children and in 10 children suffering from mild respiratory infections but without any clinical evidence of protein malnutrition or marasmus. Parents of all these subjects belong to low income groups. Normal healthy children had 6.58 ± 0.08 (S.E.) g./100 ml. of mean serum total proteins, 4.02 ± 0.11 (S.E.) g./100 ml. of albumin and 1.33 ± 0.06 (S.E.) g./100 ml. of gamma globulin. Serum vitamin B₁₂ and P.G.A. levels ranged from 50-900 μg./ml. and 3-37 mμg./ml. respectively, except in two children where the serum vitamin B₁₂ level was 1,160 and 1,280 μg./ml. In infants the total proteins were lower mainly due to a lower albumin content. The gamma globulin was also slightly lower than in the higher age group. The serum vitamin B₁₂ and P.G.A. levels were, however, much higher in some of the infants.

In children with associated respiratory infections, there was a significant reduction in the serum albumin level ($p < 0.01$) and a rise in the gamma globulin fraction ($p < 0.01$). Serum vitamin B₁₂ and folic acid levels in this group were, however, within the normal range, except in two cases where the serum vitamin B₁₂ levels were more than 1,100 μg./ml. This probably indicates that mild respiratory infection and fever, although altering the serum protein patterns and A/gamma-G ratio, exerts an insignificant effect on the serum vitamin B₁₂ and P.G.A. levels.

Severity of Disease and Type of Anaemia. The clinical findings in these cases are summarized in Table 2. There were 20 cases of protein malnutrition and eight cases of marasmus. The clinical severity of hypoproteinaemia was assessed according to the extent of oedema, the degree

of anaemia, the skin and hair changes, and the activity of the patient. Thus a case with a reduction in activity, the presence of extensive oedema and ascites and associated skin and hair changes was considered severe; patients with oedema of feet, little lassitude, anorexia and minimal skin changes were diagnosed as mild. Those with an intermediate picture were classified as moderate. In the case of marasmus, children with marked looseness of the skin, including the face, and with extreme lassitude and emaciation were considered severe. Those with looseness of the skin restricted only to the extremities, and with some reduction in activity were classified as mild. There were only three cases in the whole group of 28 children who were considered mild.

The majority of these cases had vitamin deficiencies mainly vitamins A and B. In those with B-complex deficiencies, lack of riboflavin was predominant. In 24 patients, the blood examination revealed either a microcytic or normocytic picture. Only four cases had macrocytic anaemia.

The liver could be palpated in 15 cases; in none was the spleen palpable and there was no evidence of kidney damage.

Total white blood cell count was high in those cases with some respiratory infection and fever at the time of admission.

Serum Vitamin B₁₂ and P.G.A. Levels and Liver Damage. Liver biopsy findings, serum vitamin B₁₂ and P.G.A. levels in these cases are tabulated in Table 3. Grading of biopsies was done according to the histological findings in the liver as follows:

I—Mainly swelling of the parenchymatous cells with occasional vacuolation (Fig. 1).

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TABLE 2

CLINICAL AND HAEMATOLOGICAL FINDINGS IN CASES OF HYPOPROTEINAEMIA AND MARASMUS

Case	Sex	Age (years)	Clinical Severity	Vitamin Deficiency	Liver Size (cm.)	Type of Anaemia	Total W B.C./c.mm.
MKR	M	1	Mild	—	—	Normocytic and normochromic	8,100
PRA	M	4	Mild	A, B ₂ , D	—	Macrocytic and normochromic	6,100
KAL	F	5	Moderate	—	1	Microcytic and normochromic	8,600
KIS	M	8	Moderate	A, B ₂	—	Normocytic and normochromic	10,000
RS	M	6	Moderate	D	5	Microcytic and normochromic	8,100
SUB	M	2	Moderate	A, B, D	4	Normocytic and normochromic	26,000
DAD	M	3	Moderate	A, B	2	Normocytic and hypochromic	14,600
GHR	M	3	Moderate	—	—	Normocytic and normochromic	6,200
VIL	M	4	Moderate	A, B ₂ , D	4	Normocytic and normochromic	10,100
MAL	F	1½	Severe	A	3	Microcytic and hypochromic	23,700
KAB	M	2½	Severe	—	2	Microcytic and hypochromic	24,600
MUN	M	5	Moderate	—	1·5	Macrocytic and hypochromic	10,100
LAX	M	1	Severe	A	1·5	Microcytic and normochromic	6,700
PET	M	8	Severe	A, B ₂	—	Normocytic and normochromic	14,400
SUN	F	4	Severe	A, B ₂ , D	2	Microcytic and normochromic	11,800
VAS	M	3	Severe	A, B	—	Microcytic and hypochromic	23,000
GAJ	F	6	Severe	A, B, C	—	Microcytic and normochromic	7,200
MAT	F	3	Severe	A, B	—	Microcytic and normochromic	18,000
SUS	F	3	Severe	A, B ₂	—	Normocytic and normochromic	24,200
SHL	F	1½	Severe	A, B, D	—	Normocytic and normochromic	15,000
SHO*	F	1½	Mild	A, D	5	Microcytic and normochromic	12,700
SAM*	F	1½	Severe	B	—	Normocytic and normochromic	11,100
AMM*	F	4	Severe	A, B	—	Macrocytic and hypochromic	8,900
GUL*	F	2	Severe	A, D	2	Microcytic and normochromic	8,900
KAD*	F	1	Severe	A, B	—	Macrocytic and normochromic	24,600
ROS*	F	4	Moderate	—	—	Normocytic and hypochromic	9,800
PLA*	F	5	Moderate	—	6·5	Microcytic and normochromic	7,200
ZAH*	F	4	Moderate	B ₂ , C	2	Microcytic and normochromic	10,100

* Marasmus.

TABLE 3

SERUM PROTEINS, VITAMIN B₁₂, AND FOLIC ACID (P.G.A.)
LEVELS IN HYPOPROTEINAEMIA AND MARASMUS

Case	Liver Biopsy	Total Proteins (g %)	Albumin (g. %)	Gamma Globulin (g. %)	A/G Ratio	A/γ-G Ratio	Serum B ₁₂ (μg./ml.)	Serum P.G.A. (mμg./ml.)
MKR	Swelling of parenchymatous cells	4·1	1·72	1·11	0·71	1·53	900	17
PRA	Swelling of parenchymatous cells with occasional vacuolation	4·1	1·40	1·17	0·52	1·20	240	5
KAL	Swelling of parenchymatous cells	5·1	1·56	1·59	0·44	0·98	300	4
KIS	Swelling of parenchymatous cells	4·9	1·40	2·00	0·40	0·70	60	5·6
RS	Moderate fatty change	3·0	1·00	1·09	0·50	0·92	3,800	100
SUB	Moderate fatty change	5·7	1·94	2·08	0·51	0·93	2,200	6·2
DAD	Moderate fatty change	3·9	0·74	1·82	0·23	0·41	4,800	36
GHR	Moderate fatty change	2·2	0·43	0·84	0·24	0·51	6,500	42
VIL	Moderate fatty change	3·2	0·80	1·51	0·33	0·53	420	3·6
MAL	Severe fatty change	3·1	0·51	1·42	0·20	0·36	2,090	—
KAB	Severe fatty change	3·0	0·61	1·35	0·25	0·45	650	—
MUN	Severe fatty change	3·2	0·95	0·97	0·42	0·98	1,700	5·6
LAX	Severe fatty change	4·1	1·30	1·54	0·46	0·84	390	15
PET	Severe fatty change	4·0	0·85	1·65	0·27	0·51	1,790	6
SUN	Severe fatty change	3·3	0·74	1·63	0·29	0·45	6,500	100
VAS	Severe fatty change and cirrhotic change	3·6	1·06	1·21	0·52	0·88	3,280	6·4
GAJ	Necrosis and cirrhotic change	5·0	0·79	3·34	0·19	0·24	2,600	2·8
MAT	Moderate fatty change	3·9	0·78	1·40	0·36	0·56	2,100	—
SUS	Moderate fatty change	4·1	1·47	1·51	0·56	0·97	2,100	—
SHL	Swelling of parenchymatous cells	5·4	2·80	1·18	1·07	2·37	680	—
SHO*	Occasional fatty change and cirrhotic change	6·2	2·22	2·72	0·56	0·82	480	21
SAM*	Swelling of parenchymatous cells	5·4	2·81	1·14	1·08	2·46	1,720	—
AMM*	Swelling of parenchymatous cells	4·0	1·02	1·82	0·34	0·55	980	4·4
GUL*	Swelling of parenchymatous cells	6·9	2·68	2·09	0·64	1·30	60	4
KAD*	Swelling of parenchymatous cells	4·5	1·82	1·45	0·68	1·26	2,220	3
ROS*	Moderate fatty change and precirrhotic change	4·3	1·22	1·55	0·40	0·79	2,700	—
PLA*	Severe fatty change	4·1	1·17	1·74	0·40	0·67	2,600	21
ZAH*	Severe fatty change and cirrhotic change	4·1	1·24	1·70	0·43	0·74	600	—

* Marasmus.

Fig. 1.—Liver biopsy photomicrograph (H. and E.), showing swelling of the parenchymatous cells.

Fig. 3.—Liver biopsy photomicrograph (H. and E.), showing severe fatty change.

Fig. 2.—Liver biopsy photomicrograph (H. and E.), showing moderate fatty change.

- II—Moderate fatty change, where a moderate amount of fat was present, occupying half or more of the cytoplasm (Fig. 2).
- III—Severe fatty change in which almost the whole lobule was affected and the sinusoids were very narrowed (Fig. 3).
- IV—Precirrhotic changes, wherein the lobules showed moderate to marked fatty changes combined with increasing fibroblastic connective tissue arising from the portal tracts and spreading into the liver parenchyma, but without connecting up the portal tracts.
- V—Cirrhotic change in which there was diffuse hepatic fibrosis in a fatty liver.

In all these cases the total serum proteins were low, mainly at the expense of marked reduction in serum albumin content. In 10 patients the serum albumin level was below 1.0 g./100 ml. Nearly two-thirds of the cases had high gamma globulin levels as compared to levels of 1.33 ± 0.25 (S.D.) g./100 ml. in healthy children. Many of these cases had evidence of respiratory or gastro-intestinal infections. Very high values for gamma globulin above 2.75 g./100 ml. were observed in three out of four cases, and the liver biopsies showed cirrhotic changes. In one of these, the serum albumin level

was only 0.79 g./100 ml., while the gamma globulin was 3.34 g./100 ml.

A decrease in A/G ratio may be due to a drop in the albumin, a rise in the globulin or both. Since the liver damage mainly alters the serum albumin and gamma globulin levels, the albumin/gamma globulin ratio (A/γ-G) might be a more useful index in assessing the extent of hepatocellular damage; the figures for A/γ-G ratios are included in the Tables. The A/G ratios were markedly reduced in all the cases. Only four had A/G ratios more than 0.6. The changes are more clearly demonstrated by A/γ-G ratios. There was, however, no correlation between the A/G or A/γ-G ratios and the extent of the liver damage as seen by liver biopsies, although they were markedly low in all the cases with distinct fatty change in the liver.

In four cases clinically diagnosed as marasmus, the liver biopsy studies revealed fatty changes similar to those observed in hypoproteinaemia. One patient (K.A.D.) died a few days after admission. The liver biopsy showed swelling of the parenchymatous cells, but serum vitamin B₁₂ was 2,220 μμg./ml. Autopsy revealed severe fatty change in the liver. The changes in the liver observed in these cases of marasmus could have been due to an association of marked proteinaemia in addition to calorie deficiency.

Serum vitamin B₁₂ was higher than 1,000 μμg./ml. in 16 cases and in two of these it was as high as 6,500 μμg./ml. In all these cases repeated estimations were done to confirm the results. The levels of serum vitamin B₁₂ could not be correlated with the extent of liver damage, but were found to be associated with the fatty change in the liver (Fig. 4). In some cases with cirrhotic change the serum vitamin B₁₂ was lower than 1,000 μμg./ml.

Serum vitamin B₁₂ levels could not be correlated with total α, α₂ or β globulin, and they were not related to the clinical severity of the disease; neither was there any correlation with the total white blood cell count.

Serum P.G.A. levels showed marked variations, so that no definite conclusions could be drawn.

Serum Vitamin B₁₂ after Treatment. All these cases were treated with protein therapy without any additional vitamin B₁₂ or folic acid and they received vitamin A or other factors of B complex to correct the appropriate deficiency. Some of these cases were followed up for the period of two months. From Table 4 it can be seen that in all the cases followed up, serum vitamin B₁₂ levels showed a marked drop with the progressive improvement. Studies on second liver biopsies, obtained four to

Fig. 4.—Correlation of serum vitamin B₁₂ levels with liver biopsy studies.

- I—The mean serum vitamin B₁₂ level in normals with the range.
- II—Swelling of the parenchymatous cells.
- III—Moderate fatty change.
- IV—Severe fatty change.
- V—Precirrhotic change.
- VI—Cirrhotic change in a fatty liver.

six weeks after treatment, also showed definite improvement. Because of the lack of any correlation initially, serum P.G.A. estimations were not repeated.

Discussion

There seems to be a considerable variation in serum vitamin B₁₂ levels in children reported from various countries (Macdougall and Ross, 1960). Besides the differences in techniques of estimation, various other factors, such as variations in diet, type of intestinal flora and the sub-clinical liver damage, might be responsible for such a variation. Healthy Indian adults, who are not vegetarians, have serum vitamin B₁₂ levels similar to those reported by Western workers. However, in healthy lacto-vegetarians serum vitamin B₁₂ and P.G.A. levels show significantly lower values, without any significant differences in haematological data or protein patterns (Satoskar *et al.*, 1961b). Some of the newborn Indian infants may show markedly elevated serum vitamin B₁₂ and P.G.A. levels, and these have been correlated with similar high serum vitamin B₁₂ values in their mothers. The probable cause for such high values has been discussed previously (Satoskar *et al.*, 1961a). Healthy Indian children belonging to a similar group have serum

TABLE 4

SERUM PROTEINS AND VITAMIN B₁₂ LEVELS IN HYPOPROTEINAEMIA AND MARASMUS, BEFORE AND AFTER TREATMENT

Case	Follow-up (days)	Haemato- crit (%)	Hb (g. %)	Total Proteins (g. %)	Albumin (g. %)	Gamma Globulin (g. %)	A/G Ratio	A/γ-G Ratio	Serum B ₁₂ (μg./ml.)
DAD	0	—	6.0	3.9	0.74	1.82	0.23	0.45	4,800
	21	—	10.0	7.3	3.00	2.09	0.70	1.43	440
SUN	0	22	7.5	3.3	0.74	1.63	0.29	0.45	6,500
	21	—	—	5.1	1.62	1.85	0.46	0.88	220
	60	40	12.0	6.1	3.05	1.38	1.00	2.21	50
PET	0	29	9.0	4.0	0.85	1.65	0.27	0.51	1,790
	15	—	—	4.9	1.70	1.78	0.53	0.96	310
	30	36	13.0	6.3	2.95	1.79	0.88	1.65	170
VAS	0	27	8.0	3.1	1.06	1.21	0.52	0.88	3,280
	15	35	12.0	4.7	1.65	1.48	0.54	1.11	756
	45	37	13.0	6.3	3.04	1.60	0.93	1.90	120
ZAH*	0	24	9.0	4.1	1.24	1.67	0.43	0.74	600
	15	—	11.0	6.1	2.77	1.90	0.83	1.46	165
AMM*	0	20	3.5	4.0	1.01	1.82	0.34	0.55	980
	15	23	4.0	5.0	2.22	1.43	0.80	1.55	880
	30	—	7.0	5.8	2.43	2.01	0.74	1.21	330

* Marasmus.

B₁₂ and P.G.A. levels of 50-900 μg./ml. and 3-37 μg./ml. respectively. Serum vitamin B₁₂ values lower than 100 μg./ml., observed in some of these healthy children, are consistent with our results in adult lacto-vegetarians. Serum vitamin B₁₂ values above 1,000 μg./ml. were observed only rarely in healthy children or adults.

It is clear that kwashiorkor is essentially a disease of poverty and is associated with an inadequate diet. Although the predominant deficiency is that of proteins, other nutritional deficiencies particularly of calories and various vitamins and minerals also contribute to the syndrome (Trowell, Davies and Dean, 1954; Gopalan and Ramalingaswami, 1955). Cases reported here were suffering from multiple deficiencies and this is reflected in the clinical manifestations and type of anaemia observed. In the majority of cases, the blood picture was either normocytic or microcytic, and only four patients had macrocytic anaemia, and in these the serum vitamin B₁₂ levels were high, while P.G.A. levels were low. The anaemia in kwashiorkor does not present a clear or constant morphological picture. Usually it is normocytic or slightly macrocytic and often microcytic (Trowell *et al.*, 1954). In a previous study from India, haematological studies revealed a normocytic blood picture in 87% of the cases and macrocytic in 13%. The anaemia was hypochromic with low mean corpuscular haemoglobin concentration in 12 patients (Gopalan and Ramalingaswami, 1955). In a study reported from Durban the anaemia was normocytic in 24, microcytic in four and macrocytic in four cases out of 36

children (Scragg and Rubidge, 1960). In a series of 21 cases of kwashiorkor in Africans, appreciable normocytic or macrocytic anaemia was found in six cases, while two-thirds of the children had haemoglobin levels of 9.0 g./100 ml. Megaloblastic changes were present in only two cases (Adams, 1954). Those megaloblastic anaemias in African children which respond to folic acid but not to penicillin had serum vitamin B₁₂ values ranging from normal to very high. In non-megaloblastic, microcytic, iron-responding anaemias in Africans, the vitamin B₁₂ levels also ranged from normal to high (Foy, Kondi and Manson-Bahr, 1955). All the children in the present series with hypoproteinaemia and marasmus were severely undernourished and their home diet contained little animal protein. However, serum vitamin B₁₂ levels in many of these were markedly raised.

Various pathological changes in the liver and the muscle tissue have been described in kwashiorkor (Trowell *et al.*, 1954). In this series changes ranging from parenchymatous swelling to cirrhosis in fatty liver, were observed in cases of protein malnutrition. A few cases of marasmus also had fatty livers. Generally, the high serum vitamin B₁₂ levels could be correlated with the fatty change. Reduction in the A/G or A/gamma-G ratios due to other causes, in the absence of liver damage such as a fatty change, was rarely associated with high serum B₁₂ values. Previously very high serum vitamin B₁₂ levels up to 13,000 μg./ml. have been reported in certain liver disorders (Rachmilewitz *et al.*, 1956; Jones *et al.*, 1957; Mackay *et al.*, 1957;

Grossowicz, Hochman, Aronovitch, Izak and Rachmilewitz, 1957; Rachmilewitz *et al.*, 1958; Nelson and Doctor, 1960). In most of the studies, the common denominator of the high B₁₂ levels in serum in acute as well as chronic liver diseases was the presence of hepatocellular damage (Rachmilewitz *et al.*, 1958). In some cases vitamin B₁₂ roughly paralleled the functional state of the liver as judged by the clinical and laboratory findings and served as a useful diagnostic test for the presence of the degree of hepatocellular damage (Jones *et al.*, 1957; Rachmilewitz *et al.*, 1958). Other authors have reported no significant correlation of abnormal serum or liver B₁₂ values with any liver function tests (Nelson and Doctor, 1960). In our studies there was no correlation between high serum vitamin B₁₂ levels and the clinical severity of the condition or the degree of liver damage as judged by A/G, A/γ-G ratios and liver biopsy. It is realized that liver biopsy was not always be diagnostic of the degree of hepatocellular damage (Zamcheck and Sidman, 1953). Results of the serum folic acid estimations revealed no correlation with the liver damage.

The increase of serum vitamin B₁₂ in liver disease is considered to be due to the release of the stored vitamin B₁₂ from the damaged liver cells, since, on occasions, excessive amounts of B₁₂-binding proteins are released from a damaged liver (Rachmilewitz *et al.*, 1956; Mackay *et al.*, 1957); also a definite decrease in hepatic B₁₂ content in liver disorders has been demonstrated (Nelson and Doctor, 1960). However, the inability of the damaged liver to take vitamin B₁₂ from circulation could also contribute to the increase in serum vitamin B₁₂ levels. Such impairment of radio-vitamin B₁₂ uptakes has been demonstrated in liver diseases (Glass, Boyd and Ebin, 1958). Furthermore, as in the liver, damaged muscle tissue may also play a similar role. In some of our cases muscle biopsies showed definite pathological changes.

Present evidence regarding the usefulness of vitamin B₁₂ in the treatment of kwashiorkor is equivocal. It is difficult to correlate the findings of high serum vitamin B₁₂ levels with the beneficial effects of B₁₂ therapy in patients and it seems doubtful whether the administration of large doses of vitamin B₁₂ in cases with high serum levels would in fact modify the course of the disease in protein malnutrition.

Summary

The serum proteins, vitamin B₁₂, P.G.A. levels and the type of anaemia were studied in Indian children suffering from hypoproteinaemia and

marasmus. The blood picture was normocytic in 11, microcytic in 13 and macrocytic in four children. The serum vitamin B₁₂ levels were significantly higher in 16 out of 28 children studied and these could be correlated with the fatty change in the liver. As a result of therapy, the serum vitamin B₁₂ dropped to normal values. The P.G.A. levels, however, revealed no correlation.

The implications of these findings are discussed.

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