Effect of Dietary Protein on Blood Regeneration of Anemic Patients Suffering from Parasitic Infestation

PRELIMINARY REPORT

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ANEMIA is relatively widespread in Iraq, especially among inhabitants of the rural areas where the condition results from the frequency of parasitic infestation, notably ankylostoma and bilharzia. Also, the diet of these people is deficient in certain nutritional elements, particularly animal protein, and is probably an additional factor in the causation of anemia. It was considered of interest to study the effect of various levels of protein in the diet on the regeneration of hemoglobin and red blood corpuscles, the object being to find the optimum diet in the treatment of anemia and to find out whether the administration of iron together with the irradication of parasitic infestation in a community would be all that is needed for proper treatment.

METHOD OF STUDY

The patients on whom the study was carried out were farmers or mud workers hospitalized for treatment of anemia. They were suffering from ankylostomiasis, and some of them were also suffering from bilharziasis. All the patients chosen for study were of the same socio-economic level; they were from the rural areas outside the city of Baghdad, or from the neighboring provinces. Their diet had previously consisted mainly of bread, dates, and vegetables when available. Rice was eaten two or three times weekly, and milk, meat, and eggs were occasionally consumed. On the whole, one could consider their diet to be lacking particularly in animal protein.

This preliminary report is based on the results of 53 cases studied so far. Forty-eight patients were males and five were females. The average age of the group studied was 21.68 years, with a range of 12 to 55 years. The majority of the patients were between 18 and 30 years of age. All female patients suffered from amenorrhea.

Stool examinations revealed that 51 patients were infested with ankylostoma; 16 of them were also suffering from urinary bilharzia, and three patients had ascaris as well. Two patients were suffering from bilharzia only.

The patients were divided into two major groups: the first group consisted of 27 patients who received a relatively low protein diet, and the second group consisted of 26 patients who received a modified standard hospital diet. The constituents of the two diets are shown in Tables I and II. The low-protein diet supplied 3,200 calories and 64 grams of protein; the modified standard hospital diet supplied 3,440 cal and 102.5 g protein. It was not considered practical to raise the calories in the low-

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This work has been done at the suggestion of Professor H. Gounelle, F.A.O. Nutrition Expert for Iraq.

The biochemical tests have been performed by Drs. Hasan Rabii and Mohammed Abdulnabi assisted by Leila Yousef Dhia and Nessima Abuthrab, the National Nutrition Institute Laboratories. Results will be the subject of a further publication.

The dietetic studies have been conducted by Miss Thérèse Béné, dietitian, the National Nutrition Institute of Baghdad, under the F.A.O. Technical Assistance Program. For her aid we are very grateful.

protein diet to the level of the other diet, since such a rise would have entailed the consumption of more fat and sugar. This would have rendered the diet unpalatable and at the same time intolerable, especially since it was intended that the diet be followed for one month. However there were enough calories in the low-protein diet to make available sufficient protein for tissue regeneration.

TABLE I

Daily Constituents of the Low-Protein Diet

Quantities indicated as edible part	
Breakfast	
Tea + sugar	20 g
Jam	25
Butter	20
Fruit (apple type)	100
Bread	100
Lunch	
Meat	40
Vegetables	200
Rice	150
Fruit (apple type)	250
Bread	100
Jam	25
Butter	15
4 o'clock	
Dibis*	30
Leban†	100
Tea + sugar	20
Dinner	
Salad	100
oil	10
Potatoes or	150
macaroni	60
Bread	100
Fruit	250
Jam	25
Butter	15

This diet supplies 3,200 calories and 64 g protein (8 per cent of the total calories) of which 10.7 g are animal protein.

* Date syrup

† Yoghurt

The average daily consumption of the group that received the low-protein diet was 2,900 cal and 56.4 g total protein, representing 7.8 per cent of the calories; the average daily quantity of animal protein consumed was 15 g. The group that received the modified standard hospital diet consumed an average of 3,277 cal and 103 g total protein, representing 12.6 per cent of the calories; the average daily consumption of animal protein was 37.2 g.

TABLE II

Daily Constituents of the Modified Standard Hospital Diet

Quantities indicated as edible part	
Breakfast	
Tea + sugar	20 g
Milk	150
Eggs (2) or	
"gaimar"	40
Bread	200
Lunch	
Meat	60
Rice	200
Vegetables	250
Fruit	225
Bread	100
4 o'clock	
Tea + sugar	20
Dinner	
Soup containing cereals	20
and pulses	20
Meat	50
Potatoes	150
or macaroni	60
or pulses	60
Salad	100
oil	10
Bread	100
Custard:	
milk	100
sugar	20
flour	10

This diet supplies 3,440 cal and 102.5 g protein (12 per cent of the total cal) of which 35.7 g are animal protein.

Duration of the Experiment

The majority of the patients were kept under experimental control from 26 to 32 days. In three patients, the study had to be terminated on the 21st day; in one, on the 17th day; and in another, on the 12th day.

Since there are several nutritional factors essential for hemopoiesis and in order to eliminate the most important one in the causation of ankylostoma anemia, a satisfactory supply of iron was given by mouth to all patients. Ferrous sulfate in a dosage of 2 g was administered daily. Practically all patients tolerated the drug well, and none suffered from vomiting or diarrhea. Vitamin C was not

given with the iron, nor was any liver extract or vitamin B_{12} given. However, there was some difference in the vitamin C content of both diets; the low protein diet contained more fruits and thus supplied more vitamin C than the modified standard hospital diet.

A dietitian weighed the diet of each patient and kept it on a separate tray clearly marked with the patient's bed number. This work involved the weighing of 4,548 meals for the total number of patients during the experimental period, as well as the reweighing of what was left in the dishes. During meals, patients were supervised to prevent them from offering part of their meals to other patients. All trays were checked at the end of each meal, and any foodstuff left was weighed and the amount recorded on the "ingesta" sheet for that patient.

At the end of the experimental period, calculations were made of the total consumption of each foodstuff, from which the average daily consumption was derived. The results were then expressed in terms of calories and proteins, using the International Food Composition Table (compiled by F.A.O.) or data supplied by our laboratory. Precautions were taken to prevent relatives and visitors from bringing foodstuffs to patients.

Hematologic Studies

Blood was collected from the anticubital vein, avoiding undue venous congestion. As an anticoagulant, a mixture of 0.4 per cent potassium oxalate and 0.6 per cent ammonium oxalate in the dry form was used.[1] Hemoglobin was estimated by the oxyhemoglobin method using the "Grey wedge photometer," so calibrated that the reading 100 corresponded to 14.8 g Hb/100 ml blood. Cell counts were made in duplicate, and the packed cell volume was determined by use of the Wintrobe tube centrifuged for 30 min at 3,000 revolutions per min. After being read, the tube was recentrifuged for another 15 min to ascertain that no further fall occurred in the level of the red blood cells.

The mean corpuscular volume (M.C.V.) and the mean corpuscular hemoglobin concentration (M.C.H.C.) were calculated. Tables III and IV show the results of the various hematologic studies carried out on the two groups of patients. The range of normality used for the M.C.V. was 75–96 c.μ. and for the M.C.H.C., between 28 to 34 per cent.[2] According to the classification of Wintrobe, the types of anemia in the cases studied were as noted in Table V.

TABLE III

Results of Hematologic Studies Carried Out at the Beginning of the Experiment on Patients Receiving the Low-Protein Diet

No. of patient	Hb %	R.B.C. in millions	P.C.V.	M.C.V. in c.μ.	M.C.H.C. %
1	61	3.92	33	84.2	26.8
2	28	1.97	17	86.3	24.3
3	33	2.00	14	70	34.8
4	44	4.02	32.5	80.8	19.6
5	25	1.59	16	100.6	22.6
6	60	3.73	33	88.4	26.3
7	81	3.80	38	100	30.8
8	84	4.25	43.5	102.3	28.
9	38	3.23	26	80.5	21.2
10	30	2.64	18.5	70	23.5
12	45	3.69	26	70.4	25.
13	35	2.34	17	72.6	30.4
14	43	2.64	22.5	85.2	28.2
15	36	2.62	19	72.5	28.
16	31	2.78	21	75.5	21.8
17	64	4.19	37	88.3	24.8
18	34	2.21	19	86.3	26.5
19	55	3.54	26	73.4	30.6
20	36	2.89	20.7	71.8	27.7
21	54	3.71	30	80.8	26.6
22	30	1.50	16	106.6	27.7
23	36	2.43	20	82.3	26.6
24	37	2.79	20	71.7	27.4
25	42	2.53	22	86.6	28.2
26	43	2.18	23	105.5	27.6
27	45	2.32	24	103.5	27.7
28	56	3.33	31	93.1	28.1
Mean	44.6	2.92	24.6	84.7	26.7

P.C.V. = packed cell volume; M.C.V. = mean corpuscular vol; M.C.H.C. = mean corpuscular hemoglobin concentration.

Biochemical Studies

Blood proteins, plasma iron, and the unsaturated iron binding capacity in serum were determined for most of the patients on admission as well as at the end of the study period. Analysis of these results will be the subject of a further publication.

Clinical Examination

In the group that received the low-protein

diet, one patient had an enlarged liver, three fingers' breadth below the costal margin and a spleen which reached the umbilicus. In another patient, the liver was enlarged two fingers' breadth below the costal margin. In seven patients, it was just palpable. Pitting edema was not demonstrated in any of the patients in this group, although puffiness of the face was noted in three cases. In three cases, the spleen was palpable two to three fingers' breadth below the costal margin; in four cases, it was just palpable.

In the group that received the modified standard hospital diet the liver was just enlarged in six cases. The spleen was significantly palpable in two cases, slightly in three cases, and just palpable in eight cases. There was slight pitting edema in one patient.

Body Weight: The weights of more than half of the patients (52.8 per cent) could be considered to be normal according to the "Standard Weight" table published by the Association of Life Insurance Medical Directors and Actuarial Society of America (1912).[3] The normal range was considered 10 per cent above or below the average weight. Thirty-four per cent of the patients had a weight deficit falling in the range of 10–20 per cent below average weight, and 13.2 per cent in the range of 20–30 per cent below average weight.

The greater part of the patients in both groups were dewormed at the start of the experimental period. Tetrachlorethylene in a dose of 3 ml was administered weekly for three consecutive weeks, and those patients simultaneously infested with urinary bilharziasis were also treated with fouadin. At the completion of the anti-parasitic treatment, repeated stool and urine examinations were made. In a few cases, stool examinations remained positive for ankylostoma ova even after three doses of tetrachlorethylene.

Since the dietary histories of the patients were practically the same and since the major cause of the anemia was due to intestinal blood loss caused by ankylostoma, it was postulated that the level of anemia bore some relation to the number of worms in the intestine. It was therefore decided that the blood regeneration of certain patients in both groups would be compared while they still harbored the parasites. Accordingly, two sub-groups were created for this experimental procedure as follows:

TABLE IV

Results of Hematologic Studies Carried Out at the Beginning of the Experiment on Patients Receiving the Modified Standard Hospital Diet

No. of patient	Hb %	R.B.C. in millions	P.C.V.	M.C.V. in c.μ.	M.C.H.C. %
50	35	2.59	20.5	79.1	24.7
51	44	2.90	22	75.8	29.6
52	24	2.01	14	69.6	24.8
53	40	3.20			
54	50	3.84	27	70.3	26.8
55	62	3.35	33	98.5	27.2
56	47	3.45	27.5	79.7	24.7
57	52	3.56	27	75.8	28
58	60	4.35	30	69.	29
59	50	3.62	28	77.3	25.9
60	27	1.58	15	94.3	26.6
61	40	3.04	24	78.9	25.0
62	50	3.35	26.5	79.1	28.
63	56	4.34	36.5	84.1	22.6
64	37	2.79	20.5	73.5	26.7
65	85	3.86	39	101.	32.2
66	38	2.82	21.5	76.2	26.1
67	36	2.56	22	86	24.2
68	26	1.71	14.5	84.8	26.4
69	44	3.73	29	77.7	22
70	60	3.85	31	80.5	28.6
71	49	3.15	25	79.3	29.
72	35	2.78	19	69	27.2
73	31	2.30	17	74	26.9
74	28	1.94	15	77.3	27.6
75	40	1.86	21	112.9	28.2
Mean	44	3.02	24.2	75.8	26.7

26 Patients on Modified Standard Hospital Diet		*27 Patients on Low-Protein Diet*	
Dewormed at the start	Not dewormed	Dewormed at the start	Not dewormed
13	13	20	7

RESULTS

In analyzing the results, patients had to be further classified with respect to the level of hemoglobin at the beginning of the experimental period. It has been found that the mean daily rise of hemoglobin varies with the degree of anemia at the start. Thus, a patient whose hemoglobin level at the beginning

TABLE V

Types of Anemia in Patients Receiving the Two Diet Programs

Type of anemia	Number of patients	
	Low-protein diet group	Standard diet group
Macrocytic orthochromic	2	2
Macrocytic hypochromic	4	1
Normocytic orthochromic	3	5
Normocytic hypochromic	10	11
Microcytic orthochromic	4	1
Microcytic hypochromic	4	5
Total	27	25

is 30 per cent will have a higher daily rise of hemoglobin than a patient whose hemoglobin level is 60 per cent at the start. Accordingly, patients within each sub-group were arbitrarily classified into three classes according to the level of hemoglobin: (class A) level below 40 per cent, (class B) level between 40 to 59 per cent and (class C) 60 per cent and over. Tables VI and VII show the average daily rise of hemoglobin as well as the average daily increase of red blood corpuscles in the various groups and classes.

Considering the results for the group that was simultaneously dewormed (Table VI) it will be seen that the patients whose hemoglobin level was under 40 per cent and who received the Modified Standard Hospital diet (henceforth called the MSH diet) registered an average daily rise in hemoglobin of 1.93 per cent as compared with 1.42 per cent registered by those receiving the low-protein diet. Although the number of patients is not large, the difference in rise is statistically significant. Similarly, the difference in the average daily rise in red blood cells for the two groups of the class under question is significant—a daily increase of 0.0745 million R.B.C. for patients on the MSH diet as compared with a daily average rise of 0.0487 million R.B.C. for patients on the low-protein diet.

The better effect of the MSH diet on the speed of recovery from anemia as compared with the low-protein diet is also shown in Class "B" (hemoglobin level between 40 to 59 per cent) of the same group (Table VI). An average daily hemoglobin rise of 1.86 per cent is registered on the MSH diet as compared with 1.45 per cent on the low-protein diet. This difference is also statistically significant. However, there is no difference in the average daily rise of red blood corpuscles in this class of patients.

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TABLE VI

Average Daily Increase of Hemoglobin and Red Blood Cells of Anemic Patients Who Were Dewormed During Experimental Period

Type of diet	Class A Hb level below 40%			Class B Hb level between 40–59%			Class C Hb level over 60%		
	Number of patients	Hb rise %	RBC rise in millions	Number of patients	Hb rise %	RBC rise in millions	Number of patients	Hb rise %	RBC rise in millions
Modified standard hospital diet	3	1.93	0.0745	6	1.86	0.0521	4	1.31	0.0365
Low-protein diet	9	1.42	0.0487	6	1.45	0.0530	5	0.71	0.0264

TABLE VII

Average Daily Increase of Hemoglobin and Red Blood Cells of Anemic Patients Who Were Not Dewormed

Type of diet	Class A Hb level below 40%			Class B Hblevel between 40-59%		
	Number of patients	Hb rise %	RBC rise in millions	Number of patients	Hb rise %	RBC rise in millions
Modified standard hospital diet	7	1.99	0.0700	6	1.7	0.0298
Low-protein diet	4	1.34	0.0550	3	1.4	0.0300

level above 60 per cent) is marked (1.31 per cent on the MSH diet as compared with 0.71 per cent on the low-protein diet). Statistically it has not been found to be so. Similarly, no statistical significance is found in the difference between the average daily rise of red blood corpuscles in both groups.

Consideration of the group of patients who were not dewormed (Table VII) shows that the patients who fell under class "A" registered an average daily rise of hemoglobin of 1.99 per cent on the MSH diet as compared with 1.34 per cent on the low-protein diet. Statistically, the difference is very significant. The average daily rise of red blood cells for the same class of patients was 0.0700 million per cu mm of blood on the MSH diet as compared with 0.0550 million on the low-protein diet. This difference is not statistically significant. In the class "B" patients the difference in average daily rise of hemoglobin was not very significant statistically. There also was no difference in the average daily increase of red blood cells for the comparable groups.

A shift to macrocytosis following treatment with iron was found at the end of the experimental period in the blood picture of quite a number of patients. Six of the 20 patients who received the low-protein diet in the group that was dewormed at the start developed macrocytosis. Three other patients remained macrocytic. In a fourth patient, the blood picture was macrocytic at the start but changed to normocytosis. Four patients out of 11 who received the MSH diet in the corresponding group developed macrocytosis, and two already macrocytic remained unchanged.

Among the group that was not dewormed, four patients out of seven on the low-protein diet developed macrocytosis, and one already macrocytic remained so. The blood picture of eight patients out of 13 on the MSH diet also changed to macrocytosis, and one patient already macrocytic remained so.

In a previous work on the anemia of ankylostomiasis, Demarchi and Jalili[4] found similar results as regards the development of macrocytosis during treatment with iron. This phenomenon, as Lehmann[5] suggested, may be due to an outpouring of reticulocytes from a bone marrow stimulated by constant blood loss. The development of macrocytosis may be due to the existence of a dual deficiency of iron and antianemic factor; the macrocytosis of one deficiency may be masked by iron deficiency and on correction of one deficiency the other deficiency develops.[6] On the other hand, the macrocytosis may be simply the result of a macro-normoblastic reaction of the bone marrow activated by a good supply of iron in the presence of blood loss.[2,7]

CONCLUSION

Although the number of patients in each group under study is not large enough to enable one to draw a positive conclusion, there is strong indication that in severe ankylostoma anemia, a diet high in protein is more effective than a relatively low protein diet in the treatment of the anemia. The rate of recovery has been without doubt quicker on the modified standard hospital diet for the severely anemic patients. Qualitatively, there was not much difference between the two diets, since both of them contained animal protein. However, there was a difference of about 38 g in the protein content. The low-protein diet, on the other hand, was in a more favorable position as regards its vitamin C content, but it was certainly not in a similar position as regards its vitamin B_{12} content. The problem of the difference in the iron content of the two diets has been amply counteracted by the administration of a high dose of iron by mouth. Further study is in progress to find out whether a diet containing a still higher percentage of protein would give a more favorable result.

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Catalytic Enzyme for Medical Practice

"Today's medicine's need for an internal critique is even greater than the need of general science for self-correcting forces. Medicine is a curious mixture of arts and science. Where its practice accomplishes useful ends the arts retain their primacy and provide the medium through which science is applied to the welfare of patients. An inner critique has provided self-correcting and adjusting forces in the graphic arts, drama, and music. Politics has its correctives, be they election or revolution. But medicine has never had an effective forum for critique within and only at times fair criticism from outside. Since the conserving arts of medicine, though essential, tend to hold back progress if not examined and refreshed by the experiment and experience of practice, and since the essential characteristic of science is that it is provisional, forever being finished but never finished, *change* is the life blood of medicine. But change, unless directed, rarely correlates with progress. The crucial and painful defect of present-day medical practice is the lack of effective critical introspection. A deficiency of the catalytic enzyme, criticism, can be harmful, can produce as much morbidity and mortality in medical practice, teaching, and research as a vitamin deficiency can produce in a growing, living creature."
—W. B. Bean, *A. M. A. Archives of Internal Medicine* 97: 497, 1956.