of possible tuberculous infection than a contrast series: and that it approaches that of a group of patients suffering from pulmonary tuberculosis. Bass and Vader (1957), in Eindhoven, collected a series of 128 patients with sarcoidosis, the diagnosis being made on clinical grounds mainly, biopsy evidence being positive in 16. Contact with active tuberculosis, often with longer intervals than two years, within and without the family totalled 23 (18%), to which they added contact with inactive tuberculosis in 17 (13%) and with cattle in 6 (5%), giving them a total of 36% with tuberculous contacts; both latter groups were inaccessible in our patient questionnaire retrospective survey. It seems that their higher incidence may be partly due to different means of selection of the patients, different definition of contact history, and the advantages of a full radiological survey of the possible contacts.

These significant findings clearly bear upon the problem of the part which tuberculous infection may play in the genesis of sarcoidosis. They suggest that contact with tuberculosis may well be a substantial rather than a minor cause; for, if the contact history is a mere coincidence, it is difficult to explain why it should differ from that of the contrast group. This evidence of a relationship between tuberculous infection and the onset of sarcoidosis raises many further problems. It may, for instance, well be that the role of infection with *M. tuberculosis* is catalytic for an immune process of a highly specific type. Evidence for altered immune reactions in patients with active sarcoidosis has been recorded by Greenwood *et al.* (1958).

The familial aspects of tuberculosis in this series of patients with sarcoidosis lends support to this in that there seems to be some evidence of inherited resistance to tuberculosis. There are five families in this series with sarcoidosis. The relationship is close in all of them, and yet in only one of these families is another relative known to have tuberculosis, and there the contact was not recent. Although this is a small experience it does suggest that there may well be an immune process which is determined genetically. There seems to be a place for a longer survey of the contacts of patients with tuberculosis, particularly where the population is compact and stable.

Summary

Three series of patients, with tuberculosis, sarcoidosis, and asthma or bronchitis, have been investigated for contact with tuberculosis, and this has been correlated with the onset of the disease in the first two series. Similar incidence of recent contact was found in the series with sarcoidosis (12% of 210) and with tuberculosis (16% of 315), contrasting with the control group (2% of 214). The relationship of this to the aetiology of sarcoidosis is discussed.

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KWASHIORKOR IN AFRICAN CHILDREN IN DURBAN

BY

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Since Williams's (1933) classic description of kwashiorkor in West Africa and Trowell's (1937) comprehensive study in Uganda, a considerable amount has been contributed to the literature on this subject. It is now apparent that there are many minor variations on the major theme of this malnutritional syndrome, and this becomes apparent from the 1,565 cases of kwashiorkor studied at this hospital during 1955 and 1956. This is a record of in-patients only, and selection has been applied here in the sense that as only the worst cases were admitted these are the ones described. The less severe cases (and these were very numerous) had to be treated as out-patients because of the heavy demand for beds. Since the condition is, unfortunately, so common in Durban, we are unusually well placed to record the incidence of various clinical signs, their relation to biochemical data, the influence of infections on prognosis, and the response to treatment.

Criteria for Diagnosis

Our criteria for diagnosis were: (1) a dietary history suggesting protein malnutrition; (2) oedema associated with hypoalbuminaemia—the latter unexplained on the basis of renal, cardiac, or other disease; (3) retardation of growth, irritability, apathy, and anorexia; (4) a variable dermatosis.

Cases diagnosed as suffering from "malnutrition" and "marasmus" are not included in this study, for we have not been able to determine with confidence whether such cases (Fig. 1, a, b) were of the atrophic type (Altman, 1948) and were simply *undernourished* (starved), as opposed to being *malnourished* as in kwashiorkor. Adequate pathological and biochemical studies have not yet been done in these cases.

As stated by Brock (1955), "... the greatest difficulty lies in the fact that there is a spectrum of clinical

appearances from classical kwashiorkor with considerable subcutaneous fat through the intermediate degrees to undernutrition and marasmus." Bearing in mind this very real clinical problem, we have erred on the side of excluding cases from the kwashiorkor series when any

FIG. 1.—(a) Atrophic case many weeks after admission and (b) six months later on discharge.

doubt existed and unless both of us concurred unhesitatingly in the diagnosis.

Incidence

A total of 4,944 cases of all diseases were admitted to the paediatric unit during 1955, and of these the several varieties of "malnutrition" (including 731 cases of kwashiorkor) comprised 1,014 (20.5%). In 1956 the total admissions numbered 5,285, and of these 1,009 (19.1%) were suffering from frank malnutrition, 834 of which were cases of kwashiorkor. Thus about one-fifth of the cases, sufficiently ill to warrant urgent admission to this unit, suffer from a pre-

ventable nutritional condition with a very high mortality.

The sharp rise in case incidence during the hot humid summer months of January and February, with a distinct fall during the cooler months, is shown in Fig. 2.

Contributory Causes of Malnutrition

Poverty and bad housing conditions, deprivation of maternal care, a high illegitimacy rate among the urban African community, and ignorance all play a part in producing the high incidence of kwashiorkor among

FIG. 2.—Seasonal incidence of kwashiorkor.

African infants in Durban. We believe, too, that the development of an associated infection such as measles or dysentery in a child who is maintaining a precarious nutritional balance on a grossly inadequate diet often precipitates the development of frank kwashiorkor.

Clinical Features

Sex and Age Distribution.—Tables I and II show the distribution by sex and age. Our figures do not disclose any significant sex predominance, and the majority (81%) of cases were between 6 and 36 months old, the average age being 22 months.

TABLE I.—Kwashiorkor—Age and Sex Distribution

		Mean Age in Months	Under 6 Months	Over 4 Years
Males	839	22.1	19	58
Females	726	21.7	29	55
Total	1,565	22.0	48	113

TABLE II.—Age and Mortality in Different Age Groups

Age in Months	Admissions		Deaths	
	No.	%	No.	%
2-5	29	1.9	20	69.0
6-11	160	10.2	120	75.0
12-23	734	46.9	432	58.9
24-35	374	23.9	161	43.0
36-47	155	9.9	54	34.8
48-59	68	4.3	25	36.8
60-71	25	1.6	7	28.0
72-83	17	1.1	2	11.8
84-96	3	0.2	—	—
Total	1,565	100	821	52.5

TABLE III.—Main Clinical Features in 1,565 Cases

	Total	%
Oedema	1,462	93.4
Dermatoses	1,284	82.0
Hair changes	751	48.0
Stomatitis	404	25.1
Hepatomegaly	353	22.6
Ulceration	314	20.1
Initial albuminuria	129	8.2
Keratomalacia	14	0.9

The incidence of the more important clinical features is shown in Table III.

Oedema.—Peripheral oedema of the degree and distribution described by many authors was present in 93.4% cases. Ascites occurred in only one case, in a child who developed what appeared clinically to be cirrhosis when recovery from kwashiorkor was almost complete. We have never seen effusions into joints in any of our cases, and none developed congestive cardiac failure, but at necropsy a small pericardial effusion was found in one case and pulmonary oedema in three cases.

Initial Albuminuria.—Albuminuria was seldom more than slight (recorded as a trace or rarely as "one plus"), and this mild proteinuria rapidly disappeared on treatment. No relationship could be established between the presence of albumin in the urine and the severity of the case as judged by other criteria.

Dermatosis.—Skin lesions were present in 82% of cases. Constant observation disclosed the evolution of the dermatosis through the stages of hyperpigmentation ("enamel-paint" dermato-

sis), desquamation and pigmentation (Fig. 3), fully described clinically by Trowell *et al.* (1954) and both clinically and histologically by Gillman and Gillman (1951). The fully developed dermatosis is on the whole a bad prognostic sign in our experience, though many children slowly recover despite initially gross skin changes. Extensive purpura-like dermatosis was often found (Fig. 4).

In addition, we have not infrequently noted, on subsidence of periorbital oedema (which may be gross), the appearance in its place of a dark, almost black, pigmentation, particularly below the eyes.

Ulceration and Nutritional Gangrene.—Ulceration or actual tissue necrosis, as opposed to the typical desquamation, was relatively common, being found in mild or gross form in 20.1%. It was usually encountered in the flexures, on the buttocks, or on the dorsum of the feet as circular punched-out ulcers (Fig. 5). Other forms of

FIG. 3.—“Enamel paint” dermatosis with desquamation and pigmentation.

FIG. 4.—Purpura-like dermatosis.

FIG. 5.—Deep punched-out ulcer on dorsum of foot.

necrosis were also seen in the post-auricular and natal clefts, the nasolabial folds, and at the junction of the helix of the ear with the scalp. The raw edges of the eyelids have also been found to ulcerate. Occasionally part of the ear or nose sloughed away, although no case of cancrum oris was encountered in this series.

Ocular Lesions.—During 1955 and 1956 we encountered corneal ulceration in 14 cases of frank kwashiorkor. Since 11 of the 14 cases occurred in 1956, these lesions would appear to be increasing in frequency, as our figures since then show (17 cases with 12 deaths

FIG. 6.—Corneal ulceration with subsequent destruction of eye.

in a series of 1,102 cases of kwashiorkor during the year period July, 1958, to June, 1959). A striking feature was the rapid development of the corneal ulceration with perforation and prolapse of the iris (Fig. 6). We have found perforation of one or both eyes developing within 12 hours of noticing the first indications of dryness and haziness of the cornea. With one exception, all the patients with corneal involvement in the present series died. Five of them were admitted in extremis and died within a few hours.

Stomatitis.—A bright-red tongue, fissuring of the lips, angular stomatitis, and, quite frequently, ulceration of the buccal mucosa were common features.

Hair Changes.—Hair changes were present in 48% of cases. Sparseness of the eyebrows was another fairly common finding.

Hepatomegaly.—Our difficulty has been to decide when a liver should be regarded as enlarged on clinical grounds alone. In our experience in apparently healthy African children the liver is so often palpable one to two fingerbreadths below the costal margin that we have come to regard this as a normal finding. On this basis, then, the liver was found to be more than two fingerbreadths below the costal margin in 22.6% of cases. Gross enlargement was found in only 6.3% of cases. The liver was never tender on palpation.

Liver biopsies were not done, but fatty livers were found at necropsy in all but one of 53 cases.

Convulsions.—Convulsions occurred in 37 cases, the cerebrospinal fluid being normal in every case.

Rickets.—Rickets was detected in association with kwashiorkor in only three cases, but mild and even severe bony changes, as noted by Gillman and Gillman (1951), may have been overlooked as radiographs of ribs and epiphyses were taken only where clinical evidence of rickets was manifest.

Intestinal Helminths.—Although common in kwashiorkor, helminths were not found more often than in other patients in the wards.

Incidence of Associated Infections

More than one infection was often present in a single case, but for statistical purposes these have been noted separately in Table 4. By gastro-enteritis we mean

TABLE IV.—Associated Infections in 1,565 Cases

Type of Infection	No. of Cases
Bronchopneumonia	380
Gastro-enteritis	361
Bacillary dysentery	157
Measles	91
Acute otitis media	83
Pulmonary tuberculosis	67
Chronic otitis media	63
Amoebic dysentery	25
Pyelonephritis	20
Diphtheria	7
Pertussis	6
Mastoiditis	3
Urinary bilharzia	2
Cerebral sinus thrombosis	2
Chicken-pox	2
Poliomyelitis	1

vomiting and diarrhoea thought to be of infective origin and not simply the frequent loose stools so common in kwashiorkor. Although many cases presented with an associated infection, cross-infection in the wards played a part in producing the high incidence shown here, and there was a notable lack of response to antibiotic therapy. Measles was often a serious complicating factor.

Laboratory Investigations

Haematology

The mean haemoglobin level (Table V) on admission in 808 cases was 10 g./100 ml., and on discharge, in 226 cases, was 10.5 g./100 ml.—indicating the slow

TABLE V.—Mean Haemoglobin Levels

	No. of Determinations	Mean Hb g. 100 ml.
On admission	808	10.0
On discharge	226	10.5

erythropoietic recovery. During the two-year period, bone-marrow examinations were performed on only 183 cases; megaloblastic anaemia was present in 36 of these (19.7%).

Figures given in Table VI should not be regarded as indicating the overall incidence of the marrow reactions specified, for marrow studies were done only

TABLE VI.—Results of Bone-marrow Examination in 183 Cases

Type of Marrow	No. of Cases	Mean Hb on Admission (g. 100 ml.)
Megaloblastic	36*	5.2
Non-megaloblastic	147	7.0

* Associated with infection in 21 cases.

on obviously anaemic patients. Moreover, on occasion, infants moribund on admission exhibited a severe clinical anaemia, but died before bone-marrow examinations could be done. Others may have died with haemoglobin levels over 7 g./100 ml., and with normal peripheral smears.

Biochemical Data

Serum Proteins.—(Table VII). Serum protein estimations, done on admission in 588 cases, showed a mean

total protein of 4.1 g./100 ml., and a mean albumin level of 1.2 g./100 ml. In the majority of cases plasma proteins improved *pari passu* with the general condition, but in 25 of these death due to various intercurrent

TABLE VII.—Serum Proteins

	No. of Determinations	Total Proteins; Mean and Range g. 100 ml.	Serum Albumin Mean and Range g. 100 ml.	Serum Globulin Mean and Range g. 100 ml.
On admission: All cases	588	4.1 (2.2-5.4)	1.3 (0.1-2.2)	2.9 (1.4-4.3)
Cases dying	264	3.9 (2.2-5.2)	1.2 (0.1-2.1)	2.8 (1.4-4.1)
Cases recovering	324	4.4 (2.6-5.4)	1.3 (0.6-2.2)	3.1 (1.7-4.3)
On discharge	306	6.6 (4.5-8.6)	2.7 (1.6-3.9)	4.3 (3.0-6.4)

infections occurred, even when the total proteins had risen to a mean of 6.6 g./100 ml., and the albumin from 1.2 to 2.3 g./100 ml.—a finding in conformity with that of Gillman and Gillman (1951).

Serum Cholesterol.—(Table VIII). Our results in 526 cases showed a low mean level on admission (78.6 mg./100 ml.), with a significant rise on discharge (120.5 mg./100 ml.) in 250 cases.

TABLE VIII.—Serum Cholesterol and Blood Urea

	On Admission	On Discharge
Serum cholesterol (mean—mg. 100 ml.)	78.6 (526)	120.5 (250)
Blood urea (mean—mg. 100 ml.)	18.2 (586)	25.3 (226)

Figures in parentheses denote number of cases investigated.

Blood Urea.—(Table VIII). The blood urea levels, on admission and on discharge, were estimated in 586 and 226 cases respectively. Levels on admission were usually lower than those on discharge, while levels estimated during convalescence were occasionally higher than normal. Thus, in 17 convalescent cases the blood urea level rose above 40 mg./100 ml., and in one case as high as 91 mg./100 ml. These high levels were not associated with signs of uraemia or dehydration.

Treatment

Our treatment followed that recommended by Trowell *et al.* (1954) and Pretorius *et al.* (1956). We used fresh acidified skimmed milk in frequent small feeds, alternating with oral Darrow's solution, increasing the quantity of milk feeds as appetite increased. To the skimmed milk was added calcium caseinate powder.

In severe cases, and particularly in those not showing a rapid response to oral feeding, blood, plasma, and serum transfusions were often of great benefit as suggested by Achar (1950) and Brock *et al.* (1955). Intravenous electrolyte therapy was also necessary on many occasions, since dehydration was a serious complicating factor in cases with an associated gastro-enteritis or dysentery.

In this series routine prophylactic antibiotics, as recommended by Brock *et al.* (1955), were not given, though the vast majority of patients did, in fact, receive antibiotic therapy because of the very high incidence of associated infections.

Length of Stay in Hospital.—The average length of stay in hospital was 30 days. It was impossible to

accommodate these children after the "initiation of cure" for the period of what Brock *et al.* (1955) describe as the "consolidation of cure."

Relapses.—When it is considered that, on leaving hospital, children return to the same unsatisfactory home conditions, relapses were surprisingly infrequent (4.5%).

Results

Mortality.—(Table IX). Total deaths from all causes were 821 (52.5%). Many of these patients died within a few minutes to a few hours of admission. Deaths from associated infections numbered 546 (Table X). There were 203 deaths from uncomplicated kwashiorkor within 48 hours of admission (Table IX).

TABLE IX.—Deaths from Kwashiorkor

Cause of Death	1955	1956	1958–59*
Kwashiorkor only:			
Deaths within 48 hours ..	115	88	21
„ after 48 „ ..	24	48	17
Total	139	136	38
(percentage of all admissions)	(19%)	(16.3%)	(3.4%)
Kwashiorkor complicated by infections:			
Deaths within 48 hours ..	67	134	179
„ after 48 „ ..	186	159	180
Total	253	293	356
(percentage of all admissions)	(34.6%)	(35.1%)	(32.3%)
Kwashiorkor—deaths, all causes	392	429	394
Total admissions for kwashiorkor (Overall mortality)	731 (53.6%)	834 (51.4%)	1,102 (35.7%)

* July 1, 1958, to June 30, 1959. The criteria for diagnosis and for admission to hospital remained unchanged as compared with 1955 and 1956.

TABLE X.—Causes of Death (1955 and 1956)

Bronchopneumonia	175
Gastro-enteritis	168
Bronchopneumonia and gastro-enteritis	78
Bacillary dysentery	62
Bronchopneumonia and bacillary dysentery	27
Pulmonary tuberculosis	23
Amoebic dysentery	6
Measles	5
Diphtheria	2
No cause other than kwashiorkor	275
Total	821

Necropsy Findings

From the main necropsy findings in 53 cases it was apparent that the major lesions were similar to those reported by Gillman and Gillman (1951), by Trowell *et al.* (1954) and by other authors. The high incidence of clinically detected associated infections was confirmed at necropsy, where no fatal case was found to be free of infection. In several cases there was more than one infection. Our most recent figures confirm this high incidence of associated infection. During the year July, 1958, to June, 1959, 336 necropsies were carried out on 394 kwashiorkor patients who died, and only 33 were found to be free from an associated infection.

Discussion

This study reveals that undernutrition and malnutrition in the African child population in Durban form a most serious and formidable problem and are the direct or indirect cause of severe morbidity and death.

The usual dietary history obtained was that the infant had been breast-fed for a variable period and then

various maize products were given as porridge. Infants under 6 months suffering from frank kwashiorkor had invariably not been breast-fed at all, their diet consisting of some concoction of maize such as mealie-meal or purified corn starch and water and not infrequently condensed milk alone. As stated by Williams (1933), kwashiorkor often develops in the child when the next child is born; in fact, typically it is the disease of the "deposed child." To this problem there is added that of the mother who works to augment the family income. The child or children are often deprived of maternal care in this way and are attended by a grandmother or other relatives. Trowell and Davies (1952) suggest that the reasons for the occasional development of kwashiorkor in the fourth and fifth years of life are either a serious deterioration in the diet or the development of a prolonged and debilitating disease such as tuberculosis. Amongst older children in this series 54.5% had associated severe infections. In the absence of some chronic disease, in this older group, we often found that the child had been in the care of an overzealous grandmother, who, for safety's sake, prevented him from roaming around the neighbourhood and scavenging from other sources.

The high illegitimacy rate among Durban Africans frequently deprives children of the little financial support of the father. Ignorance on matters of feeding also undoubtedly plays a major part in the urban African population in Durban. Quite often mothers agree that they could afford to buy milk for their children, but tend rather to buy bulky carbohydrate foods devoid of proteins, fats, and other essential nutrients.

The distinct seasonal incidence found in Johannesburg by Gillman and Gillman (1951) and in Durban by Klenerman (1950) and Walt *et al.* (1950) is confirmed by our findings. We attribute the sharp rise in case incidence during the hot humid summer months to the high incidence of gastro-enteritis and dysentery at this time of the year. Whatever the aetiology of the diarrhoea, whether infective or metabolic, it often constitutes a final precipitating cause of kwashiorkor (Brock, 1955). As suggested by Gillman and Gillman (1951), the metabolic demands of the hot humid season in already malnourished babies may be of considerable importance in producing the distinct seasonal incidence noted here.

The finding that the majority of our cases were 6 to 36 months of age is similar to that of many authors (Trowell and Davies, 1952; Brock *et al.*, 1955).

The clinical features commonly found in this series differ only slightly from the many excellent descriptions given by several authors. However, in contrast to the cases studied by Gomez *et al.* (1952) and Woodruff (1955), ascites was a most unusual finding in the cases studied by us in Durban, and, in fact, was found on only one occasion. We agree with the conclusions of Dean and Schwartz (1954) at Kampala that no relation exists between the presence of albumin in the urine and the severity of the condition as judged by other criteria.

Minor traumata have been shown to play some part in localizing the skin lesions (Gillman and Gillman, 1951; Dean and Schwartz, 1954). This has been confirmed by our experience, and, in addition, we suggest that the periorbital hyperpigmentation is the result of trauma to this skin by distension with gross oedema. However, it is also possible that this pigmentation may be the equivalent in these children of a similar pigment

associated with liver disease in adults and referred to as "masque biliare" (Urbach and Le Winn, 1946).

Although ulceration or actual tissue necrosis was a common finding in our most severe cases, no case of cancrum oris occurred. Gillman and Gillman (1951) in South Africa, and Jelliffe (1953) in Nigeria, noted several cases of cancrum oris in kwashiorkor. We had, however, seen two cases of cancrum oris in kwashiorkor in Durban in years prior to the present study, and in a third case the dorsum of both feet sloughed extensively, leaving both the metatarsal bones and tendons exposed. All these lesions may represent the equivalent, in our cases, of similar and other forms of nutritional gangrene described by Gillman and Gillman (1951). We have also observed gangrene of the feet and legs in two cases in whom surprisingly good pulsations were noted in the affected limbs. The mechanisms producing such nutritional gangrene are still obscure and may involve basic intracellular nutritional and enzymatic disorders, rather than any disturbance in vascular supply. We were struck by the suddenness with which such gangrenous lesions could appear and the speed of their progress.

How far the corneal lesions, noted in increasing numbers of kwashiorkor cases in Durban, are attributable to "nutritional gangrene" of ocular tissues, analogous to that seen in the skin, still remains to be determined. It is possible that some dysfunction of the lacrimal glands (perhaps comparable with that reported in the pancreas) is basically responsible. Despite Williams's reference to corneal ulceration in severe cases in her original series (Williams, 1933) and her later report of two cases of corneal sloughing (Williams, 1935), ocular lesions are still inadequately described in kwashiorkor and malnutrition generally. Kark (1943) reported 34 cases of the syndrome, 21 of which had conjunctivitis and blepharitis, but he did not mention the occurrence of corneal lesions. Blumenthal (1950) described malnutritional "kerato conjunctivitis." He opined that ocular disease is attributable to the consumption of a predominantly carbohydrate diet devoid of vitamins, which is far more dangerous than subsistence on a quantitatively inadequate but relatively varied diet. Ocular signs, attributed to vitamin A deficiency, were described in 44% of 150 cases of kwashiorkor studied by Achar and Benjamin (1953). Oomen (1954) described xerophthalmia in 29 patients, 22 of whom could be classified as cases of kwashiorkor according to the definition of Brock and Autret (1952). Oomen did not attribute this xerophthalmia to the deficiency of a single vitamin, but rather regarded it as indicative of an ominous overall malnutrition. Keratomalacia was present on the cornea of one or both eyes of four of Oomen's patients; there was lack of lustre of the cornea in all cases, six had ulcers, and three developed perforations. We prefer to apply the term keratomalacia to the corneal lesions in our cases rather than Blumenthal's name—kerato-conjunctivitis.

We have often seen children with obvious kwashiorkor who have good curly black hair. This confirms Altman's (1948) report that hair changes may be completely absent in severe cases of kwashiorkor. Brock (1954) also stated that hair changes are not essential for the diagnosis of kwashiorkor. Moreover, as noted by others, dyspigmentation of the hair occurs in malnutritional syndromes which would not ordinarily be classified as kwashiorkor. For example, ginger or almost flaxen hair may be seen in African children suffering from chronic

wasting diseases such as tuberculosis. Nor does the colour of the hair (reddish, golden, grey, or even white) seem to be related to the severity of the malnutritional condition.

With regard to the mental state of children with kwashiorkor—the very sensitive description given by Dean and Schwartz (1954) epitomizes the clinical impression given by our cases. These authors state that "... the almost complete apathy makes the child behave as though it wanted nothing so much as to be left alone to die."

Authors differ on the finding of hepatomegaly in kwashiorkor. Trowell, Davies and Dean (1954) did not find it as a feature in the cases seen at Kampala. However, Gillman and Gillman (1945a, 1945b, 1951) and Altman (1948) stressed enlargement of the liver as an important feature of the cases in Johannesburg. Likewise, Gelfand (1946) reported enlargement of the liver as common in his cases and noted that pressure over the liver caused pain. Brock (1955) stated that the liver was often but by no means invariably enlarged. All authors agree on the occurrence of fatty livers in kwashiorkor. Thus Gillman and Gillman (1945a, 1945b, 1951) found, in biopsies, that a fatty liver of varying severity was the most constant single pathological reaction in the syndrome. They thought that the state of the liver, as determined by biopsy, was a better indication of prognosis than any of the clinical or biochemical findings studied by them. The fatty changes present on admission in the livers of a large series of cases usually resolved completely on recovery of the patient and were certainly not a precursor to cirrhosis. This finding was later confirmed by Altman (1948). Suckling and Campbell (1957) further confirmed this opinion in a follow-up study of 27 cases of kwashiorkor in coloured children in Capetown. Moreover, although malnutrition and frank kwashiorkor are so common here, cirrhosis is rare among African children in Durban. If the invariably fatty liver in this syndrome of kwashiorkor were a precursor to cirrhosis, the incidence of cirrhosis should be very much higher in infants in populations in which kwashiorkor is so common.

Although Trowell *et al.* (1952) state that the very slow pulse often accompanying hunger oedema in adults is not found in kwashiorkor, bradycardia was not an uncommon finding in some of our severe cases; it was always regarded as a very grave prognostic sign.

Whereas Altman (1948) reported many cases of active rickets associated with kwashiorkor in African children in Johannesburg, in our series frank rickets was a rarity. This may have been due to the rarity of the overt rachitic rosary and other lesions for reasons outlined by Gillman and Gillman (1951).

Convulsions occurred in only a small number of our cases, and most of these may have been febrile in origin. However, since Brock *et al.* (1955) and Hansen (1956) stressed the importance of electrolyte disturbances in kwashiorkor, routine electrolyte studies may help to determine whether, in some instances, convulsions are metabolic in origin, for example, as found in hypernatraemia (Finberg and Harrison, 1955).

The high incidence of associated infections is one of the most alarming features of kwashiorkor as seen in Durban. Gelfand (1956) has stated that diarrhoea is an outstanding feature of the syndrome in Salisbury, and in our cases the incidence of gastroenteritis was remarkably high. Heavy infestations with intestinal

parasites were also very common, ascaris being among the most frequent. However, infestation with the latter helminth was no more common in kwashiorkor cases than in other patients in our wards not manifestly suffering from kwashiorkor. This fact leads us to suggest that roundworm infestation plays only a minor part, if any, in precipitating kwashiorkor in our cases. This view is suggested despite Jelliffe's (1953) opinion that heavy ascaris infestations seen in Nigeria probably interfered with food absorption, and even though there is some evidence that ascariasis results in the production of a substance inhibiting protein absorption. We advise against therapy for helminths in seriously ill children until they are better able to tolerate the toxic drugs administered.

Our haematological findings are in keeping with those of many authors who have reported on anaemia in kwashiorkor; for most authors agree that the anaemia in kwashiorkor is usually only moderate in degree (Trowell, 1944; Gelfand, 1946; and Brock and Autret, 1952). Altman and Murray (1948) found the anaemia to be normocytic in 24 of 36 cases studied by them, microcytic in 4, and macrocytic in 4. Trowell *et al.* (1952) state that the anaemia does not present clear or constant morphological features. They found it to be usually normocytic or slightly macrocytic and often slightly microcytic, but the bone marrow was seldom if ever, megaloblastic in their cases. Trowell and Simpkins (1957) concluded that when due care was given to all technical details of staining, typical megaloblasts of Ehrlich were not seen in their cases.

In Durban, Walt *et al.* (1950) found a moderate macrocytic normochromic anaemia unassociated with megaloblastic anaemia in a series of 36 cases, while Adams (1954), describing the haematological findings in 21 cases of kwashiorkor (19 of which were in the paediatric unit from which our series of cases are drawn), found a level of haemoglobin of less than 9 g./100 ml. in two-thirds of cases, but megaloblastic changes in the bone marrows of only two cases. Abnormal but not frankly megaloblastic changes were found by Adams in the marrows of a further six cases. However, Walt *et al.* (1956) reported 42 cases of megaloblastic anaemia, 22 (52%) of which had typical kwashiorkor. These authors suggest that the number of cases of megaloblastic anaemia may be increasing in Durban, and they believe that any anaemia developing suddenly in kwashiorkor should be suspected as being megaloblastic. We agree with this opinion, but have found that many anaemias which supervened acutely in our cases were normoblastic. Moreover, as stated by Trowell *et al.* (1954), any severe bacterial infection can cause anaemia, sometimes very suddenly. Associated infections were very common in our cases, and as we also see megaloblastic anaemia in infants unassociated with kwashiorkor, it is difficult to assess whether the infection or the kwashiorkor was the precipitating factor. Adams (1954) noted that the anaemia sometimes increased considerably as oedema decreased and the plasma proteins rose, a severe anaemia being unmasked during recovery. This finding was confirmed in our series in those cases in which repeated haemoglobin estimations were possible. All writers agree that the anaemia is slow to respond to treatment. Despite resolution of the clinical lesions and biochemical abnormalities, the haemoglobin may not be significantly higher on discharge than on admission.

Trowell and co-workers (1954) found that children with the most severe oedema had the lowest total proteins,

and especially albumin levels. We are unable to find a clear relationship between the total plasma protein, total albumin or albumin/globulin ratio, and the presence or absence of oedema. Our findings are thus in conformity with those of Gillman and Gillman (1945a; 1951), Janssen and Le Roux (1950), and Brock (1954).

Too few serum bilirubin estimations were done in our kwashiorkor cases during 1955 and 1956 to give us significant information. Kinnear and Pretorius (1957) stated that serum bilirubin levels showed neither diagnostic nor prognostic significance in fatal kwashiorkor. Our experience since 1957, when serum bilirubin estimations were begun as a routine investigation, indicates that serum bilirubins are rarely raised, but when elevated the prognosis is bad. During the period July, 1958, to June, 1959, when 1,102 cases of kwashiorkor were admitted to this unit, 30 cases were found to have a raised level of serum bilirubin, and all but five of these died.

Depression of serum cholesterol and blood urea levels has been reported in kwashiorkor, and our findings of low initial levels with a rise during treatment were similar to those of Dean and Schwartz (1953).

Trowell *et al.* (1954) state that under the best conditions the mortality is probably below 10%. A review of the literature reveals that the mortality rate of kwashiorkor varies widely from year to year and from place to place—a finding stressed by Gillman and Gillman (1951). Thus, Williams (1933) reported a mortality of 90%, Altman (1948) a rate of 20%, and Gelfand (1956) that of 90% in 1946, falling to 77% in 1953 and 50% in 1955. A similar fall of mortality rate was reported by Kahn *et al.* (1958) in Johannesburg from 40% in 1950 to 20% in 1958. In Durban, Klenerman (1950) had a mortality rate of 49%. In our own large series of cases the total mortality rate from kwashiorkor and its complications was 53.6% in 1955 and 51.4% in 1956. The reduction of the mortality rate in this hospital for the period July, 1958, to June, 1959 (35.8%—Table IX) may be explained by the fact that this unit acquired 120 additional convalescent beds, which we believe reduced the incidence of cross-infection and hence the death rate.

The surprisingly low relapse rate found in Durban is probably partly attributable to the fact that many of our cases are returned to their rural grandparents, where they may relapse and not return to hospital. It may also be explained on the suggestion of Dean and Schwartz (1954) that "... the short period of good feeding may have a permanent effect if it comes at a critical time . . . , so that relapse may not be inevitable even if the diet cannot be greatly improved."

Were it not for the fact that milk powder is dispensed by child welfare clinics run by the Durban City Health Department, and sponsored by various charitable organizations, the incidence and death rate would probably be higher than it is already. The University Department of Social, Preventive, and Family Medicine, through its Institute of Family and Community Health, has shown the inestimable value of educational and prophylactic work in preventing severe malnutrition in infancy, even though this Institute has embraced only a limited section of the local African community. Expansion of prophylactic work in this field in the future would appear to be a vital factor in the prevention of this type and all other forms of malnutrition in the African and lowest income groups of the population.

Summary

During a two-year period (1955-6) 1,565 cases of kwashiorkor were studied in the paediatric unit of the King Edward VIII Hospital, Durban.

The clinical criteria for the diagnosis of kwashiorkor are stated. No case presenting predominantly with emaciation was included in this series.

A marked seasonal incidence in Durban is noted, the disease being far more common during the summer months.

The common clinical findings and their incidence are described. Special attention has been drawn to the prevalence (20% of cases) of ulceration or actual tissue necrosis (possibly "nutritional gangrene") and of the increasing incidence of ulcerating corneal lesions in Durban.

The very high incidence of associated infections is stressed.

While detailed haematological and biochemical investigations were not possible in all instances, the findings are given in a considerable number of cases investigated.

The frequency of anaemias (including megaloblastic types) is discussed in the light of available literature, the slow erythropoietic recovery being characteristic.

The bad prognostic signs of bradycardia and elevation of the level of serum bilirubin are noted.

Reasons for the high incidence of kwashiorkor in Durban are discussed. The high death rate, due mainly to associated infections in an eminently preventable condition, is deplored.

A brief description of the treatment prescribed in this unit is given.

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AN ABNORMALITY OF BLOOD LIPIDS
IN HEREDITARY SPHEROCYTOSIS

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Several metabolic differences between blood of patients with hereditary spherocytosis and blood of normal subjects have been described; these include differences in inorganic phosphate levels, sodium transport, and intermediary carbohydrate metabolism (see review by Pranker, 1959). It appears likely that these changes are secondary to a defect in the red-cell membrane which is manifested by the reduced surface area to volume ratio in spherocytes. The primary genetically controlled defect is not yet known, but the striking abnormality in shape of the red cells suggests that a component of the cell membrane, possibly a phospholipid, may be involved. For this reason we have investigated the phosphatide composition of spherocytes, as compared with normal cells, as well as the rate of incorporating of ^{32}P into phosphatides of normal and abnormal blood cells. A characteristic difference between normal and spherocytic blood lipids has been revealed, and this difference may possibly explain the development of spherocytosis in susceptible subjects.

Materials and Methods of Study

Blood was obtained from two young women with typical hereditary spherocytosis and family histories of the condition; one subject had had a splenectomy. Normal and abnormal bloods were incubated with ^{32}P -orthophosphate in citrate-dextrose for five hours at 37°C . as previously described (Lovelock *et al.*, 1959). The cells were separated from plasma and extracted with methanol-chloroform (Bligh and Dyer, 1959). The lipids recovered were separated by chromatography on silicic-acid-impregnated paper (Marinetti *et al.*, 1957), identified by their R_f value and staining behaviour, and analysed quantitatively by determining the phosphorus