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The third number of the *Bulletin of the International Corresponding Club (Preventive and Social Medicine)* appeared early this year. It is available to non-members (obtainable from the Department of Social and Industrial Medicine, The University, Sheffield, 10, price 5s.). The aim of the Club is to have a corresponding member in as many departments of preventive and social medicine as possible which are actively doing teaching and research. At present there are 42 members from 15 countries. Membership costs 10s. a year, and the bulletin is published twice a year, from Sheffield and Cornell alternately. Among the reports from members is the news from Queen's University, Belfast, that a generous grant from the Nuffield Foundation has made possible an extension of the department's genetic research on populations. Among schemes organized by the Social Medicine Unit at Oxford is a retrospective survey of all children in England, Scotland, and Wales who have recently died either of leukaemia or of malignant disease, work on which began last November. The aim of the survey is to obtain details about the social pathology of the disease and whether its incidence is related to x-ray diagnostic and therapeutic procedures.

MEGALOBlastic ANAEMIA OF INFANCY IN KWASHIORKOR AND OTHER DISEASES

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Megaloblastic anaemia in infancy has been thoroughly reviewed by Zuelzer and Rutzy (1953), who believe that most cases develop as a result of severe infection or malnutrition; a few of their cases occurred in negroes (4 out of 59). Although a similar picture has been described in African infants no large series has been reported. Altmann and Murray (1948) found macrocytosis in only some of their cases, while Wills did not find any true megaloblasts in the bone marrow of the 36 cases of malignant malnutrition (kwashiorkor) recorded by Walt *et al.* (1950). In East Africa, Trowell (1949) had similar results, but in 1954 Adams reported two cases in patients with kwashiorkor.

We also believed megaloblastic anaemia of infancy to be a rare disease until 1953, when megaloblasts were recognized by one of us (S. H.) in the peripheral blood smears of some six patients with anaemia. Because of this a fuller investigation was instituted in 1954, and its results are reported here.

Material and Methods

The period of this investigation ran from February 17, 1954, to February 7, 1955, during which time 776 patients were admitted to the paediatric wards of the McCord Zulu Hospital. Children up to the age of 10 years are accepted in these wards, although the majority are under 3 years. A small daily hospital fee is charged, making this group somewhat selective, as free hospital care is available in Durban to those who wish to use it. About 90% of the patients admitted are of Bantu extraction, while Asiatic and Coloured (mulatto) make up the other 10%. Almost all come from very poor homes where sanitation is bad, poverty and ignorance are rife, and superstition flourishes, causing undernutrition and recurrent infections. The infants are usually breast-fed to begin with and are weaned on to maize porridge with very little milk or first-class protein; they may receive a little vegetable and sugar, and if milk is used it is usually well diluted. All patients with a suggestive clinical picture or with a haemoglobin level of less than 6.7 g./100 ml. were subjected to aspiration of bone marrow from the iliac crest as described by Rubinstein (1950). Later, local analgesia has not been used and no difficulties or complications have been encountered. The haemoglobin of 6.7 g./100 ml. was arbitrarily arrived at in 1953, when the first cases were discovered, and has served us well.

A megaloblastic bone marrow was found in 42 cases, 40 being African (Bantu), one Asiatic, and one Coloured. Of

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the 42 cases, 22 (52%) had typical kwashiorkor. The average age was 14.4 months, with a range from 1 month to 30 months.

The patients were all examined by one of us (F. W.) at McCord Zulu Hospital. Haemoglobins were estimated routinely on or shortly after admission, on blood taken from a finger-prick, using a Sahli haemoglobinometer, and thereafter in most cases were repeated daily.

All other haematological examinations, including bone-marrow examinations, were done at King Edward VIII Hospital Laboratory. This is about four miles from McCord Hospital, and the distance and transport difficulties often led to quite long delays. Venous blood was taken from the jugular veins (external or internal) into Heller and Paul's mixed oxalates. Haemoglobin was estimated with an EEL Photoelectric colorimeter (as oxyhaemoglobin), standardized from time to time with blood sent from London under the Haemoglobin Standards Scheme. Haemoglobins throughout are recorded as grammes per 100 ml. of blood. Red-cell counts were not done, because of the impossibility of performing accurate counts in a busy routine laboratory.

Full blood and reticulocyte counts were done two or three times a week, reticulocytes being estimated by the method described by Dacie (1950).

Blood and marrow films were stained by May-Grünwald-Giemsa stain, using a phosphate buffer pH 6.8, and all were examined by one person (S. H.) at King Edward VIII Hospital. Other haematological investigations were done by standard methods.

Megaloblastic Erythropoiesis

It is now generally accepted that the megaloblast is a pathological cell found only in a group of conditions known as megaloblastic anaemias (Davis and Brown, 1953). In a typical case recognition of megaloblasts and megaloblastic erythropoiesis is a simple indisputable matter. However, as more cases of possible megaloblastic anaemia are examined one becomes more and more persuaded that there are all degrees of megaloblastic change in the bone marrow from very obvious to quite minimal (Zuelzer and Ogden, 1946; Dacie and White, 1949; Zuelzer and Rutzky, 1953).

The group showing the smallest change—that is, the least deviation from the normal—will naturally be the most difficult to recognize, and it may, and often does, happen that a bone marrow which one worker classifies as “partial or incomplete megaloblastic change” will be classified by another as “normoblastic.”

We have been faced with this difficulty and have been unable to find a solution. For recognition of megaloblasts as opposed to normoblasts we have relied almost entirely on the nuclear change. The “lacy pattern,” “scroll-work,” or “woven-skein” appearance of the nuclear chromatin, albeit only partial or incomplete, has been to us the most convincing evidence. Enlargement of the nucleated red cells, marked disproportion in size between nucleus and cytoplasm, Howell-Jolly bodies, and trefoil and clover-leaf nuclei in the nucleated red cells are useful ancillary signs, but have never been used alone without the basic nuclear chromatin alteration as a final arbiter.

Bizarre myelocytes, metamyelocytes, and bizarre giant “stab” cells we have found most helpful in diagnosis. Rarely, if ever, have we observed megaloblasts without granulocyte alterations, although we have been confronted often with the reverse picture—that is, marked changes in the white-cell series *without* megaloblasts being present. This problem is not unique and has been commented on by Altmann and Murray (1948), Zuelzer and Rutzky (1953), and Adams (1954). In some patients we have been able to demonstrate the transformation of marrows containing only abnormal white cells to frankly megaloblastic marrows, and, though we feel that the presence of a large number of bizarre myelocytes in the marrow in most cases indicates a “pre-megaloblastic” change, this must remain for the moment speculative. Davidson (1954) has indicated

that bizarre giant stab cells occur with some frequency in the bone marrows of patients with iron-deficiency anaemia. While this is so in our experience, too, the change has never been as marked or as frequent as in megaloblastic marrows and there is little possibility of confusion between these two conditions. In this series we have not used bizarre myelocytes alone to diagnose a megaloblastic marrow.

Peripheral Blood.—Megaloblasts are quite often found, although a prolonged search may be necessary, but in our experience the most valuable single finding in the peripheral blood suggesting megaloblastic anaemia has been the haemoglobin level. Only very rarely has a case been diagnosed as megaloblastic anaemia with a haemoglobin of more than 7.4 g./100 ml. (50%). Macrocytosis and ovalocytosis were helpful, but were not invariably present. Mean cell volume has in the past proved most unreliable and has not been estimated in our cases. Large multilobed polymorphs were of great assistance in diagnosis and are easily found in the majority of cases. They are probably the derivatives of the bizarre giant myelocytes, and have the same significance diagnostically. The blood findings are suggestive, but have not been used to diagnose megaloblastic anaemia in this series. The presence of megaloblasts in the bone-marrow smears has been the sole criterion for diagnosis.

In the final analysis, the diagnosis of the milder grades of megaloblastic anaemia is entirely subjective. We see only one way of overcoming this problem, and that is by free interchange of slides among various workers investigating this disease. Dr. W. W. Zuelzer, of the Children's Hospital of Michigan, U.S.A., very kindly examined seven different bone-marrow films sent to him; his findings agreed with ours in almost every detail.

Clinical Picture

Diagnosis of the disease is by bone-marrow examination. We have found three types of clinical picture: (I) those patients who were severely anaemic on admission; (II) those who developed their anaemia insidiously while being treated for the primary disease; and (III) those who (also while under treatment) suddenly developed a marked anaemia within 48 to 72 hours as if a “crisis” had occurred.

Type I cases were usually desperately ill, with a haemoglobin below 5 g./100 ml.; they usually had kwashiorkor or some infection such as pneumonia, gastro-enteritis, or otitis media, and in many cases a combination of two or more of these diseases occurred. Pallor in African infants is easily overlooked because of their colouring, but careful examination of the tongue, gums, and lips will show the best evidence of anaemia; there are no other clear-cut clinical signs. The type II cases were not particularly ill on admission, usually overcoming their initial illness rapidly. Thereafter their progress was not satisfactory because, despite a fair appetite, normal stools, and freedom from cough and from clinical signs of infection, they continued with an unexplained fever, lay apathetically, and failed to gain weight. The haemoglobin in this type averages 6–7 g./100 ml. and bone-marrow examination shows megaloblasts. Type III is possibly a further stage of type II but even more treacherous, and before one's suspicions are thoroughly aroused a sudden and marked anaemia becomes self-evident and the patient severely ill. The haemoglobin may drop 3 to 4 g. in 48 hours without showing any clinical signs of haemolysis. Unless one is aware of this syndrome the child may die before treatment is started. The spleen is palpable in many cases.

In our patients parasitic infections such as hookworm do not occur frequently or cause ill-health, while malaria is almost unknown; in this age group ascariasis does occur, but the infections are never heavy and rarely need specific therapy. Most of these patients were very ill, no fewer than 23 needing parenteral fluid therapy. Because the diarrhoea of kwashiorkor and infective gastro-enteritis is most difficult to distinguish clinically we have assumed most cases to be due to infection and have treated them as such.

Three cases (Nos. 17, 18, and 22) had radiological evidence very suggestive of pulmonary tuberculosis.

Treatment

Oral folic acid, 5 mg. three times a day, was given to 38 cases, but 8 of these also received 7½ mg. intramuscularly on the first day of treatment or later if the response to oral therapy was thought to be poor; it was continued orally for the complete hospital stay, and for a month after discharge 5 mg. daily was given as maintenance therapy, but this may not be necessary.

Two cases (Nos. 8 and 14) were also given vitamin B₁₂ because it was thought that there had not been a reticulocyte response. In Case 8, however, folic acid had been given intramuscularly two days before vitamin B₁₂,

and six days later the reticulocyte count was 10.8%, while in Case 14 there was a reticulocyte count of 18.8% on the day vitamin B₁₂ was administered, intramuscular folic acid having been given six days previously.

In four cases (Nos. 18, 30, 35, and 42) folic acid was not given at all. Case 18 was admitted with kwashiorkor, developed pneumonia, and was treated with "maas" (skimmed acidophilous milk) plus penicillin and sulphonamides. On the third day the haemoglobin was 9 g./100 ml. and the bone marrow mildly megaloblastic, but clinical grounds did not warrant such a diagnosis and folic acid was not prescribed. Eleven days later both bone marrow and total serum protein (3.3 g./100 ml. on admission) were normal. The patient was then found to have primary tuberculosis and remained in hospital for 2½ months till her

TABLE I.—Summary of Cases

Case No.	Disease	Admission Date	Age in Months	Sex	Admission Haemoglobin (g./100 ml.)	Nearest Bone Marrow (g./100 ml.)	Bone Marrow Result	Hospital Day of Bone Marrow	Hospital Day Folic Acid Started	Peak Reticulocytes %	Day of Retic. Peak after Folic Acid	Hospital Day of Blood Transfusion	Final Haemoglobin (g./100 ml.)	Clinical Result	Treatment
1	Gastro-enteritis	17/2/54	5	F	9.6	7.7	Mod.	34	34	8.8	3	—	6.5	Cured	Pen. Strep. Aur. PT.
2	Kwashiorkor (Kwkor.)	23/2/54	24	F	7.2	3.2	"	18	19	50.0	2	16	7.3	"	Pen. Sul.
3	Gastro-enteritis	5/3/54	7	M	9.0	6.6	Normo.	22	38	17.4	3	—	7.4	"	Pen. Sul. Aur. PT.
4	Kwkor.	8/3/54	18	F	5.6	5.6	Mild	8	8	—	—	—	5.6	Died (8)	Pen. Sul.
5	"	8/3/54	15	M	—	—	Normo.	14	31	7.6	5	24	—	Cured	Pen. Strep.
6	Ulcerative stomatitis	20/3/54	15	M	6.9	5.2	Mild	10	12	13.0	3	—	—	R.H.T. (16)	Pen. Aur.
7	Kwkor.	6/4/54	18	M	6.1	4.8	Mod.	4	8	—	—	—	—	Died (10)	Pen. Sul.
8	Bronchopneumonia	14/4/54	15	F	6.7	6.3	Mild	8	11	10.8	13	17	11.4	Cured	Pen. Sul. Vit. B ₁₂
9	Undernutrition	21/4/54	2	F	6.7	5.9	"	8	10	26.4	7	17	7.9	Died (19)	Aur. PT.
10	Gastro-enteritis	21/4/54	2	M	6.7	5.5	"	6	8	14.2	5	—	7.5	" (17)	Aur. PT.
11	Kwkor.; cancrum oris	1/6/54	30	F	2.7	5.9	Mod.	6	9	—	—	1, 6	—	" (13)	Pen. Chlor. Ter. PT.
12	Kwkor.	15/6/54	6	M	6.7	6.1	"	15	2	11.2	19	—	7.0	Cured	Pen. Sul. PT.
13	"	21/6/54	15	M	7.7	7.6	"	3	1	14.8	28	—	7.6	"	Pen. Sul.
14	"	25/6/54	9	M	9.1	7.3	"	11	15	19.4	21	8	7.7	"	Pen. Sul. Vit. B ₁₂
15	"	12/7/54	15	F	9.3	8.1	? Mild	4	9	27.0	25	12	7.9	"	Pen. Sul.
16	"	14/7/54	30	M	4.1	6.3	Normo.	28	3	19.8	5	1	8.1	"	" "
17	"	1/8/54	18	F	8.7	6.7	Mild	2	2	14.0	4	—	6.2	R.H.T. (67)	Pen. Sul. Strep. INH.
18	"	18/8/54	8	M	9.0	8.0	Mild	3	No folic acid			—	7.5	Cured	Pen. Sul. Strep. INH. Aur. PT.
19	"	29/8/54	12	M	4.8	3.2	Severe	2	2	13.4	8	2	9.4	Transferred (25)	Pen. Sul.
20	Bacill. dys.; pneumonia	30/9/54	18	M	8.7	6.5	Mod.	32	32	9.8	5	40	8.1	Cured	Pen. Sul. Strep. Aur. PT.
21	Kwkor., gastro-ent.	12/10/54	24	M	11.4	4.7	Severe	11	11	—	—	11, 16	8.0	Died (19)	Pen. Sul. Strep. PT.
22	Gastro-ent.; P.T.B.	29/10/54	18	F	3.0	3.0	Mod.	1	2	—	—	2	7.0	" (7)	Strep. INH. PT. Cort.
23	Kwkor.; gastro-ent.	6/11/54	12	F	8.7	—	Mild	10	13	10.4	13	22	9.8	Cured	Pen. Sul. Strep. PT.
24	" "	15/11/54	12	F	7.4	—	Mod.	5	10	6.2	14	13	7.7	"	Pen.
25	Gastro-enteritis	26/11/54	14	F	9.0	4.1	Mild	20	25	16.5	6	—	6.7	"	Pen. Sul. Strep. Aur. Cort. PT.
26	"	18/12/54	2	F	8.3	4.8	Mod.	13	20	5.8	8	20	10.2	"	Pen. Sul. Cort. PT.
27	Undernutrition	25/12/54	9	M	9.3	6.1	Mild	17	18	8.6	24	—	10.6	"	Pen. Sul. PT.
28	Bacill. dysentery	26/12/54	8	M	10.1	—	"	12	19	9.0	13	—	9.5	"	Sul. PT.
29	Kwkor.; gastro-ent.	26/12/54	10	M	8.6	6.7	Mod.	7	12	15.0	17	—	7.4	"	Pen. Sul. Cort. PT.
30	Gastro-enteritis	27/12/54	13	M	6.1	4.5	Mild	2	No folic acid			2	4.0	Died (2)	Sul. Strep. Aur. Cort. PT.
31	"	28/12/54	4	M	9.9	8.0	Mod.	17	17	14.0	13	—	10.4	Cured	Aur. PT.
32	Undernutrition	31/12/54	4	F	7.4	7.5	"	11	12	24.2	24	—	9.3	"	Sul. Aur. PT.
33	Bronchopneum.; ot. media	2/1/55	13	M	6.7	5.3	Mild	6	10	13.0	15	16	8.0	"	Pen. Sul. PT.
34	Ulcerative stomatitis	3/1/55	11	F	5.0	4.8	Mod.	2	7	26.8	20	1	10.2	Transferred (54)	Pen. Sul. Strep. Achro. PT.
35	Kwkor.	5/1/55	19	F	8.6	12.7	"	2	No folic acid			2	6.7	Cured	Pen. Aur. PT.
36	Gastro-enteritis	5/1/55	1	M	12.6	9.3	Mild	15	24	—	—	—	8.3	Died (28)	Pen. Sul. Aur.
37	Kwkor.	7/1/55	13	F	4.6	4.5	Severe	1	7	25.0	22	1	9.0	Cured	Pen.
38	Kwkor. gastro-ent.	8/1/55	17	F	7.0	6.1	Mod.	29	8	12.6	20	—	8.4	"	Pen. PT.
39	Gastro-enteritis	9/1/55	8	F	6.2	5.3	"	2	4	23.2	14	4	9.8	"	Pen. Sul. PT.
40	Kwkor.; gastro-ent.	18/1/55	14	M	9.0	6.9	Mild	8	11	16.2	11	—	11.1	"	Pen. Sul.
41	Kwkor.	26/1/55	24	M	8.6	7.2	"	8	23	13.8	6	19	8.0	Transferred (30)	Pen. Sul.
42	Ulcer. stomat.	7/2/55	15	M	6.7	6.7	"	1	No folic acid			—	—	Died (2)	Pen. Sul.

Bone marrow result: Mild=Mild megaloblastic; Mod.=Moderately severe megaloblastic; Severe=Severe megaloblastic; Normo.=Normoblastic.
 Treatment: Pen.=Penicillin; Sul.=Sulphonamides; Cort.=Corticosteroid; Aur.=Aureomycin (chlortetracycline); Chlor.=Chloramphenicol;
 Strep.=Streptomycin; Ter.=Terramycin (oxytetracycline); Achro.=Achromycin; INH=Isoniazid; PT.=Parenteral fluid therapy.
 Result: Died (8)=Died on 8th hospital day; R.H.T.=Refused hospital treatment.

discharge. Case 30 was desperately ill on admission and died within 72 hours, before folic acid could be started, despite intravenous infusion, blood transfusion, and antibiotics.

Case 35 began with a normoblastic bone marrow which changed to megaloblastic on the thirteenth hospital day with a drop in haemoglobin to 8.5 g./100 ml., but became normoblastic again seven days later. Folic acid was not administered at the time because the patient was improving clinically. Unfortunately reticulocytes were not counted; on discharge the patient was well despite a haemoglobin of 6.7 g./100 ml. In Case 42 death occurred 2½ days after admission before folic acid could be started.

Blood transfusions were necessary in 22 cases, 5 of which were fatal. Table I shows the hospital day on which transfusion was given, and its relation to folic acid therapy; in seven cases it was given some days before folic acid was started and in five on the same day. Two patients (Cases 11 and 21) needed more than one transfusion, but both died.

All patients were treated with antibiotics when necessary and intravenous therapy was also used liberally. Maas was the sole diet for all cases of kwashiorkor for the first 14 days, except for two patients who received a specially prepared casein food which was under trial for two months in 1954. Streptomycin and isoniazid were given to the three cases with tuberculosis. Corticotrophin was given to five cases with collapse.

Results

Of the 776 admissions, 42 (5.4%) had megaloblastic bone marrows, and 22 of these cases occurred in kwashiorkor. Of the 42 patients, 10 (24%) died, the haemoglobin on admission being less than 6.7 g./100 ml. in eight cases. Table I does not show the immediate cause of death, which was bronchopneumonia in three, acute gastro-enteritis in two, and kwashiorkor, cancrum oris, circulatory failure, pulmonary tuberculosis, and sudden anaemic crisis in one each.

Of 15 patients who had a sudden drop in haemoglobin, 13 survived as a result, we think, of emergency treatment with blood transfusions. In most cases the haemoglobin did not rise rapidly after folic acid therapy and was of little use as an index of cure; many cases were discharged much improved but with a haemoglobin level below that on admission (Table I).

Many reticulocyte counts were high and very satisfactory after treatment, but their response to folic acid was not as uniform as has been reported elsewhere in the literature (Altmann and Murray, 1948; Zuelzer and Rutzky, 1953), and they were not as useful as we had hoped and was of little use as an index of cure; many cases were discharged much improved but with a haemoglobin level below that on admission (Table I).

Comment

Anaemia in kwashiorkor is very common, but megaloblastic anaemia has been thought to be rare. Woodruff (1955) reviewed the natural history of anaemia in protein malnutrition, but failed to find megaloblasts in the bone marrow. Because his age group differed greatly from ours, we do not think the cases are strictly comparable. Five years ago, under similar conditions, in 36 cases of kwashiorkor in which the bone marrows were studied we did not report a single case of this disease (Walt *et al.*, 1950).

Altmann and Murray (1948) and Adams (1954) have recorded a few cases of megaloblastic anaemia associated with kwashiorkor, and in our series 22 cases have occurred with this disease. It is possible that the number of cases is actually increasing, in Durban at any rate. There is now

an incidence of 5.4% of all admissions, but we will not speculate on the possible factors of the change in diet due to the increased cost of living, or the more liberal use of antibiotics, or some change in the manufacture of basic foodstuffs leading to a deficiency of folic acid. We believe that they were discovered because of what Zuelzer calls "a high index of suspicion" in an anaemic infant. This report records the facts gleaned so far; another, but controlled, investigation is in progress in which bone-marrow studies are being made on all new admissions to determine the incidence, bone-marrow response to oral folic acid, and seasonal occurrence of this disease. In the present series 16 cases (38%) occurred during the summer months of December and January (Table II).

TABLE II.—Seasonal Incidence of Megaloblastic Anaemia

	No. of Cases		No. of Cases
Feb. 17 to 28, 1954	2	September	1
March	4	October	2
April	4	November	3
May	0	December	7
June	4	January, 1955	9
July	2	February 1 to 7	1
August	3		

Almost all of our cases occurred in Africans, while only 4 out of 59 in Zuelzer's series were negroes; he found that associated or preceding infections were common. This is true for our cases too. The commonest diseases by far were acute gastro-enteritis, otitis media, and pneumonia, although many developed severe anaemia suddenly.

A reticulocyte response of 8% or more occurred in 30 cases of the 34 in which a count was done, and from Table I it can be seen that the day of the reticulocyte peak varied greatly. Despite a satisfactory reticulocytosis, there was little effect on the haemoglobin, which did not always rise although the patient was clinically well.

Lack of folic acid in these infants is not the only cause of anaemia, which may well be due to other factors such as infection, diarrhoea, or even protein malnutrition as suggested by Woodruff (1955). Because the megaloblasts disappear rapidly from the bone marrow after folic acid is given, re-examination after a short interval may be a better guide to improvement than reticulocyte counts or haemoglobin estimations. In two cases of kwashiorkor (Nos. 18 and 35), however, no folic acid was given, yet both recovered and had normal bone marrows on discharge; this shows that the "megaloblastosis" can be influenced by other factors, possibly such agents as diet or antibiotics. Case 18 did not receive folic acid and yet four weeks after admission had a reticulocytosis of 19.6%, after being treated for otitis media and while on streptomycin and isoniazid for pulmonary tuberculosis. Case 35 had a normoblastic bone marrow on admission, then developed diarrhoea, and 11 days later had a mildly megaloblastic bone marrow, was treated with chlortetracycline and intravenous therapy, and reverted to a normoblastic marrow seven days later. Both of these patients received a full diet after two weeks.

Prophylactic oral folic acid may not prevent the disease, possibly because of insufficient absorption. At the time of this investigation a separate research was also being carried out in which kwashiorkor patients were given special high-protein food, with 5 mg. of folic acid added daily as a routine. Cases 12 and 13 were so treated on admission; in Case 12, on the fourteenth day, because of a sudden drop in haemoglobin, the bone marrow was examined and showed a moderately severe megaloblastic anaemia which responded to an increase of dosage to 5 mg. three times a day with an 11% reticulocytosis. Case 13 was also started on 5 mg. of folic acid daily as a routine on admission, but the bone marrow on the third day was megaloblastic.

Deficiency of folic acid may be due to lack of absorption from the bowel, an insufficiency in the diet, decreased bacterial synthesis, or an increase in body metabolism. The merit of oral over intramuscular folic acid therapy, if any,

and the response to vitamin B₁₂ still need to be investigated. May *et al.* (1950) have suggested that vitamin-C deficiency plays a large part in this disease, but we think this unlikely, as scurvy is very rare in our wards. Zuelzer and Rutzky (1953) state that vitamin C is not specific and that its lack does not prevent the action of folic acid. They further state that all cases invariably responded to folic acid. We agree with this generalization because the "megaloblastosis" of the bone marrow disappears quickly, and have gained the impression that responses are more rapid if treatment includes intramuscular folic acid.

Summary

Forty-two cases of megaloblastic anaemia in infancy (5.4% of all admissions) diagnosed during a year by bone-marrow examinations are described.

Twenty-two cases suffered from kwashiorkor, the remainder from various infections.

The clinical picture and the criteria for bone-marrow diagnosis are described.

The results of treatment with folic acid are reported.

The mortality rate was 24%, but in all but one case these deaths were thought to be due to the primary disease or some acute complication.

Megaloblastic anaemia of infancy is thought to be a secondary disease; the megaloblastosis of the bone marrow can be cured by giving folic acid, which is specific.

We can only speculate on the reasons for now finding this disorder, when five years ago a similar search was unrewarding.

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According to a correspondent in the *Journal of the American Medical Association* (February 4, 1956, p. 415) the Navajo Indians are the sickest group of people in the United States and have the least medical care. Life expectancy among the Indians is 20 years, and one baby out of every four dies before the age of 5. Two dispensaries are provided on the Navajo reservation by Catholic Indian missions; trained nurses are in charge. One of these dispensaries is 100 miles from the nearest hospital, doctor, or drug store.

RESPIRATORY VIRUS INFECTIONS IN R.A.F., 1954-5

WITH PARTICULAR REFERENCE TO INFLUENZA AND A.P.C. VIRUSES

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Acute respiratory disease is of considerable importance in the Royal Air Force, in particular because of its effects on the efficiency of aircrew. As good opportunities exist in the Service for the investigation of this problem, a survey was made during the winter of 1954-5.

The main objects of the survey were (1) to observe the prevalence of identifiable respiratory virus infections in selected units, and to see whether evidence could be found of illness associated with infection by the adenoidal-pharyngeal-conjunctival (A.P.C.) group of viruses; and (2) to study the relationship between the level of circulating antibody to soluble antigen and susceptibility to influenza.

Viruses of the A.P.C. group were first isolated by Rowe *et al.* (1953), and further reports on the group were made by Huebner *et al.* (1954) and Rowe *et al.* (1955). Hilleman and Werner (1954) reported the cultivation of an agent designated R1-67, and subsequently shown to be one of the A.P.C. group, from patients with acute respiratory illness. The outbreak in which these cases occurred was at Fort Leonard Wood, Missouri, and was later described in detail (Hilleman *et al.*, 1955a). Hilleman *et al.* (1955b) have since reported upon the high prevalence of infection with viruses of this family among recruits in Fort Dix, New Jersey, and Berge *et al.* (1955) among recruits in Fort Ord, California. Serological evidence of infection associated with respiratory illnesses in northern England has recently been reported by Zaiman *et al.* (1955). In October, 1954, before the beginning of the present study, we investigated a small outbreak of respiratory illness in an R.A.F. unit in Kirkham (Lancs), and found a fourfold or greater rise in complement-fixing antibody to an A.P.C. antigen (R1-67) in three patients with influenza-like symptoms: a virus strain of the A.P.C. group was isolated from throat washings from one.

The survey described here lasted four months—from the beginning of December, 1954, to the end of March, 1955. Special studies were made at 10 selected units scattered throughout England. These were Chivenor (Devon), Driffield (Yorks), Horsham St. Faith (Norfolk), Middleton St. George (Durham), Middle Wallop (Hants), Newton (Notts), North Weald (Essex), Stafford (Staffs), Syerston (Notts), and Warton (Lancs). In one of the 10 stations evidence was found of an outbreak of acute respiratory illness associated with A.P.C. virus infection. This outbreak occurred in March, 1955, soon after an outbreak of influenza B in the same unit, and was