THE ASSOCIATION OF GALL-STONES WITH
ACHOLURIC JAUNDICE IN CHILDREN

REPORT OF A CASE IN A CHILD AGED THREE YEARS
WITH A NOTE ON THE CRISSES OF ACHOLURIC JAUNDICE

BY

DOUGLAS GAIRDNER, B.M., M.R.C.P.

(From the Hospital for Sick Children, Great Ormond Street)

The majority of cases of acholuric jaundice in adults are associated with
gall-stones. In children the same association is mentioned in some of the
text-books, although the literature contains references to few cases, the follow-
ing ten cases being all that a search has yielded.

Two cases, both aged about fifteen years, are reported from the Mayo
Clinic (Potter, 1928); splenectomy was performed for 'haemolytic anaemia' and
gall-stones were found at operation, but no other details are available. Murray-Lyon (1935) reports a case of acholuric jaundice in a boy aged ten
years; multiple-facetted gall-stones were found unexpectedly when splenectomy
was performed. Snelling and Brown (1936) report a similar case in a child of
six years. In the case reported by Brooks, Clinton and Ashley (1935) of a
child aged four years, gall-stones in a chronically inflamed gall-bladder were
found at operation; their presence had not been suspected, although some of
the symptoms described, such as intense icterus, may well have been due to
them. Roberts (1938) mentions two sisters, aged twelve and fourteen years; in
both gall-stones were diagnosed radiologically and subsequently removed. The
only available series of children who have been splenectomized for acholuric
jaundice is that of Barrington-Ward (1937). In his series of ten cases under
twelve years, three (30 per cent.) were found to have gall-stones, the youngest
of these being six years. In none had their presence been suspected prior to
operation (personal communication).

The small number of the reported cases in the literature is thus in contrast
to Barrington-Ward's findings. This may be due to failure to examine for the
presence of gall-stones when splenectomy is performed. If, as Barrington-
Ward's figures suggest, acholuric jaundice in children is often associated with
gall-stones, occasional cases would be expected in children, as in adults, to
present with symptoms due to the gall-stones. Up to the present, however,
this possibility does not appear to have been recognized. It is the purpose of
this communication to draw attention to it.

The diagnosis of gall-stones in children

Gall-stones, from whatever cause, are uncommon in children. Potter
in 1928 was able to collect only 141 cases from the literature. An analysis of

109
ARCHIVES OF DISEASE IN CHILDHOOD

his series shows that the majority fall into one of two categories: (1) Foetuses and young infants, when the gall-stones of pigment type are found at autopsy in subjects dying from some unrelated complaint. Here the gall-stones rarely give rise to symptoms. (2) Children usually in the second decade of life, when the adult type of disease with cholecystitis and lithiasis occasionally occurs and enables a pre-operative diagnosis sometimes to be made.

Acholuric jaundice is not an uncommon disease: there have been nineteen cases at the Hospital for Sick Children, Great Ormond Street, during the past ten years. If the conclusion is accepted that in these cases gall-stones are common, there must exist a third category—children of any age with acholuric jaundice associated with gall-stones of the pigment type. These stones being radio-opaque should be easily demonstrated; Roberts' two cases appear to be the only previous ones in which use was made of this fact in children.

Previously the diagnosis of cholelithiasis in a young child during life has only been made either when a stone was passed per rectum or at operation. I have been able to collect seven such cases from the literature in children under four years.

<table>
<thead>
<tr>
<th>DATE</th>
<th>AUTHOR</th>
<th>SEX</th>
<th>AGE</th>
<th>REMARKS</th>
</tr>
</thead>
<tbody>
<tr>
<td>1879</td>
<td>ANDUARD</td>
<td>?</td>
<td>Under 4 years</td>
<td>Gall: stone in faeces.</td>
</tr>
<tr>
<td>1880</td>
<td>MASSIE</td>
<td>F</td>
<td>4 years</td>
<td>Gall-bladder symptoms: stone in faeces.</td>
</tr>
<tr>
<td>1882</td>
<td>WALKER</td>
<td>M</td>
<td>3 months</td>
<td>Stone in faeces.</td>
</tr>
<tr>
<td>1884</td>
<td>RICARD</td>
<td>?</td>
<td>Under 4 years</td>
<td>Colic: stone in faeces.</td>
</tr>
<tr>
<td>1925</td>
<td>SNYDER</td>
<td>M</td>
<td>4 years</td>
<td>Cholecystitis and lithiasis found at operation for acute appendicitis.</td>
</tr>
<tr>
<td>1927</td>
<td>POTTER</td>
<td>?</td>
<td>3 years</td>
<td>Cholecystectomy (no details available).</td>
</tr>
<tr>
<td>1935</td>
<td>BROOKS et al.</td>
<td>M</td>
<td>4 years</td>
<td>Acholuric jaundice: gall-stone unsuspected until operation.</td>
</tr>
</tbody>
</table>

Case report

A female child aged three years and a quarter was admitted to the Hospital for Sick Children on March 4, 1938, on account of increasing jaundice. Six days previously the jaundice had first been noticed, and on that day there had been some mild abdominal pain, but no nausea or vomiting, and the child had seemed well and had taken her food normally. A day or two later it was noticed that the motions were pale and the urine dark. There had been no further pain, and apart from the increasing jaundice the child had not seemed unwell.

Past history.—The patient had had pertussis a year previously and tonsillec- tomy six months previously. There had been no previous jaundice or anaemia, the child having always been healthy.

Family history.—The parents were unrelated. The mother suffered from chronic nephritis, from which she has since died; at autopsy there were no findings suggestive of haemolytic disease. Neither parent had ever suffered from jaundice or anaemia, nor was there any history of these complaints amongst their relations. This inquiry included twenty-three first cousins of the patient. There had been one sibling, born a year before the patient. It was a month premature following an ante-partum haemorrhage, and lived one week.
**GALL-STONES WITH ACHOLURIC JAUNDICE**

**Condition on admission.**—A well-developed child, weighing twenty-eight pounds (normal for age thirty-four pounds). She was in apparently normal health except for intense icterus. The tongue was furred. The liver was palpable two fingersbreadths below the costal margin, was of normal consistency and was not tender. The spleen was not palpable. The temperature and pulse rate were normal.

Urine: bile salts and pigments + +, no excess urobilin.

**Van den Bergh (direct): + +.**

**Serum bilirubin:** 39 units; one week later, 9·5 units (normal up to 0·4 units).

**Plasma phosphatase:** 23·5 units; one week later 22·5 units (normal 5–20 units).

**Laevulose liver function test (oral): normal.**

**Sedimentation rate:** 33 mm. in one hour.

A tentative diagnosis of catarrhal jaundice was made, although it was recognized that there were two facts which were not typical: the onset with little or no constitutional upset and the unusually intense degree of icterus. However, the gradual return to normal of the colour of the urine and faeces appeared to confirm the diagnosis.

On March 18, 1938, the child was discharged home. She was then well, having gained one pound in a fortnight; icterus was just discernible; there was no anaemia clinically (no blood count was done at this time), but the liver was still enlarged.

On March 24, 1938, she was re-admitted with the following history: Three days after discharge she became unwell, drowsy, complaining of toothache and pains in the limbs; she appeared pale. Next day the urine was ‘tea-coloured’ and pallor was now severe. On the day before re-admission she became ill with fever and sweats; she passed several liquid stools which were almost black in colour.

**Condition on admission.**—The child was almost moribund, with gross pallor and a slightly icteric tinge. The liver was more enlarged than previously, but was not tender. The gall-bladder was not felt. The spleen was easily palpable. The temperature was normal and the pulse rate 140. The urine showed a slight excess of urobilin; bile salts and pigments were absent; there were 10 mgm. per cent. of albumin present. The faeces contained no blood; bile pigments were present.

**Blood picture:** Haemoglobin 20 per cent. ; red blood cells 1·06 millions; normoblasts 0·5 per cent. ; recticulocytes 0·1 per cent ; microcytosis + +, poikilocytosis +. White blood cells 19,300 per c.mm. (polymorphs 55 per cent. ; lymphocytes 29·5 per cent. ; monocytes 8 per cent.; basophils 1 per cent. ; neutrophil myelocytes 5 per cent. ; metamyelocytes 1·5 per cent.). Platelets 197,240 per c.mm.

On clinical examination and before a haematological examination was available, a diagnosis was made of yellow atrophy of the liver complicating a previous catarrhal jaundice. Treatment was thereupon instituted as follows: by means of an intravenous drip alternate transfusions were given of 10 per cent. glucose in saline, and of whole blood (mother as donor, the mother and child both being group A). In this way she received 100 grammes of glucose and 600 c.c.m. of blood during the course of the twenty-four hours. Following this her condition improved swiftly and her haemoglobin rose to 60 per cent. (table 1).
### Table 1

**Blood Picture in a Case of Acholuric Jaundice Showing Effect of Blood Transfusion During a Haemolytic Crisis, and of Subsequent Splenectomy. Note Disappearance of Spherocytosis Soon After Recovery from the Crisis**

<table>
<thead>
<tr>
<th>Days after crisis</th>
<th>0</th>
<th>1</th>
<th>2</th>
<th>4</th>
<th>9</th>
<th>16</th>
<th>20</th>
<th>29</th>
<th>35</th>
<th>42</th>
<th>43</th>
<th>48</th>
<th>58</th>
<th>136</th>
<th>330</th>
</tr>
</thead>
<tbody>
<tr>
<td>Haemoglobin per cent. (Haldane)</td>
<td>20</td>
<td></td>
<td></td>
<td></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>Red blood cells, millions</td>
<td>1.06</td>
<td>45</td>
<td>55</td>
<td>60</td>
<td>58</td>
<td>53</td>
<td>62</td>
<td>62</td>
<td>72</td>
<td>64</td>
<td>75</td>
<td>75</td>
<td>75</td>
<td>75</td>
<td>85</td>
</tr>
<tr>
<td>Colour index</td>
<td>1.0</td>
<td>2.86</td>
<td>3.5</td>
<td>3.16</td>
<td>2.9</td>
<td>3.04</td>
<td>3.34</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Reticulocytes per 100 R.B.C.</td>
<td>0.1</td>
<td>7.6</td>
<td>1.0</td>
<td>10.8</td>
<td>10.1</td>
<td>9.6</td>
<td>18.0</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Normoblasts per c.mm.</td>
<td>96</td>
<td>330*</td>
<td>351</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>65</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Erythroblasts per c.mm.</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>195</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Megaloblasts per c.mm.</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Fragility limits (normal 0.30-0.39 per cent.)</td>
<td>0.36-0.60</td>
<td>0.36-0.60</td>
<td>0.39-0.60</td>
<td></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>Anisocytosis</td>
<td>+ +</td>
<td>+ +</td>
<td>+ +</td>
<td>+ +</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>Spherocytosis</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</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>Van den Bergh (direct reaction)</td>
<td>2.8</td>
<td>1.7</td>
<td>2.1</td>
<td></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>Serum bilirubin (normal, up to 0.4 units)</td>
<td>19.3</td>
<td>15*</td>
<td>7.8</td>
<td>5.2</td>
<td>9.5</td>
<td>8.8</td>
<td>6.5</td>
<td>6.4</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>White blood cells, thousands</td>
<td>115</td>
<td>59</td>
<td>54</td>
<td>50</td>
<td>58</td>
<td>56</td>
<td>56</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Polymorphs, per cent.</td>
<td>55</td>
<td>57.5</td>
<td>59</td>
<td>54</td>
<td>50</td>
<td>58</td>
<td>56</td>
<td>56</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Basophils</td>
<td>1</td>
<td>0</td>
<td>0.5</td>
<td>2</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Eosinophils</td>
<td>0</td>
<td>0.5</td>
<td>5</td>
<td>6</td>
<td>2</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lymphocytes</td>
<td>29.5</td>
<td>15.5</td>
<td>27</td>
<td>32</td>
<td>40</td>
<td>32</td>
<td>38</td>
<td>38</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Monocytes</td>
<td>8</td>
<td>7.0</td>
<td>8.5</td>
<td>6</td>
<td>8</td>
<td>10</td>
<td>2</td>
<td>2</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Myelocytes</td>
<td>5</td>
<td>0.5</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Metamyelocytes</td>
<td>1.5</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Platelets, thousands</td>
<td>197</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

* These figures are approximate.
GALL-STONES WITH ACHOLURIC JAUNDICE

Meanwhile Dr. D. G. ff. Edward reported that the majority of the red cells were densely staining microcytes (microspherocytes). Microspherocytosis was obvious in the wet films for the first nine days after the crisis; thereafter the red cells appeared normal apart from well-marked anisocytosis and polychromasia. On the twenty-second day after the crisis a Price-Jones curve was constructed (fig. 1), and the following dimensions of the red cells estimated:

- Mean corpuscular haemoglobin: 25.5\% (normal 27–32).
- Mean corpuscular diameter: 7.3\mu (normal 6.7–7.7).
- Coefficient of variation: 10.2 (normal 5.7–7.3).
- Mean corpuscular volume: 110\mu^3 (normal 80–94).
- Mean corpuscular thickness: 2.6\mu (normal 1.7–2.5).
- Diameter-thickness index: 2.8 (normal 2.4–4.2).
- Volume-thickness index: 1.45 (normal <1.5 (Hill, 1938)).

![Price-Jones curve](fig.1.png)

**Fig. 1.**—Price-Jones curve, twenty-second day after haemolytic crisis. Normocytosis and anisocytosis shown. At this stage the reticulocytes numbered 10 per cent., accounting for the number of macrocytes present, 5 per cent. of the cells having diameters of over 9\mu. (By courtesy of Dr. C. J. C. Britton.)

These measurements confirm, on the whole, the absence at this time of spherocytosis: the cells are of normal average diameter, the diameter-thickness index is well within normal limits, and Haden’s volume-thickness index is just below the upper limit of normal as estimated recently by Hill (1938). In contrast to this change in shape undergone by the red cells following recovery from the crisis, their fragility was constantly increased [table 1, normal fragility limits for this age (washed cells), 0.30 to 0.39 per cent.].
The persistent fragility and high level of the reticulocytes (table 1) now suggested that the crisis had been superimposed upon a chronic haemolytic process. With this in mind the original attack of obstructive jaundice was reviewed, and the possibility arose that it had been due to a gall-stone. Cholecystography failed to demonstrate the gall-bladder, but a shadow suggestive of a stone was seen in the region of the gall-bladder.

Operation.—After a blood transfusion from a donor unrelated to the patient, splenectomy was performed by Sir Lancelot Barrington-Ward. A stone was found at the junction of the cystic and common ducts, and this, along with the gall-bladder, was removed. Convalescence was uneventful.

Pathological report.—(Dr. D. N. Nabarro)—

Spleen: weight ninety-seven grammes. Histology: the splenic pulp is largely replaced by a suffusion of blood. The Malpighian bodies are prominent, many with large germinal centres. The appearances are those seen in acholuric jaundice.

Gall-bladder: small and contracted with considerable thickening of the walls. Histology: the muscular layer is increased, the serosa oedematous and congested, and the epithelium normal. There is little evidence of inflammation. The appearances suggest simple hypertrophy due to obstruction, with slight inflammatory reaction in the mucosa.

Gall-stone: 1 × 0.5 cm., the appearance being that of a pigment stone.

Result.—The usual satisfactory effect of splenectomy on the blood picture was seen (table 1), and the signs of abnormal haemolysis disappeared. One year later the child was very well. The liver was now not enlarged. The only abnormal findings were persistent anisocytosis and fragility of the red cells.

Discussion

Three features of the case require comment: the familial aspect of the disease, the nature of the crisis and the transient appearance of microspherocytosis.

1. No evidence was obtained that other members of the patient's family suffered from acholuric jaundice. Although both the child's father and mother were somewhat anaemic (haemoglobin 75 per cent. and 70 per cent. respectively), the fragility of their red cells was found to be normal, using a qualitative method. No attempt was made to employ a more delicate method in order to uncover slight departures from the normal, as suggested by Vaughan (1936), nor was it possible to estimate the fragility of the red cells of other relatives of the patient.

2. The history of dark motions and dark urine forms the chief evidence upon which is based the assumption that the acute anaemia was caused by a haemolytic process. Actually the signs of active haemolysis were largely absent by the time the child was seen in hospital, as the level of urobilin in the urine was then only moderately raised. The absence of blood in the faeces appeared to rule out the possibility that a cryptic haemorrhage had caused the sudden development of anaemia. The absence of any past history of anaemia or of jaundice (apart from the obstructive jaundice accounted for by the gall-stone), is noteworthy in contrast to the presence of the pigment stone, which is strongly indicative of a long-standing haemolytic process.
GALL-STONES WITH ACHOLURIC JAUNDICE

3. Microspherocytosis was apparent in the blood films during the first nine days following the haemolytic crisis. Thereafter the red cells were shown to be within the limits of normality in this respect, though their dimensions showed perhaps a slight tendency to what Vaughan (1937) has described as megalospherocytosis; that is, a thick cell with a normal or large diameter and so having a large corpuscular volume. This change in shape of the red cells after the crisis was not reflected in their fragility, which remained constantly raised.

It is not proposed to discuss here the whole question of the significance of spherocytosis and of its relation to fragility. Much recent work on this subject has shown that it is more complex than had been thought hitherto. It will suffice to indicate the contributions which the study of this case can make towards the different theories.

Briefly there are two views: one regards spherocytosis as the essential abnormality which absolutely distinguishes familial acholuric jaundice from the other haemolytic anaemias. This theory was initiated by Naegeli in 1919 and elaborated by Haden (1934).

The opposite view is that spherocytosis is not pathognomonic of any one form of haemolytic anaemia, but may occur whenever active haemolysis is present. On this theory spherocytosis results from the effect of haemolysins on the red cell. Convincing clinical and experimental evidence in favour of this view has recently been produced by Dameshek and Schwartz (1938).

Whichever view of the significance of spherocytosis is accepted, it has usually been concluded that fragility was a manifestation of, and hence ran parallel to, spherocytosis. Haden and Dameshek and Schwartz all emphasize this. A number of workers, however, have shown that in acholuric jaundice splenectomy usually abolishes the spherocytosis while leaving the fragility unaltered (Hawksley, 1936; Vaughan, 1937). This fact favours an alternative view, that fragility, not spherocytosis, is the pathognomonic feature of acholuric jaundice. It is important to emphasize that in acholuric jaundice the fragility tends to be persistently raised, because in acute haemolytic processes, such as that of Lederer, increased fragility may occur temporarily (Parsons and Hawksley, 1933; Joules and Masterman, 1935), but does not persist after the haemolysis is over (Dameshek and Schwartz, 1938).

On the basis of these various opposing theories, the facts of the reported case may be regarded as follows:

The appearance of spherocytosis at the haemolytic crisis, and its virtual disappearance subsequently, is in keeping with the view that spherocytosis is associated with active haemolysis, rather than that it is the cause of it. At the same time it is worthy of note that no support is furnished in favour of the existence of haemolysins in this disease. Thus two blood transfusions, one just after the crisis and one later, proceeded without reaction, the first being even particularly effective therapeutically. Before each transfusion the patient's serum was mixed with the donor's red cells for fully half an hour without haemolysis being observed. These findings are in contrast to those of Dameshek and Schwartz and others, who have demonstrated haemolysins in the patient's serum and have proved that blood transfusion in these cases is ineffective or even dangerous.

That the fragility of the red cells remained persistently raised after their
shape had returned from spherocytic to normal argues against the theory that fragility is a function of spherocytosis. It favours, on the contrary, the view that such a persistent fragility is the essential feature of one group of the haemolytic anaemias.

There remains to discuss the justification for describing the case as one of acholuric jaundice. According to Vaughan (1936), acholuric jaundice can be clearly differentiated from all other haemolytic anaemias, as every case can be shown to have abnormal fragility, as also have some of the relatives. As has been stated, the exclusion of this familial aspect of the disease was not complete, and its apparent absence hence of no significance. On the other hand, the abnormal fragility of the patient's cells was persistent and well marked. The chronic nature of the haemolytic process was shown by the reticulocytosis which persisted during the six weeks between the crisis and splenectomy, and also by the presence of a pigment gall-stone. Lastly the splenic histology was characteristic of acholuric jaundice. In spite, therefore, of the striking transience of the spherocytosis, this case falls within the acholuric jaundice group.

A NOTE ON THE CRICES OF ACHOLURIC JAUNDICE

Many authors emphasize that severe degrees of anaemia are rarely met with in acholuric jaundice. Some cases, however, are on record in which the haemoglobin has been reduced to 20 per cent. or less during an acute haemolytic crisis (Kahn, 1913; Nobel, 1914; Götzky and Isaac, 1914; Salmonsen, 1926; Jørgensen and Warburg, 1927; Scott, 1935; Murray-Lyon, 1935; Dedichen, 1937). A study of these cases of severe crises results in the following conclusions:

1. Severe crises occur chiefly in children.
2. There is usually fever and the appearances of an infection, though no infective agent is discoverable.
3. Intestinal symptoms are common, such as vomiting, diarrhoea, and abdominal pain.
4. Jaundice is slight.
5. Blood picture: the blood picture at the height of the crisis in ten representative cases is set out in table 2. In all these cases the haemoglobin was reduced to below 30 per cent. Although the blood picture in these ten cases is not uniform, yet the following description can usefully be given.

RED CELLS: Normoblasts and megaloblasts are often numerous. The reticulocyte count at the height of the crisis is generally normal. Microspherocytosis is usually marked.

WHITE CELLS: Some degree of leucocytosis is common, often absent and occasionally extreme (cases 2, 3, 9). The most striking feature of the differential count is the presence of primitive granulocytes, myelocytes, and less often metamyelocytes and myeloblasts in the majority of cases.

6. Effect of blood transfusion: eight out of the ten cases received blood transfusions, and in seven of these an immediate clinical improvement followed,
BLOOD PICTURE IN TEN CASES OF ACHOLURIC JAUNDICE WITH SEVERE HAEMOLYTIC CRISIS. NOTE THE TENDENCY TO LOW RETICULOCYTE LEVEL BEFORE TRANSFUSION

<table>
<thead>
<tr>
<th>CASE</th>
<th>AUTHOR</th>
<th>AGE</th>
<th>HAEMOGLOBIN, PER CENT.</th>
<th>RED BLOOD CELLS, MILLIONS</th>
<th>COLOUR INDEX</th>
<th>SPHEROCYTOSIS OR MICROCYTOSIS</th>
<th>RETICULOCYTES BEFORE TRANSFUSION, PER CENT.</th>
<th>RETICULOCYTES AFTER TRANSFUSION, PER CENT.</th>
<th>NORMOBLASTS, PER CENT.</th>
<th>MEGALOBLASTS, PER CENT.</th>
<th>WHITE BLOOD CELLS, THOUSANDS</th>
<th>PRIMITIVE WHITE BLOOD CELLS</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Götzky and Isaac</td>
<td>9</td>
<td>20</td>
<td>1:1</td>
<td>0:9</td>
<td></td>
<td>12:5</td>
<td>4:6</td>
<td>11:5</td>
<td>3:5</td>
<td>27:3</td>
<td>Myelocytes, 9 per cent.</td>
</tr>
<tr>
<td>2</td>
<td>&quot;</td>
<td>3</td>
<td>12</td>
<td>1:2</td>
<td>0:5</td>
<td></td>
<td>12:5</td>
<td>4:6</td>
<td>11:5</td>
<td>3:5</td>
<td>27:3</td>
<td>Myelocytes, 15:5 per cent.</td>
</tr>
<tr>
<td>3</td>
<td>Jørgensen and Warburg</td>
<td>9</td>
<td>20</td>
<td>1:1</td>
<td>0:9</td>
<td>+</td>
<td>12:5</td>
<td>4:6</td>
<td>11:5</td>
<td>3:5</td>
<td>27:3</td>
<td>Myelocytes ++</td>
</tr>
<tr>
<td>4</td>
<td>Scott</td>
<td>2</td>
<td>20</td>
<td>1:0</td>
<td>0:9</td>
<td>+</td>
<td>12:5</td>
<td>4:6</td>
<td>11:5</td>
<td>3:5</td>
<td>27:3</td>
<td>Myeloblasts +</td>
</tr>
<tr>
<td>5</td>
<td>&quot;</td>
<td>5</td>
<td>17</td>
<td>0:8</td>
<td>1:1</td>
<td>+</td>
<td>12:5</td>
<td>4:6</td>
<td>11:5</td>
<td>3:5</td>
<td>27:3</td>
<td>Myelocytes, 12 per cent.</td>
</tr>
<tr>
<td>6</td>
<td>&quot;</td>
<td>8</td>
<td>20</td>
<td>0:8</td>
<td>1:1</td>
<td>+</td>
<td>12:5</td>
<td>4:6</td>
<td>11:5</td>
<td>3:5</td>
<td>27:3</td>
<td>Myelocytes, 5 per cent.</td>
</tr>
<tr>
<td>7</td>
<td>&quot;</td>
<td>7</td>
<td>26</td>
<td>1:5</td>
<td>0:9</td>
<td>+</td>
<td>12:5</td>
<td>4:6</td>
<td>11:5</td>
<td>3:5</td>
<td>27:3</td>
<td>Myelocytes +</td>
</tr>
<tr>
<td>8</td>
<td>Murray-Lyon</td>
<td>10</td>
<td>16</td>
<td>0:8</td>
<td>0:3</td>
<td>+</td>
<td>12:5</td>
<td>4:6</td>
<td>11:5</td>
<td>3:5</td>
<td>27:3</td>
<td>Myelocytes +</td>
</tr>
<tr>
<td>9</td>
<td>&quot;</td>
<td>3</td>
<td>27</td>
<td>1:7</td>
<td>0:8</td>
<td>+</td>
<td>12:5</td>
<td>4:6</td>
<td>11:5</td>
<td>3:5</td>
<td>27:3</td>
<td>Metamyelocytes, 1:5 per cent.</td>
</tr>
</tbody>
</table>
which coincided with a sudden and sustained rise in the reticulocyte count from a low figure to from 4 to 41 per cent. (The exception was case 8, which only responded in this way after a second transfusion. Case 9 was the only one with a fairly high reticulocyte count at the crisis, but here transfusion raised the reticulocyte level from 5 to 41 per cent).

From the records of these cases it is difficult to avoid the conclusion that the recovery which followed transfusion was not merely coincidental. Nevertheless, that recovery can occur spontaneously from even the severest crises, is shown by cases 1 and 2, in which recovery occurred, though more slowly than in the remaining eight cases which received transfusion.

**Differential diagnosis of acute haemolytic anaemia**

A description of the acute haemolytic anaemia of Lederer as seen in childhood has recently been given by Parsons (1938). His description resembles in a striking way that given above of the crises of acholuric jaundice. Both diseases occur often in the young, and the symptomatology of their onset is similar. As regards the blood picture, Parsons describes what he terms the ‘aregenerative phase,’ in which reticulocytosis may at first be absent, red cell regeneration being preceded by a leucocytosis with many primitive granulocytes. Finally, cases of Lederer’s anaemia respond immediately to blood transfusion, in the same way as do the majority of severe acholuric crises.

This similarity between the two types of acute haemolytic anaemia has been noted by others. One of Murray-Lyon’s cases was at first thought to be a Lederer’s anaemia. Vaughan (1936) stresses the inadequate fragility investigations recorded in published cases of Lederer’s anaemia, and considers that these were probably examples of acholuric jaundice. West-Watson and Young (1938) also emphasize the slender evidence on which differentiation of the two diseases is supposed to be made.

It has been shown that an acholuric crisis or a Lederer’s anaemia may give no past history of illness, may present an identical clinical and haematological picture, may have fragile red cells and may respond to transfusion. Microspherocytosis is usually, possibly always, present during a crisis of acholuric jaundice, and since macrocytosis is said to be characteristic of Lederer’s anaemia this is probably an important differential point. The work of Dameshek and Schwartz, however, suggests that spherocytosis may occur in any acute haemolytic process, so that its presence cannot be diagnostic of any particular type. It would seem, therefore, that the two types of acute haemolytic anaemia may be indistinguishable during the crisis.

After recovery from the crisis a Lederer’s anaemia returns haematologically to normal, so that the two following criteria should be satisfied:

(1) Differential fragility curves should be normal. (No cases of acholuric jaundice with normal fragility by the differential method has been described.)

(2) Reticulocytosis and other evidence of abnormal haemolysis should be persistently absent.

Published cases of Lederer’s anaemia have sometimes been fairly adequately
GALL-STONES WITH ACHOLURIC JAUNDICE

investigated as regards the second of these criteria (Parsons and Hawksley, 1933; Joules and Masterman, 1935), but not the first. This requires to be done.

Meanwhile it would seem best to regard acute haemolytic anaemia of the type under discussion as a syndrome. This syndrome occurs in several conditions in which the erythron is persistently abnormal, e.g. spherocytic, fragile or sickled. Occasional cases of leukaemia present the same syndrome, and in them blood transfusion may also bring about a remission.

The evidence that the syndrome also occurs in the absence of these conditions (i.e. Lederer's anaemia) is at present suggestive but inconclusive.

Summary

1. Gall-stones are probably more commonly associated with acholuric jaundice in children than is generally recognized.
2. Such cases may present with symptoms due to the gall-stones.
3. Diagnosis of such cases is simple, as the pigment stones are radio-opaque.
4. A case is described illustrating these points.
5. Microspherocytosis disappeared soon after a crisis: fragility was persistently raised. The significance of these facts is discussed.
7. Severe crises of acholuric jaundice tend to resemble those of Lederer's anaemia. The differential diagnosis is discussed.

Thanks are due to Dr. Donald Paterson and to Dr. Bernard Schlesinger for permission to report the case; to Sir Lancelot Barrington-Ward for kindly allowing the use of his case notes, and to Dr. D. N. Nabarro, Director of Pathology. Dr. W. W. Payne performed a number of biochemical investigations. Much help has been received in haematological matters from Dr. D. G. ff. Edward and from Dr. C. J. C. Britton, of the Middlesex Hospital.

References

ARSCHIVES OF DISEASE IN CHILDHOOD

Ricard (1884). *Thèse de Paris,* quoted by Potter.
The association of gall-stones with acholuric jaundice in children: Report of A Case in a Child Aged Three Years with a Note on the Crises of Acholuric Jaundice

Douglas Gairdner

Arch Dis Child 1939 14: 109-120
doi: 10.1136/adc.14.78.109

Updated information and services can be found at:
http://adc.bmj.com/content/14/78/109.citation

These include:

Email alerting service
Receive free email alerts when new articles cite this article. Sign up in the box at the top right corner of the online article.

Notes

To request permissions go to:
http://group.bmj.com/group/rights-licensing/permissions

To order reprints go to:
http://journals.bmj.com/cgi/reprintform

To subscribe to BMJ go to:
http://group.bmj.com/subscribe/