Serum protein and transferrin determinations to distinguish kwashiorkor from iron deficiency anaemia

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Masawe, A. E. J., and Rwabwogo-Atenyi, J. (1973). Archives of Disease in Childhood, 48, 927. Serum protein and transferrin determinations to distinguish kwashiorkor from iron deficiency anaemia. Serum proteins and serum transferrin levels were studied in 38 African children of whom 10 were normal controls, 18 had severe iron deficiency anaemia, and 10 had kwashiorkor. The results showed that the patients with iron deficiency anaemia had relatively higher total serum proteins and serum globulins than a comparable normal control group. Conversely, patients with kwashiorkor had lower total proteins and normal globulins. The albumin fraction was raised above the control in 50% of the patients with iron deficiency anaemia and diminished in the other 50%. In kwashiorkor the levels were uniformly diminished.

The transferrin levels were uniformly raised in the iron deficiency anaemia group and uniformly diminished in the kwashiorkor group. The transferrin level was deemed the best screening test to distinguish the two disorders.

Kwashiorkor and iron deficiency anaemia are common causes of morbidity and mortality in childhood in the tropics (World Health Organization, 1968, 1971). Kwashiorkor results from early weaning followed by an overall inadequate protein intake. Iron deficiency anaemia is a consequence of inadequate dietary intake of iron, chronic blood loss, or both. Heavy hookworm infestation is the commonest cause of blood loss and iron deficiency anaemia in East Africa (Blackman, 1962; Vanier, 1966; Nhonoli, 1969). From 2 to 100 ml blood is lost in faeces per patient per day depending on the load of the worms (Roche and Layrisse, 1966; Martinez-Torres et al., 1967).

Often the two conditions coexist, their features overlap, and differentiation of one from the other is usually difficult. Recently McFarlane et al. (1970) reported that patients with severe kwashiorkor have diminished serum transferrin and that early iron therapy may be dangerous. Treatment should be deferred until the levels of the transferrin are improved by intensive dietary management, and this usually takes a few days (Gabr, El-Hawary, and El-Dali, 1971). In iron deficiency anaemia, on the other hand, iron replacement is the cornerstone of treatment and must not be delayed. Accordingly, it is imperative to have a good criterion for screening patients with iron deficiency anaemia from those with kwashiorkor.

Reported here is a study of serum proteins, serum transferrin, and haematological profiles in normal control children, in patients with severe kwashiorkor (grade IV malnutrition), and in patients with severe iron deficiency anaemia to attempt to define a good screening criterion.

Material

For this study, 18 children with severe iron deficiency anaemia, 10 with kwashiorkor, and 10 healthy controls were selected. The children included those attending the paediatric services of Mulago Hospital between January and May 1971. The selection criteria included (a) iron-deficiency anaemia, clinical evidence of anaemia: Hb concentration of < 8 g/100 ml, absent stainable iron in bone marrow, positive hookworm ova, and heavy occult blood in stools; (b) kwashiorkor, clinical features of severe protein-calorie malnutrition: retarded growth (low weight for expected height), generalized oedema, flaky-paint skin lesions, and woolly depigmented hair; (c) controls, healthy-looking children with Hb concentrations of 11 g/100 ml and over.

These were selected from specialized clinics (surgical and skin) and had no apparent evidence of malnutrition or infections. The serum protein fractions were in addition comparable to those reported by Edozien and Udoozo (1960) on 231 healthy Nigerian children.
All three categories were closely matched for age and sex.

**Methods**

Blood specimens were collected by venepuncture in heparinized and plain bottles. The plain bottles were then centrifuged and the serum was stored at −20 °C until used. Haemolysed specimens were discarded. All the specimens were collected before starting therapy.

**Assays.** Total serum proteins were assayed by modified biuret method (Wootton, 1964) and protein fractions were determined by electrophoresis (Varley, 1967). Cellulose acetate membrane 10 cm long and barbitone buffer pH 8·6 were used for electrophoresis. 5 μg of the specimen was applied and run for 1 hour at stabilized DC current of 10V/cm length. The strips were then stained with Ponceau reagent and quantified by Beckman microzone densitometer R-110 model.

The transferrin concentrations were determined by radial immunodiffusion technique of Mancini, Carbonara, and Hersmans (1965).

Haematological profiles in all cases were carried out as described by Dacie and Lewis (1968). Stools were examined for occult blood by Hematest tablets.

**Results**

The Table summarizes the haematological and biochemical findings for the three categories of subjects.

**Age.** Age distribution was similar in the three groups. 12 patients with iron deficiency anaemia, 9 with kwashiorkor, and 9 control children were aged 5 years or less.

**Sex.** Males predominated in all three categories.

**Haematological profiles.** Haemoglobin packed cell volume (PCV) and the mean corpuscular haemoglobin concentration (MCHC) were markedly diminished below the normal control in the iron deficiency anaemia group and only moderately so in the kwashiorkor group. 3 children with iron deficiency anaemia had homozygous sickle cell haemoglobin (Hb SS), and 2 of those with kwashiorkor had megaloblastic anaemia.

The peripheral picture was hypochromic microcytic in all patients with iron deficiency anaemia, normocytic normochromic in the control children, and variable in the children with kwashiorkor. In the last group, some films were hypochromic and microcytic, others were normocytic and normochromic, and others still were macrocytic normocytic.

**Stool examinations.** All 18 children with iron deficiency anaemia had heavy hookworm infestation and strongly positive occult blood test. 5 control children had mild hookworm infestation. Of these, 4 had MCHC of less than 31%. All 10 children with kwashiorkor had moderate to severe parasitic infestations. The parasites included hookworms, Ascaris, Trichuris trichiura, and tapeworms. Occult blood test was positive in all.

**Serum transferrin.** The results are summarized both in the Table and the Fig. The concentrations were increased above the normal control in the iron deficiency anaemia group, and were markedly diminished in the kwashiorkor group. The difference between the iron deficiency anaemia and the kwashiorkor groups is significant (P < 0·001) by Student’s ‘t’ test.
Serum protein and transferrin determinations to distinguish kwashiorkor from iron deficiency ta in 38 children

<table>
<thead>
<tr>
<th>Serum transferrin (mg/100 ml)</th>
<th>Serum proteins (g/100 ml)</th>
<th>Total</th>
<th>Albumin</th>
<th>α1-globulin</th>
<th>α2-globulin</th>
<th>β-globulin</th>
<th>γ-globulin</th>
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</thead>
<tbody>
<tr>
<td>328.7*</td>
<td>6.87</td>
<td>2.55</td>
<td>0.47</td>
<td>0.85</td>
<td>0.88</td>
<td>2.12</td>
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</tr>
<tr>
<td>11.66</td>
<td>0.25</td>
<td>0.15</td>
<td>0.04</td>
<td>0.05</td>
<td>0.07</td>
<td>0.15</td>
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</tr>
<tr>
<td>257-419</td>
<td>4.4-8.3</td>
<td>1.3-3.8</td>
<td>0.16-0.75</td>
<td>0.44-1.36</td>
<td>0.53-1.74</td>
<td>1.2-3.5</td>
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<tr>
<td>273.95</td>
<td>6.33</td>
<td>2.96</td>
<td>0.36</td>
<td>0.67</td>
<td>0.75</td>
<td>1.57</td>
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<tr>
<td>27</td>
<td>0.22</td>
<td>0.18</td>
<td>0.03</td>
<td>0.08</td>
<td>0.07</td>
<td>0.13</td>
<td></td>
</tr>
<tr>
<td>248-317</td>
<td>5.4-7.9</td>
<td>2.1-4.2</td>
<td>0.2-0.5</td>
<td>0.3-1.26</td>
<td>0.36-1.22</td>
<td>1.08-2.61</td>
<td></td>
</tr>
<tr>
<td>170.59</td>
<td>5.0</td>
<td>1.62</td>
<td>0.37</td>
<td>0.72</td>
<td>0.75</td>
<td>1.49</td>
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<tr>
<td>6.18</td>
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<td>0.13</td>
<td>0.03</td>
<td>0.13</td>
<td>0.10</td>
<td>0.19</td>
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<td>139-200</td>
<td>3.9-5.5</td>
<td>1.2-2.4</td>
<td>0.23-0.54</td>
<td>0.36-1.59</td>
<td>0.24-1.17</td>
<td>0.58-2.4</td>
<td></td>
</tr>
</tbody>
</table>

Serum proteins.

**Total.** Total proteins for the iron deficiency anaemia group were similar to those in the control children, but the total proteins for the kwashiorkor group were significantly less than the control. 4 patients with iron deficiency anaemia had low plasma proteins and classical clinical features of kwashiorkor.

**Albumin.** The results are summarized in the Table and Fig. Taking 2.5 g/100 ml arbitrarily as the lower range of normal, 9 (50%) of the children with iron deficiency anaemia, 2 (20%) of the control children, and all 10 children with kwashiorkor had subnormal albumin levels.

**Globulin.** Results are summarized in the Table and Fig. The globulin fractions were slightly

![Diagram](http://adc.bmj.com/)

**Fig.**—Serum albumin, serum transferrin, and serum β-globulin in patients with kwashiorkor, in control children, and in patients with chronic iron deficiency anaemia. Transferrin concentrations are in μg/100 ml on the right-hand scale, while the other fractions are in g/100 ml on the left hand scale.
increased in the iron deficiency group and were within normal limits in the kwashiorkor group, but the differences are not significant.

Discussion

The above results confirm the introductory remarks that iron deficiency anaemia and kwashiorkor often overlap. 4 children with iron deficiency anaemia had classical features of kwashiorkor and 3 children with kwashiorkor had iron deficiency anaemia. In a study of iron stores in healthy and malnourished children in India, Manchanda, Lal, and Khanna (1969) also found that 56% of the healthy children and 85% of the malnourished children had iron deficiency.

Previously, both conditions have been considered together as nutritional disorders and iron replacement therapy has been advocated for both. Iron therapy is also advocated for mass campaigns in various parts of the world (World Health Organization, 1968). Recently, evidence has emerged to show that the liberal use of iron may not be rational, and that careful distinction of patients with kwashiorkor from those with iron deficiency anaemia may be necessary before therapy is given. In kwashiorkor the serum transferrin levels are depleted (Edozien and Udeozo, 1960; Antia, McFarlane, and Soothill, 1968; McFarlane et al., 1970; Gabr et al., 1971) and early replacement of iron may inflame underlying infections and accelerate death (McFarlane et al., 1970). The transferrin is bacteriostatic and protective (Weinberg, 1966; McFarlane, Okubadejo, and Reddy, 1972). In iron deficiency anaemia, on the other hand, the transferrin levels are raised and in vitro growth of bacteria in blood from such patients is much less than the growth in blood from patients with kwashiorkor (A. E. J. Masawe and H. Nsanzumuhire, unpublished data).

Of the screening criteria studied, only the transferrin estimations appear promising. The levels were uniformly raised above the normal control in iron deficiency anaemia and uniformly diminished in kwashiorkor. The secondary kwashiorkor changes in some patients with iron deficiency anaemia did not influence the transferrin levels, nor did the secondary iron deficiency in some patients with kwashiorkor alter the transferrin levels appreciably.

The other criteria were less specific. The haematological profiles were abnormal in both groups and tended to overlap. Total plasma proteins were uniformly diminished in patients with kwashiorkor but variable in patients with iron deficiency anaemia. Finally, the albumin levels were uniformly diminished in kwashiorkor but bimodal in iron deficiency anaemia—in some patients the levels were raised and in others they were diminished. The albumin findings in the patients with iron deficiency anaemia were very similar to those reported by Blackman et al. (1965) on adult patients with similar anaemia in Kampala.

Transferrin estimation has been recommended for assessing prognosis in patients with kwashiorkor; reduced levels bear a close relation to severity and bad prognosis (McFarlane et al., 1970; Gabr et al., 1971). A further practical application is suggested by the study, namely screening of patients with kwashiorkor from patients with iron deficiency anaemia before iron therapy. The procedure is technically simple and straightforward and can be carried out in many laboratories in the tropics.

We are greatly indebted to the Medical Superintendent and to all paediatricians, Mulago Hospital, for allowing us to study their patients, and to Dr. H. Nsanzumuhire for his comments. This project was supported jointly by the WHO Regular Funds and by Makerere University Research Grant No. 622.

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