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## Serum electrolytes and proteins in kwashiorkor

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(Received 5 June 1956—Revised 18 September 1956)

The purpose of this investigation was to study the pattern of serum sodium and potassium in kwashiorkor and to ascertain whether it can be related to the presence or absence of oedema or diarrhoea, whether it alters with the rise of serum protein levels in response to a high-protein diet, and whether abnormalities in the electrolyte pattern are responsible for the deaths which sometimes occur in children suffering from this disorder.

### EXPERIMENTAL

*Subjects.* Investigations were carried out on sixty-three children, sixty Africans and three of mixed race, who were admitted to the Paediatric Department of Baragwanath Hospital. All were suffering from severe kwashiorkor, the diagnostic criteria being irritability, dermatosis, oedema, discoloration and change in the texture of the hair, and low weight for age, all of which were present in most of the subjects. Their ages varied from 8 months to 6 years, the mean age being 20 months. There were thirty-seven males and twenty-six females. On admission all but four of the patients had marked oedema, which added to their initial weight. Weight for age is shown in Fig. 1, in comparison with average weights of normal controls.

Patients with renal or cardiac oedema, and those known to be suffering from tuberculosis, dysentery or parasitic infestations were excluded from this study.

*Examination of blood.* Blood was taken from the internal jugular vein, in most patients within 1 h of admission, and always within the first 18 h. Blood examinations were repeated every 6th or 7th day until discharge from hospital. When the subjects were out of danger, were taking feeds well and all evidence of oedema had disappeared, they were discharged from hospital prematurely because of the shortage of beds. In some of these subjects repeat estimations could not be done. Owing to conditions prevailing in the ward, balance studies could not be carried out. The average period in hospital was 23 days. The specimens of blood taken before discharge are those tabulated under the heading 'During recovery'.

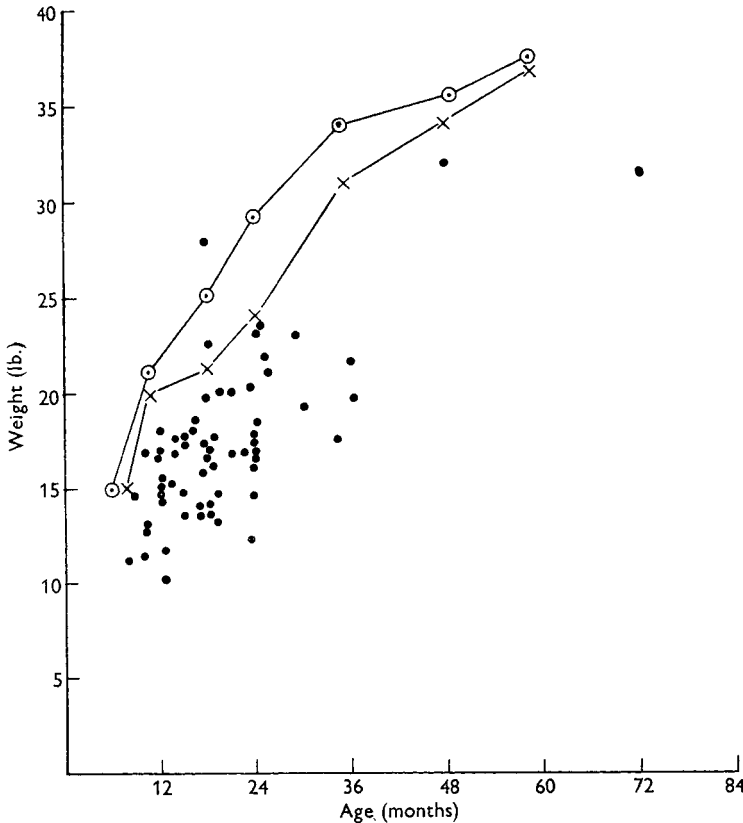


Fig. 1. Weight distribution by age of kwashiorkor patients in comparison with mean weights of normal children. ○—○, normal for European children; ×—×, normal for African children.

Serum was separated by centrifuge within 1 h of collection of the blood. Determinations of serum sodium and potassium were carried out with an EEL flame-photometer (Evans Electro-selenium, Ltd) (Varley, 1954). In order to give a more complete picture, serum proteins were also estimated by a modification of the method of Wolfson, Cohn, Calvary & Ichiba (1948), 27.2% sodium sulphate being used.

The assessment of results was based on normal values obtained from twenty-one subjects showing no evidence of malnutrition and not suffering from conditions known to affect electrolyte balance. These values were: sodium 136.3 (s.d.  $\pm$  4.0) m-equiv./l.,

potassium 5.0 (S.D.  $\pm$  0.6) m-equiv./l., total serum proteins 7.0 (S.D.  $\pm$  0.39) g/100 ml., serum albumin 3.7 (S.D.  $\pm$  0.39) g/100 ml., and serum globulin 3.3 (S.D.  $\pm$  0.63) g/100 ml.

*Treatment of patients.* Most patients were treated with skim milk, though older children without diarrhoea were given half-cream or full-strength cow's milk. All mixtures were acidified with lactic acid. After the first few days in hospital approximately 3 g milk protein/lb. body-weight were given in 24 h. Naso-gastric tube feeds were given when required. Twenty-four of sixty-three patients (38%) showing evidence of hypokalaemia (hypotonia and abdominal distension) were given potassium chloride intravenously. Patients without symptoms but with low potassium levels were given a solution of equal quantities of potassium acetate, bitartrate and citrate orally (Leonsins, 1951).

Vitamins C and D were given in prophylactic doses during convalescence.

#### RESULTS

##### *Serum sodium*

As indicated in Table 1, the serum sodium was 130 m-equiv./l. or less in forty-two out of sixty-three (67%) of the patients on admission and in 61% remained low during recovery. No significant difference was apparent in these sodium levels before and after treatment. The presence or absence of diarrhoea in oedematous patients appeared to make no difference to the serum sodium levels.

##### *Serum potassium*

As can be seen in Table 2, serum potassium levels varied widely. Twenty-seven of sixty-three subjects (43%) had levels of 4.0 m-equiv./l. or less and four of those with extremely low values died. In three patients the serum potassium level remained low after treatment, but they showed no symptoms. No subject with an abnormally high serum potassium level died.

Of the patients with and without diarrhoea, 60% and 27% respectively had low levels. Fifty-nine patients were oedematous and of these twenty-nine (49%) had low serum potassium levels; in most of these the levels became normal after treatment.

##### *Serum protein*

Serum protein levels are shown in Table 3. Low albumin levels in particular were observed and, in a few patients, high globulin levels. On treatment, both albumin and globulin levels increased, the former to a greater degree (56% as against 36% for globulin). One 4-year-old oedematous subject showed a normal total protein (6.2 g/100 ml.) on admission with an albumin:globulin ratio of 1.9:4.3.

There was no difference in serum protein levels between the groups with and without diarrhoea.

In twenty-five out of forty-four subjects whose serum proteins were re-examined at weekly intervals there was a definite relationship between rise of serum proteins (albumin or globulin or both) and subsidence of oedema (Table 4). In twenty-one

Table 1. Serum sodium levels in kwashiorkor patients with and without diarrhoea

Serum sodium level (m-equiv./l.)	Patients with diarrhoea				Patients without diarrhoea				All patients	
	Before treatment		During recovery		Before treatment		During recovery		Before treatment	During recovery
	No. of patients	Mean sodium level (m-equiv./l.)*	No. of patients	Mean sodium level (m-equiv./l.)*	No. of patients	Mean sodium level (m-equiv./l.)*	No. of patients	Mean sodium level (m-equiv./l.)*	Mean sodium level (m-equiv./l.)*	Mean sodium level (m-equiv./l.)*
† 106-120	2		1		1		4			
121-125	5		1		6		1			
126-130	12	128 ± 6.0	10	129 ± 7.4	1	16	9	129 ± 7.6	129 ± 5.7	129 ± 7.3
131-135	9		5		5		5			
136-145 †	2		3		5		4			
				Total		4		Total		7

\* Value and standard deviation.

† Lowest observation.

‡ Highest observation.

Table 2. Serum potassium levels in kwashiorkor patients with and without diarrhoea

Serum potassium level (m-equiv./l.)	Patients with diarrhoea				Patients without diarrhoea				All patients	
	Before treatment		During recovery		Before treatment		During recovery		Before treatment	During recovery
	No. of patients	Mean potassium level (m-equiv./l.)*	No. of patients	Mean potassium level (m-equiv./l.)*	No. of patients	Mean potassium level (m-equiv./l.)*	No. of patients	Mean potassium level (m-equiv./l.)*	Mean potassium level (m-equiv./l.)*	Mean potassium level (m-equiv./l.)*
† 2.4-3.0	7		0		3		0			
3.1-3.5	5		0		1		1			
3.6-4.0	6		2		5		0			
4.1-4.5	5	3.7 ± 0.83	0	5.0 ± 0.61	1	7	2	5.2 ± 0.67	4.2 ± 1.00	5.1 ± 0.63
4.6-5.0	4		7		5		5			
5.1-5.5	3		8		0		9			
5.6-6.0	0		3		1		4			
6.1-6.9 †	0		1		5		2			
				Total		4		Total		7

\* Value and standard deviation.

† Lowest observation.

‡ Highest observation.

subjects the time taken for the subsidence of clinically detectable oedema was 6-14 days and in four subjects 34-37 days (mean 10 days).

*Fatalities.* Table 5 summarizes information about eleven patients who died. In two of them (numbers 1 and 10) a low serum potassium level was associated with a low serum sodium.

Table 3. *Serum protein levels in patients with kwashiorkor*

Serum protein level (g/100 ml.)	Total proteins*			Albumin*			Globulin*		
	A	B	C	A	B	C	A	B	C
0.7-1.0	—	—	—	2	1	1	—	—	—
1.1-1.5	—	—	—	30	4	4	—	—	—
1.6-2.0	—	—	—	22	4	4	8	—	1
2.1-2.5	—	—	—	6	11	—	28	4	4
2.6-3.0	3	—	1	—	9	—	22	11	4
3.1-3.5	10	1	1	—	10	—	1	18	—
3.6-4.0	18	1	3	—	4	—	—	9	—
4.1-4.5	18	2	4	—	1	—	1	2	—
4.6-5.0	9	6	—	—	—	—	—	—	—
5.1-5.5	1	5	—	—	—	—	—	—	—
5.6-6.0	—	12	—	—	—	—	—	—	—
6.1-6.5	1	5	—	—	—	—	—	—	—
6.6-7.0	—	5	—	—	—	—	—	—	—
7.1-8.0	—	7	—	—	—	—	—	—	—
Total no. of cases	60	44	—	60	44	—	60	44	—
Mean level	4.1	5.9	—	1.6	2.5	—	2.5	3.4	—
Standard deviation	0.45	0.77	—	0.36	0.81	—	0.39	0.58	—

\* A, number of patients before treatment; B, number of patients during recovery; C, number of deaths.

Table 4. *Serum protein (g/100 ml.) on admission and after loss of clinical oedema of patients with kwashiorkor*

(Mean values with standard deviations for twenty-five subjects)

	Oedematous subjects	Non-oedematous subjects
Albumin	1.6 ± 0.30	2.6 ± 0.65
Globulin	2.5 ± 0.45	3.2 ± 0.51
Total proteins	4.0 ± 0.48	5.8 ± 0.84

Table 5. *Summary of information about eleven fatal cases of kwashiorkor*

Age (months)	Weight (lb.)	Sex	Serum sodium (m-equiv./l.)	Serum potassium (m-equiv./l.)	Serum albumin (g/100 ml.)	Serum globulin (g/100 ml.)
24	16 $\frac{3}{4}$	M.	118	2.6	0.9	2.1
12	14 $\frac{1}{2}$	F.	135	5.1	1.1	2.6
19	18 $\frac{1}{4}$	M.	126	4.5	1.5	2.8
24	14 $\frac{1}{2}$	M.	135	4.1	—	—
34	20	M.	135	3.8	—	—
23	18	F.	113	5.6	1.9	2.0
24	18 $\frac{1}{4}$	M.	130	2.6	1.6	2.6
16	14	M.	139	2.6	1.6	2.6
18	19 $\frac{3}{4}$	F.	135	3.7	1.5	2.3
18	16 $\frac{1}{2}$	F.	122	2.6	1.2	2.3
10	14 $\frac{1}{2}$	M.	122	5.4	1.2	2.3

## DISCUSSION

In the sixty-three subjects the mean serum sodium concentration was 129 m-equiv./l. on admission to hospital. The levels were not significantly different before and after treatment or when patients with and without oedema and with and without diarrhoea were compared. Sixty-seven per cent showed low serum sodium levels on admission and 64% during recovery, although the oedema had subsided completely. Thus it does not appear that serum sodium plays an important part in the oedema of kwashiorkor or its subsidence. This agrees with the conclusions of Hansen & Brock (1954).

In four out of eleven fatal cases the serum sodium levels were greatly reduced (113–122 m-equiv./l.) and in the remainder varied from 126 to 139 m-equiv./l. (see Table 5). The serum sodium levels of these eleven fatal cases (two died within 24 h, five within 48 h and nine within 72 h of admission) did not differ from those of many of the survivors.

The occurrence of diarrhoea was frequently associated with a low serum potassium level. Eighteen of thirty patients (60%) showed a level of 4.0 m-equiv./l. or less. Of the thirty-three patients without a history of diarrhoea nine (27%) had low serum potassium levels.

Of fifty-nine oedematous patients twenty-nine (49%) showed low serum potassium levels but at the same time twelve of the latter suffered from diarrhoea. No relationship between oedema or its subsidence and serum potassium levels could be established. In our opinion these figures indicate that lowered serum potassium levels were the result of diarrhoea.

Treatment resulted in the restoration of normal serum potassium levels in all but three subjects who showed no oedema or clinical symptoms of hypokalaemia. Several of our patients whose serum potassium levels were low lost their oedema on being treated with milk mixtures, without the administration of extra potassium salts. Of the eleven fatal cases six had serum potassium levels below 4.0 m-equiv./l., four of these having levels of 2.6 m-equiv./l.

Amongst our patients 25% showed an increase of oedema and weight in the first 2 or 3 days of treatment.

In kwashiorkor oedema is partly attributed to the reduced osmotic pressure caused by the lowered serum proteins, particularly serum albumin. In twenty-five of forty-four subjects a rise of serum proteins showed a correlation with the diminution of oedema; but the remaining subjects varied, some showing a loss of oedema without a parallel increase of serum proteins.

## SUMMARY

1. Serum electrolytes were investigated in sixty-three patients suffering from advanced malnutrition (kwashiorkor), of whom eleven died.
2. No correlation was found between the degree of oedema and serum sodium or potassium levels.
3. No correlation was found between the severity of diarrhoea and the serum sodium levels.

4. The serum potassium level was reduced in subjects suffering from diarrhoea, and severe hypokalaemia was present in four of the eleven fatal cases.

5. There was only limited correlation between the changes in total serum protein and albumin and subsidence of oedema.

We wish to thank Dr R. Cassel, his staff and Mrs D. van Jaarsveldt of the South African Institute for Medical Research for their technical assistance and Dr E. Kahn for helpful advice.

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## The effect of various levels of penicillin and chlortetracycline in the diet of fattening pigs

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(Received 14 July 1956—Revised 15 January 1957)

The benefits to be derived from a dietary antibiotic supplement have been adequately demonstrated in pigs, poultry, calves and other animal species, but there are several factors that influence the magnitude of the antibiotic response. In this connexion the relation between the quantity of antibiotic administered and the growth response obtained requires further investigation.

Braude, Kon & Porter (1953) suggested that the optimum level of inclusion of antibiotics in the diet of pigs probably lies within the range 5–15 g/ton food. Childs & Cuthbertson (1954) reported that under normal farm conditions in the British Isles levels of 10 or 15 g of procaine penicillin/ton food did not produce a significantly greater response than that obtained with a level of 5 g.

Several reports have suggested, however, that with chlortetracycline and oxytetracycline higher levels of administration may be associated with a greater antibiotic response. Catron, Maddock, Speer & Vohs (1951) studied the effect of 0, 5, 10, 20 and 40 mg chlortetracycline hydrochloride/lb. ration and found that 20 and 40 mg

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