

# Serum Siderophilin in Kwashiorkor

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Kwashiorkor is known to be associated with low plasma proteins (Edozien, 1960) and low serum iron-binding capacity (Edozien and Udeozo, 1960). Unpublished observations of Neale and Soothill (1958) confirmed that the iron-binding capacity was down to about one-third of a normal level, but showed that the siderophilin (syn. transferrin) was much more profoundly depressed—down to 6 mg./100 ml., compared with a normal European level of about 200. We therefore report a study of the serum siderophilin concentration estimated immunologically in a series of children with typical kwashiorkor and of some control data. These values are correlated with a clinical grading of the severity of the disease and the effect of treatment.

## Materials and Methods

The patients were 24 random attenders at the Nutrition Clinic of the Department of Paediatrics at the University College Hospital, Ibadan in whom the diagnosis of kwashiorkor was made on standard clinical grounds. These were classified clinically into three groups—mild, moderate, and severe. Criteria on which the classification was based were oedema, mental status, skin changes, and state of mobility. Serum siderophilin was estimated by the double gel diffusion precipitin technique (Soothill, 1962). Serum pooled from Nigerian healthy adults was used as standard. Results are presented in terms of this standard (% PS), which was estimated in terms of a purified siderophilin preparation kindly supplied by Dr. Tristram Freeman and found to contain 150 mg./100 ml. of siderophilin. It was also compared with the reference normal serum standard used by Soothill (1962) for which some data from a healthy European population were reported. The Nigerian standard was 90% of the European. Total serum proteins were estimated by the technique of Gornall, Bardawill, and David (1949).

Comparable data were obtained from four breast-fed infants who had marasmus due to breast milk insufficiency, and from 10 children with other diseases—infected, developmental, and neoplastic—not obviously associated with malnutrition.

## Results

The results for the kwashiorkor series are shown in Table I, and for the marasmic and the control series in Table II. The mean values for siderophilin, total protein, and packed cell volume (PCV) for the three series are given. The siderophilin concentrations of the kwashiorkor series are significantly lower than either the marasmus series or the miscellaneous control series ( $t = 2.26$ ,  $p < 0.05$ , and  $t = 6.09$ ,  $p < 0.001$ , respectively on log data). The values for the control and the marasmic series and those from patients with kwashiorkor, classified both according to the clinical severity and to the course and management adopted (i.e. those who died, and those who received in-patient or out-patient treatment), are shown in Fig. 1. All the fatal cases were receiving in-patient treatment.

A  $3 \times 3$   $\chi^2$  analysis shows a highly significant relation between the levels of the siderophilin grouped into 3 equal batches: less than 13, 13 to 39, and more than 39, and the clinical course of the patients ( $\chi^2 = 14$ ,  $p < 0.01$ ), but not with the clinical assessment of the severity of the disease ( $\chi^2 = 3.7$ ,  $p > 0.4$ ), though the severe group includes the lowest values detected and the only case classified as mild was the highest. Serum total protein, and PCV fitted little better, even with the outcome classification (Fig. 2). Repeated values on some of the patients, treated either as in-patient or as out-patient by dietary measures alone, are given in Fig. 3.

## Discussion

The low levels of siderophilin in kwashiorkor observed by Neale and Soothill (1958) are confirmed by these results. This may well be the most profound defect known of acquired disturbance of production of a plasma protein. Though there is a significant correlation between serum total protein and the siderophilin levels ( $r = 0.5115$ ,  $p < 0.02$ ), the proportional depression of the siderophilin concentration is considerably greater than that of

TABLE I  
Serum Siderophilin in Kwashiorkor

Age (yr.)	Sex	Duration of Symptoms (wk.)	Clinical Features Laboratory Data					
			Weight (kg.)	Clinical Grading	Clinical Outcome	PCV (%)	Total Protein (g./100 ml.)	Siderophilin % of PS
5	F		9.5	Severe	Died		3.5	4
1½	M	6	10.9	Severe	Died	17	4.3	6
1½	M	2	11.9	Moderate	Out-patient	24	3.4	7
1½	F	1		Moderate	Out-patient	22	4.3	8
2	M	2	8.6	Severe	Died	33		12
2	M	4	7.7	Severe	Died		4.4	12.5
3½	F	8	9.1	Severe	Died	28	3.8	12.5
5	F	10	9.5	Severe	Died	24	4.7	12.5
1½	F	6	5.9	Severe	In-patient	27	4.9	17
1½	F	3	6.4	Severe	Out-patient	27	4.9	25
5	F	4	9.1	Severe	In-patient	28	3.4	27
2½	F	12	10	Moderate	Out-patient	31	5.7	28
3	F	8	7.3	Moderate	In-patient	20	3.9	29
2	M	3	6.8	Severe	Out-patient	33	4.4	30
2½	F	8	6.8	Moderate	In-patient		4.2	33
2	M	2	14.1	Moderate	Out-patient			34
1½	M	4	7.7	Moderate	Out-patient	34	5.1	40
2	F	3	8.6	Moderate	Out-patient	32	4.2	50
1½	F	2	5.9	Moderate	Out-patient	31	5.4	50
5	F	9	8.2	Severe	In-patient		4	56
2½	M	3	8.2				4.2	59
5	F	8	17.7	Moderate	Out-patient	25	4.2	67
5	F	3	6.8	Severe	Out-patient	29	5.9	71
2	M	4	7.3	Mild	Out-patient	24	6.5	125
Kwashiorkor mean			8.9			27	4.5	34

the total plasma protein, which is never below half of the lowest value of the control series, though the siderophilin value fell to one-fifth of the lowest control value. The considerably higher values in

the severely marasmic children, in the control series containing a number of diagnoses, and in healthy newborns and adult Nigerians (McFarlane and Udeozo, 1968) and our experience in a wide

TABLE II  
Serum Siderophilin in Nigerian Children with Miscellaneous Diseases and with Marasmus

Diagnosis	Age (yr.)	Sex	Weight (kg.)	Siderophilin % of PS	Total Protein (g./100 ml.)
Tonsillitis .. .. .	2½	F	11.6	67	6.3
Tuberculosis .. .. .	5	F	14.3	500	6.4
Bronchiolitis .. .. .	½		6.9	200	6.9
Tuberculosis .. .. .	7	F	14.1	286	7.1
Empyema .. .. .	1½	F	10.9	57	6.6
Tuberculosis .. .. .	3	M	14.1	200	7.2
Tuberculosis .. .. .	2	F	10	200	6.2
Ventricular septal defect .. .. .	1½	F	9.7	100	6.3
Osteomyelitis .. .. .	2	M	10.9	125	—
Burkitt's tumour .. .. .	—	—	—	200	—
Miscellaneous .. .. .	mean		11.4	194	6.6
Marasmus .. .. .	5/12	F	3.6	33	7.0
Marasmus .. .. .	10/12	F	4.7	100	7.6
Marasmus .. .. .	9/12	M	3.5	67	7.6
Marasmus .. .. .	9/12	F	3.5	84	7.8
Marasmus .. .. .	mean		3.8	71	7.5

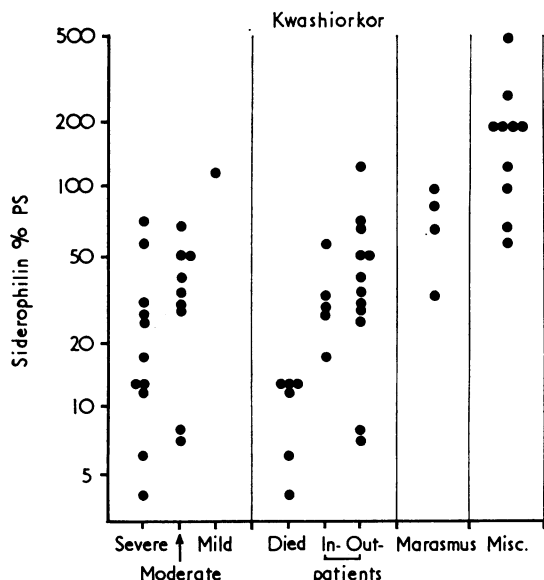


FIG. 1.—Serum siderophilin levels in 24 patients with kwashiorkor, classified clinically into severe, moderate, and mild, and into those who died and those who were treated as in-patients or out-patients, in 4 children with marasmus, and in 10 children with miscellaneous diseases.

range of disease processes in Great Britain (Neale and Soothill, 1958), suggests that the very low levels of siderophilin found in kwashiorkor may well be a diagnostic abnormality of this disease with the possible exception of asiderophilinaemia. The defect is almost certainly one of production, and it would be interesting to know whether it would affect the genetically controlled various siderophilin types differently. It is probable that these differences have little effect on the immunochemical assay. It is interesting that the grading, derived from outcome, and from the accustomed decision making entailed in clinical management, namely whether the patients died or were treated as in-patients or out-patients, fitted the siderophilin values far more closely than

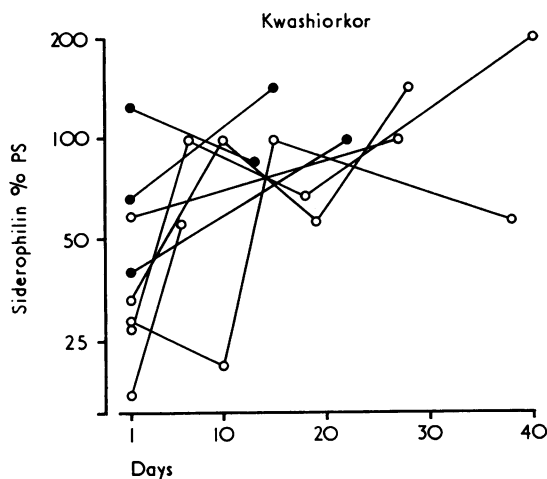


FIG. 3.—Sequential values of serum siderophilin in 8 patients with kwashiorkor treated with diet; ● = out-patients and ○ = in-patients.

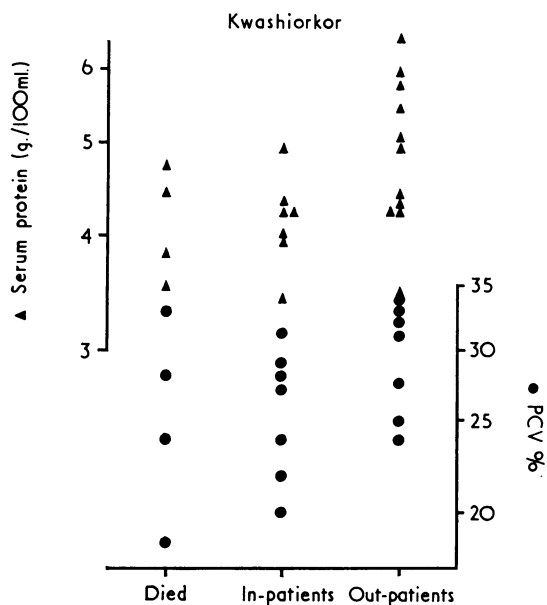


FIG. 2.—Serum total protein and packed cell volume (PCV) in patients with kwashiorkor, classified according to whether they died or whether they were treated as in-patients or out-patients.

the attempt at a clinical grading of the severity of the condition when first seen. Clearly the test provides an objective assessment of the severity of the disease, of use for both treatment and research purposes. The remarkable response of the siderophilin level to a high protein diet (see Fig. 2—in one patient it rose nearly tenfold in a week) suggests that it would be useful for control of the efficacy of different treatment regimens. Such immunochemical determinations are easy and cheap.

If the observation is confirmed that the serum iron-binding capacity is not so profoundly depressed as the siderophilin (Neale and Soothill, 1958), it may be that this defect is less relevant in handling iron than might be expected. Indeed, it seems likely that the serum siderophilin has a considerable

functional reserve. There is little correlation between the siderophilin level and the packed cell volume in our series ( $r = 0.508$ ,  $p > 0.05$ ), suggesting that other factors are probably more relevant in the anaemia. More detailed knowledge of the amino acid requirement for production of each individual protein is required before one can speculate on the mechanism of this extreme and highly reversible defect.

### Summary

Serum siderophilin levels were profoundly depressed in a series of 21 patients with kwashiorkor.

The level correlates with independent grading of the severity of the disease.

Siderophilin level was far more profoundly depressed than the total serum protein level. It correlated poorly with the packed cell volume.

The defect was rapidly reversible by high protein diet.

The possible usefulness of this simple test in

diagnosis, in grading the severity of the disease, and in research on means of treatment is discussed.

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