DISCUSSION

The origin of RTF and R-determinants is obscure. One view is that different RTF picked up single R-determinants by recombination with bacterial chromosomes and then acquired multiple resistance by combining with one another. Another explanation is that a single RTF serially picked up the different chromosomal resistance sites. Against these arguments are the facts that the biochemical mechanisms of multiple drug resistance may differ from those of non-RTF mediated resistance, and that RTF transmitted resistance comes to expression immediately in a new recipient whereas chromosomal gene pick-up is delayed. Anderson and Datta presented evidence that quadruple transmissible resistance was present from the start of their investigations. These facts are difficult to reconcile with chromosomal gene pick-up theories and a de novo origin of R-factors has been suggested. Anderson and Datta presented evidence that treatment of calves with ampicillin resulted in an increase in the proportion of ampicillin-resistant strains of S. typhimurium and that this resistance was contagious. Whatever their ultimate origin, the R-factors appear to be selected by drugs and this fact may necessitate a review of the use of these agents in human and veterinary medicine.

It is not known whether both the S. typhimurium and Citrobacter originally possessed the R-factor or (more likely) if one strain infected the other in the intestine of the patient. Salmonella typhimurium is a common animal parasite which often infects man. If it was the primary resistant organism in this case it could mean that a reservoir of R-factors already exists in the local animal population.

It is surprising that no multiple-resistant E. coli were isolated from the patient, particularly as the S. typhimu-

rism strain could transmit its resistance to the patient’s E. coli in vitro. The rate of transmission was low, however, and resistant clones may have been missed. The rate of transmission of multi-drug resistance factors differs among various recipients and is also influenced by the presence of other epimnes. However, the existence of strains which harbour R-factors have now been demonstrated in South Africa, and in vivo transmission of their drug-resistance to other Enterobacteriaceae may interfere with future therapeutic efficacy.

SUMMARY

This paper reports the isolation of strains of Enterobacteria ceae with the property of transmissible multiple drug-resistance in South Africa. The strains are a Salmonella typhimurium and an organism belonging to the Citrobacter group, both of which were isolated from the stools of a White child. The strains are resistant to sulphonamide, tetracycline, chloramphenicol, streptomycin and ampicillin and are capable of contiguously transmitting this pattern of resistance en bloc to sensitive E. coli and Providencia strains. The public health importance of the phenomenon is mentioned.

We thank Prof. P. J. Pretorius for permission to publish details of the patient. One of us (J.N.C.) is in receipt of grants from the South African Council for Scientific and Industrial Research.

REFERENCES


Case Report

ATYPICAL SPHEROCYTOSIS IN AN AFRICAN GIRL

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Hereditary spherocytosis is best known as a disorder affecting people of European origin, although it is by no means confined to this group. The disease has been reported in Egyptians by Salah, in Filipinos by Stransky and Dausis-Lawas, and in a comprehensive search of the literature reported that 42 bona fide cases had been described in Negroes. In the African this condition is considered to be a distinctly rare entity. Gelfand has not seen it in an African in the Rhodesias, and Foy and Kondi recorded, without mentioning any details, one typical case of hereditary spherocytosis in KwaZulu. In the South African Bantu, Merskey and Baskind and Gon each reported a case of chronic haemolytic anaemia resembling acholuric jaundice. In neither case was a family study carried out and in the former, comprehensive techniques for the exclusion of antibodies had not been evolved at the time of recording. Metz was the first to report a Bantu family where the diagnosis of hereditary spherocytosis could be established and he mentioned a further case in a Bantu male. Recently, Spector and Metz recorded another Bantu family with hereditary spherocytosis. The true incidence of this disease in races other than European is not known. Whether the paucity of reports in Africans indicates that the disorder is rare in this race, or results from failure in diagnosis, or in reporting of known cases, is not possible to assess. In view of the apparent rarity of this disorder in Africans, this paper presents a case in a Bantu girl which, for reasons to be mentioned later in the report, is considered to be a case of atypical spherocytosis or 'type-B' of Young, Izzo, Altman and Swisher.

METHODS

Routine haematological studies were performed by standard methods. Autohaemolysis studies were done by the method described by Cartwright; glucose utilization studies by the
method described by Tanaka, Valentine and Miwa, and the blood glucose was determined by the Somogyi method. The serum iron, iron-binding capacity, urinary urobilinogen, faecal urobilinogen, serum haptoglobins, haemoglobin electrophoresis, and fetal haemoglobin determination, and the glucose-6-phosphate dehydrogenase estimations were all performed by established methods.

CASE REPORT
R.M., a 10-year-old Bantu girl, was admitted to the Queens-town Hospital in February 1963 on account of gross anaemia and splenomegaly. The haemoglobin was found to be 26 G/100 ml. and she was transfused with 2 pints of blood. During the interval between this admission and her referral to the Red Cross War Memorial Children's Hospital, Cape Town, she was given 1,400 mg. of iron-dextran (Imferon) intramuscularly. No malarial parasites were detected on the smear. The initial diagnosis was iron-deficiency anaemia and she was given a further 600 mg. of intramuscular iron-dextran complex.

Family history. Her parents and 4 siblings had no history of anaemia or jaundice and when examined by Dr. G. J. Lotter, District Surgeon of Queenstown, they did not have anaemia or splenomegaly. The father's blood was available for study and was found to be completely normal, as was the osmotic fragility.

Physical examination showed a well-developed, well-nourished Bantu girl with slight pallor and scleral icterus. Her height was 4 ft. 8 in. and weight 61 lb. She had a splenomegaly of 6 cm. and the liver was palpable 1.5 cm. below the costal margin. Cardiomegaly was present and a pre-systolic sound, confirmed on phonocardiography, was audible. Radiological examination of the chest showed moderate cardiac enlargement.

The relevant haematologic findings are shown in Table I. Many of the red cell inclusions stained with prussian blue for iron. It was not possible to transfer these inclusions by incubating the patient's serum with normal compatible erythrocytes at 37°C for 24 or 48 hours. The bone marrow aspirate showed erythroid hyperplasia in keeping with haemolytic anaemia, and staining for iron showed increased iron content.

**TABLE I. HAEMATOLOGIC FINDINGS**

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Before Splenectomy</th>
<th>After Splenectomy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Haemoglobin (G/100 ml.)</td>
<td>9.2</td>
<td>13.7</td>
</tr>
<tr>
<td>Volume of packed erythrocytes (%)</td>
<td>26</td>
<td>38</td>
</tr>
<tr>
<td>Mean corpuscular haemoglobin concentration</td>
<td>86</td>
<td>80</td>
</tr>
<tr>
<td>Red cells (%)</td>
<td>35</td>
<td>36</td>
</tr>
<tr>
<td>Spherocytes</td>
<td>17</td>
<td>12</td>
</tr>
<tr>
<td>Polychromatophilia</td>
<td>0.00</td>
<td>0.00</td>
</tr>
<tr>
<td>Basophilic stippling</td>
<td>0.00</td>
<td>0.00</td>
</tr>
<tr>
<td>Howell-Jolly bodies</td>
<td>0.00</td>
<td>0.00</td>
</tr>
<tr>
<td>Pappenheimer bodies</td>
<td>0.00</td>
<td>0.00</td>
</tr>
<tr>
<td>Serum iron (µg/100 ml.)</td>
<td>96.4</td>
<td>96.4</td>
</tr>
<tr>
<td>Total iron-binding capacity µg/100 ml.</td>
<td>304.0</td>
<td>304.0</td>
</tr>
<tr>
<td>Saturation (%)</td>
<td>32</td>
<td>32</td>
</tr>
<tr>
<td>Serum bilirubin (mg./100 ml.)</td>
<td>0.7</td>
<td>0.7</td>
</tr>
<tr>
<td>Direct</td>
<td>0.4</td>
<td></td>
</tr>
<tr>
<td>Indirect</td>
<td>0.3</td>
<td></td>
</tr>
<tr>
<td>Urinary urobilinogen mg./2 hours</td>
<td>10</td>
<td>82</td>
</tr>
<tr>
<td>Faecal urobilinogen mg.</td>
<td>495</td>
<td>Absent</td>
</tr>
<tr>
<td>Plasma methaemoglobin</td>
<td>Absent</td>
<td>Absent</td>
</tr>
<tr>
<td>Plasma methaemalbumin</td>
<td>Absent</td>
<td>Absent</td>
</tr>
<tr>
<td>Plasma sulphhaemoglobin</td>
<td>Absent</td>
<td>Absent</td>
</tr>
<tr>
<td>Serum potassium mg.</td>
<td>4.0</td>
<td>4.0</td>
</tr>
<tr>
<td>Mechanical fragility (%)</td>
<td>8</td>
<td>8</td>
</tr>
<tr>
<td>Tc chromium 51-labelled erythrocyte survival time (autotransfusion)</td>
<td>12 days</td>
<td>30 days</td>
</tr>
</tbody>
</table>

**Antibody tests:**
(a) Direct antiglobulin (Coombs test) - Negative
(b) Indirect Coombs test - Negative
(c) Ham's acid-serum test - Negative
(d) Auto-antibodies at 37°C - Negative
(e) Auto-antibodies at 22°C - Negative
(f) Auto-agglutinins at 4°C - Negative

Haemoglobin electrophoresis
(1) Fetal haemoglobin 0.0
(2) Haemoglobin A 99
(3) Haemoglobin A2 0.0
(4) Haemoglobin A1c 0.0
(5) Hb S 0.0
(6) Hb C 0.0
(7) Hb D 0.0

The red cell osmotic fragility and autohaemolysis estimations were markedly increased and the results are shown in Tables II and III. Unlike the typical cases of hereditary spherocytosis,
also dilated and engorged. Haemosiderin-laden macrophages were abundant.

**FIG. 2.** Organ-scanning data following injection of radioactive labelled patient's erythrocytes and normal compatible donor's erythrocytes.

The post-splenectomy course was uneventful. The haematological status improved and the data are shown in Table I. The osmotic fragility was unchanged (Table II). There was considerable improvement in the autohaemolysis studies (Table III). The latter in the post-splenectomy period behaved in a manner similar to typical hereditary spherocytosis in so far as the presence of glucose and adenosine in the incubating blood markedly retarded haemolysis. The red cell survival was now within normal limits, the T1 being 30 days (Fig. 1). Within one month postoperatively, her cardiac size returned to normal and no abnormal heart sounds or murmurs were audible.

**DISCUSSION**

In typical cases of hereditary spherocytosis the family history is positive and autohaemolysis proceeds at an abnormally fast rate. Dacie showed that in 21 patients with hereditary spherocytosis the range of haemolysis at 48 hours, without additional glucose, was 7.5-47.5% with a mean of 28.5%. Dacie and other workers showed that haemolysis was markedly slowed in the presence of glucose and that adenosine was also effective in retarding haemolysis.

In atypical spherocytosis (group B) described by Young and his co-workers in 1956, the disorder differed in that the rate of autohaemolysis of the patient's erythrocytes was not reduced by the addition of glucose. They described 2 patients under this title. After splenectomy, from which the patients derived striking clinical benefit, glucose had as marked an effect in reducing autohaemolysis as in typical cases of hereditary spherocytosis. The reason for these discrepancies is unknown. Dacie has made similar observations in 2 children of different families whose parents were apparently normal, as well as in an adult with a positive family history who had the nephrotic syndrome and amyloid disease in addition to hereditary spherocytosis. The patient described in this paper appears to be as a result of 2 G of intramuscular iron-dextran complex injected into a person who was not iron-deficient but in fact had a disease which caused iron overload. Many of these inclusions stained positively with prussian blue, indicating their iron content.

**SUMMARY**

Attention is drawn to the rarity of hereditary spherocytosis in the African. A case of atypical spherocytosis is described in a Bantu girl.

Thanks are due to Dr. M. C. Botha and his staff, for some of the studies included in this paper. Dr. D. McKenzie, for providing the facilities of his pathology laboratory; and Miss R. Schein, for her technical assistance. I would like to acknowledge the assistance of Dr. M. I. Papilsky, of Queenstown, for providing the early clinical and haematologic data on this patient.

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