GAUCHER'S DISEASE

DIAGNOSIS BY STERNAL PUNCTURE AND IMPROVEMENT FOLLOWING SPLENECTOMY

BY

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The disturbance of lipoid metabolism, known as Gaucher's disease, is a relatively rare condition, although in the past twenty years there has been an increase in the number of reports of the disease, due to its more frequent recognition.

First described in France by Ernest Gaucher in 1882, the second report was made in England by Collier in 1895. Subsequent accounts mostly came from the Continent and America, and by 1926 Pick was able to collect thirty-nine authenticated cases from the literature, of which five were seen and reported by him personally. In 1929 Hoffmann and Makler collected and analysed eighty-nine reports. Since then case reports have gradually increased in number, and the total must now be nearing two hundred. The number of cases recorded from Britain form a comparatively small percentage of these.

The disease, apparently congenital, is due to an upset of lipoid metabolism, in which cerebroside (kerasin) is found in the typical Gaucher cells of the affected tissues and organs. The occurrence of the disease in several members of the same family has frequently been observed, and although there is slight evidence that it may be hereditary (Anderson, 1933; Bloem, Groen and Postma, 1936), such cases are exceptional.

It is noteworthy that many of the cases have occurred in Jews, although this is by no means a constant finding. Packman (1938) recorded the disease in a brother and sister who were negroes, and Aballi and Kato (1938) reported two cases in a Japanese family. Females are more often affected than males, and symptoms usually appear during the first decade of life, although several cases have been reported in which the symptoms did not appear till middle age (Bloem, Groen and Postma, 1936). The infantile type of the disease is acute and less typical (Oberling and Woringer, 1927; Moncrieff, 1930; Rowland, 1936; Aballi and Kato, 1938).

Case report

A Jewish boy, aged ten years, was brought by his parents to the Royal Infirmary, Manchester, on October 2, 1939. He complained of swelling of the abdomen, weakness and loss of flesh. His parents stated that they had noticed
that the child's abdomen had been swollen since infancy, and as time had gone
on this had become more pronounced.

Up to the age of nine the boy had felt perfectly fit and had had no com-
plaints. He was energetic, and was in the 'scholarship class' at school. In
the spring of 1938 he became listless and easily tired, but after his summer
holidays he seemed to improve. In the following November he complained of
pain in the left side of the chest and abdomen, and was admitted to a hospital,
where he remained for two weeks under observation.

The pain having disappeared he was discharged, but was re-admitted to the
same hospital two days later on account of epistaxis. On this occasion he was
reated with a prolonged course of oral iron and parenteral liver extract for
splenomegaly associated with anaemia and leucopenia. During this time
epistaxis, although not severe, had occurred on several occasions, and he had
also suffered from subconjunctival haemorrhages. His abdomen had become
more swollen and he had lost further weight. No pigmentation of the skin had
been noticed. He was discharged in July, 1939, and during the three months he
had been at home his condition had got progressively worse. There had been
no further haemorrhages, however. By September, 1939, the boy could only
walk a short distance on account of the dragging weight of his abdomen.

Previous health. At the age of eighteen months he had suffered from
enlarged cervical glands, but these had subsided in a few weeks. He had also
suffered from mild attacks of whooping cough, measles, ? scarlatina and
chickenpox. Since the age of nine years he had worn glasses on account of
myopia.

Family history. His sister, aged six years, had always been perfectly
healthy, as were his parents. Their clinical findings and blood counts were
normal. There was no known history of blood disease, jaundice or abdominal
swelling in his forebears on either side of the family.

Clinical examination. Clothed, the boy looked pale and ill. He had a
pronounced malar flush. The abdomen was very prominent, and he walked
with his shoulders thrown back so as to counteract the drag of the swelling.
Stripped, he looked a pathetic sight, there being gross abdominal swelling
associated with wasting of the thorax and limbs (fig. 1). The greatest circum-
ference of the abdomen was two inches above the umbilicus where it measured
twenty-eight inches. His weight was 3 stone 12 lb., and he was 4 feet 1 inch in
height. There was visible pulsation in the vessels of the neck, and a few small
dilated veins were noted in the epigastrium and around the umbilicus, which
was everted.

There was pronounced pallor of the skin and mucous membranes, and small
discrete movable glands were palpated in both sides of the neck, and in the
groins and axillae. There was no jaundice, cyanosis or oedema, and no evidence
of pigmentation of the skin, apart from a melanotic naevus below and to the
right of the umbilicus. The sclerae were of a bluish tinge but no pingueculae
were present. Both tonsils were considerably enlarged.

An enormous spleen could be felt filling practically the whole abdomen.
The margin of the hand could just be put between the lower edge of the spleen
and pubes. A splenic notch was easily felt. There was no abdominal tender-
ness. The liver was just palpable below the right costal margin. There were no
signs of ascites. The lungs were apparently clear; at the left base the per-
cussion note was impaired due to the enlarged spleen. Pulse rate varied from
80 to 90 per minute, and the heart sounds were soft, there being frequent extra-
systoles. Blood pressure 115/70 mm. Hg.

No abnormalities were noted on examination of the genito-urinary and
nervous systems. Apart from general pallor of the fundi no abnormality was
found on ophthalmoscopic examination.
Special investigations. Blood counts showed a hypochromic anaemia, associated with leucopenia and thrombocytopenia (table 1). The mean cell volume of the erythrocytes was 83 microns. Haemolysis of the red cells began at 0.46 per cent. saline and was complete at 0.32 per cent. saline. The direct van den Bergh reaction was negative, and the serum contained 0.8 units bilirubin.

Bleeding time was 2 min. 3 sec. (normal for method 2 to 5 min.), coagulation time 2 min. 40 sec. (normal for method 1½ to 3 min.). Examination of material obtained by sternal puncture showed a hyperactive cellular marrow with an increase of erythroblasts and normoblasts. Leucopoietic elements appeared reduced in number. In addition Gaucher cells, with typical reticulated cytoplasm and eccentric nuclei were seen. These characteristic large cells, however, were comparatively few in number.

Other investigations:

- Blood cholesterol . . . . . . 130 mgm. per cent.
- Blood lipoid phosphorus . . . 13.2 mgm. per cent.
- Blood fat . . . . . . 1.08 grammes per cent. (fasting).
- Serum calcium . . . . . . 10.6 mgm. per cent.
- Blood phosphatase . . . . 3.6 units (Bodansky's method).
- Blood urea . . . . . . 24 mgm. per cent.

The urine was normal as judged by routine tests. The Wassermann reaction gave an unsatisfactory result on two occasions, fixation of complement occurring in the absence of antigen. The Kahn and Meinicke tests were both negative.

Glucose and laevulose tolerance tests were within normal limits, and x-rays of the skeleton showed no changes in the bones, apart from a slight trabeculation in the middle thirds of both tibiae which, in the opinion of the radiologist, was probably not of pathological significance.

Subsequent progress. As his parents were unwilling that the boy should come into hospital, he was brought regularly by them to the out-patient clinics,
### Table 1

<table>
<thead>
<tr>
<th>DATE</th>
<th>2.10.39</th>
<th>9.10.39</th>
<th>2.11.39</th>
<th>8.11.39</th>
<th>23.11.39</th>
<th>8.2.40</th>
<th>11.4.40</th>
<th>13.6.40</th>
<th>20.7.40</th>
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<tr>
<td>Erythrocytes, per c.mm.</td>
<td>3,470,000</td>
<td>3,190,000</td>
<td>2,910,000</td>
<td>5,050,000</td>
<td>4,540,000</td>
<td>4,820,000</td>
<td>4,766,000</td>
<td>4,940,000</td>
<td>4,900,000</td>
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<td>Leucocytes, per c.mm.</td>
<td>3,600</td>
<td>1,800</td>
<td>3,000</td>
<td>5,800</td>
<td>16,000</td>
<td>24,400</td>
<td>26,800</td>
<td>12,800</td>
<td>19,600</td>
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<td>Haemoglobin, per cent. (Haldane)</td>
<td>62</td>
<td>54</td>
<td>46</td>
<td>74</td>
<td>80</td>
<td>89</td>
<td>90</td>
<td>93</td>
<td>92</td>
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<td>Colour index</td>
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<td>0.85</td>
<td>0.81</td>
<td>0.74</td>
<td>0.88</td>
<td>0.92</td>
<td>0.94</td>
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<td>Neutrophil polymorphs, per cent.</td>
<td>64.5</td>
<td>52.5</td>
<td>54.0</td>
<td>54.0</td>
<td>61.0</td>
<td>44.0</td>
<td>82.0</td>
<td>47.0</td>
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<td>Lymphocytes, per cent.</td>
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<td>41.5</td>
<td>41.0</td>
<td>38.0</td>
<td>28.0</td>
<td>40.0</td>
<td>17.0</td>
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<td>38.5</td>
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<td>Monocytes, per cent.</td>
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<td>6.0</td>
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<td>5.0</td>
<td>2.5</td>
<td>4.5</td>
<td>1.0</td>
<td>6.5</td>
<td>6.0</td>
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<tr>
<td>Myelocytes, per cent.</td>
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<td>Nil</td>
<td>1.0</td>
<td>2.0</td>
<td>Nil</td>
<td>Nil</td>
<td>Nil</td>
<td>Nil</td>
<td>Nil</td>
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<td>Eosinophils, per cent.</td>
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<td>Nil</td>
<td>Nil</td>
<td>1.0</td>
<td>8.5</td>
<td>11.5</td>
<td>Nil</td>
<td>5.5</td>
<td>3.5</td>
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<tr>
<td>Basophils, per cent.</td>
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<td>Nil</td>
<td>Nil</td>
<td>Nil</td>
<td>Nil</td>
<td>Nil</td>
<td>Nil</td>
<td>Nil</td>
<td>Nil</td>
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<tr>
<td>Platelets, per c.mm.</td>
<td>38,800</td>
<td>39,600</td>
<td>45,000</td>
<td>269,000</td>
<td>400,000</td>
<td>386,000</td>
<td>392,000</td>
<td>442,000</td>
<td>408,000</td>
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<td>Reticulocytes, per cent.</td>
<td>9.6</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>1.1</td>
<td>0.8</td>
<td>—</td>
<td>—</td>
<td>1.1</td>
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<td>Anisocytosis and poikilocytosis</td>
<td>Marked</td>
<td>Marked</td>
<td>Marked</td>
<td>Marked</td>
<td>Slight</td>
<td>—</td>
<td>—</td>
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A few nucleated red cells were noted in the peripheral blood during the week following the operation.
where he was treated with oral iron. By the end of three weeks, however, his general condition was deteriorating so rapidly that he had to be admitted. By this time the sternal puncture result had clinched the diagnosis of Gaucher's disease (fig. 2), and although operation risk seemed great the opinion of a surgeon was sought with a view to performing splenectomy. The patient's condition became even worse and he had another epistaxis on October 30, 1939. His temperature had been intermittently raised.

The boy's parents consented to the operation in spite of the obvious risk involved, and on November 8, 1939, after a pre-operative drip transfusion of 600 c.c. citrated blood, splenectomy was successfully carried out by Mr. H. H. Rayner.

The spleen was delivered through a right paramedian incision six inches in length. Dense adhesions were found between the upper pole of the spleen and the diaphragm and, on attempting to break these a necrotic area ruptured with the escape of grumous material, yellow in colour and odourless. The liver, which was enlarged about one-and-a-half inches below the right costal margin, was noted as being pale with fine yellowish mottling.

After the operation another drip transfusion, of 450 c.c. blood and 200 c.c. saline was given. The patient made satisfactory progress subsequently and five weeks later he was up and walking about. He felt very well and was putting on weight and improving in colour. Glands were still palpable in the neck, groins and axillae as before, although probably due to his improved nutrition they were not so easily detected (fig. 3).

The blood count figures rose dramatically after the transfusion and splenectomy (table 1), and this improvement was maintained without further treatment.

At the end of two months his weight was 4 stone 3 lb. Sternal puncture, at this time, showed the erythropoietic hyperplasia to have diminished, and the proportion of leucopoietic elements to have increased. Gaucher cells were...
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present in about the same numbers as before. Reticulocytes in the peripheral blood had fallen to normal. X-rays of the skeleton showed no pathological change.

At the beginning of April, 1940, he reported complaining of a sore throat and swollen cervical glands. His tonsils were greatly enlarged. Removal of tonsils and adenoids was performed by Mr. F. G. Wrigley on April 10, 1940. His general health has continued to improve up to the time of writing (nine months after the operation). Recently (July, 1940) his weight was 5 stone and sternal puncture showed Gaucher cells to be present in approximately the same numbers as before the operation. There was, however, no radiological evidence of disease throughout the skeleton.

Morbid anatomy of the spleen, tonsils and adenoids

The weight of the spleen removed at operation was 3,530 grammes. It was firm and of a dark purple colour with yellow mottling. The surface showed numerous infarcts of varying size and the capsule was thickened. There was a large ruptured necrotic area at the upper pole where it had been adherent to the diaphragm (fig. 4). On section the spleen was dense in consistency and of a deep red colour. Numerous small greyish-white spots were noted on the cut surface. Histological examination showed the spleen to be packed with Gaucher cells and the lymphoid follicles were widely separated from one another. The large characteristic Gaucher cells varied in shape and size, but were mostly spherical or ovoid. The great majority of them had a relatively small single nucleus, often eccentrically placed within the cell but some were multinuclear. The cytoplasm of the cells was pale and reticulated and some showed vacuoles. These appearances were well seen in sections stained with Mallory's stain and Masson III in paraffin sections of both formalin and Helly fixed material (fig. 5). Frozen sections, stained by Sudan III, did not show any fat staining. The Schultze reaction for cholesterol was negative. Frozen sections of formalin fixed spleen and also fresh dry smears from bone marrow did not show any doubly-refractile bodies in the Gaucher cells under ordinary conditions, but when mounted in pure glycerin and employing a strong illuminant feebly anisotropic bodies suggesting the form of vesicular crystals were seen in the cells. These apparently crystalline forms corresponded very well to the spaces present in the reticulated cytoplasm of the cells. This appearance, possibly due to the refractive index of the mounting medium, was present at room temperature and was not increased to any appreciable extent by heating and cooling the frozen sections of the spleen. Heating in water was not found
to cause doubly-refractile bodies to appear in the cells (cf. Graham and Blacklock, 1927).

Histological examination of the tonsils and adenoids, removed at operation, showed signs of chronic inflammation but no Gaucher cells were found.

**Chemical analysis of the spleen**

(In collaboration with Dr. F. X. Aylward)

Six hundred and twenty grammes of the spleen were minced and extracted with three litres of cold alcohol and three litres of ether. The alcohol-ether extract contained most of the glyceride cholesterol and phosphatides of the spleen. The residue was extracted exhaustively with chloroform at 60° C. and filtered through a hot funnel. The hot chloroform extract contained mainly cerebrosides and sphingomyelin. The extract was taken to dryness and weighed. 20·9 grammes were obtained, or approximately 4 per cent. of the wet weight of the spleen.

The solid obtained agreed with the known properties of cerebrosides, being insoluble in cold alcohol and ether, and being soluble in hot alcohol or hot chloroform. On cooling these hot concentrated solutions a white precipitate readily appeared, in the form of a gel.

On crystallizing out from a dilute hot alcoholic solution, a white solid resulted which macroscopically appeared to have a definite crystalline form. Under the microscope crystalline needles which formed star-shaped aggregations, somewhat similar to crystals of kerasin illustrated by Pick (1933) were seen (fig. 6). The form of the crystals varied in arrangement but were mostly star shaped. Under the polarizing microscope they were strongly doubly-refractile.

Of the crude material obtained 3·3 grammes were dissolved in hot alcohol, precipitated with saturated solution of HgCl₂ and the precipitate separated off by centrifuging. The precipitate was dissolved in hot alcohol and Hg was removed by means of H₂S. The filtered solution was then taken to dryness and recrystallized from alcohol yielding 0·86 grammes of a white solid.

**Fig. 5.—Gaucher cells in spleen. (Masson III × 300.)**
The physical properties of the purified material were similar to those of the crude dry extract. Similar doubly-refractile crystals were obtained. Analysis showed that phosphorus was absent, thus excluding sphingomyelin. Micro-

![Crystalline aggregations of kerasin obtained from Gaucher spleen (x 400).](image)

analysis of the purified material (Weiler and Strauss, Oxford) gave the following percentages:

<table>
<thead>
<tr>
<th></th>
<th>C</th>
<th>H</th>
<th>N</th>
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<tbody>
<tr>
<td></td>
<td>70-26</td>
<td>11-21</td>
<td>2-2</td>
</tr>
</tbody>
</table>

The results reported compare favourably with the findings of several other workers (table 2), although the nitrogen figure is somewhat higher.

<table>
<thead>
<tr>
<th></th>
<th>C PER CENT.</th>
<th>H PER CENT.</th>
<th>N PER CENT.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lieb (1927)</td>
<td>...</td>
<td>69-76</td>
<td>11-24</td>
</tr>
<tr>
<td>Lieb and Mladenonic (1929)</td>
<td>...</td>
<td>70-74</td>
<td>11-35</td>
</tr>
<tr>
<td>McConnell, Forbes and Apperley (1939)</td>
<td>...</td>
<td>70-60</td>
<td>11-23</td>
</tr>
<tr>
<td>Present Case</td>
<td>...</td>
<td>70-26</td>
<td>11-21</td>
</tr>
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</table>

Examination of the crystals (Dr. H. E. Buckley) employing the selenite plate test as described by Rosenheim (1914) showed that the appearances were consistent with the substance being pure kerasin. No phrenosin was present as judged by this test.
Gaucher's disease: etiology and pathology

Gaucher originally described the condition as a primary epithelioma of the spleen, whereas Bovaird (1900) considered it to be an endothelial hyperplasia of the spleen, liver and lymph nodes. Brill, Mandlebaum and Libman (1905) first discovered the typical cells in the bone marrow, and in 1907 Schlagenhauffer designated the condition an affection of reticulum cells of all the lymphatic and haemopoietic organs. In the same year Marchand emphasized the importance of the foreign substance in the cells.

Mandlebaum and Downey (1916) founded the modern conception of the disease as a metabolic disturbance, and Lieb (1924) and Epstein (1924) showed that the cerebroside, kerasin, was the abnormal substance stored. It is now recognized that reticulum cells are almost exclusively affected by the disease, but the exact nature of the process is unknown. Whether 'storage' corresponds to an increased ingestion or diminished excretion by the cells involved, remains an open question. Pick (1933) favours the view that increased intake by the cells is the most likely explanation, although Jaffé (1938) quotes Tropp as holding the view that the piling up of kerasin in affected cells is due to a defect of mobilization and transport, or an increased production by the cells, and Tannhauser (1933) suggests that kerasin is produced at the expense of either the sphingomyelin or sphingosine present in the body.

Certain workers (Lieb and Mladenonic, 1929; Capper, Epstein and Schless, 1934) have reported the presence of small amounts of phrenosin as well as kerasin in Gaucher spleens, but the amount is small and is not constantly found (McConnell, Forbes and Apperly, 1939). The cholesterol content of the spleen is not increased (Cushing and Stout, 1926; Thomson and Wright, 1937).

According to Rosenheim (1916) the formula for kerasin is C_{47}H_{91}O_{8}N + H_{2}O, and analyses have shown that kerasin may form up to 10 per cent. or more of the dry weight of the spleen. Cushing and Stout (1926) found crude cerebroside to form 16 per cent. of its dry weight. Chemical studies of the blood have failed to show any definite changes.

The morbid anatomy of the disease gives a clear-cut picture, although the degree of involvement of various organs varies considerably. The spleen may weigh over 8,000 grammes (Brill, Mandlebaum and Libman, 1909), and although the liver enlargement is relatively less it is frequently twice its normal weight (Pick, 1933). Bone marrow and lymphatic glands (more frequently intrathoracic and intra-abdominal) are also affected, and rarely the lungs (Merklen, Waitz and Warter, 1933; Myers, 1937) and kidney (Horsley, Baker and Apperly, 1935) may contain Gaucher cells. Although it is likely that Gaucher cells may be present in the brain and meninges (Myers, 1939) definite evidence of this appears to be lacking.

The characteristic Gaucher cells found in affected organs and tissues are of large size (20 to 80 μ in greatest diameter) with pale reticulated cytoplasm in which vacuoles may be seen. The nucleus is relatively small and eccentrically placed and multinuclear cells may be found occasionally. They are ovoid or polyhedral in shape, although those present in bone marrow are frequently elongated, with an irregular cytoplasmic outline.

In the spleen and liver haemosiderin deposits occur in endothelial cells, but the Gaucher cells themselves contain hardly any pigment. Those in lymphatic
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Glands contain haemosiderin in greater quantity (Pick, 1933). The cells do not react with stains for fatty substances, and are not doubly refractile. Graham and Blacklock (1927) made the observation that if frozen sections of fresh spleen were heated in water or glycerin to 100°C, the cells took on Sudan III stain to a slight extent and became doubly refractile. They attributed this phenomenon to hydrolysis or the running together of lipoids present in the diffuse phase. Although the lipoid substance is not doubly refractile in fresh tissues under ordinary conditions, it appears anisotropic after chemical extraction and crystallization, as was shown in the present case.

The disease is associated with a hypochromic anaemia, although in some cases this may be slight (Bonta, 1930). Leucopenia, frequently with relative lymphocytosis, is almost constantly present. The finding of a 'rather marked leucocytosis' (Enzer, 1933) must be regarded as exceptional. Thrombocytopenia is also a feature of the disease. Hyperfunction of the spleen and involvement of the bone marrow by Gaucher cells have both a part in causing anaemia.

Clinical findings and the course of the disease

In the infantile type of the disease, the clinical picture is usually one of acute involvement of the nervous system, there being paralysis, nuchal rigidity and opisthotonus associated with cachexia and enlargement of the spleen and liver. These cases are rapidly fatal.

The chronic form of the disease may be present for several decades before giving rise to symptoms, although the condition is usually recognized in childhood. The splenic enlargement may be detected in routine examination, or medical advice may be sought on account of abdominal distension, discoloration of the skin or haemorrhages.

An ochre pigmentation of the skin, more especially of the exposed parts, has been found in approximately half the cases reported. Bloem, Groen and Postma (1936) noted a patchy pigmentation of the legs, which had a sharply defined lower margin, just below the ankles. About 15 per cent. of the cases exhibit wedge-shaped thickenings of the sclerae (Hoffmann and Makler, 1929). Pick (1933) regards both these phenomena as evidence of haemochromatosis which becomes more pronounced during the course of the disease. Malar flush and myopia have been noted in several cases by Bloem, Groen and Postma (1936).

The spleen is greatly enlarged and may extend into the pelvis. Enlargement of the liver is also present but is relatively less than that of the spleen. Only occasionally are superficial lymphatic glands involved. Pains in the lower ends of the femora, tibiae, sternum or spine indicate skeletal involvement by the disease process, and swellings near the joints may be present. On occasion bone involvement has been so pronounced as to warrant the term 'osseous form of Gaucher's disease' (Pick, 1926; Melamed and Chester, 1938).

The course of the disease is slowly progressive and some cases live to over fifty years of age. Even with the enormous enlargement of the spleen and liver...
symptoms may be extraordinarily slight. Death takes place from intercurrent disease, leucopenia favouring infection. In the terminal stages cachexia may be pronounced.

Diagnosis

In the differential diagnosis of the disease the following conditions must be excluded: leukaemia, haemolytic anaemia, ‘splenic anaemia,’ congenital syphilis, tuberculosis, rickets, Niemann-Pick’s disease, Tay Sachs’ disease and parasitic infections such as malaria. Some cases of the osseous type of the disease have been primarily regarded as osteomyelitis (Capper, Epstein and Schless, 1934; Myers, 1937). The infantile type may simulate intracranial disease such as meningitis.

Blood examination and probability help to rule out many of the above possibilities. There are no pathognomonic signs or symptoms, but the finding of leucopenia and thrombocytopenia associated with gross splenomegaly and liver enlargement should always bring to the mind the possibility of Gaucher’s disease; if in association with skin pigmentation and thickenings of the sclerae the diagnosis is even more likely. X-rays may show destructive changes and rarefaction of the bones, and flask-like expansions of the lower ends of the femora (Junghagen, 1926; Reiss and Kato, 1932; Welt et al., 1929; Worth, 1936).

Only by biopsy can an absolute diagnosis be made. The method most frequently described is that of splenic puncture. Originally described by Bernstein (1915) it has been reported as a reliable method devoid of danger (Graham and Blacklock, 1927). Excision of a lymph gland has also been described as a method of making a pathological diagnosis (Hoffmann and Makler, 1929). There are now several cases on record in which examination of the bone marrow has effected an absolute diagnosis. Among these may be quoted the reports by Welt et al. (1929), Sokolowsky (1932), Fleischhaker and Kilma (1936), Aballi and Kato (1938) and Schartum-Hansen (1938). However, a case described by Schleussner and Schnee (1939) showed no Gaucher cells on sternal puncture, but splenic puncture established the diagnosis. Thus, although it cannot be claimed that the absence of the typical cells excludes the possibility of Gaucher’s disease, a positive result dispenses with the procedure of splenic puncture, a proceeding to be avoided if possible in a patient with a haemorrhagic diathesis.

Treatment

Medical treatment of the disease is unsatisfactory; Potter and Macrae (1933) noted some clinical improvement following injections of liver extract, but other patients, including the one described here, have failed to show any benefit from this form of treatment. Radiotherapy may cause some diminution in size of the spleen, but has no effect on the course of the disease (Pick, 1933).

With regard to splenectomy, opinions are divided. Some authorities state that the operation is contraindicated, whilst others claim successful results following removal of the spleen. Pick (1933) states that the operation is
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associated with a mortality of about 20 per cent. and that in most cases removal of the spleen causes skeletal involvement to become more pronounced. He admits, however, that a number of cases show improvement in general nutrition and condition of the blood after the operation, and that from a symptomatic standpoint splenectomy has a definite value.

Reviewing the literature there is now a fair proportion of cases where the operation has resulted in marked general improvement, and although no claim can be made of a 'cure' the patients may remain in a satisfactory clinical condition for many years.

Hunter and Evans (1929) recorded a case of a woman aged sixty, who was well thirteen years after splenectomy. They stated that the operation caused complete relief of symptoms. The Mayos (1935) reported a series of nine cases treated by splenectomy, in which there were two hospital deaths and two deaths subsequently. Five of the patients were alive, one of them having had four children during the eleven years following the operation.

Ogilvie (1937) operated on two sisters suffering from Gaucher's disease; one of them who had marked skeletal involvement died six hours after splenectomy, but the other was well two years afterwards, with a normal blood picture.

Among others who found splenectomy to be followed by general improvement may be mentioned Mandlebaum (1919), Bloom (1925), Graham and Blacklock (1927), Bonta (1930), Capper, Epstein and Schless (1934), Lowinger (1935), Bessie (1937), Pack and Silverstone (1938) and Webster (1938).

The size of the spleen is no contraindication to the operation; Ogilvie (1937) successfully removed one weighing 13 1/2 lb. Although the procedure is admittedly associated with risk, it is justifiable from the standpoint that all other forms of treatment are useless. It is hardly worth while considering the operation when skeletal involvement is present to any appreciable extent. Haemorrhagic diathesis does not necessarily exclude the performance of splenectomy, but in such cases pre-operative transfusions are required.

It is not possible to state how long a patient may remain well after the operation, but the resulting improvement may be maintained for many years, although this is by no means always the case. Detailed reports of cases followed up after operation are not numerous, but it would seem that some cases may remain well for fifteen years or more after splenectomy. Naturally the degree of involvement of other organs besides the spleen at the time of operation bears a direct relationship to the prognosis. In an appreciable number of cases splenectomy seems to have checked the progress of the disease to some extent. The ultimate prognosis, however, is always bad.

Comment

The history and clinical and haematological findings in the case described strongly suggested a diagnosis of Gaucher's disease. The superficial lymphadenopathy was of interest as very few of the recorded cases have shown this.

The absence of skin pigmentation, thickenings of the sclerae and x-ray evidence of skeletal involvement, in spite of the apparent advanced stage of the
disease, were also noteworthy. The anaemia did not respond to iron or liver extract.

The pathological diagnosis, made by sternal puncture, obviated the employment of splenic puncture, which was considered hazardous on account of the low platelet count and poor general condition of the child.

It is suggested that sternal puncture which causes the patient little or no inconvenience should always be performed before splenic puncture in a suspected case. The former has the additional value of giving information concerning the haemopoietic activity of the marrow, and can exclude such conditions as atypical leukaemias.

The spleen (3,530 grammes) formed slightly over an eighth of the body weight of the patient. His immediate post-operative improvement was striking. The platelet count rose to 680,000 per c.mm. then gradually fell to within the normal range. Without further treatment eight months after splenectomy, the anaemia had improved, the red cell count and haemoglobin values being normal. The leucocyte count, which rose abruptly following the operation, remained at a level above the normal limits, and a proportional increase of eosinophils was frequently observed.

Although sternal puncture performed during the eight months following the operation showed Gaucher cells present in about the same numbers as before no radiological evidence of osseous disease was noted.

The boy’s general condition has continued to improve dramatically since the operation. Examination of his tonsils and adenoids, which were removed on account of chronic enlargement, failed to show any Gaucher cells. Chemical investigations carried out on the spleen gave results comparable with those of other workers. A lipoid fraction obtained, which was insoluble in ether and soluble in hot alcohol, was identified as cerebrosides.

**Summary**

(1) A case of Gaucher’s disease occurring in a nine-year-old Jewish boy is described.

(2) Diagnosis was effected by sternal puncture.

(3) There was great clinical improvement following splenectomy.

(4) Chemical analysis showed that crude cerebrosides formed approximately 4 per cent. of the wet weight of the spleen. This material, when purified, was shown to have the physical and chemical characteristics of kerasin.

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**References**

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