Hyponatraemia in Diarrhoeal Infants in Lagos

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Hyponatraemia has been recognized in Western countries as a frequently occurring phenomenon in the fluid and electrolyte imbalance which accompanies infantile diarrhoea (Weil and Wallace, 1956; Macaulay and Blackhall, 1961; Bruck, Abal, and Aceto, 1968), but this association is believed to be rare in the tropics and in malnourished children, and reports are few, there being none from West Africa. Our experience in Lagos with patients suffering from diarrhoea led us to suspect that hyponatraemia was not at all rare and in the present paper we describe the condition as it occurs here.

Subjects and Methods

We reviewed the records of 48 children (24 male, 24 female) with diarrhoea seen in our hospital from December 1966 to May 1968, who showed a serum sodium concentration of 148 mEq/l. or more. 30 were less than 6 months old; 13 were in the 6–9 month group; 2 were between 9 months and 1 year; and only 3 children were above 1 year. The oldest child was 3½ years of age. Body weight was recorded in 23 patients, and all of these were below the average weight of healthy children in social Class I (Institute of Child Health, Lagos Report 1963–68).

Of the 48 children, 39 presented as emergencies, and had been admitted to hospital earlier (Table I). All patients were from families of indigenous people.

In 41 patients blood was collected in a paraffin bottle before the start of treatment for determination of sodium, potassium, chloride, and bicarbonate. In 7 patients blood samples were collected after they had received varying amounts of intravenous fluids (Cases 1–7, Table I).

Results

Most of the patients were brought to hospital between 3 and 7 days after the onset of illness. Gastro-enteritis was the most frequent provisional diagnosis, stools being watery and frequent: 5–10 times a day. Vomiting was frequent, especially after feeds. 3 patients were admitted with bronchopneumonia and diarrhoea; 4 had urinary tract infections; and 1 child, 3½ years old, had abdominal and pulmonary tuberculosis. Accurate records of fluid intake just before and during the illness were available in only 9 in-patients and these are summarized in Table I; of these, 4 patients were on intravenous fluids. One patient received 220 ml. Darrow’s solution intraperitoneally. In Case 7 (Table I) the leakage of intravenous fluid was only discovered after 24 hours. 7 patients attended health centres and had received oral normal saline with glucose or Darrow’s solution in unknown quantities. 34 patients, including Cases 8 and 9 (Table I), had received no fluids therapeutically, and during the illness had been fed on breast milk supplemented with milk recon-
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TABLE I

Fluid Intake in 9 Patients in First 24-48 Hours and During Illness

<table>
<thead>
<tr>
<th>Case No.</th>
<th>Sex/Age</th>
<th>Weight (g.)</th>
<th>Immediate Cause of Dehydration</th>
<th>Initial Serum Na (mEq/l.)</th>
<th>Fluid Intake</th>
<th>Max. Serum Conc. (mEq/l.)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>* 9 mth.</td>
<td>5443</td>
<td>Bronchopneumonia and diarrhoea</td>
<td>122</td>
<td>0.9% sodium chloride solution; 2740 ml. in 5 days</td>
<td>166</td>
</tr>
<tr>
<td>2</td>
<td>F 5 mth.</td>
<td>5443</td>
<td>Diarrhoea and vomiting</td>
<td>115</td>
<td>250 ml. 0.9% and 500 ml. NaCl solution</td>
<td>160</td>
</tr>
<tr>
<td>3</td>
<td>F 9 mth.</td>
<td>4989</td>
<td>Diarrhoea and vomiting</td>
<td>150</td>
<td>1200 ml. 0.9% NaCl solution</td>
<td>160</td>
</tr>
<tr>
<td>4</td>
<td>F 1 yr.</td>
<td>4989</td>
<td>Diarrhoea and vomiting, kwashiorkor</td>
<td>150</td>
<td>1460 ml. 0.18% NaCl solution</td>
<td>162</td>
</tr>
<tr>
<td>5</td>
<td>F 5 mth.</td>
<td>4535</td>
<td>Diarrhoea and vomiting</td>
<td>150</td>
<td>220 ml. full strength Darrows solution intraperitoneally</td>
<td>162</td>
</tr>
<tr>
<td>6</td>
<td>F 1 mth.</td>
<td>4989</td>
<td>Diarrhoea and vomiting</td>
<td>150</td>
<td>610 ml. 0.18% saline</td>
<td>148</td>
</tr>
<tr>
<td>7</td>
<td>F 13 mth.</td>
<td>5443</td>
<td>Diarrhoea and vomiting</td>
<td>131</td>
<td>Intravenous fluid leakled; no oral fluids</td>
<td>160</td>
</tr>
<tr>
<td>8</td>
<td>F 1 mth.</td>
<td>2550</td>
<td>Diarrhoea and vomiting</td>
<td>142</td>
<td>F.S. Lactogen 720 ml./24 hr.</td>
<td>160</td>
</tr>
<tr>
<td>9</td>
<td>F 1 yr.</td>
<td>5556</td>
<td>Bronchopneumonia and diarrhoea</td>
<td>142</td>
<td>F.S. Lactogen 540 ml./24 hr.</td>
<td>160</td>
</tr>
</tbody>
</table>

* Sex not recorded.

Fluid intake in 9 patients in the first 24-48 hours and during illness is presented in the table. The fluid intake varied from 220 ml. to full strength Darrows solution intraperitoneally.

stitted from powdered milk, in most cases Lactogen. All except 5 children showed clear clinical signs of dehydration, often severe.

Thirty-one patients had fever of 37.8 °C or more; the temperature reached 40 °C in 11, and 41.1 °C in 2. Hyperirritability was present in 31 patients; of these, 16 were irritable when disturbed though lethargic otherwise. Thirst was present in all except those who were very sick and comatose. Only 5 patients were in shock with thin radial pulse and cold extremities. In 14 patients pulse volume and peripheral circulation were noted as good despite signs of severe dehydration.

Thirty-seven patients had hyperpnoea with acidoic breathing. In 3 respiration was depressed and breathing shallow, in spite of a very low bicarbonate concentration in blood.

Cerebral symptoms were present in 22 patients (46%). The salient features of these cases are summarized in Table II. Consciousness varied from hyperirritability to gross depression in 14 patients. 6 patients had generalized or focal convulsions. Involuntary movements, coarse tremors, and generalized hypertonia were present in 5. 6 patients showed signs of meningeal irritation such as neck stiffness, positive Kernig sign, and a shrill cry. In only 2 patients was the anterior fontanelle found to be tense. Subarachnoid haemorrhage was found in 2 patients.

Fourteen (29%) out of the 48 patients died, all but one death occurring among patients with CNS signs. 7 necropsies were carried out; 3 (Cases 5, 13, 14, Table II) revealed petechial haemorrhages on the surface and in the substance of the brain, especially the cerebellum; numerous intravascular thrombi were found in 2 and massive intraventricular haemorrhage in 1 of them (Case 5, Table II). In the remaining 4, cerebral oedema and extreme vascular congestion were the main findings. In 2 of them microscopy showed oedema and severe hyperaemia with marked stasis in blood vessels of meninges and extravasation of erythrocytes. These lesions were of the type known to be associated with hypernatraemia (Finberg, Lutterell, and Redd, 1959; Finberg, Kiley, and Lutterell, 1963).

Laboratory Investigation

The results are given in Table III. The serum sodium concentration ranged from 148-175 mEq/l. In 3 patients, the bicarbonate content of blood was above 20 mEq/l.; all others had significant metabolic alkalosis.

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### TABLE II
Clinical Features in 22 Patients with CNS Signs

<table>
<thead>
<tr>
<th>Case No., Sex, and Age</th>
<th>Aetiology or Underlying Disease</th>
<th>Urea</th>
<th>Max. Serum Na(mEq/l.)</th>
<th>Clinical Features</th>
<th>Result of CSF</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>1, F, 7 mth.</td>
<td>Diarrhoea and vomiting</td>
<td>153</td>
<td></td>
<td>Apathetic, irritable; anterior fontanelle tense; signs of meningeal irritation</td>
<td>Clear, normal biochemistry</td>
<td>Recovered</td>
</tr>
<tr>
<td>2, F, 2 mth.</td>
<td>Diarrhoea and vomiting treated at Gbaja with ? Darrow's orally</td>
<td>170</td>
<td></td>
<td>Hyperpyrexia, coma, gasping</td>
<td>Clear, normal biochemistry</td>
<td>Died; no necropsy</td>
</tr>
<tr>
<td>3, M, 3 mth.</td>
<td>Diarrhoea and vomiting</td>
<td>86</td>
<td>170</td>
<td>40 °C., unconscious, anterior fontanelle became tense, opisthotonos, tremor, convolution, developed on 3rd day after admission</td>
<td>Uniformly blood-stained and xanthochromic; protein 800 mg./100 ml.</td>
<td>Recovered, but was spastic and mentally retarded</td>
</tr>
<tr>
<td>4, M, 15 mth.</td>
<td>Diarrhoea and vomiting</td>
<td>282</td>
<td>160</td>
<td>Hyperpyrexia, comatose, shill cry, involuntary movements, convolution</td>
<td>Protein 10 mg./100 ml. Cl 900 mg./100 ml.</td>
<td>Died, necropsy showed cerebral oedema and vascular congestion</td>
</tr>
<tr>
<td>5, M, 2 mth.</td>
<td>Diarrhoea</td>
<td>160</td>
<td></td>
<td>Hyperpyrexia, comatose, jittery, involuntary movements, and convolution</td>
<td>Xanthochromic protein 860 mg.</td>
<td>Died, necropsy; intravascular thrombi, haemorrhage in brain and ventricular haemorrhage</td>
</tr>
<tr>
<td>6, F, 5½ mth.</td>
<td>Diarrhoea and vomiting</td>
<td>164</td>
<td></td>
<td>Hyperpyrexia, comatose, and depressed respiration</td>
<td>Died, necropsy, cerebral oedema and marked vascular congestion</td>
<td>Recovered</td>
</tr>
<tr>
<td>7, F, 6 mth.</td>
<td>Diarrhoea and vomiting</td>
<td>150</td>
<td></td>
<td>Semiconscious, meningeal irritation, hypotension</td>
<td>Clear, protein normal</td>
<td>Recovered</td>
</tr>
<tr>
<td>8, F, 4 mth.</td>
<td>Diarrhoea and vomiting; received 250 ml. normal saline subcutaneously</td>
<td>160</td>
<td></td>
<td>Irritable, restless, meningeal irritation</td>
<td>Clear, protein 140 mg./100 ml.</td>
<td>Died, no necropsy</td>
</tr>
<tr>
<td>9, M, 9 mth.</td>
<td>Diarrhoea and vomiting; received 250 ml. normal saline subcutaneously</td>
<td>76</td>
<td></td>
<td>Unconscious and gasping</td>
<td>Clear, protein not done, sugar 20 mg./100 ml. Cl 933 mg./100 ml.</td>
<td>Recovered</td>
</tr>
<tr>
<td>10, F, 2 mth.</td>
<td>Diarrhoea and vomiting</td>
<td>154</td>
<td></td>
<td>Irritable, signs of meningeal irritation</td>
<td>Clear, protein 30 mg./100 ml.</td>
<td>Recovered</td>
</tr>
<tr>
<td>11, M, 1½ mth.</td>
<td>Diarrhoea and vomiting</td>
<td>257</td>
<td>160</td>
<td>Restless, irritable, convolution</td>
<td>Normal CSF</td>
<td>Died, no necropsy</td>
</tr>
</tbody>
</table>
TABLE II—continued

<table>
<thead>
<tr>
<th>Case No., Sex, and Age</th>
<th>Aetiology or Underlying Disease</th>
<th>Urea</th>
<th>Max. Serum Na (mEq/l.)</th>
<th>Clinical Features</th>
<th>Result of CSF</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>12, M, 4 mth.</td>
<td>Diarrhoea and vomiting, urinary infection, IVP non-functioning left kidney</td>
<td>252</td>
<td>160</td>
<td>Comatose, signs of meningeal irritation</td>
<td>Protein 100 mg./100 ml</td>
<td>Recovered</td>
</tr>
<tr>
<td>13, F, 6 mth.</td>
<td>Diarrhoea and vomiting</td>
<td>114</td>
<td>150</td>
<td>Comatose, restless, convulsion</td>
<td>Protein 120 mg./100 ml</td>
<td>Died; oedema of brain and petechial haemorrhage on the brain surface</td>
</tr>
<tr>
<td>14, M, 8 mth.</td>
<td>Diarrhoea and vomiting</td>
<td>42</td>
<td>158</td>
<td>Restless, irritable, neck retraction</td>
<td>CSF normal</td>
<td>Died, haemorrhage on surface and in brain; numerous intravascular thrombi Recovered; CNS signs cleared up after recovery</td>
</tr>
<tr>
<td>15, M, 1 mth.</td>
<td>Diarrhoea and vomiting</td>
<td>164</td>
<td></td>
<td>Semicongious, hypertonic, brisk reflexes, bilateral ankle clonus</td>
<td></td>
<td>Died of hyperkalaemia</td>
</tr>
<tr>
<td>16, F, 13 mth.</td>
<td>Diarrhoea and vomiting</td>
<td>148</td>
<td></td>
<td>Restless, thirst, tremor of hands</td>
<td></td>
<td>Died; tuberculosis lesions in lungs and abdomen; cerebral oedema and hyperaemia</td>
</tr>
<tr>
<td>17, M, 3½ yr.</td>
<td>A case of primary TB; diarrhoea and vomiting</td>
<td>166</td>
<td></td>
<td>Semicongious, hyperpyrexia, deep acidotic breathing</td>
<td></td>
<td>Recovered</td>
</tr>
<tr>
<td>18, M, 1½ mth.</td>
<td>Diarrhoea and vomiting</td>
<td>158</td>
<td></td>
<td>Semicongious, restless, head retraction, acidotic breathing</td>
<td>Protein 100 mg./100 ml</td>
<td>Recovered</td>
</tr>
<tr>
<td>19, F, 1 yr.</td>
<td>Bronchopneumonia; malnourished</td>
<td>54</td>
<td>160</td>
<td>Unconscious, hypertonic, convulsion</td>
<td>Protein 35 mg./100 ml</td>
<td>Died, no necropsy</td>
</tr>
<tr>
<td>20, M, 3 mth.</td>
<td>Diarrhoea and vomiting</td>
<td>64</td>
<td>160</td>
<td>Irritable; slight hypertonia</td>
<td>Protein raised</td>
<td>Recovered</td>
</tr>
<tr>
<td>21, F, 9 mth.</td>
<td>Diarrhoea and vomiting</td>
<td>52</td>
<td>166</td>
<td>Comatose, hyperpyrexia, carpopedal spasm</td>
<td></td>
<td>Died, no necropsy</td>
</tr>
<tr>
<td>22, M, 8 mth.</td>
<td>Diarrhoea and vomiting</td>
<td>168</td>
<td></td>
<td>Comatose</td>
<td></td>
<td>Died, necropsy: cerebral oedema and congestion</td>
</tr>
</tbody>
</table>

Acidosis. Potassium was above 6 mEq/l. in 4 patients and below 3 mEq/l. in 5 patients; none of the latter had signs of hypokalaemia.

Blood urea was estimated in 19 patients and ranged from 42 to 282 mg./100 ml.

Lumbar puncture was performed in 16 patients. CSF was uniformly blood stained and xanthochromic in 2 patients (Case 3 and 5, Table II); in others it was clear and under normal pressure. In 8 patients the protein content was high, ranging from 35 to 860 mg./100 ml. Sugar was normal or increased in all specimens. Chloride was increased in all and ranged from 800 to 933 mg./100 ml. (normal 750 mg./100 ml.).
TABLE III
Concentration of Electrolytes and Urea in Blood Serum

<table>
<thead>
<tr>
<th>Electrolyte</th>
<th>Range</th>
<th>No. of Patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Na (mEq/l.)</td>
<td>148-175</td>
<td>48</td>
</tr>
<tr>
<td>Cl (mEq/l.)</td>
<td>110-150</td>
<td>42</td>
</tr>
<tr>
<td>HCO₃ (mEq/l.)</td>
<td>6-25</td>
<td>38</td>
</tr>
<tr>
<td>K (mEq/l.)</td>
<td>2-4-7-2</td>
<td>39</td>
</tr>
<tr>
<td>Blood urea (mg./100 ml.)</td>
<td>42-282</td>
<td>19</td>
</tr>
</tbody>
</table>

Discussion

Incidence. Hypernatraemic dehydration in diarrhoea is believed to be uncommon in the tropics. Ahmed and Webb (1963) found hypernatraemia in 1 single infant in a series of 65 infants presenting with diarrhoea at Vellore in South India and this infant had been given concentrated salt solution (500 mEq/l.) by mistake. A similar low incidence has been reported from Karachi (Zubeida et al., 1968, personal communication).

By contrast, in our experience at Lagos, hypernatraemic dehydration in infants with gastroenteritis is not uncommon. Of 643 patients with diarrhoea who attended the Casualty Department from June 1967 to January 1968, 120 had their serum sodium measured. In 25 of these, serum sodium was 150 mEq/l. or more, an incidence of 20%. A similar incidence of hypernatraemic dehydration in diarrhoeal infants has been reported from the U.S.A. and other Western countries (Darrow et al., 1949; Weil and Wallace, 1956; Finberg and Harrison, 1955; Bruck et al., 1968).

Hypernatraemic dehydration is commoner in infants under 1 year and this is well illustrated in two recent studies on hypernatraemia (Morris-Jones, Houston, and Evans, 1967; Bruck et al., 1968). In the present series also all infants except 3 were under 1 year, and of these, 30 (62%) were under 6 months.

Causes of hypernatraemic dehydration in infants. Hypernatraemia, i.e. serum sodium concentration of 150 mEq/l. or more, is due to excessive loss of water from body fluids or to reduced intake of water in relation to electrolytes. It is more often due to a total deficit of water than to an excess of sodium. The potential channels of excessive loss of water in infants are insensible water loss through skin and respiratory passages, diarrhoeal stools, and dilute urine. In normal infants more than 50% of daily water loss is from the surface of the skin and the lungs, and fever, hyperventilation, and high environmental temperature tend to aggravate this loss. Heeley and Talbot (1955) observed average rates of insensible water loss of 1150 ml./m.² per day in sick infants, which is considerably higher than those for resting healthy infants. The average rate of insensible water loss in resting well infants is about 470-620 ml./m.² per day (Guest and Pettit, 1957).

Diarrhoeal stools are usually hypertonic when compared with blood. If the stools are large and frequent there is proportionately a greater loss of water than sodium (Skinner and Moll, 1956; Weil and Wallace, 1956; Bruck et al., 1968).

Insufficient water intake. This is common in infants. In the present series, all patients except 4 (Table I, Cases 1, 2, 3, 4) had received insufficient quantities of water during the acute illness because of vomiting and anorexia.

Increased renal water requirement. Because of renal immaturity, dehydrated young infants are unable to form maximally concentrated urine. If they are fed on undiluted cow's milk and skimmed powder milk mixture which provides high protein intake, or given saline orally or parenterally, which gives a high solute load, the renal water requirement obligatory for excretion of electrolytes and urea is increased, thus increasing the water deficit (Pratt and Snyderman, 1953). 37 of 48 patients in the present series continued to be fed on powdered milk mixture in addition to breast feeding during the illness. It is possible that this could have contributed to the water deficit and to the hypertonicity of the blood.

In the majority of our patients no single cause could be identified as being responsible for the hypertonicity of the body fluids. A combination of several factors related to acute illness, i.e. water loss in a hypotonic diarrhoeal stool, excessive insensible water loss, insufficient water intake, and continued feeding of infants on powdered milk mixture in addition to breast-feeding accounted for or contributed to hypernatraemia. The rarity of this condition in India and Pakistan could be explained by the fact that mothers as a rule stop all feeds, including milk, and give only sugar and barley water to infants with diarrhoea.

Excessive administration of salt solution was the probable cause of hypernatraemia in only 11 of 48 patients. Of these, 4 patients (Cases 1, 2, 3, 4, Table I) had received large amounts of salt solution intravenously, while 7 patients, who were referred from Health Centres, had received orally unknown quantities of isotonic NaCl solution or Darrow's solution.

Cerebral manifestations in association with acute
Hyponatraemia are common and well documented (Rapoport, 1947; Finberg and Harrison, 1955; Skinner and Moll, 1956; Weil and Wallace, 1956; Macaulay and Blackhall, 1961; Morris-Jones et al., 1967), and subdural and subarachnoid haemorrhages have been observed in infants with hyponatraemia (Finberg, 1959). These clinical observations have been amply confirmed experimentally (Finberg et al., 1959), and experimental studies have also shown that the osmolality of the extracellular fluid is the relevant factor rather than the sodium concentration alone (Finberg et al., 1959). Thus, when a hypertonic solution, whether of sodium chloride, sodium bicarbonate, sucrose, mannitol, or urea, was injected into laboratory animals, cerebral lesions were produced which were closely akin to those found in human beings. Morris-Jones et al. (1967) showed a close relation between frequency of fits and serum sodium levels; thus the risk of fits was 10% when serum sodium was in the range of 140 to 158 mEq/l. but 71% at serum sodium levels above 158 mEq/l. The danger was further increased when high blood urea levels also contributed to extracellular osmolality.

Accepting the standard of Morris-Jones et al. (1967), that a serum Na concentration of 158 mEq/l. indicates severe hyponatraemia, 65% (17/26) of such patients in the present series had cerebral symptoms. 15 of these 17 had symptoms of severe cerebral disturbances, such as coma, convulsions, generalized hypertonia, gross involuntary movements, and neck retraction, whereas when the serum sodium level was below 158 mEq/l., 27% (5/22) of the patients had cerebral signs, and only one of them (Case 13, Table II) was unconscious and had convulsions. It is, therefore, clear that cerebral disturbances are correlated with high serum sodium concentration ($\chi^2 = 8.7$, $p < 0.01$) (Fig.).

Macaulay and Watson (1967) in a follow-up report on 100 hyponatraemic patients, who had no antecedent nervous disease, found that 16 patients had sustained permanent brain damage and of these only 8 patients were alive. Morris-Jones et al. (1967) reported neurological abnormalities in 37 (12/32) of the survivors; in several, however, abnormalities were unrelated to earlier hypotonia, and only 3 out of 32 (9%) had both related and symptomatically important lesions. Several other authors (Finberg, 1959; Weil and Wallace, 1956) have also reported permanent brain damage among survivors from acute hyponatraemic dehydration.

In the present series neurological signs were present in 22 (46%) of 48 patients, and of these 13 died, though in one (Case 16, Table II) hypernatraemia was the probable cause of death. The patients who, at the time of admission, had signs of severe brain damage, showed no improvement on treatment; coma deepened, respiration became irregular, and death followed. Of the 9 survivors, 1 child (Case 3, Table II) sustained permanent brain damage. 3 other children have been followed for one year and so far their physical and mental development have been normal.

Conclusions

This study shows that hyponatraemic dehydration is not infrequent in Lagos in infants suffering from diarrhoea. In our experience the clinical features that helped us to arrive at a diagnosis of this condition were: pyrexia, often high, hyperpyrexia, irritability, lethargy, increased thirst, absence of shock, good peripheral circulation in spite of moderate to severe dehydration, and presence of acidotic respiration.

In view of the high risk of brain damage and mortality attendant on this condition, it is important to prevent hyponatraemia. In the majority of patients hyponatraemia results from excessive loss of water in relation to sodium, and it can be prevented by ensuring an adequate fluid intake in an infant who has fever and is hyperventilating, especially when diarrhoea is also present. The daily fluid requirement of a normal infant is approximately 150 ml/kg body weight in 24 hours. More may be needed in hot climates. During the diarrhoeal illness, twice the normal intake may be necessary. Injudicious administration of fluids with a high solute content such as 0.9% NaCl solution with 5% dextrose, or Darrow's solution should be discouraged. Mothers should be advised to stop milk feeds during the illness, and instead to offer the infant at frequent intervals a solution...
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containing sodium chloride 0.85 g., KHCO₃ 1 g., and sugar 25 g. in a pint of water. If the diarrhoea continues and the child cannot take the fluids because of anorexia and vomiting, intravenous fluids will have to be given and this will necessitate admission to hospital.

We thank Professor Ransome-Kuti, Ag. Head of the Department of Paediatrics, College of Medicine of the University of Lagos, and Professor John Davis of Manchester for their help and advice in preparing this paper, and Dr. Odunjo of the Department of Pathology, College of Medicine of the University of Lagos, for giving us the results of the necropsy. We are also grateful to our other colleagues for allowing us access to their patients.

REFERENCES