AFRICAN REGIONAL SCIENTIFIC CONFERENCE JOHANNESBURG 1949

Communication No. D(m) 13.

ANAEMIA IN AFRICANS: THE FIELD OF WORK ON NUTRITION AND ITS ROLE IN DISEASE

by

*E. G. Holmes**

SUMMARY

A communication is made on the red blood counts of Africans and their relationship to those of dwellers at similar altitudes in other parts of the world.

Other work in Uganda is directed towards the study of Anaemia, which appears to be due to lack of iron, and is precipitated by infection or infestation. There may well be a background of dietary deficiency, but there is no evidence of deficiency of any known haematinic principle other than iron. Gross dietary deficiency is common, resulting, in gross cases, in a picture similar to the "famine Oedema" recognised elsewhere.

Studies are in progress on nitrogen metabolism, and on water metabolism, and work has been published on the carbohydrate metabolism in this condition.

Lesions of the liver and digestive glands are also being studied, as well as the possibility of the presence of excess oestrogens which escape destruction due to the defective hepatic function. How far chronic malnutrition, which does not bring the patient to hospital, contributes to these lesions is the subject of study. Peculiar cardiac lesions (of which the aetiology is unknown) have been found to be common.

Investigations are in progress on the chemotherapeutics of tuberculosis.

The nutritional level of the population as a whole is largely conjectural, and dietary surveys, to provide accurate information, and to enable the sociological and economic bearings of malnutrition to be assessed, are an urgent necessity.

Mr. F. L. Gee, students in the Physiology class at Makerere College and the writer, have recently undertaken a study of the blood counts of 20 healthy male Africans between the ages of 17 and 26. The subjects were all students of Makerere College. Their homes were in different parts of East Africa but all had been in Kampala for two months or more when the observations were made. The results are shown in Table 1, together with the figures for two other groups in which blood counts only were performed. The counts of groups 1 and 2 were made on venous blood, those in group 3 on capillary blood. The students live together in hostels, which are on a hill. Anti-malarial precautions are observed. They wear shoes. If sick, they have easy access to medical treatment. Their diet is as follows:—

Protein.....	109 grams per day, including 30 grams animal protein.
Carbohydrate.	496 grams per day.
Fat.....	104 grams per day.
Iron.....	30 milligrams per day.
Calories.....	3,277 per day.

Group	Number in group	Hb. g. %		R.B.C. × 10^6		M.C.V.		M.C.H. (yy)		M.C.H.C. %	
		mean	σ	mean	σ	mean	σ	mean	σ	mean	σ
1.....	20	16·55	1·81	5·99	0·52	82·5	5·08	28·1	3·95	32·3	4·03
2.....	26	—	—	6·11	0·57	—	—	—	—	—	—
3.....	72	—	—	6·45	0·54	—	—	—	—	—	—

Originally with a view to testing the evidential value of these data, values for red blood counts of healthy adult males were collected from the available literature. The table below shows all the values collected up to 10.7.1949. It will be observed that the data are incomplete both with respect to statistical details and values for 1,000′–4,000′ and for high altitudes.

The most obvious features of the table are the general rise of count with altitude and the large and quite often significant differences between mean values obtained at one altitude and even at one place. These differences may be due to systematic errors in techniques, to real differences between capillary and venous blood, to the lack of randomness in the samples, to the vagueness of the term "healthy" or to the incidence of factors other than oxygen tension. There is certain internal and collateral evidence that all these causes operate.

The attempt to reconstruct a complete regression and correlation (with healthy limits) for individual counts thus fails, not merely for lack of some statistical detail but because the validity of such statistics must depend either on the assumption that the samples are random (clearly untrue) or, more doubtfully, on the assumption that the number of individuals in a sample is randomly distributed among the samples (which does not seem particularly likely to be true). If we replace these dubious assumptions by the single assumption that the group of samples is a random sample of all the samples that might have been taken (i.e. that the systematic differences between the sam-

*Makerere College, Kampala, Uganda.

Place	Altitude nearest 100′	Number in sample	Mean	Standard deviation	
Boston.....	0	18	5·35	·287	
Bombay.....	0	121	5·11	·387	
London.....	0	100	5·43	·306	
London.....	0	90	5·42	·293	
Copenhagen.	0	60	5·07	·326	
Baltimore...	0	100	5·87	—	
Copenhagen.	0	10	5·45	—	
Tulane.....	100	100	5·26	·869	
Buenos Aires	100	45	5·50	·294	
Oslo.....	100	50	5·52	—	
Calcutta.....	100	50	5·36	—	
Calcutta.....	100	17	5·55	—	
Munster.....	200	90	5·18	·298	
St. Louis.....	700	23	5·29	·310	
Detroit.....	700	20	5·08	·268	
Detroit.....	700	20	4·86	·259	
Leavensworth	700	25	4·93	·336	
Kansas City..	700	15	5·09	·371	
Cleveland...	700	100	4·95	—	
Indianapolis.	800	10	5·58	·300	
Omaha.....	1,100	100	5·00	·264	
Zurich.....	1,500	10	5·35	·366	
Saskatoon...	2,000	20	5·50	·284	
Kampala....	4,000	48	4·56	·580	
Makerere.....	4,100	26	6·11	·573	
Makerere.....	4,100	20	5·99	·521	
Makerere.....	4,100	72	6·46	·541	
—	4,400	—	5·24	—	
Nairobi.....	5,000	400	5·02	·970	
Denver.....	5,000	40	5·42	·241	
Nairobi.....	5,000	29	5·57	—	
Davos.....	5,200	4	6·25	·526	
—	5,200	—	6·55	—	
—	5,300	50	6·07	—	
—	5,300	50	5·42	—	
Johannesburg	5,700	11	5·75	·413	
Johannesburg	5,700	30	5·59	·240	
Johannesburg	5,700	35	6·10	·466	
Johannesburg	5,700	118	6·04	·532	
Johannesburg	5,700	60	5·99	·465	
Johannesburg	5,700	35	6·12	—	
Johannesburg	5,700	46	6·02	—	
Johannesburg	5,700	70	5·47	—	
Johannesburg	5,700	100	5·49	—	
—	5,900	—	7·00	—	
Kasauli.....	6,300	75	6·81	·872	
Kasauli.....	6,300	52	6·44	·820	
Mexico City.	7,600	30	7·25	—	*
—	8,000	—	6·04	—	
Maro Cocha.	14,400	8	7·19	—	*
Pamirs.....	14,700	7	7·96	—	*
Maro Cocha.	16,700	132	6·66	—	*

*May contain some women.

ples form, when regarded as a group, a random distribution) and take account of the fact that the standard error of the means is much smaller than the standard deviation of the group of mean values, it would seem that we can obtain a fairly valid estimate of the correlation and regression of count with altitude by treating each mean as a single value.

The results of doing so are:—

$r = \cdot 75$; $t = 8$; $P < 10^{-10}$

Regression of count on altitude = 5·23 + ·134 per 1,000′. S.D. of *mean* counts (allowing for altitude) = ·46 & $\frac{27}{52}$ values lie between the 50 per cent. limits. (Standard error of means is of the order ·1).

It is clear that the correlation of count with a factor determined by altitude is established beyond question.

In so far as it is a useful approximation to regard the regression as linear, the regression equation suggests certain " normal " values for each altitude and in view of the comparatively large standard deviation of the group of mean values and of the effectively small number of means available it is probably futile to attempt fitting a curved regression line (necessarily of at least the third order on general consideration).

The assignment of healthy limits for individuals must be even more tentative as not only do the means vary considerably, but the standard deviation of samples also does so, and shows a tendency to be smaller at sea level than at higher altitudes (linear variance of the group of s.d. = ·20; standard error of standard deviation being of the order ·05). A speculative estimate is perhaps obtained by taking the mean value of the variance of samples from such samples as enable the calculation (·232) and combining it with the variance of the group of mean values after the altitude regression has been allowed for (·212). This gives a 50 per cent level of ± ·444, but it is doubtful if it is worth stating the 5 per cent. and 1 per cent. limits. The limits at sea level are almost certainly narrower than this and those at high altitudes wider.

These observations, of course, serve only to confirm the already widely accepted theory that there is a progressive increase in the red blood count and haemoglobin (provided that there has been time for acclimatization) with height above sea level, and that a *selected* group of Africans in Uganda conform in this respect to the world picture. But in East Africa they will have a much greater local significance, since there is reason to suspect that a truly random sample of the local population might yield much lower results both for haemoglobin and red count.

Lehmann and Milne, for instance, estimating haemoglobin by the rather crude copper sulphate gravity method, have obtained the following results on African school children in Kampala:—

Age group (years)	Number of children	Percentage with haemoglobin less than 14 gms./100 cc.
5–10	133	31
11–15	481	14
16–25	227	0·4

It will be recalled that the mean Hb. of Makerere students was 16·55 (σ = 1·81) gms./100 cc. H. F. Welbourne (to be published) has carried out a more extensive survey of haemoglobin values in school children of all races in Uganda.

Other data for the East African territories are no doubt scattered through various reports, which will gradually be unearthed.

Harvey has recently reported the following mean figures for a group of 29 railway workers (males) in Nairobi (5,000 feet). Hb. 17·15; R.B.C. 5·57; M.C.V. 92·5; M.C.H. 31·0; M.C.H.C. 33·3 per cent.

The general clinical impression is that patients admitted to Mulago hospital, for whatever cause, more often have red counts between four to five million than over five million. Tonkin performed a series of 400 red cell counts on apparently healthy male prisoners in Nairobi prison. These men were under medical supervision, and were frequently wormed. The mean figure was $5·02 \times 10^6$. From the European Hospital records, he found that the average count of an apparently considerable (but unstated) number of sick Europeans was $5·73 \times 10^6$. Hennessey performed 48 counts on male convicts in the Central prison, Uganda, (approx. 3,9000 feet) and found a mean value of $4·56 \times 10^6$ ($\sigma = 0·58 \times 10^6$) with a mean haemoglobin of 13·1 g. per cent.

It is of course clear that before it can be considered that the blood picture presented by any group is optimal, a number of groups (e.g. of persons consuming diets of different types, of persons more or less exposed to infections or parasitic infestations, etc.), must be studied, and consideration must also be given to other factors. Among such factors would naturally be similarity between the findings, and those obtained from healthy individuals in other parts of the world at similar altitudes.

Whatever may be the conclusions about the normal blood picture of Africans, there is no doubt but that in Uganda gross anaemia is very common. Trowell and his collaborators have published a number of papers on the subject.

Recently Lehmann has advanced the view that these cases can be cured by simple iron therapy coupled with removal of infections and/or infestation (of which latter hookworm infestation is by far the most important). He does not find evidence that any haematinic principle, other than iron, is involved. He does not consider the condition to be a macrocytic anaemia in the accepted sense, but suggests that the large cells described by other observers as megalocytes are in fact reticulocytes and young erythrocytes. Lehmann and Baird have recently described a modification of the cyan-haematin method of haemoglobin determination.

Holmes noted the adverse effect of infections particularly of the respiratory tract on an anaemia, which was probably of this type, seen in East African soldiers in Burma. Having few haematological facilities he accepted the condition, probably wrongly, as tropical macrocytic anaemia.

Lehmann and Milne suggest that, though the sickle-cell trait is even commoner in Uganda than formerly supposed, there is no evidence that it is a common cause of anaemia, and that sickle-cell anaemia is extremely rare. Lehmann and Raper have investigated the ethnological distribution of the sickle-cell trait. Raper has demonstrated intravascular sickling as a cause of sudden death in Africans who carried the sickle-cell trait but were not necessarily anaemic.

Gross undernutrition is commonly seen in the hospitals of Uganda. The presenting symptoms of the severe cases are oedema and diminished serum proteins, changes in skin and hair, and an anaemia. Naturally, parasitic infestation and malarial infection are common in these cases, and the condition may accompany such conditions as tuberculosis and nephritis. Nevertheless a great many of the cases showing the symptoms described are primarily nutritional in origin. The similarity to the " famine oedema " which has followed social catastrophes in Europe and elsewhere is obvious. In all probability " Kwashiorkor," originally described in West Africa, and other syndromes described in other parts of the world represent the same syndrome, modified by local conditions. Trowell has used the term " Malignant Malnutrition " for the condition and has discussed it fully. He has in another publication indicated some of the possible economic and social implications.

An attempt is being made in Uganda to study this condition from a number of different angles. Holmes and Trowell have found abnormal sugar tolerance and inability to store hepatic glycogen after glucose injection.

Work is in progress on nitrogen metabolism and water distribution and balance (Holmes and Stanier).

Trowell projects a study of the secretory function of various digestive glands.

Davies, besides making a histo-pathological study of the liver lesions (which have been described by many authors) has also found lesions in the pancreas and in nearly all the exocrine glands discharging into the alimentory canal. On the theory that the liver inactivates aestrogenic compounds and that the damaged liver may fail to do this adequately, he is considering the possible role of excess oestrogens in the production of abnormalities such as gynaecosmastia, carcinoma of the male breast, feminization of the skeleton, very high incidence of inguinal hernia, high incidence of cystic hyperplasia, of primary hepatic carcinoma, and of carcinoma of the reticuloendothelial system and other tissues. Vint has described abnormalities of the African pituitary.

Davies has described the pathology of a cardiac condition, common in Uganda, and described in West Africa, but not (so far as is known) elsewhere, which clinically presents the signs, symptoms and cause of cardiac failure commonly attributed to rheumatic lesions.

Many of the conditions thus briefly mentioned may be nutritional in origin, though it is not desired to make any sweeping statement on the matter. Unfortunately, though we see many severe cases of malnutrition in hospital, there is at present no reliable information as to the real dietary state of the population. It is said that malnutrition is common in Muganda children, rare in Muganda adults, but often seen in adults belonging to the group of migratory labour. Many opinions are expressed about African diets, some of them obviously coloured by precon-

ceived ideas, but scientific information is meagre. It can only be supplied by proper diet surveys, which are a most urgent requirement. Owing to the difficulties in distribution of local foodstuffs, and to tribal dietary custom and prejudice, the results of a single survey are often only locally applicable. The study of malnutrition as seen in hospital will obviously be pursued for its own intrinsic interest and for the light which it will throw on Physiology, Biochemistry and Pathology. If, however, any economic or social implications are to be seriously considered, field work, such as diet surveys, must also be carried out.

Tuberculosis is common in Uganda, and may fairly be described as an outstanding public health problem. Attack on it on public health lines will necessarily progress slowly. Dr. Hutton is particularly interested in the chemo-therapeutic approach, and is testing out various drugs as they become available on the only too plentiful material to be found in the wards. He has also published work on Pneumococcal Meningitis, a condition seen more frequently here than it is in U.K.

The work here discussed is in progress at the following Institutions:—

The Department of Physiology, Makerere College.

Research Unit R./144 (under the direction of Dr. Holmes: Senior Research Worker Dr. Lehmann).

The Laboratories of Makerere College Medical School.

The Wards of Mulago Hospital (Dr. Trowell, Dr. Hutton).

The Government Pathological Laboratories, Kampala. (Dr. Raper, Dr. Davies).

It involves close collaboration between Makerere, Medical School, and Government staff.

G.P.-S.5663—1949-50—500.