SEVERE AND PROLONGED UNDERFEEDING IN AFRICAN CHILDREN

(THE KWASHIORKOR SYNDROME OF MALIGNANT MALNUTRITION)

BY

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This communication falls into three parts: first there is a critical review of recent advances in knowledge of the effects of severe and prolonged under-feeding in African children, with consequent production of that syndrome of malnutrition, which has been called kwashiorkor; and secondly personal observations are offered of the frequency of this form of malnutrition and its relationship to other common disorders of African children, namely, malaria, congenital syphilis and sickle cell disease; and thirdly observations are offered of a limited trial of desiccated hog's stomach. It is hoped in this way to summarize the present state of knowledge of this syndrome and to consider its relationship to diseases peculiar to the tropics and to the Bantu race.

Recent literature on the kwashiorkor syndrome

Following brief descriptions by Procter (1926) in Kenya and Lieurade (1932) in the Cameroons, Cecily Williams (1933, 1935), working at Accra in the Gold Coast, first adequately described the syndrome. She noted the disease only among children and she considered that it was a new clinical entity. She suggested the term kwashiorkor, because the Ga tribe around Accra called it thus: (kwashi = the name of a boy born on Sunday—orkor = red). She noted the oedema, the pale red skin and hair, the crazy-pavement dermatosis and the fatty liver as seen at autopsy. Unfortunately Africa is divided into many hundreds, if not thousands, of small tribes, so that the term kwashiorkor is not understood outside the immediate vicinity of Accra, capital of the Gold Coast. Other medical officers, unable to find this disease in the standard text books, usually employ the local tribal name, such as Pieraerts (1942), who described cases of 'diboba' in the Belgian Congo. Observations have thus tended to remain isolated.

Trowell (1937, 1940), in reporting cases in Kenya, considered that the disease was largely a mixture of pellagra, nutritional oedema, an anaemia due to

deficiency of iron, and nutritional macrocytic anaemia. The term 'infantile pellagra' was suggested, but this term is now considered unsatisfactory. He discussed earlier work by Gillan (1934) and the view of Stannus (1934, 1936), as well as other possible cases in Mexico and the West Indies in children who were mostly the descendants of the African slaves. Although Carruthers (1941) has described possible cases in Indian children in India, no case has been traced in the literature among European, white American, Chinese or Japanese children.

The question then emerges: is this syndrome confined, almost exclusively, to Africans and their descendants, occasioned largely by race and heredity, or is it noted with greater ease in Africans? This point cannot be settled, for there are no real facts upon which a conclusion can be built. It is, however, suggestive that it is the pallor and redness of the black African skin and hair which is the most distinctive feature of the syndrome and this change has usually suggested the African tribal name of the complaint. If, however, the disease occurred in a European child what colour would the hair and the skin become? It is probable that there may be much in common between the pale skin and hair pigments in kwashiorkor and the muddy skin and the dull, lustreless hair noted in marasmus and cachexia in European children.

Trolli (1938) and Van Daele (1938) were among the first to note that African adults frequently suffered from the kwashiorkor syndrome; a point confirmed by Pieraerts (1942) and Trowell (1942, 1944). No essential clinical difference has been detected in the cases seen in children and those seen in adults; the biochemical changes and autopsy findings are similar. In adults, however, the oedema is usually less, so is the pallor of both the African skin and African hair; but these may at times be quite as severe in adults as in children.

In Africa the discussion has turned largely on the

dermatosis, since it was hoped that this, more than any other sign, would determine whether the disease was pellagrous.

Cecily Williams (1940) maintained that crazy-pavement dermatosis was unlike that of classical pellagra and Nicholls (1940) reported that this dermatosis was common in Ceylon but that pellagra was considered to be rare in that country. Trowell (1941) reported that the dermatosis sometimes peeled after nicotinic acid treatment, but that as the general condition continued to deteriorate the relationship to pellagra was still uncertain.

In South Africa the recognition of the disease was slow, but Suzman (1941) reported cases in African children; and Kark (1943), who reported the cases in children in a native reserve, considered that the condition was one of pellagra. Meanwhile the exact significance of the crazy-pavement dermatosis attracted attention; Harding le Riche (1943) found it present in 42.9 per cent. of some 3519 African schoolchildren surveyed in Johannesburg. Other features of the syndrome were not present and he refrained from saying whether the condition was considered to be pellagrous. It is the opinion of the present writers that some reticulation of the skin of the lower leg into slightly scaly glazed areas is normal; it can be seen in Europeans of all ages, especially those who walk bare-legged. Crazy-pavement dermatosis is only an exaggeration of this normal scaly reticulated skin. It is usually a sign of malnutrition, but it can often be seen even when other features of the syndrome cannot be detected.

Scott Brown and Trowell (1944) reported deficiency bowel pattern in the kwashiorkor syndrome in African children, African adults and in Polish adult refugees, in all of whom the clinical picture appeared identical. Thus the syndrome affected adults as well as children, and could affect European adults in whom the hair was dull and lustreless and the skin muddy and pale with only small areas of dermatosis. In this communication Trowell stated that he could no longer consider that the syndrome was pellagrous, for the radiological changes in the small intestine appeared to be unknown in pellagra.

It has only been possible to examine as yet the small intestine in three African children who have had a satisfactory diet for a long period of time and who have no intestinal helminths. In them, however, even in the second and third year, the x-ray outline of the small intestine showed that it was often irregular in calibre and had coarse, irregular, mucosal folds. It is considered that only gross segmentation (fig. 1 and 2) can be considered as abnormal and a sign of deficiency bowel pattern, and it is impossible to accept the stricter criteria of 'normality' described by Ross Golden (1941).

An unsatisfactory aspect of the syndrome is the absence of any very distinctive changes at post-mortem, and Trowell (1944) stressed the fact that no significant lesion has been found in the gastro-intestinal tract of tissues fixed within a few minutes of death, and he regarded as of little significance

the fatty degeneration of the liver. Gillman and Gillman (1944) in a series of communications, submitted to journals in America, of which the writers have been privileged to receive copies, have demonstrated by an improved method of liver biopsy, performed in more than 300 cases of kwashiorkor in children, that fatty degeneration was the earliest

FIG. 1.—Deficiency bowel pattern in the small intestine of an African child of some four years.

sign to appear in the liver and the last to disappear. This lesion was often so gross that the sections lost all resemblance to hepatic tissue. This fatty degeneration does not respond to any known diet supplemented by large doses of the B-complex vitamins; but it did appear to respond speedily to the oral administration of desiccated hog's stomach. It was only possible to test this preparation in some six cases. All other observers, with this single exception, have reported that the syndrome is

FIG. 2.—Deficiency bowel pattern in an African adult of some twenty years, showing segmentation in the small intestine.

refractory to all forms of treatment, and Gillman and Gillman (1944) set the mortality as high as 50 per cent. In their opinion they were able to trace all stages from fatty degeneration to pigment cirrhosis of the haemochromatosis type, which occurred later in adolescent or adult life.

In animals the disease has been reproduced in almost every respect by Rao (1941): he fed young monkeys almost exclusively on milled rice and he noted that they wasted, developed oedema, diarrhoea, and that the stools contained undigested food. A stage was soon reached at which the animals refused to eat, and their lives could not be saved by liberal additions of all the known vitamins. Fatty degeneration of the liver and inflammation of the gastro-intestinal tract were noted at post-mortem. Laycock (1944) noted the effect in Chinese adults of semi-starvation by the Japanese; he noted the oedema, diarrhoea, passage of undigested stools, the lustreless hair and the pale skin; he observed that many cases were unable to recover even when given a liberal diet.

The occurrence of anaemia in this syndrome has been noted by many observers, and Trowell (1937) suggested that it was usually due to a deficiency of iron and of the liver factors which were absent in nutritional macrocytic anaemia. Further investigation showed that the anaemia was usually macrocytic (increased mean corpuscular volume) and hypochromic (decreased mean corpuscular haemoglobin concentration).

Thus in forty-six children suffering from kwashiorkor, who were examined in this hospital during 1943, the mean blood count of the group was: R.B.C. 3,090,000, Hb 8.6 gm., M.C.V. 116.5 c.μ, M.C.H.C. 27.6 per cent. This macrocytic hypochromic anaemia was very variable and it appeared to be present even in cases which showed neither helminthic ova in the stools, nor malarial parasites in the blood. The presence of a relapsing malarial infection cannot ever be completely excluded, but was discovered in only 25 of these 46 children, all of whom were in-patients. The routine investigation of all cases of anaemia in adults and children in Uganda has revealed that most of them have a macrocytic hypochromic variety, which appears to be due to a dual deficiency. This group has been provisionally called the dimorphic group (Trowell, 1942 and 1943). When these cases of so-called 'dimorphic anaemia' are examined, a large proportion show certain signs suggestive of the kwashiorkor syndrome; thus there is often a pale skin, brown, soft hair, oedema, a reduction in the plasma albumin and an increase of its globulin; but attacks of loose stools and deficiency bowel pattern appear to be much less common. There appears to be much overlap between cases of 'dimorphic anaemia' and cases of the kwashiorkor syndrome as seen in adults and in children. There is only one further observation on the anaemia, and that is, that the megaloblasts of pernicious anaemia are seldom, if ever, seen in the bone marrow or in the peripheral blood in the kwashiorkor syndrome or in 'dimorphic anaemia.' Earlier accounts (Trowell, 1942) mentioned the abnormal types of erythropoiesis seen in

'dimorphic anaemia,' and referred to one series of cells as the 'nutritional macrocytic anaemia megaloblasts.' The latter term now appears open to grave objection, for the structure of the nucleus is not sufficiently reticular to warrant the use of a term, which should be reserved for the abnormal haemopoiesis, seen in a case of pernicious anaemia, during relapse.

Personal observations

During 1945, at a children's clinic held each week at Mulago Hospital, Kampala, Uganda, an attempt was made to assess how far this type of malnutrition was present among the sick children attending. Each week, out of the twenty to thirty cases, the first two or three cases to arrive were placed by the nurse in a special part of the room where they were examined in a more detailed manner. Histories were taken, with special attention to attacks of malarial fever, syphilis in mother or child, and particulars of feeding and of the diet were noted. Children were then examined clinically, noting especially the early and obvious physical signs, softness and brownness of the hair, pallor of the skin, oedema, and failure to gain weight. Blood counts were performed, including a sealed drop preparation for sickle cells, and blood was removed for the Kahn test and for estimation of the plasma proteins. The last were only estimated in some twenty children but some one hundred and twenty-six patients were examined in every other respect. At the same time some fifty-four in-patients were also examined during 1945.

Body weight. Fig. 3 shows the scatter distribution of their weights. It is noted that at birth many African babies are lighter than Europeans, but that they tend to gain weight more rapidly, probably due to their being suckled whenever they cry. Malaria, contracted by almost all babies soon after birth,

FIG. 3.—Scatter distribution of the weights of 126 African children.

● = black hair and dark skin.
○ = brownish hair and pale skin.

does not appear to impede growth, at least during the first five months. A check occurs about the fifth or sixth month in many cases. After that, those who maintain a healthy increase of body weight seldom show the hair and skin changes seen in this variety of malnutrition, but those whose weight is unsatisfactory usually show these changes. It will be seen from fig. 3 that after the sixth month about three-quarters of all cases attending the clinic showed signs of the kwashiorkor syndrome.

Plasma proteins. These were estimated in only twenty cases, difficulties in securing technical assistance precluding a larger number of examinations. Cases were not selected, except on the ground of age, none being below six months. Blood was removed from the external jugular vein, and this was not attempted in very young babies.

Fig. 4 shows the distribution of these cases. It will be seen that in only four cases did the albumin and the globulin both lie within the normal range for British children (Rennie, 1935; Hickman, Finch

FIG. 4.—Scatter distribution of the plasma proteins in 20 African children.

and Tonks, 1943). In most cases the plasma albumin was low and the plasma globulin was high, so that the A/G ratio was low. Every case had an A/G ratio which lay below that of the mean A/G ratio for normal children, that is the A/G ratio was decreased. It often lay below unity, that is it was 'reversed.'

Blood counts. Mean of the whole group: R.B.C. 3,340,000 (range 1.50–7.00 per c.mm.). Hb. (Sahli, per cent. of normal), approx. 59 (range 36–125). Mean of group, showing no malarial parasites: R.B.C. 4,200,000 per c.mm., Hb. 69 per cent. Mean of group, showing malarial parasites: R.B.C. 2,950,000 per c.mm. Hb. 52 per cent. Sick cells in sealed drop preparation: 25 cases (20 per cent.).

Infections. Apart from malaria and congenital syphilis it proved difficult in out-patients to state what infections were present, so in-patients, totalling some fifty-four cases of kwashiorkor, were examined in greater detail for any infection. Whenever

possible the groups were combined to assess the true incidence of infection.

MALARIA. In 180 cases, 119 with parasites in the blood smear (66 per cent.), subtertian 80, quartan 36, benign tertian 3.

CONGENITAL SYPHILIS. In 180 cases, 9 certain cases (mother and child—both strongly positive), 8 probable cases (child strongly positive, mother absent), 8 probably 'false' positives (the general biological reaction of the child, intensified by malaria, giving a 'false' positive, i.e. child feebly positive, no clinical signs, mother's Kahn negative). Probable total of 17 cases (9.5 per cent.).

PNEUMONIA. In 54 ward cases, 12 cases, 9 fatal.

INTESTINAL. In 54 ward cases, bacillary dysentery 4 cases, amoebiasis 1 case, ankylostomiasis 14 cases, ascariasis 4 cases, giardiasis 6 cases.

Desiccated hog stomach

To assess the response of cases to treatment is most difficult. Thus many minor cases respond well to an ordinary diet as soon as any infection, such as relapsing malaria, is treated, although even in them the progress is slow, at least as regards the gain of body weight. Severe anasarca is almost always very refractory to all forms of treatment. It does not respond to even large injections of vitamin B₁, and if its mechanism is the reduction of the plasma albumin, then progress must needs be slow, unless plasma can be administered intravenously. It has not been possible to try this experiment in Uganda. The biggest advance in recent years has been the introduction of high-calorie, high-protein diets. Nevertheless in advanced cases the response is slow and cases may yet die several weeks after admission. If the findings of Gillman and Gillman (1944) can be confirmed, namely that the earliest lesion is a fatty degeneration of the liver, then this may explain why severe cases cannot produce plasma albumin quickly, for it is the liver which synthesizes albumin from the amino-acids. Gillman and Gillman (1944) claimed that desiccated hog stomach quickly restored the liver to normal, as shown by serial liver biopsies.

It has not been possible to secure the apparatus employed by Gillman and Gillman and therefore routine liver biopsies have not been made in the present cases. It has been done, however, in some twenty-five adults suffering from obscure liver disease and the method, without special precautions, does not appear to be free from a certain risk of fatal haemorrhage.

A trial of desiccated hog liver has been made in some six cases of kwashiorkor. The results, although not conclusive, are encouraging. One typical response, involving the disappearance of the oedema, is given in some detail.

Male Ruanda child, aged about three years, fell sick on the way to Uganda, developed oedema, which became severe, so that the child resembled a case of acute nephritis. Diarrhoea started and may have had a bacterial origin, for on admission there was much pus and some mucus in the stools, culture

was negative and no protozoal or helminthic cause was detected. The temperature was 101° F. on admission but afterwards was normal, and no malarial parasites were detected in the blood smear. Crazy-pavement dermatosis was present on the legs, the hair and skin were pale and reddish.

No improvement occurred during two weeks, on a high-calorie, high-protein diet, together with vitamin B₁ 10 mgm., and nicotinic acid 100 mgm. daily, with also 6 grains daily of quinine. Then for four days sulphathiazole (0.5 gm. four-hourly), and injections of neohepatex 2 c.cm. daily, were tried without response.

Desiccated hog stomach (1 heaped teaspoon—about 60 grains, thrice daily), was given. A diuresis occurred, 58 ounces of urine were passed the next day, and the weight, previously stationary, fell from 29 lb. to 26 lb. with disappearance of all oedema. Appetite also improved, and a discharge was demanded; after this the child did not attend again.

Discussion

It has been suggested (Trowell, 1944) that the kwashiorkor syndrome in the tropics is usually a pattern; the strands of the warp are nutritional in origin—wasting, oedema, skin changes, a gastro-intestinal defect, anaemia, fatty liver and so forth; the strands of the weft are infections or congenital defects—malaria; respiratory infections, and intestinal helminths. From the foregoing investigation it is considered that:

Malaria is active in two-thirds of the cases at any one time; it probably affects almost all cases at one time or another; it intensified the anaemia, which otherwise is usually mild.

Congenital syphilis affects rather under a tenth, and may affect far less if malaria gives many 'false' positive reactions, a point still undecided, and still under investigation.

Intestinal helminths and protozoa affect about one-third of the cases.

Pneumonia is the commonest fatal infection.

Sickle cells are present in about one-fifth of the cases; few of these show an anaemia which can be ascribed to sickle cell haemolysis. The question of sickle cell trait and sickle cell anaemia has been discussed elsewhere (Trowell, 1945).

In the tropics the kwashiorkor syndrome is seldom seen uncomplicated by infection of which the most important is malaria (in at least two-thirds), and

also intestinal protozoa and helminths (in about a third). At the present time the majority of clinicians in the tropics do not recognize the condition and refer to it as malarial marasmus or hookworm anaemia and so forth. There is considerable truth in this point of view, since relapsing and untreated malaria may well cause long bouts of restricted intake of food, and thus produce secondary nutritional defects. These may be largely overcome by treating the malaria and allowing appetite and a normal diet to do the rest. Far too often this form of treatment is unsatisfactory; as even after weeks of quinine, the gain of weight is very poor; in fact the kwashiorkor syndrome, when well established, is always extremely refractory to all forms of treatment.

The true constituent elements in the syndrome are only seen in clear perspective when the condition occurs, almost uncomplicated by tropical disease, as seen in the observations of Gillman and Gillman (1944) in Johannesburg in South Africa.

The difficulties which attend weaning in tropical countries, where milk, eggs, and meat may be in short supply and seldom purchased by poor peasants, can be envisaged by reference to table 1. This shows how the estimated requirements of 1200 calories for a child of two years can be secured by the staple carbohydrates of Uganda. In the second part of the table two of the staple cereals of Europe and Asia are listed for comparison.

It will be seen that Starling's dictum 'Look after the calories and the protein will look after itself' only applies to wheat-eaters. No one in Britain would regard it as satisfactory if a child was weaned on to a diet of bread and water, but the position of this child would be fortunate in comparison with many young children in the tropics, who must largely look to supplement of beans, groundnuts and peas to increase the amount of protein.

In addition many children receive only two meals a day and these consist of bulky carbohydrate of vegetarian origin. Thus to supply 1200 calories a Ganda child attempts to eat 24 ounces of plantains at each of its two meals (prepared by peeling 96 ounces per day, 50 per cent. wastage), whereas a British child could secure the same number of calories from 6 ounces of bread at each of the two meals. The result in the African child is pot-belly

TABLE 1.—DIET TO SUPPLY 1200 CALORIES FOR A CHILD AGED 2 YEARS

Food	Amount	Protein	Calcium	Iron	Vitamins				
					A	B ₁	Nicotinic acid	C	D
	oz.	Gm.	mgm.	mgm.	Units	Units	mgm.	mgm.	Units
Required	—	40	1000	7	2000	200	6	35	600
1. Cassava tubers . .	43	9	500	0	0	0	0	360	0
2. Sweet potatoes . .	54	11	140	0	0	100	0	140	0
3. Plantains	96	19	60	5	4000	100	0	100	0
4. Millet	13	23	130	2	100	200	7	0	0
5. Maize	13	39	30	13	0	100	2	0	0
6. Rice	12	22	10	1	0	240	7	0	0
7. Wheat	12	42	100	10	0	360	17	0	0

and umbilical hernia and separation of the recti abdominis muscles; these are present in many African children.

In conclusion, the relationship of the kwashiorkor syndrome to marasmus, to nutritional (or famine) oedema, and to coeliac disease is discussed. It is well recognized that marasmic children may have scanty dull hair, pale and muddy complexions, oedema, gastro-intestinal attacks, reduced blood proteins, anaemia, and often prove refractory to all forms of treatment. Distinctive features in kwashiorkor are the macrocytic anaemia, steatorrhoea, fatty liver, deficiency bowel pattern and raised plasma globulin. Nevertheless kwashiorkor may well be only severe marasmus, after weaning, in African children with a few additional variants, such as the fatty liver, due to the peculiarities of the African diet.

Superficially the cases resemble nutritional (famine) oedema; but the clinical picture of the latter disease has seldom included the grossly fatty liver, the macrocytic anaemia or the raised plasma globulin of kwashiorkor. Nevertheless during times of war and famine, it is seldom possible to investigate adequately the cases of oedema. All is confusion when relief comes. So far, however, the picture of famine oedema is almost restricted to wasting, oedema and a reduction of the plasma albumin; until this picture can be enlarged or modified, it would appear unwise to state that kwashiorkor is merely nutritional oedema.

In the established case of kwashiorkor it is doubtful if there is any single clinical or bio-chemical investigation which can unequivocally distinguish a case of kwashiorkor from one of coeliac disease (fig. 5). These are the only two common conditions in childhood in which marked deficiency bowel pattern occurs. It is true that African children, who may almost be on a fat-free diet, may pass little fat, but if given milk, then steatorrhoea is present, though seldom gross (Gillman and Gillman, 1944), and the fat is well split (Trowell, 1937). Tetany is uncommon, but has been observed; it should be borne in mind that African children probably make most of their vitamin D in the skin in large amounts in the tropical sunshine; rickets has never been seen in any x-ray taken in Uganda. Slight generalized osteoporosis has been observed especially in adult cases, but true bony deformities have not been observed in kwashiorkor. Pot-belly, macrocytic anaemia, retarded growth and irritability have all been noted. Oedema, however, is far more common in kwashiorkor and in this disease many cases proceed rapidly to inanition and death. Both kwashiorkor and coeliac disease are refractory to all forms of treatment; crude liver extracts aid both diseases, not only with regard to the blood picture, but also as regards the gastro-intestinal defect. Both diseases are apt, like sprue, to develop secondary vitamin deficiencies.

With regard to terminology, kwashiorkor, meaning the red boy or man, holds pride of place in Africa. It is unfortunate that this term is only

FIG. 5.—Failure of growth and pot-belly in a child of some eight years, measuring 35 inches. This type resembles in certain respects coeliac disease; there was steatorrhoea, macrocytic anaemia, deficiency bowel pattern, low plasma albumin, but no bone deformity or tetany.

understood by one of the smallest tribes in the Gold Coast. It is even more unfortunate that cases occurring in adult life, resemble in every respect these infantile cases, except that redness of the hair and skin are seldom seen in adults. They can hardly be called 'the red disease.' Neither was this colour seen in two Polish refugees (Scott Brown and Trowell, 1944) who suffered from this condition. It has therefore been proposed (Trowell, 1944) that this syndrome might provisionally be called 'malignant malnutrition.'

Summary

1. A critical review is offered of a severe syndrome of malnutrition, seen in African children, and called kwashiorkor. It manifests itself chiefly as failure of growth, oedema, macrocytic anaemia, steatorrhoea, crazy-pavement dermatosis, fatty liver and decreased plasma albumin but increased plasma globulin, and deficiency bowel pattern.

2. In varying degrees this syndrome affects about three-quarters of the sick children in Kampala, Uganda, between the ages of six months to three years.

3. A detailed study is offered of the infections detected in 180 cases. Malaria was present in about two-thirds, intestinal infections by protozoa and

helminths in about one-half, and congenital syphilis in one-tenth.

4. The syndrome may be very refractory to all forms of treatment; a limited trial of desiccated hog's stomach supplementing a high-protein, high calorie diet, has given encouraging results, and is worthy of a more protracted trial.

Thanks are due to Mr. F. R. Bell, Veterinary Officer, for the estimations of the plasma proteins and to Mr. J. Kyobe for the blood counts; to Messrs Bengers for the desiccated hog stomach (extomak); and to the Director of Medical Services, Uganda, for permission to publish this article.

REFERENCES

- Carruthers, L. B. (1941). *Trans. roy. Soc. trop. Med. Hyg.*, **35**, 21.
- Gillan, R. U. (1934). *E. Afr. med. J.*, **11**, 38.
- Gillman, J., and Gillman, T. (1944). *Nature*, **154**, 210.
- Golden, R. (1941). *Radiology*, **36**, 262.
- Hickman, E. M., Finch, E., and Tonks, E. (1943). *Arch. Dis. Childh.*, **18**, 96.
- Kark, S. L. (1943). *S. Afr. J. med. Sci.*, **6**, 106.
- Laycock, H. T. (1944). *Brit. med. J.*, **1**, 667.
- Le Riche, H. (1943). Health survey of African children in Alexandra Township, Johannesburg, Witwatersrand University Press.
- Lieurade (1932). *Bull. Soc. Path. Exot.*, **25**, 46.
- Nicholls, L. (1940). *Trans. roy. Soc. trop. Med. Hyg.*, **34**, 291.
- Pieraerts, G. (1942). *Receuil de travaux de science médicale au Congo Belge.*, **1**, 104.
- Procter, R. A. W. (1926). *Kenya med. J.*, **3**, 289.
- Rao, M. V. R. (1941). *Indian J. med. Res.*, **30**, 273.
- Rennie, J. B. (1935). *Arch. Dis. Childh.*, **10**, 415.
- Scott Brown, J. S., and Trowell, H. C. (1944). *Lancet*, **2**, 812.
- Stannus, H. S. (1934). *Arch. Dis. Childh.*, **9**, 115.
- (1936). *Trop. Dis. Bull.*, **33**, 729.
- Suzman, M. M. (1942). *Clin. Proc.*, **1**, 205.
- Trolli, G. (1938). Résumé des observations réunies au Kwango, au subject des deux affections indéterminées. Foréami d'après les médecins du l'années 1936-1937. Brussels.
- Trowell, H. C. (1937). *Arch. Dis. Childh.*, **12**, 193.
- (1940). *Trans. roy. Soc. trop. Med. Hyg.*, **33**, 389.
- (1941). *Ibid.*, **35**, 13.
- (1942). *Ibid.*, **36**, 151.
- (1943). *Ibid.*, **37**, 19.
- (1944). *Clin. Proc.*, **3**, 381.
- (1945). *E. Afr. med. J.*, **22**, 34.
- Van Daele, G. (1938). *Ann. Soc. belge Méd. trop.*, **18**, 563.
- Williams, C. D. (1933). *Arch. Dis. Childh.*, **8**, 423.
- (1935). *Lancet*, **2**, 1151.
- (1940). *Trans. roy. Soc. trop. Med. Hyg.*, **34**, 85.