Absorption of xylose, glucose, glycine, and folic (pteroylglutamic) acid in Zambian Africans with anaemia

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SUMMARY Rates of glucose, glycine, and folic (pteroylglutamic) acid absorption were determined for a 30 cm jejunal segment in vivo, with a double-lumen tube perfusion system, in 10 Zambian African women with a mean haemoglobin concentration of 5·1 (3·5-9·2) g/dl. In four the anaemia was megaloblastic (due to folate deficiency) and in six hypochromic. Perfusion solutions contained (1) glucose 200 mmol/l, (2) glycine 100 mmol/l, and (3) folic acid 250 μg/l. D-xylose absorption after a 25 g oral load was determined in them, and also in 18 additional patients (11 had megaloblastic and seven either hypochromic or haemolytic anaemia). Xylose absorption tests were significantly impaired in the patients with megaloblastic compared with hypochromic or haemolytic anaemia (p < 0·001); those with untreated megaloblastic anaemia had a greater abnormality than those who had started treatment. Mean glucose, glycine, and folic acid absorption rates were similar to those in controls, and the rates in patients with megaloblastic and hypochromic anaemia were not significantly different. Correlation between glucose absorption rate and xylose excretion was, however, significant (p < 0·02). If more patients had been studied it seems likely therefore that a significant impairment of glucose absorption rate in the presence of megaloblastic anaemia would also have been demonstrated. In this investigation anaemia per se did not affect glucose, glycine, or folic acid absorption rates or xylose absorption, but xylose absorption was reduced in patients with megaloblastic anaemia. That abnormality was probably related to folate deficiency, and the underlying mechanism seems to be different from that causing impairment of monosaccharide absorption in patients with systemic bacterial infections. Mean glucose and folic acid absorption rates were not altered by megaloblastic anaemia, indicating that folate deficiency does not cause a general depression of absorption.

Glucose and D-xylose malabsorption is widespread in indigenous people of Zambia and other tropical countries (Cook, 1967, 1974a). Systemic infection is an important aetiological factor (Cook, 1971a, 1972a), but the mechanism is unknown. An inverse association between serum γ-globulin and IgG concentrations, and absorption of glucose and xylose has been demonstrated in the absence of overt infection (Cook, 1973a, 1974b).

Anaemia is very common in tropical Africa. In Lusaka it is usually hypochromic (due to hookworm infestation) or haemolytic (due to malaria or haemoglobinopathy). Subclinical folate deficiency is widespread and megaloblastic anaemia, usually associated with pregnancy and the puerperium accounts for numerous hospital admissions in the latter part of the dry season.

The present study was undertaken to determine whether anaemia and subclinical malabsorption, both common in Africans, are associated. Xylose absorption tests were performed in 28 anaemic patients. With the use of a double-lumen tube jejunal perfusion system, glucose, glycine, and folic (pteroylglutamic) acid absorption rates in 10 of them were compared with non-anaemic controls.

Methods

Table 1 summarizes details of 10 consecutively admitted cases of severe anaemia (haemoglobin < 10 g/dl) in the Department of Medicine, The Uni-
Aneamia and absorption in man

Table 1  Clinical and laboratory details of 10 Zambian African women who had jejunal perfusions of glucose, glycine, and folic acid (main investigation)

<table>
<thead>
<tr>
<th>Patient no.</th>
<th>Age (yr)</th>
<th>Body wt (Kg)</th>
<th>Tribe²</th>
<th>Haemoglobin (g/dl)</th>
<th>Serum protein (g/l)</th>
<th>Stool parasites</th>
<th>Serum urea (mmol/l)</th>
<th>D-xylene excretion (g/15 h)</th>
<th>Tube position (distance of proximal opening past duodo-nenoejejunal flexure) (cm)</th>
<th>Order of perfusions²</th>
</tr>
</thead>
<tbody>
<tr>
<td>Megaloblastic anaemia</td>
<td></td>
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<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>23</td>
<td>47</td>
<td>Tonga</td>
<td>4-8</td>
<td>33</td>
<td>37</td>
<td>16</td>
<td>Chilomastix</td>
<td>3-8</td>
<td>5-0</td>
</tr>
<tr>
<td>2</td>
<td>18</td>
<td>44</td>
<td>Chikunda</td>
<td>6-0</td>
<td>35</td>
<td>47</td>
<td>26</td>
<td>None</td>
<td>5-3</td>
<td>5-7</td>
</tr>
<tr>
<td>3</td>
<td>21</td>
<td>48</td>
<td>Tonga</td>
<td>3-9</td>
<td>35</td>
<td>33</td>
<td>16</td>
<td>None</td>
<td>5-8</td>
<td>3-1</td>
</tr>
<tr>
<td>4</td>
<td>19</td>
<td>50</td>
<td>Tumbuka</td>
<td>4-1</td>
<td>32</td>
<td>36</td>
<td>17</td>
<td>None</td>
<td>2-5</td>
<td>3-0</td>
</tr>
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<td>Hypochromic anaemia</td>
<td></td>
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<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>5</td>
<td>23</td>
<td>47</td>
<td>Lala</td>
<td>3-5</td>
<td>35</td>
<td>50</td>
<td>28</td>
<td>Hookworm</td>
<td>3-6</td>
<td>5-6</td>
</tr>
<tr>
<td>6</td>
<td>13</td>
<td>45</td>
<td>Tonga</td>
<td>5-6</td>
<td>42</td>
<td>40</td>
<td>14</td>
<td>None</td>
<td>3-8</td>
<td>6-3</td>
</tr>
<tr>
<td>7</td>
<td>21</td>
<td>46</td>
<td>Lenje</td>
<td>9-2</td>
<td>24</td>
<td>33</td>
<td>17</td>
<td>Hookworm</td>
<td>2-7</td>
<td>6-6</td>
</tr>
<tr>
<td>8</td>
<td>17</td>
<td>41</td>
<td>Neenga</td>
<td>4-5</td>
<td>34</td>
<td>39</td>
<td>16</td>
<td>Hookworm</td>
<td>2-0</td>
<td>9-4</td>
</tr>
<tr>
<td>9</td>
<td>18</td>
<td>46</td>
<td>Lozi</td>
<td>3-8</td>
<td>36</td>
<td>47</td>
<td>21</td>
<td>None</td>
<td>4-1</td>
<td>9-1</td>
</tr>
<tr>
<td>10</td>
<td>33</td>
<td>73</td>
<td>Shona</td>
<td>5-7</td>
<td>40</td>
<td>31</td>
<td>12</td>
<td>None</td>
<td>2-5</td>
<td>4-3</td>
</tr>
</tbody>
</table>

¹Brelsford (1965).
²A, glucose (200 mmol/l); B, glycine (100 mmol/l); C, folic acid (250 µg/l).

University Teaching Hospital, Lusaka, between mid-November, 1973 and mid-January, 1974 (main investigation). All had jejunal infusions of glucose, glycine, and folic acid, and xylose tests. They agreed to the procedure after the purpose of the study had been fully explained through an interpreter. None had clinical evidence of malnutrition or gastrointestinal disease; body temperatures were normal. None drank excess alcohol. The type of anaemia was confirmed by sternal-marrow examination; those with megaloblastic anaemia seemed to have adequate iron stores, and all of those with hypochromic anaemia had evidence of iron deficiency. Four, who had recently delivered a live infant (in no. 2 four months, and in the others approximately one month before) had megaloblastic anaemia. Numbers 1 and 2 had ankle swelling, and 2, 3, and 4 mild diarrhoea for several days before admission; all were initially pyrexial (in nos. 2 and 3 at least 40°C). Numbers 2 and 4 had splenomegaly, and no. 4 a urinary infection. Numbers 3 and 4 had had tetracycline and chloroquine before the investigations, which were done three to 12 (mean eight) days after admission. Six cases had hypochromic anaemia; in nos. 5 and 6 there was a suggestion of folate deficiency in the marrow specimen. Numbers 5 and 7 had delivered three and one month before, respectively, and no. 10 had had a spontaneous abortion one month before. Number 8 had had abdominal pain and diarrhoea; nos. 9 and 10 were initially pyrexial. Numbers 5 and 8 had splenomegaly, and nos. 5 and 9 hepatomegaly. Number 7 had a Schistosoma haematobium infestation. Number 8 had had an oral sulphonamide, and no. 10 an intramuscular iron injection and oral folic acid two days before the investigations, which were done one to nine (mean four) days after admission. Table 2 summarizes haematological data for those 10 patients. Number 4 had a reticulocyte response to oral folic acid; nos. 1-3 were discharged before adequate evaluation. Mean serum immunoglobulin concentrations in those with megaloblastic and hypochromic anaemia were (g/l): IgG 19 (16-26) and 18 (13-25), IgA 2-8 (2-2-3-5) and 2-2 (1-1-4-2), IgM 1-2 (0-6-1-8) and 1-9 (1-6-2-3), and IgD 0-13 (0-0-28) and 0-17 (0-0-2-0) respectively. In no. 4 the xylose test was repeated after two weeks of oral folic acid therapy; haemoglobin was 6-8 g/dl.

Table 3 summarizes details of the controls, who were also inpatients at The University Teaching Hospital, Lusaka. Haemoglobin concentration was more than 10-0 g/dl. They were clinically well-nourished and had no evidence of gastrointestinal disease or systemic bacterial infection. Glucose (Cook, 1971b; 1972b, c; 1973b), glycine (Cook, 1971b; 1972b, c; 1973c), and folic acid (Cook et al., 1974) absorption rates have been reported.

Table 4 summarizes data for 18 anaemic patients who had xylose tests (additional investigation). The type of anaemia was confirmed by sternal-marrow examination; those with megaloblastic anaemia seemed to have adequate iron stores, and those with hypochromic anaemia had evidence of iron deficiency. Body temperatures were normal. Six patients (a) had untreated megaloblastic anaemia; one had delivered a normal infant two months before and
another was eight months pregnant. Ankle swelling and excessive tiredness were prominent symptoms in 1 and 3 respectively. Two drank excess alcohol. Three had splenomegaly and hepatomegaly. All had evidence of an infection when admitted: two of the urinary tract, two acute diarrhoea (which was probably infective), one cellulitis of the left leg, and one glandular tuberculosis. They were all initially pyrexial. One had had penicillin, and another ampicillin, vitamin B complex and ferrous sulphate before investigation. Mean polymorphonuclear leucocyte count was 4.5 (1.6-14.2) × 10⁹/l. Mean serum

Table 2  Haematological details of 10 Zambian African women who had jejunal perfusions of glucose, glycine, and folic acid (main investigation)

<table>
<thead>
<tr>
<th>Patient no.</th>
<th>PCV*</th>
<th>Serum folate concentration (µg/l)</th>
<th>Red-cell folate concentration (µg/l)</th>
<th>Serum iron (µmol/l)</th>
<th>Total iron-binding capacity (µmol/l)</th>
<th>Reticulocyte count (%)</th>
<th>Polymorphonuclear leucocyte count (× 10⁹/l)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>0.18</td>
<td>1.8</td>
<td>114</td>
<td>44.7</td>
<td>53.7</td>
<td>5.8</td>
<td>4.7</td>
</tr>
<tr>
<td>2</td>
<td>0.22</td>
<td>1.8</td>
<td>114</td>
<td>2.5</td>
<td>43.0</td>
<td>3.2</td>
<td>2.4</td>
</tr>
<tr>
<td>3</td>
<td>0.15</td>
<td>0.8</td>
<td>72</td>
<td>17.9</td>
<td>37.6</td>
<td>3.4</td>
<td>6.0</td>
</tr>
<tr>
<td>4</td>
<td>0.16</td>
<td>3.2</td>
<td>158</td>
<td>25.9</td>
<td>37.6</td>
<td>3.4</td>
<td>21.1</td>
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<table>
<thead>
<tr>
<th>Hypochromic anaemia</th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
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<tbody>
<tr>
<td>5</td>
<td>0.12</td>
<td>4.8</td>
<td>382</td>
<td>5.4</td>
<td>80.5</td>
<td>2.0</td>
<td>2.9</td>
</tr>
<tr>
<td>6</td>
<td>0.22</td>
<td>4.2</td>
<td>512</td>
<td>4.5</td>
<td>94.0</td>
<td>4.2</td>
<td>3.5</td>
</tr>
<tr>
<td>7</td>
<td>0.32</td>
<td>3.2</td>
<td>112</td>
<td>6.3</td>
<td>40.0</td>
<td>3.0</td>
<td>1.8</td>
</tr>
<tr>
<td>8</td>
<td>0.18</td>
<td>8.8</td>
<td>404</td>
<td>4.5</td>
<td>61.7</td>
<td>3.3</td>
<td>3.3</td>
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<tr>
<td>9</td>
<td>0.14</td>
<td>4.8</td>
<td>242</td>
<td>3.6</td>
<td>94.0</td>
<td>4.3</td>
<td>4.4</td>
</tr>
<tr>
<td>10</td>
<td>0.18</td>
<td>14.2</td>
<td>602</td>
<td>18.8</td>
<td>96.7</td>
<td>4.3</td>
<td>4.1</td>
</tr>
</tbody>
</table>

1 Determined on fasting samples obtained on the morning of perfusion.
2 Packed cell volume.

Table 3  Clinical and laboratory details of non-anaemic controls who had no evidence of malnutrition, gastrointestinal disease, or systemic infection

<table>
<thead>
<tr>
<th>Solution perfused</th>
<th>No. studied</th>
<th>Sex</th>
<th>Age (yr)</th>
<th>Body-wt (kg)</th>
<th>Haemoglobin (g/dl)</th>
<th>Serum protein (g/l)</th>
<th>Albumin (g/l)</th>
<th>Total globulin (g/l)</th>
<th>y-globulin (g/l)</th>
<th>Tube position (distance of proximal opening of jejunal flexure) (cm)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Glucose (200 mmol/l)</td>
<td>14</td>
<td>9 F</td>
<td>39</td>
<td>(16-60)</td>
<td>57 (43-79)</td>
<td>13.8</td>
<td>(11-5-17)</td>
<td>33 (27-44)</td>
<td>44 (29-54)</td>
<td>22 (14-30)</td>
</tr>
<tr>
<td>Glycine (100 mmol/l)</td>
<td>17</td>
<td>13 4</td>
<td>38</td>
<td>(16-65)</td>
<td>53 (43-70)</td>
<td>12.9</td>
<td>(10-4-16)</td>
<td>36 (30-44)</td>
<td>40 (28-52)</td>
<td>20 (15-26)</td>
</tr>
<tr>
<td>Folic acid (250 µg/l)</td>
<td>5</td>
<td>4 1</td>
<td>43</td>
<td>(20-60)</td>
<td>64 (55-75)</td>
<td>13.5</td>
<td>(11-9-15)</td>
<td>38 (33-43)</td>
<td>40 (16-28)</td>
<td>20 (16-28)</td>
</tr>
</tbody>
</table>

1 Mean (and range) are shown for each index.

Table 4  Clinical and laboratory details of 18 anaemic patients who had xylose tests (additional investigation)

<table>
<thead>
<tr>
<th>No. studied</th>
<th>Sex</th>
<th>Age (yr)</th>
<th>Body-wt (kg)</th>
<th>Haemoglobin (g/dl)</th>
<th>Reticulocyte count (%)</th>
<th>Serum protein (g/l)</th>
<th>Albumin (g/l)</th>
<th>Total globulin (g/l)</th>
<th>y-globulin (g/l)</th>
<th>Stool parasites</th>
<th>Serum urea (mmol/l)</th>
</tr>
</thead>
<tbody>
<tr>
<td>6</td>
<td>3 3</td>
<td>35</td>
<td>(16-60)</td>
<td>48 (31-60)</td>
<td>6.2</td>
<td>2.1</td>
<td>(1-3-3-2)</td>
<td>39 (28-46)</td>
<td>34 (28-40)</td>
<td>17 (13-21)</td>
<td>Hookworm in 3 (n = 5)</td>
</tr>
<tr>
<td>M. anaemia (untreated)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>5</td>
<td>3 2</td>
<td>43</td>
<td>(23-56)</td>
<td>55 (50-62)</td>
<td>8.6</td>
<td>7.7</td>
<td>(5-0-10)</td>
<td>37 (34-38)</td>
<td>43 (37-49)</td>
<td>21 (15-26)</td>
<td>Hookworm in 1</td>
</tr>
<tr>
<td>M. anaemia (treated)</td>
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<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
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<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>7</td>
<td>3 4</td>
<td>48</td>
<td>(17-41)</td>
<td>48 (32-60)</td>
<td>6.6</td>
<td>2.5</td>
<td>(2-5-2-6)</td>
<td>(n = 2)</td>
<td>33 (28-37)</td>
<td>46 (35-55)</td>
<td>Hookworm in 2; Ascites lumbricoides</td>
</tr>
<tr>
<td>Hypo anaemia</td>
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<td></td>
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<td></td>
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<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

1 Mean (and range) are shown for each index.
folate concentration in four was 2·6 (2·0-3·8) μg/l. Mean serum iron and iron-binding capacity in four were 35·8 (17·0-56·4) and 49·2 (32·2-64·4) μmol/l respectively. All subsequently responded to oral folic acid; one also had an antibiotic and another specific treatment for tuberculosis. Haematological response was slow in the patient with tuberculosis. Xylene tests were done 0·5-six (mean two) weeks after admission, and repeated in one after three weeks of oral folic acid and antibiotic therapy; haemoglobin concentration had risen from 3·0 to 7·3 g/dl. Five patients (b) were undergoing treatment for megaloblastic anaemia. Two of them had had ankle swelling and two weight loss; none had evidence of gastrointestinal disease. Two drank excess alcohol.

Three had evidence of infection at admission: one of the urinary tract, one acute bronchitis, and in one the site was not determined. All were initially pyrexial. The mean polymorphonuclear leucocyte count was 5·4 (1·2-6·5) × 10⁹/l. Serum folate concentration in two was 1·0 and 2·7 μg/l, and in three mean serum concentration was 311 (105-560) ng/l. Mean serum iron and iron-binding capacity in four were 20·6 (3·6-36·7) and 40·3 (37·6-43·0) μmol/l respectively. All showed a haematological response to oral folic acid at investigation; two had also had an antibiotic. Xylene tests were done once to eight (mean five) weeks after admission. Seven patients (c) had a non-megaloblastic anaemia (five hypocromic and two haemolytic). Hypochromic anaemia in two was associated with early pregnancy, and in three with malaria (Plasmodium malariae), Salmonella typhi (convalescent), and hookworm infections. Two patients with haemolytic anaemia had P. falciparum and P. malariae infections. One had had ankle swelling. Two had splenomegaly and three hepatomegaly. Four were initially pyrexial. Mean polymorphonuclear leucocyte count was 5·4 (1·7-11·6) × 10⁹/l. Mean serum iron in four was 9·8 (5·4-20·6) and iron-binding capacity 66·2 (53·7-75·2) μmol/l. Three were receiving oral iron when investigated. Xylene tests were done two to 15 (mean eight) days after admission. Mean serum immunoglobulin concentrations in groups (a), (b), and (c) were (g/l): IgG 15 (12-18), 20 (16-23) and 23 (17-27), IgA 2·4 (0·9-4·8), 3·2 (1·0-5·8) and 2·9 (2·2-3·7), IgM 1·1 (0·8-1·7), 1·7 (1·5-2·1) and 1·9 (1·1-3·8) and IgD 0·06 (0·0-0·16), 0·07 (0·0-0·22) and 0·07 (0·0-0·18) respectively.

**Experimental procedures**

The perfusion technique has been described (Cook, 1971a, 1972b). A double-lumen tube was swallowed on the evening before the investigations; they took place after a 14-18 hour overnight fast, during which sips of water were permitted. The position of the tube was checked radiographically before (Table 1) and after the studies (Cook and Carruthers, 1974); the proximal (infusion) opening had moved distally by a mean of 5 (maximum 9) cm by the end of the study. The perfusion fluid was infused at a constant rate of 12·0 ml/min from the proximal opening, and intestinal content was obtained by siphoning through the distal opening 30 cm further along the tube. The perfusion solutions contained (A) 200 mmol/l glucose (Hopkin & Williams Ltd., England), (B) 100 mmol/l glycine (Hopkin & Williams Ltd., England), and (C) 250 μg/l folate (pteroylglutamic) acid (Boots Ltd., Nottingham, England A4155). All solutions were made iso-osmotic with sodium chloride and contained 5·0 g/l polyethylene glycol (PEG) 4000 as a non-absorbable marker. The solutions were infused in varying order (Table 1). After an equilibration period of 35 minutes, three successive 10-minute collections of intestinal content were made. Samples during the glucose and glycine infusions were immediately frozen solid. All perfusion solutions were treated in an identical way to the intestinal contents. Serum samples were obtained mid-way through the folate acid infusion—that is, 50 minutes after the start—for folate concentration.

Methods for glucose, glycine, and PEG determination have been described before (Cook, 1971a; 1972b) and that for folate below. Glucose and PEG determinations were made in duplicate and those for glycine in triplicate. Calculations of absorption rates (Cook, 1971a) and reproducibility of those results for the three 10-minute collections (Cook, 1972b) have been described. For glucose absorption rate the standard deviation was 0·05 g/30 cm of jejunum/min, and the coefficient of variation 21·2% (n = 10). For glycine, the corresponding figures were 4·1 mg and 7·5% (n = 10), and for folate 0·196 μg and 8·6% (n = 10). For net water absorption the SD was 1·12 ml/30 cm of jejunum/min (n = 30).

Folate concentrations in serum, red-cells, perfusion solutions, and intestinal contents were determined by a Lactobacillus casei technique (Waters and Mollin, 1961; Hoffbrand et al., 1966). Ascorbic acid (5 mg/ml) was added to the serum samples immediately after separation, and the red-cells were immediately haemolyzed by dilution of the blood (1:10) in a 10-0 g/l ascorbic acid solution. Volatile preservative was added to all of the samples (0·04 ml/ml), which were immediately frozen solid and transported, by air, to London surrounded by CO₂ ice.

Methods for the xylose test and serum urea (Cook, 1972a), and protein (Cook, 1973a) concentrations have been described. Serum immunoglobulin
concentrations were determined using immuno-diffusion plates (Meloy Laboratories, Inc., Springfield, Virginia, U.S.A.); standard curves were constructed with serum samples prepared by the same laboratory.

Jejunal biopsy-specimens were taken from six patients (nos. 1, 4, 5, 7, 8, and 9): the site was 1-34 (mean 19) cm past the duodenojejunal flexure. They all had a normal dissecting-microscope appearance, histology and disaccharidase, brush-border lactase and acid and hetero-β-galactosidase concentrations for Africans in Africa (Cook et al., 1969; Cook et al., 1973). In nos. 1, 5, and 8 maltase, iso-maltase, sucrase, and trehalase concentrations were towards the lower limit of normal; all total and brush-border lactase concentrations were low compared with northern European subjects. In one additional patient with treated megaloblastic anaemia a jejunal biopsy specimen was also normal. Detailed results are being published separately.

Significance was determined by Student’s *t* test. Figures shown means ± 1 SEM.

**Results**

Figure 1 shows the results of xylose tests in the 28 patients. The mean for those with hypochromic and haemolytic anaemia (6-7 [4-3-9-4] g/5 h) is similar to that in non-anaemic Zambian African patients (Cook, 1972a). Those with megaloblastic anaemia (treated and untreated) had a significantly lower mean excretion than those with hypochromic and haemolytic anaemia (*p* < 0-001). Mean values for those with untreated and treated megaloblastic anaemia were 3-6 [1-4-5-7] and 5-0 [2-9-6-7] g/5 h respectively. After starting folic acid, excretion increased from 3-0 to 5-8 and from 2-7 to 4-8 g/5 h in the two patients studied.

Figure 2 shows glucose absorption rates in the 10 anaemic patients, and controls; difference between means is not significant. Mean values for the patients and controls were 0-23 (0-14-0-28) and 0-22 (0-15-0-35) g/min respectively. Lowest absorption rates were in nos. 3 and 10. Figure 3 shows glycine absorption rates in the 10 anaemic patients, and controls; difference between means is not significant. Mean values for the patients and controls were 56 (38-70) and 50 (32-60) mg/min respectively. Highest absorption rates were in nos. 4, 6, 7, and 9, and the lowest in no. 5. Figure 4 shows folic acid absorption rates in the 10 anaemic patients, and controls; difference between means is not significant. Mean values for the patients and controls were 2-25 (1-06-2-97) and 2-58 (2-31-2-96) µg/min. Lowest absorption rates were in nos. 5, 6, and 8 (in no. 8 the rate was 1-06 µg/min). Mean serum folic acid concentration during the folic acid infusions was 5-5 (2-0-15-5) µg/l; in eight of them that was slightly higher than the fasting concentration. Figures 2, 3, and 4
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**Fig. 3** Glycine absorption rate (mg/30 cm of jejunum/min) from a 100 mmol/l solution in 10 anaemic patients (●, megaloblastic; ○, hypochromic) and 17 controls (▲). Difference between means is not significant (t = 1.55; df = 25; p < 0.20). Mean net water absorption rate in the anaemic patients (○) and controls (▲) is also shown; difference between means is not significant (t = 0.17; df = 25; p < 0.90).

**Fig. 4** Folic (pteroylglutamic) acid absorption rate (mg/30 cm of jejunum/min) from a 250 μg/l solution in 10 anaemic patients (●, megaloblastic; ○, hypochromic) and 5 controls (▲). Difference between means is not significant (t = 1.29; df = 13; p < 0.30). Mean net water absorption rate in the anaemic patients (○) and controls (▲) is also shown; difference between means is not significant (t = 0.68; df = 13; p < 0.60).

summarize mean net water absorption rates; differences are not significant.

Figure 5 shows a significant positive correlation between glucose absorption rate and xylose excretion in the 10 patients in the main investigation.

Patients nos. 1, 2, 4, 6, 7, and 10 had diarrhoea (up to three fluid stools) soon after the three perfusions.

**Discussion**

A high proportion of Africans in tropical Africa is anaemic, and that applies especially to women. The present study shows that anaemia per se does not significantly alter glucose, glycine, or folic (pteroylglutamic) acid absorption rates, or the xylose test; apart from low folic acid absorption rates in a minority, those compounds were absorbed normally in the presence of hypochromic and haemolytic anaemia. However, megaloblastic anaemia (due to folate depletion) was associated with impairment of the xylose test. The patients who were undergoing treatment had a higher mean xylose excretion than those who were untreated, and, furthermore, two individuals tested serially showed an improvement after treatment had started. Those results suggest that

**Fig. 5** Significant correlation between xylose excretion (g/3 h) after a 25 g oral load and glucose absorption rate (mg/30 cm of jejunum/min) from a 200 mmol/l solution in 10 anaemic patients (●, megaloblastic; ○, hypochromic). (y = 0.136 + 0.016 (x); r = + 0.720; p < 0.02).
Folate depletion may be an important factor in xylose malabsorption. Although a minority of the patients with megaloblastic anaemia and folate deficiency in the present study drank alcohol, most did not; folate deficiency combined with high alcohol intake is known to produce functional abnormality of the small intestine (Halsted, 1975). A significant depression of glucose absorption in association with megaloblastic anaemia has not been demonstrated, but that might well be due to the small numbers studied; a significant positive correlation between glucose absorption rate and xylose excretion (Figure 5) (Cook, 1971a) lends support to that suggestion. Jejunal morphology, and glycine and folic acid absorption were in those tested similar to controls; that indicates that the present results are not the outcome of a general absorptive defect due to the megaloblastic anaemia.

Previous investigations of intestinal function in nutritional folate deficiency unassociated with alcoholism have yielded conflicting results (Halsted, 1975). Thus, although Forshaw (1969) and Dawson (1971) demonstrated xylose malabsorption in nutritional folate deficiency, which returned to normal after treatment with folic acid, Winawer et al. (1965) were unable to detect a functional abnormality. In Kuala Lumpur, Tasker (1961) found that mean xylose excretion after a 5 g oral load was 0·71 g/5 h in 36 patients with nutritional megaloblastic anaemia, and 1·43 g/5 h in 21 controls. However, in Singapore Siang et al. (1966) demonstrated xylose malabsorption in only two out of eight patients with megaloblastic anaemia associated with malnutrition and accompanied by folate deficiency. The evidence from Africa is limited. A significant correlation between haemoglobin concentration and xylose excretion after a 5 g oral load has been demonstrated in patients with megaloblastic anaemia in Nairobi, Kenya; as in the present study, folate depletion was largely dietary, had a seasonal incidence, was often associated with pregnancy and the puerperium, and responded rapidly to oral folic acid (Foy and Kondi, 1971).

The mechanism of monosaccharide malabsorption in folate depleted subjects is unknown. In the present study, jejunal morphology and disaccharidase concentrations were normal in three patients with megaloblastic anaemia, despite the fact that enterocytes have a high turnover rate and folate requirement (Halsted, 1975). Minor alterations in jejunal mucosal integrity have not however been ruled out. Relative anoxia of the enterocyte is clearly not important because xylose and glucose absorption in the patients with non-megaloblastic anaemia were similar to that in non-anaemic controls (Cook, 1972a; 1974a). Monosaccharide malabsorption in the presence of systemic infection is probably in part via folate deficiency; serum γ-globulin and IgG concentrations are usually high in infections, however, and a separate mechanism seems likely.

Many patients had a systemic infection on admission, although most had been adequately treated at investigation; such infections are associated with impaired glucose and xylose absorption (Cook, 1971a; 1972a). However, mean serum γ-globulin and IgG concentrations were not raised in the patients with megaloblastic anaemia; serum IgG was, in fact low in them compared with Zambian Africans with out anaemia or systemic infection (Cook and Lewis 1975). Systemic infection might have been a contributory factor in the depression of xylose absorption, but it seems extremely unlikely that it was entirely responsible. The patients in the present investigation did not have tropical sprue (Klipstein, 1968; Baker, 1972; Cook, 1974a). The clinical presentation and absence of severe morphological changes in the jejunum, in those in whom it was studied, are inconsistent with that diagnosis. Although difficult to define (Baker, 1972), sprue seems to be very unusual in tropical Africa (Cook, 1967; 1974a; Foy and Kondi, 1971; Thomas and Clain, 1975) and no cases have been reported from Lusaka. Low serum immunoglobulin (especially IgG) concentrations have been reported in that disease (Jarnum et al., 1968; Klipstein and Falaiye, 1969). Subclinical malnutrition was not excluded in the present study, but that has been shown to be associated with normal glucose, glycine, glycylglycine, and xylose absorption (Cook, 1974c).

The present observation may explain in part the high incidence of subclinical malabsorption in tropical Africa, where folate depletion is very common. Together with systemic infections, previously associated with glucose and xylose malabsorption (Cook, 1971a; 1972a; 1973a; 1974a, b), that may be important in human nutrition.

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References
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28, 87-92.


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