Fifty years later infant mortality, the subject of the London conference in 1906, has been brought under strong control in many countries, and to this massive achievement the new service of education has made an indispensable contribution. But great, difficult, and unfinished tasks of promoting the health of infants and children remain; and these tasks will lie largely in the hands of the child welfare service.

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ANAEMIA IN KWASHIORKOR

BY

E. B. ADAMS, M.B., B.Sc., M.R.C.P.

Assistant Physician, King Edward VIII Hospital, Durban

Kwashiorkor has been defined by Brock and Autret (1952) as a nutritional syndrome of African infants and children comprising retarded growth, alterations in skin and hair pigmentation, oedema, fatty infiltration, cellular necrosis or fibrosis of the liver, and frequently a variety of dermatoses. Mortality is heavy in the absence of proper dietary treatment.

The anaemia often found in kwashiorkor is usually mild in degree, normocytic or slightly macrocytic, and has responded somewhat slowly during treatment of the syndrome by high-protein diets (Altmann and Murray, 1948; Trowell *et al.*, 1952). In East Africa, where tropical infestations are common, sometimes there is hypochromia, responding to iron treatment; often there is slight macrocytosis, but megaloblastic change rarely if ever occurs (Trowell, 1949). Lehmann (1952) believes that this macrocytosis without megaloblastic change is due to the presence of reticulocytes following blood loss. In Johannesburg, where parasitic infestations are infrequent, Altmann and Murray have observed a more constant blood picture. They considered anaemia to be due to deficiency of protein. Three of their 34 cases showed macrocytosis, while others became macrocytic on high-protein diets. In the marrow smears of six cases abnormal cells were seen suggestive of lack of liver principle or folic acid, but, as Trowell has also observed, the red-cell precursors were of an intermediate type or macronormoblastic, there were some giant metamyelocytes, but true megaloblasts of Ehrlich were not seen. Walt *et al.* (1950) also record a moderate, slightly macrocytic normochromic anaemia in their cases in Durban. In three, all fatal, anaemia was severe, but there was no megaloblastic change. Macrocytosis was reported by van der Sar (1951) to be common in his 31 cases of kwashiorkor in Curaçao, but in only one was the bone marrow megaloblastic.

It is now generally accepted that the syndrome is due to deficiency of protein in the diet, and that it responds well to treatment with high-protein diets, anaemia slowly improving at the same time. It is said that the anaemia does not respond to folic acid, vitamin B₁₂, or liver extracts (Trowell *et al.*, 1952), although Piéraerts (1950) believes it will respond to these after protein replacement.

The possible relationship of this anaemia to protein deficiency, the occurrence of macrocytosis, and the reports that in the bone marrow there are features of megaloblastic change without the full picture seen in

megaloblastic anaemias have prompted the present investigation, in which haematological findings in a series of cases of kwashiorkor are described.

Clinical Material

Twenty-one cases have been studied—nineteen of African and two of Indian origin. The ages ranged from 1 to 5 years, with a mean of 2 years 3 months. Eleven were male and ten female.

In each case pitting oedema, dermatosis, and lowered plasma proteins were present. With the absence of complicating diseases these were the only criteria used in the selection of cases. Pitting oedema was always found in the legs and usually in the hands. Often facial oedema and generalized anasarca were marked. The dermatosis was similar to that described by Gillman and Gillman (1951) and by Brock and Autret (1952). Total plasma proteins ranged from 3.5 to 4.9 g.%, with a mean of 4.05 ± 0.10 g.%, and the albumin fraction from 1.2 to 2.6 g.% about a mean of 1.89 ± 0.04 g.% (see Table I).

TABLE I.—Plasma Proteins Before and After Treatment, and Plasma Bilirubin on Admission

Case No.	On Admission			After Treatment	
	Total Protein (g.%)	Albumin (g.%)	Bilirubin (mg./100 ml.)	Total Protein (g.%)	Albumin (g.%)
1	4.3	1.6	0.9		*
2	4.0	—	0.9	6.7	4.0
3	3.8	1.8	0.2		*
4	4.0	1.7	0.1	6.3	3.6
5	4.4	2.1	0.2	7.0	4.0
6	3.8	1.5	0.3	7.5	3.8
7	3.5	1.6	0.2	—	—
8	4.9	2.2	0.2	5.9	3.9
9	3.5	2.3	0.3		d
10	3.5	2.3	0.4		*
11	4.7	2.4	0.4		*
12	4.5	1.7	0.7	5.8	3.6
13	3.5	2.6	0.3	8.2	4.3
14	4.9	2.6	0.3	5.8	—
15	3.5	1.9	0.5	7.0	4.0
16	3.8	1.2	0.3		*
17	3.8	1.9	0.4		*
18	3.5	1.5	0.4		d
19	4.5	1.9	0.3	6.7	3.8
20	4.4	1.7	0.3		d
21	4.1	2.0	0.3		*
	4.6	1.8	0.3		*
Means	4.05 ± 0.10	1.89 ± 0.04		6.70 ± 0.23	3.89 ± 0.07

d = died. * = removed from hospital before recovery complete.

No case was included without all these features, but other manifestations of the syndrome such as mental apathy, retardation of growth, and thinning of the hair with reddish pigmentation were present in varying degree. The liver was enlarged in 12 cases. In none was the spleen palpable. Abnormalities were not detected in the heart or nervous system, and lymph nodes were never enlarged. No specific changes were observed in the tongue although it was sometimes red, and there were no significant lung changes clinically or on x-ray examination except in two of the fatal cases which showed radiological evidence of bronchopneumonia.

Stools were sometimes watery and occasionally oily, but diarrhoea was not a marked feature. Stools were always examined, usually on three consecutive days. *Entamoeba histolytica* was isolated in two cases, but there was no dysentery. Ova of ascaris were observed in three cases, while in one of these there were hookworm ova, but here the test for occult blood was negative. This low incidence of parasites indicates the small chance that intestinal infestations were responsible for the anaemia in this series.

Plasma bilirubin was estimated in every case, but in none was it elevated (see Table I).

Treatment consisted of soured milk (maas) or this and a hydrolysed protein preparation ("casydrol") given in alternate feeds until convalescence, when ward diet was added.

Eleven patients made an excellent recovery, with disappearance of all symptoms, loss of oedema and skin changes,

and gain in weight and vitality. Hair changes often persisted. Three children died, permission for necropsy being refused. Seven were removed from hospital against advice before recovery was complete. There was a return of total plasma proteins and albumin to normal values in all cases, with complete clinical recovery except in one in which a final estimation was not made (see Table I).

Methods

Blood was obtained from the jugular veins in all cases, and all haematological investigations were done by me, using dry sterile syringes with ammonium and potassium oxalate as anticoagulant. Haemoglobin was determined by a photometric method. Packed cell volumes were estimated in duplicate and red cells counted in a double chamber filling. Reticulocytes were counted by the method of Dacie (1950). Aspiration specimens of iliac marrow were obtained from every case by iliac puncture and stained with May-Grunwald-Giemsa. Mean corpuscular diameters were measured by the method of Price-Jones (1933).

The Anaemia

On admission most cases showed only mild anaemia. Often, however, there was a drop in haemoglobin, red cells, and packed cell volume in the first week, although this sometimes occurred later. This drop took place without evidence of haemolysis or blood loss. If the lowest haemoglobin levels recorded are examined it is seen that the degree of anaemia encountered in these cases is not so mild. In 14 cases haemoglobin was below 9 g.%, while in six it was less than 7 g.% (see Table II).

White-cell counts tended to be high, with a range from 7,450 to 19,200 per c.mm., about a mean of 12,700 per c.mm. but otherwise they usually showed no departure from normal. Platelets always appeared to be plentiful and platelet counts were not done.

Hypochromia was seen only once—in Case 14 after treatment, when it was of mild degree. Mean corpuscular haemoglobin concentrations varied from 26 to 36%, with a mean of 31%.

Examination of the bone marrow showed normoblastic erythropoiesis in 13 cases and in these there were no abnormalities in the myeloid series. In the remaining eight cases the marrow deviated from normal in varying degree. In two there were some megaloblasts of Ehrlich as well as normoblasts and giant metamyelocytes (Cases 17 and 20). There were also macronormoblasts, some of which had nuclei with several lobes. The bone marrow in the other six cases showed a few giant metamyelocytes and occasional macropolycytes. The red-cell precursors were mainly normoblastic, but a few showed megaloblastic features. In these the cartwheel appearance of the nuclei was absent, a finer chromatin structure taking its place. They are presumably the cells described by Altmann and Murray as being of intermediate type. Premature haemoglobinization was sometimes seen; fully haemoglobinized erythroblasts were sometimes large, occasionally with lobed nuclei, but orthochromatic megaloblasts were not seen.

These cases with bone-marrow abnormalities appear to form a series, at one end of which the marrow is almost normal with only giant metamyelocytes, while at the other there is some definite megaloblastic change.

Cell Size

There was mild macrocytosis in 11 cases in which the mean corpuscular volume was above $100 \mu^3$. It did not appear to be related to the bone-marrow changes just described: in those with normoblastic erythropoiesis the mean was $98.0 \pm 2.7 \mu^3$, while in the group with abnormal marrows there was a mean of $103.9 \pm 2.8 \mu^3$, the difference not being significant (see Table II). In most of the blood films the red cells appeared somewhat large, with some anisocytosis, but little poikilocytosis. Even in the two patients with partial megaloblastic change, the cells in the

blood films were round, but in one anisocytosis was marked (Case 17). This is demonstrated in the Price-Jones curve from this case, which shows broadening of the base and macrocytosis (see Fig. 1). Less variation was observed in other cases. There was some macrocytosis even in cases

FIG. 1.—Erythrocyte diameter distribution curve from Case 17.

FIG. 2.—Erythrocyte diameter distribution curve from Case 16.

FIG. 3.—Erythrocyte diameter distribution curve from Case 8.

with normal marrow—for example, Case 16, in which the M.C.V. was 98 μ^3 , the mean of the group (see Fig 2)—and in others with giant metamyelocytes and some intermediate red-cell precursors—for example, Case 8 (Fig. 3). Reticulocytosis did not seem to be the cause of the macrocytosis in any of these cases.

TABLE II.—Blood Counts on Admission and After Recovery, and Lowest Haemoglobin Recorded

Case No.	On Admission						After Recovery		
	Hb (g./100 ml.)	Red Cells (mill./c.mm.)	M.C.V. (μ^3)	M.C.H.C. (%)	Retic. (%)	White Cells (per c.mm.)	Lowest Hb (g./100 ml.)	Hb (g./100 ml.)	Red Cells (mill./c.mm.)
<i>Cases with Normal Bone Marrow</i>									
1	10.5	3.21	106	31	3.5	14,600	9.0	10.2	2.86
2	7.9	2.42	124	26	7.1	15,600	6.6	10.6	3.97
3	8.2	2.78	103	29	0.6	13,100	8.2		
6	10.5	4.33	83	29	0.7	13,500	8.9	9.5	4.07
7	8.2	2.80	94	31	2.3	12,500	8.2		
9	6.3	2.24	89	32	1.4	18,400	6.3		
10	11.2	3.55	94	33	0.9	7,450	11.2		
11	11.5	3.67	99	32	2.7	9,150	11.5	12.2	3.26
13	12.0	3.76	92	35	2.9	10,500	12.0	11.9	3.37
14	10.8	3.76	90	32	1.2	7,600	6.1	11.2	4.51
15	10.5	3.20	100	33	0.7	11,900	10.5	10.6	3.55
16	8.6	3.15	98	28	1.7	9,150	7.3		
21	10.2	3.20	102	31	2.1	15,450	9.7		
<i>Cases with Abnormal Bone Marrow</i>									
4	7.7	2.58	107	28	3.0	11,050	7.6	9.4	3.23
5	9.5	2.52	119	32	0.3	19,200	8.7	10.6	3.73
8	6.6	2.06	104	30	2.6	9,550	4.7	13.0	3.95
12	9.0	2.46	102	36	3.0	16,400	6.8	11.7	3.85
17	5.5	1.95	97	29	2.9	16,500	5.5		
18	10.0	3.45	90	32	1.6	9,900	8.6	11.9	4.51
19	9.5	2.97	104	31	1.9	16,000	7.1		
20	10.8	3.18	108	31	1.1	9,950	10.8		

d=died. *—removed from hospital before recovery complete.

Case Histories

(i) Normoblastic Anaemias

In this group of 13 patients, the bulk of the series, anaemia was usually mild, although in one child who died haemoglobin on admission was only 6.3 g.%. The mean haemoglobin on admission was 9.7 g.%, while in the seven cases that recovered completely the mean on discharge was 10.9 g.%. Folic acid was used in one and vitamin B₁₂ in another without effect, and ferrous sulphate was ineffective in both. Usually the anaemia increased in severity while the condition of the child improved in all other respects, the blood count after full recovery being slightly higher than on admission, as illustrated by the following example.

Case 14.—An African girl aged 3 years was admitted with gross oedema and patchy pigmentation and desquamation of the groins. Plasma proteins were 3.5 g.%, with 1.9 g.% albumin. Haemoglobin was 10.8 g.%, with 3,760,000 red cells per c.mm., haematocrit 34%, reticulocytes 1.2%. The bone marrow was normoblastic. On maize diet only oedema disappeared in three weeks—when plasma proteins had reached 5.3 g.%, with 3.2 g.% albumin. Hb was then 8.6 g.%, but despite general improvement the blood count dropped steadily. Injection of 50 μ g. of vitamin B₁₂ had no effect. The lowest count was 6.1 g.% Hb, 2,360,000 red cells per c.mm., haematocrit 21.5%, while at the same time plasma proteins were 7 g.% and albumin 4 g.%. Slight hypochromia was now observed in the blood film. Later ferrous sulphate was given by mouth, although the count had already begun to rise. The rate of increase did not appear to be altered. When the child had fully recovered the Hb was 11.2 g.%, red cells 4,510,000 per c.mm., and haematocrit 35.5%.

(ii) Anaemias With Giant Metamyelocytes and Some Red-cell Precursors of Intermediate Type in the Bone Marrow

In this group of six cases the effect of diet only was observed in three. In one with 7.7 g.% Hb on admission (Case 4) anaemia slowly decreased as the child recovered, the Hb reaching 9.4 g.%. The haemoglobin of another with 10 g.% on admission dropped to 8.6 g.% in four days, rising slowly to 11.9 g.% when clinical recovery was complete (Case 18). Reticulocytes, counted daily for two weeks, reached a peak of 7.2% on the ninth day. The fourth child

(Case 19) was admitted with 9.5 g.% (haematocrit 31%), which dropped rapidly to 7.1 g.% (haematocrit 22%) on the sixth day, when he died. There was a peak reticulocyte count of 2.8% on the third day.

One child was given folic acid five weeks after admission. Haemoglobin was rising slowly on diet alone, and there was no reticulocyte increase.

In contrast, two patients with similar bone-marrow pictures responded to treatment with a crude liver extract and vitamin B₁₂.

Case 8.—An African child aged 20 months was admitted with a two-weeks history of swelling of the whole body, vomiting after feeds, anorexia, cough, and passing soft yellow stools. The temperature was 101.6° F. (38.7° C.), pulse 120, and respirations 20, weight 14½ lb. (6.6 kg.). There was marked oedema of the arms, legs, and face, and a red tinge of the hair. Black-pigmented skin changes were present in the inguinal region, with central desquamation, and there were similar lesions on the legs. The mucous membranes were pale. The liver and spleen could not be felt and there were no other abnormalities. The Hb was 6.6 g.%, red cells 2,060,000 per c.mm., haematocrit 21.5%, reticulocytes 2.6%, leucocytes 9,550 per c.mm. (the Price-Jones curve from this case is shown in Fig. 3). The bone marrow was mainly normoblastic, but there were some giant metamyelocytes and the nuclear structure of a minority of the basophil erythroblasts was rather fine. Plasma proteins were 4.9 g.%, albumin 2.2 g.%, bilirubin 0.2 mg. per 100 ml. No pathogens were detected in six stool specimens. The test for occult blood was negative. Urine was normal. X-ray examination of the chest showed marked striations in the right middle lobe, but the Mantoux test was negative, and x-ray films showed no change three weeks later. Free acid was present in the gastric juice after histamine.

On high-protein diet alone reticulocytes reached 5.8% on the fifth day, and oedema began to decrease. After two weeks, however, there was rapid deterioration; on the 17th day the Hb was only 4.7 g.%, with 1,370,000 red cells per c.mm., and haematocrit 15.5%. No reticulocytes were seen. 150 ml. of compatible blood was transfused and 1 ml. of a crude liver extract ("pernaemon") given by intramuscular injection. Seven days later there was a reticulocyte peak of 10.4%.

Two further injections of the same liver preparation were given, the blood count rising steadily to 13.7 g.% Hb in seven weeks, with 4,580,000 red cells per c.mm., and haematocrit 45%. Plasma proteins were 5.9 g.%, albumin 3.9 g.%. There was now no oedema, skin changes had disappeared, and the child was well and happy.

Case 12.—An African infant aged 4 had the same pattern of disease. Anaemia became more severe as oedema subsided and plasma proteins increased, although there was again no haemolysis or blood loss. The admission Hb of 9 g.% dropped in seven days to 7 g.%, with 1,880,000 red cells per c.mm., haematocrit 21.5%, and reticulocytes 2.3%. There was histamine-fast achlorhydria. Injection of 50 μ g. of vitamin B₁₂ was followed in six days by a reticulocyte peak of 12.7%, and the blood count increased on this and further injections of vitamin B₁₂ to reach 11.7 g.% Hb, 3,850,000 red cells, and haematocrit 38.5% on full recovery.

(iii) Megaloblastic Anaemias

There was megaloblastic change in the bone marrow of two infants. In one, who was removed from hospital against advice, there were many typical megaloblasts of Ehrlich and giant metamyelocytes in the marrow (Case 20). These changes were present but less well marked in the other (Case 17), who died, so it was not possible in either to observe the response of the anaemia to treatment.

Case 17.—A male African child of 18 months was admitted with a history of swelling of the body for one month, loose stools, and a cough for two weeks. His diet had consisted entirely of samp porridge and tea. His temperature was 100.4° F. (38° C.), pulse 112, respirations 22, weight 18 lb. (8.2 kg.). He was listless and apathetic, with gross swelling of the whole body and pitting oedema of the limbs and trunk. Facial oedema had occluded one eye. The hair was fine in texture and reddish brown. Widespread dermatosis was present, with scaling on the limbs and lower trunk, large areas of desquamation, and raw bleeding lesions on the legs. The right ear was discharging. The liver was large and firm, but the spleen was not palpable. No other abnormalities were detected. The Hb was 5.5 g.%, red cells 1,950,000 per c.mm., haematocrit 19%, reticulocytes 2.9%, leucocytes 16,500 per c.mm. The blood film showed many macrocytes, some microcytes, but only occasional poikilocytes (mean corpuscular diameter

7.42 μ , standard deviation 1.3 μ , macrocytosis 15%, microcytosis 4.2%—see Fig. 1). Fifteen normoblasts and macronormoblasts and one intermediate megaloblast were seen per 100 white cells, which included one large metamyelocyte. Iliac marrow showed normoblasts, some basophilic megaloblasts, many large haemoglobinized erythroblasts with lobed nuclei, and giant metamyelocytes. Abnormalities were absent in the urine and stool, although the latter was oily. Plasma proteins were 3.5 g.%, albumin 1.5 g.%, bilirubin 0.4 mg. per 100 ml. On admission there were no abnormal chest signs, but x-ray examination on the following day showed bronchopneumonic infiltration in the right upper lobe with an associated pleural effusion, detectable clinically on the next day. This appears to have been a terminal bronchopneumonia, for the child died shortly afterwards. Permission for necropsy was refused.

Discussion

Kwashiorkor is a syndrome due to protein deficiency in the diet, and it might be expected that the anaemia accompanying it has the same cause, as Altmann and Murray have suggested. Cartwright (1947) has reviewed the evidence that protein deficiency produces anaemia in animals, while Keys *et al.* (1950) have shown experimentally in man that anaemia develops during starvation. In prisoner-of-war and concentration camps anaemia was often associated with low plasma proteins following starvation (Vaughan *et al.*, 1945; Leyton, 1946; Mollison, 1946; Walters *et al.*, 1947), but it was not established that this was a primary protein-deficiency anaemia. Leyton demonstrated a relationship between the plasma protein level and haemoglobin, but Mollison was not able to show a similar correlation. He considered anaemia to be due to lowered metabolism and not to any specific deficiency.

It is difficult to assess the role of protein deficiency in the production of anaemia in kwashiorkor. Often in severe cases anaemia is mild, and there is no correlation between the haemoglobin on admission and the plasma proteins in

FIG. 4.—Relationship between haemoglobin on admission and total plasma proteins (●), and between haemoglobin and plasma albumin (x).

this series of cases (see Fig. 4). It has been seen that there is often a drop in haemoglobin and haematocrit levels while oedema is decreasing and plasma proteins are increasing, which appears to exclude protein deficiency as the cause of anaemia. These changes, however, can probably be explained by variations in blood volume. In his oedematous cases at Belsen, Mollison found the blood volume to be lowered, but in other studies of hunger oedema there are conflicting reports (Denz, 1947). On indirect evidence in these oedematous cases of kwashiorkor, it seems likely that the blood volume is initially low and that it rises as soon as plasma proteins increase. As a result the blood count appears to drop. In no case has there been evidence of haemolysis or blood loss, and the changes in blood counts were often so rapid that they could be explained only by changes in blood volume. Under these circumstances the reticulocyte count, which is independent of changes in blood volume, will be a better index of response to treatment than haemoglobin or haematocrit levels. In most cases treated with high-protein diets only there have been small early rises in the reticulocyte count. Similar small rises were observed by Altmann and Murray. It is thus possible that some factor present in soured milk (maas) has stimulated erythropoiesis; but other factors such as increased metabolism might be responsible, and no definite conclusion can be drawn regarding the effect of protein replacement on blood production.

In Nigeria, Woodruff (1951) describes the predominant anaemia in pregnant African women living on protein-deficient diets as macronormoblastic and seldom megaloblastic. He showed by liver biopsy that the liver is diffusely fibrosed in many cases, and in others infiltrated with fat, and he believes that the similarity to kwashiorkor extends to the anaemia. Both may be due to underlying chronic liver disease, which is known to be accompanied by macronormoblastic erythropoiesis (Bodley Scott, 1939). Woodruff's bone-marrow findings are certainly similar to those described in this paper, but the two anaemias differ in some respects. It is perhaps worthy of note that, contrary to his experience in West Africa, severe megaloblastic anaemia of pregnancy, responding to folic acid and sometimes to vitamin B₁₂, is not uncommon among African and Indian women in Durban, many of whom live on diets low in protein.

In infancy, megaloblastic anaemia has been reported by Zuelzer and Ogden (1946), who described 25 cases. Zuelzer *et al.* (1947) carried out serial studies of the bone marrow in patients with infantile megaloblastic anaemia. They showed that there are patterns varying from predominantly normoblastic to frankly megaloblastic marrow pictures, and in all they record satisfactory responses to folic acid. Zuelzer and Ogden believe that nutritional deficiencies are partly responsible for the production of megaloblastic anaemia in infancy, and it would be surprising if nutritional megaloblastic anaemia were not sometimes encountered in a severe nutritional syndrome like kwashiorkor.

In the cases presented here it has been seen that megaloblastic transformation of the marrow occurs, although it is unusual. Dacie and White (1949) have described megaloblasts in the bone marrow of mild cases of Addisonian pernicious anaemia, the degree of deviation from normal being closely linked with the severity of the lack of haemopoietic factors. In East Africa, Foy *et al.* (1952) have described two groups of macrocytic or normocytic anaemia. In one there are giant stab cells in the bone marrow with erythroblasts, macronormoblasts, and megaloblasts in various stages of development; in the other giant metamyelocytes are present without megaloblasts. Both respond to haemopoietic substances. In kwashiorkor there is also a group in which the marrow contains giant metamyelocytes and some cells which are intermediate between normoblasts and megaloblasts. In two of these there have been satisfactory responses to crude liver extract or to vitamin B₁₂, so it would appear that these cases are examples of developing stages of nutritional megaloblastic anaemia.

There are also similarities between this marrow picture and the type of bone-marrow change in idiopathic steatorrhoea reported by Cooke *et al.* (1948). In kwashiorkor, Thompson and Trowell (1952) have demonstrated a deficiency of pancreatic enzyme production. Some of the stools examined in this series were microscopically oily, but clinically they were neither bulky nor fatty. Subclinical fat-absorption defects, with associated anaemia, however, have not been excluded, since fat-balance studies in African infants are technically difficult to perform.

In the detection of this type of anaemia in kwashiorkor examination of the blood alone for macrocytosis is of little help. Non-megaloblastic macrocytic anaemias occur in a variety of conditions. When appreciable anaemia is found on admission, or when it develops as oedema disappears, the bone marrow should be examined, and in those cases with megaloblastic change—partial or complete—liver extract, vitamin B₁₂, or folic acid should be administered in addition to high-protein diets.

Summary

In a series of 21 cases of kwashiorkor, selected only on the presence of pitting oedema, dermatosis, and lowered plasma proteins, appreciable normocytic or macrocytic anaemia was found in six cases, while two-thirds of the children had less than 9 g. % haemoglobin.

Anaemia may increase considerably as oedema decreases and plasma proteins rise. In this way severe anaemia may be unmasked.

Megaloblastic change was present in two cases. In six others there were bone-marrow abnormalities consisting of giant metamyelocytes and scanty red-cell precursors of intermediate type. Two of these had satisfactory haematological responses to crude liver extract or to vitamin B₁₂.

The possible relationship of this anaemia to protein deficiency, liver disease, and nutritional megaloblastic anaemia is discussed.

I thank Dr. Pauline Klenerman for giving me full access to her cases of kwashiorkor in African children, Dr. N. A. Rossiter for facilities to study Indian children under his care, and Dr. J. Parker, medical superintendent, for permission to publish these cases. Thanks are also due to Dr. J. Thomas, Director of Pathological Services, and his staff for their help with the biochemical estimations; and to Dr. Joan Scragg and the sisters for their assistance.

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The Minister of Education has issued a circular (272, 1954) about the precautions necessary to avoid food poisoning in the preparation and service of meals in school canteens. One of the objects of the Food and Drugs Amendment Bill at present before Parliament is to secure better hygienic conditions in places where food is prepared or served. The prevention of the contamination of food served in canteens depends, however, in large measure on the constant vigilance and the observance of hygienic practices by the canteen staffs. The Minister emphasizes that the risks of food poisoning are present wherever meals are prepared and served, and that there is no reason whatever to think that school canteens are more exposed to them than other forms of corporate meals. After briefly describing some typical examples of outbreaks of food poisoning in school canteens, the circular goes on to consider the prevention of food poisoning in schools under the following headings: Co-operation between medical, teaching, and kitchen staff; health of food handlers; hygienic conditions in the kitchen; the preparation and cooking of food; domestic animals and pests; milk supply; and notification of outbreaks of food poisoning to the medical officer of health. Under the last heading it is recommended that authorities should take steps to ensure that any outbreak of food poisoning is notified immediately, preferably by telephone, to the borough or district medical officer of health, so that he can begin his investigations and take precautionary measures without delay.

ADRENOCORTICAL FUNCTION IN BURNED PATIENTS

WITH SPECIAL REFERENCE TO A.C.T.H. AND
ADRENALINE TESTS

BY

SIMON SEVITT, M.D., M.Sc., F.R.C.P.I., D.P.H.

(Consultant Pathologist, Birmingham Accident Hospital and
Medical Research Council Burns Research Unit)

This paper is concerned with the activity of the adrenal cortex of burned patients, and in particular with a search for evidence of adrenocortical failure arising during the illness. The investigation is based on the spontaneous changes in the blood eosinophil count in burned patients, on the changes in the circulating eosinophils induced by injection of pituitary adrenocorticotrophic hormone (A.C.T.H.) or adrenaline, and on other findings.

In a previous paper (Sevitt, 1951) it was shown that a definite pattern of changes affects the number of blood eosinophils after burning (Fig. 1). Within a few hours their number is found either to be falling or to have fallen to low or zero values. This eosinopenia, which is accompanied by a neutrophil leucocytosis and commonly by some lymphopenia, is maintained for a variable number of days, after which the count begins to rise, to reach a peak value within the next few days. Evidence was produced which indicates that the eosinopenia after burning is a sensitive reflection of adrenocortical hyperactivity. This pattern of changes has been confirmed by Evans and Butterfield (1951) and by Wight *et al.* (1953).

The period of eosinopenia during which eosinophils are few or absent in the blood stream is maintained for varying periods in different patients and is terminated by the post-eosinopenic rise (Fig. 1). The duration of the periods of eosinopenia was estimated in 35 patients with an accuracy within $\pm \frac{1}{2}$ day. In Fig. 2 these periods are plotted against the skin area burned, which is expressed as a percentage of the total skin area. In patients with burns covering less than 10% of the body area the periods of eosinopenia are only one or two days, but are longer, usually three to five days, in those more extensively burned. The relationship between the eosinopenic period and the percentage area seems to be an exponential zone with its concavity facing to the left, rising steeply between four and six days after burning.

FIG. 1.—Serial blood eosinophil counts during the first week after burning in three patients. In one patient the falling of the count soon after burning is seen, and this is followed by a period of eosinopenia, which is present in all three. The eosinopenia lasted 1, 5, and 7 days respectively in the three patients and was followed by a rise in the count.