ADULT GAUCHER'S DISEASE, WITH SPECIAL REFERENCE TO THE
VARIATIONS IN ITS CLINICAL COURSE AND THE VALUE OF
STERNAL PUNCTURE AS AN AID TO ITS DIAGNOSIS

By J. Groen, M.D., and A. H. Garrer, M.D.

GAUCHER'S disease is a rare, often familial disease, distinguished by the
presence of characteristic cells in the organs of the reticulo-endothelial
system (spleen, liver, lymph glands, bone marrow). The protoplasm of these
cells has a typical cytologic appearance due to the presence of a special lipoid,
the so-called Gaucher substance or kerasin.

The increase in our knowledge of the underlying pathologic process has gradually
facilitated the possibility of a clinical diagnosis during life. Gaucher described
the disease in 1882 as an "idiopathic hypertrophy of the spleen, without leu-
kemia," but he mentioned in his paper that in the course of the disease the liver
also became enlarged. Another sign, the swelling of lymph glands, has proved of
little diagnostic value as the swollen glands are usually situated inside the body.
An important observation, of help in diagnosis, may be a peculiar yellow pig-
mentation which develops in some of the cases on the face and in the conjunctivae
in the form of wedge-shaped pingueculae. Bloem, Groen and Postma and
Kveim drew attention to the presence of a characteristic pigmentation that
occurred fairly commonly on the lower legs in their patients suffering Gaucher's
disease. If present, this pigmentation is almost pathognomonic of this condition.
Bloem, Groen and Postma described a few other minor signs that might be of
additional help in the diagnosis; viz., the presence of a peculiar malar flush and
the occurrence of myopia.

Examination of the blood may yield further useful information: a hypochromic
anemia with leukopenia and thrombopenia are usually present, the cholesterol
content of the blood is normal or very often, low. However, this hematologic
syndrome occurs also in other conditions associated with splenomegaly so that its
diagnostic importance is not decisive. The majority of patients exhibit some degree
of hemorrhagic diathesis.

X-ray examination has supplied us with another means of supporting a clinical
diagnosis of Gaucher's disease. Some of the early investigators, most notably
Brill, Mandlebaum and Libman, demonstrated that Gaucher cells accumulate in
various parts of the bones where they ultimately produce macroscopic areas of
bone destruction. Further experience has shown that these bone lesions, although
they may occur almost anywhere, show a predilection for certain areas. The head
and neck of the femur are often affected, which gives rise to a typical x-ray picture.
The lower ends of the femora often contain so many Gaucher cells that they become
swollen and present a shape similar to an Erlenmeyer flask.

Even in the presence of these clinical signs, however, a diagnosis of Gaucher's
disease could very often not be made with absolute certainty. The introduction of the sternal puncture was therefore a great advance. It is the purpose of this paper to present some cases of Gaucher’s disease with special reference to the importance of sternal puncture as an aid to the diagnosis. At the same time this will give us an opportunity to describe the clinical features which these cases presented. Some of the cases have been described by others, and by one of us, years ago and it seems appropriate to present their development since that time.

Case Reports

Case I

Mrs. E. R. B., born in 1890, a Jewish married woman, was first seen in the out-patient department on January 5, 1938.

History. The patient had always been a weak girl. When she was 13 years old she noticed a lump in the left side of the abdomen which grew slowly during the years that followed. A tendency to bleed manifested itself at an early age; later on bleeding was especially troublesome after tooth extractions and during menstruation. In 1922, when she was 32 years old, a splenectomy was performed by Dr. Pimentel. On microscopic examination this spleen was found to contain the typical Gaucher cells.

After the operation her condition remained fairly satisfactory until 3 years before admission, when she began to suffer from palpitation, dyspnea on exertion, and a persistent cough. Occasionally she would bring up some sputum, sometimes blood-stained. The urine had become scarce and darker than it had formerly been. She was thirsty but had not noticed any swelling of the feet.

The family history did not reveal other cases of a similar nature. The patient’s father died of cancer of the rectum, her mother of apoplexy. Both died in a hospital; no enlargement of the spleen or liver had been found in these individuals. The patient’s husband, two sisters, one brother and her two children, 25 and 19 years old respectively, were also examined by us. None of them showed any of the clinical signs of Gaucher’s disease.

Physical examination. The patient appeared weak and in a rather poor nutritional state. There was marked cyanosis of nails, ears, lips and cheeks. The entire skin had a somewhat yellowish tinge. Both conjunctivae showed typical pingueculae. There was bilateral myopia.

The heart was markedly enlarged toward the left, the apex-beat was visible in the anterior axillary line. The right border extended 1 cm. outside the right sternal line. All heart sounds were loud; the first mitral and the second pulmonary sounds were especially accentuated. There was normal percussion over both chest fields anteriorly, but posteriorly there was dullness on the right side, reaching from the spine of the 7th thoracic vertebra downward. On auscultation, fine crepitant rales could be heard over both lungs; over the right lower lobe the breath sounds were diminished. The abdomen showed a large surgical scar. The liver was enlarged and firm and reached downward to the umbilicus.

The right lower leg showed pigmentation of the skin due to the application of heat. The typical Gaucher pigmentation was not present. The blood pressure was normal.

The urine contained some albumin (1 per cent), an excess of urobilin and some casts. Morphologic blood studies showed hemoglobin, 110 per cent; erythrocytes, 5,530,000, and leukocytes, 11,400. The cholesterol, lipoid-phosphorus, and lipoid nitrogen content of the blood plasma were normal.

The x-ray picture showed a diffuse decalcification of the bones but no localized areas of destruction. The heart appeared displaced and/or dilated to the left. There was fluid in the right hemithorax. The pulmonary artery was abnormally prominent.

Sternal puncture revealed many typical Gaucher cells.

The clinical diagnosis was Gaucher’s disease with a tentative diagnosis of mitral stenosis or cor pulmonale due to increased resistance of blood flow in the smaller circulation. It was supposed that the obstruction in the smaller circulation was due to an accumulation of Gaucher cells in the lungs. It was

* The specimen was demonstrated by M. Elshout in a meeting of the Netherlands’ Pathological Society.
significant that in this case (where the spleen had been removed) leukocytosis was present instead of the usual leukopenia. The thrombopenia, however, persisted after splenectomy.

The condition gradually became worse. On August 10, 1938, the patient was admitted to the hospital. This time there was fluid on both sides of the chest. During her stay in the hospital the patient had repeated attacks of severe dyspnea with extreme cyanosis. She died suddenly during one of these attacks. Her age at death was 48 years.

Permission for postmortem examination could not be obtained, but punctures of the liver and the sternum were performed immediately after death. In both, Gaucher cells were found. The number of these cells in the bone marrow appeared to be far greater than in the liver.

**CASE 2.**

Mr. Fa., a Jewish lawyer, born in 1901, of German origin, was first seen on October 27, 1937.

**History.** The patient had no complaints at all until 1932, when he began to suffer from pain in the right leg, which started in the buttock and radiated toward the foot. The pain disappeared after a period of rest in bed. In 1933, he had similar pains in both legs, which disappeared spontaneously after ten days. In May, 1934, the same pain, which he considered to be sciatica, recurred in the left leg; this time it stayed there. All movements in the left hip joint became increasingly difficult; it was impossible for him to cross his legs when sitting. Now and then he felt distinct crepitation in the left hip joint on movement.

In October, 1934, he also experienced pain in the right side of his back. The local doctor suspected gall stones and sent him to a roentgenologist. The night before the x-ray examination, the patient took tetraiodo-phenolphthaline and the following morning he went to the hospital without breakfast. He cannot remember what happened to him that morning, but apparently he arrived at the hospital in a dreamlike state. The x-ray picture was made, but the patient's memory returned only when, after coming home at 11:00, he took his breakfast. He then told his family that he had to go to the hospital for the x-ray picture; he had no idea that he had already been there. No gall stones were found on this occasion. Subsequently he has had similar states of mental confusion. Finally, they occurred almost every morning between awakening and breakfast. After breakfast the symptoms disappeared. A sister of the patient noticed that during these "trances" his pupils became enlarged and that the patient perspired and trembled all over. At this time the patient was examined in Düsseldorf where the diagnosis of cerebral tumor was made. Lumbar puncture showed a normal result. Afterwards an enlarged spleen was found and a diagnosis of leukemia was put forward. The patient thereupon went to Frankfort where a low blood sugar was found during the attacks. The "spells" disappeared after administration of glucose; they could be induced by injection of insulin. Consequently, a diagnosis of islet cell tumor of the pancreas was established. In the same hospital an "arthritis deformans" of the hip joint with destruction of the head of the femur was also found for which an orthopedic support was prescribed.

As the condition became worse, the patient was operated on and a tumor the size of a nut was removed from the pancreas. On microscopic examination this appeared to be an islet cell tumor. After this operation the attacks of hypoglycemia disappeared. An explanation for the enlarged spleen was not found; the condition of the left leg remained unchanged. *

Family history revealed that the patient's father died of arteriosclerosis, his mother of "kidney trouble." One sister has gall stones. She showed no clinical signs of Gaucher's disease on examination by one of us. One brother is suffering from Gaucher's disease. The diagnosis was established on clinical grounds and verified by sternal puncture elsewhere. A second brother is reported as suffering from "a slightly enlarged spleen and a moderate secondary anemia." A third brother died when he was five months old. A cousin on the maternal side also suffered from Gaucher's disease; the diagnosis was said to have been established by pathological examination of an extirpated spleen.

**Physical examination.** The patient appeared in a moderately good state of health. The skin of the face was yellow, but there was no jaundice. Small pingeuculeae were present in both eyes. Skin and mucus membranes were somewhat anemic. Around both ears the skin showed some vitiligo. The skin of the entire body was somewhat pigmented, probably partly due to exposure to the sun. Examination of the eyes revealed a bilateral myopia of 2.5 diopters. Otherwise, neck, heart, and lungs were all normal. The abdomen was diffusely swollen. The liver was palpable, two fingers below the costal margin, with

* The case up until this stage has been described by Reiter. 34
rounded edge and smooth surface. The spleen was markedly enlarged, the organ reached downward to the level of the umbilicus and had a rounded edge. Both organs were firm in consistency and not tender.

The left leg was considerably shorter than the right; it was supported by an orthopedic apparatus. All movements in the left hip joint were restricted, especially adduction and rotation. Movement in the right hip was completely free. There was no tenderness on pressure. There was no abnormal pigmentation of the legs. Reflexes were completely normal.

The urine contained some urobilin but no further abnormalities. The sedimentation rate was normal. The blood picture showed hemoglobin, 85 per cent; erythrocytes, 5,300,000; leukocytes, 4,700; blood platelets decreased. The lipoid spectrum showed free cholesterol 44.5 mg. per cent, cholesterol esters 99.1 mg. per cent, total cholesterol 143.6 mg. per cent, lipoid nitrogen 14.7 mg. per cent, lipoid phosphorus 6.29 mg. per cent, total lipoid and fat (without cholesterol) 169.4 mg. per cent.

On roentgenological examination the head of the left femur appeared flattened and partly destroyed.

Fig. 1, Case 2. Localized Areas of Rarification in both Femora
In the head and in the shaft of both femora several areas of rarefaction were present. (fig. 1) The lower ends of both femora were swollen, (fig. 2) the left tibia showed several areas of decalcification (fig. 3). Microscopic examination of the sternal marrow showed the typical Gaucher's cells.

The patient was put on a vegetarian diet. Except for occasional periods of "sciatica" he had been relatively free from symptoms, when in 1940 he suffered a spontaneous fracture of the shaft of the right femur which brought him to the hospital again. It was then found that the bone lesions had increased
in many areas. The fracture was treated by surgical extension and healed with satisfactory callus forma-
tion (fig. 4). However a bone abscess formed on the spot where the nail had been driven through

the head of the tibia. The pus contained some large pale cells that might have been Gaucher cells.
The abscess healed after drainage and the patient's condition since has been stationary. Later he gave
up the diet and this did not seem to make any difference in the slow course of his condition.
Spontaneous fracture healing with callus formation of the right femur. Localized decalcification and swelling of lower end of the femur (Erlenmeyer flask appearance).

CASE 3

Mr. Fl., a 30 year old Jewish business man of German birth, presented himself for the first time on March 25, 1938.

History. For one year he had had increasing difficulty in walking because of pain in the left knee and left buttock, which had become almost unbearable in the last few months. The patient did not present these complaints in connection with another disease from which he had been known to have suffered.
for at least twenty years. Since that time he had seen several doctors, because of frequent hemorrhages from the nose, diarrhea and occasional fever. He had been told that he had a large liver and spleen. There were no known cases of a similar disease in his family. His mother was examined and found to be normal. His father had died from a heart attack. The patient was an only child. He was married to a normal wife. He had one child, a boy, five years old, who was found to be normal.

When the patient was 10 years old he was operated on for appendicitis. In 1916, he suffered from pericarditis. Tonsils and adenoids had been removed in 1926; the operation was followed by severe hemorrhage.

Physical examination. The patient appeared to be in moderately good health. He had a myopia of both eyes (D-4). There were no pingueculae, the pupils were normal. There was no abnormal pigmentation of the face. Mouth, throat and neck were normal. The abdomen was greatly distended. The spleen protruded from under the costal margin and reached almost the inguinal ligament. The liver was also enlarged and firm and almost reached the umbilicus.

Reflexes were normal. The left leg was about 1 cm. shorter than the right. Movement in the left hip joint was extremely painful and greatly restricted. There was pain on pressure in the hip and in the groin. There was no abnormal pigmentation on the legs.

The urine contained some urobilin, but was otherwise normal. The stools contained no occult blood. The sedimentation rate was 12 mm. after one hour (Westergren). The blood picture showed hemoglobin, 64 per cent; erythrocytes, 3,400,000, and leukocytes 3,000. Only a few thrombocytes were present in the smear. Calcium, inorganic phosphate and phosphatase and nonprotein nitrogen values in the blood were normal. The lipoid spectrum was essentially normal: free cholesterol, 55.6 mg. per cent, cholesterol esters, 66.6 mg. per cent, total cholesterol, 122.2 mg. per cent; lipid phosphorus 6.31, lipid nitrogen 27.82 mg. per cent, total lipid fats (without cholesterol) 176 mg. per cent. The patient was put on a low calcium diet for balance studies. No abnormalities in the excretion of calcium or phosphate in the feces were found, but the excretion of calcium in the urine was low, 44, 88 and 94 mg. per 24 hours respectively, on three consecutive days.

X-ray examination showed destruction of the head of the left femur. Sternal puncture revealed the presence of many Gaucher cells.

Course. The left leg was immobilized in a plaster cast. After six months the local condition seemed improved. The pain disappeared, and except for occasional attacks of ‘sciatica’ the patient managed to go about his business. From 1933 onward he began to suffer from attacks of severe pain in the left side of the chest and abdomen, which were followed each time by periods of fever. On one occasion a splenic friction rub was heard. It was felt that these attacks were due to splenic infarcts with perisplenitis. The attacks recurred so often that the patient was practically confined to bed. In view of this situation, splenectomy was performed in June of 1941. The operation was extremely difficult due to extensive adhesions between the spleen and the diaphragm. Profuse bleeding occurred, and the patient succumbed 12 hours postoperatively, in spite of repeated transfusions. Permission for postmortem examination could not be obtained. The spleen showed the typical picture of Gaucher’s disease. Unfortunately, the chemical investigation was interrupted when the chemist was deported to a German concentration camp from which he did not return. The dried spleen was lost on this occasion.

CASE 4

W. de B., born in 1909, a male office clerk, aged 25, the only patient in this series who was not Jewish, was first seen by one of us in February 1934, when he was admitted to the Binnewegasthuis because of abdominal discomfort.

History. Apart from scarlet fever, diphtheria, and measles, he had never been ill. For several years he had noticed an increasing tendency to bleed. His sister, the only living member of the family, was normal. There was no history of any other member of the family having had a similar disease.

Physical examination. There was a slight malar flush and bilateral pingueculae. Both eyes were myopic. The chest was normal. Both the liver and spleen were enlarged, the latter reaching the anterior-superior iliac spine. His legs showed a peculiar patchy brown pigmentation which ended sharply at the instep of each foot. The urine was normal. For laboratory examination (leukopenia and thrombocytopenia) the reader is referred to the first publication.*

This case was reported (Case 5) by Bloem, Groen and Postma.2
Since 1934 his condition remained fairly satisfactory on a vegetarian diet, but on June 28, 1938, he was admitted to the department of medicine of this hospital because of sudden severe pain in the sacral region after slight trauma.

On physical examination, it appeared that the liver and spleen had increased in size. These organs were in close contact in the left mamillary line, where they could be felt to rub against each other. A typical friction rub could be heard over the spleen. The pigmentation of the legs had also increased in area and intensity.

Liver function tests (galactose and bromsulphalein excretion) were normal. Vandenbergh (indirect), 0.96 mg. per cent. Sedimentation rate, 61 mm. after one hour.

The blood picture showed hemoglobin, 59 per cent; erythrocytes, 3,100,000, and leukocytes 1,100.

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Toxic granulation in about 30% of the leukocytes; marked anisocytosis, poikilocytosis and polychromasia.

In 1934, a diagnosis of Gaucher's disease had been made on clinical grounds only; this time a sternal puncture was performed. The typical cells were found.

X-ray examination showed no gross abnormality of the bones. The pain in the back disappeared rapidly after rest in bed and physical therapy.

The patient went home without pain but otherwise his condition had remained unchanged. He was a great believer in the favorable influence of a purely vegetarian diet on his condition. His diet consisted of whole wheat bread, oleomargarine, jam, vegetables, potatoes, peas, beans, nuts and fruit. He gradually lost a good deal of weight on this diet. He developed muscular atrophy and his muscular strength diminished markedly. He also developed pitting edema of the feet. The possibility that this might be due to a lack of animal food was pointed out to him but he continued on his exclusive vegetable diet. He died at his home in 1939 in a state of general exhaustion, possibly from protein deficiency.

**CASE 5**

R. P., a 43 year old Jewish single female school teacher was admitted in 1938 for recurrent attacks of sciatica. These attacks had started five years ago in the right leg, lasting only for about a fortnight. The pain radiated from the buttock along the back of the leg to the lateral side of the lower leg. Later she had similar periods of pain in the left leg. Gradually the pain became more severe; it lasted a longer time and the patient could hardly walk.

Apart from this she had very few complaints. She had noticed that her abdomen was a little swollen but she had attributed this to her getting fat. She had also noted a tendency to bleed, which was especially cumbersome during menstruation.

Physical examination revealed myopia, malar flushes, a somewhat increased second pulmonic sound, enlarged spleen which reached down as far as the umbilicus, a liver which was about 1 or 2 fingerbreadths enlarged, and a diffuse yellowish tinge of the skin of the whole body. There was a typical Lassègue sign bilaterally. Reflexes and sensitivity were normal. Movements, such as turning around in bed, were extremely difficult. The blood picture showed leukopenia and thrombopenia, with little or no anemia.

Numerous Gaucher's cells were found in the sternal marrow.

Family history did not reveal any known cases of Gaucher's disease. The patient's mother had died of carcinoma of the uterus. The father was examined and found to be normal. She was one of twelve siblings. Two of the siblings, who could not be examined, had a suspicious history of Gaucher's disease. The disease, however, was found with certainty in a younger brother (case 6).

Course. The patient's condition fluctuated, when one day she developed a typical biliary colic with jaundice. She was operated upon and a gallbladder full of stones was removed. She made a satisfactory recovery, but her sciatica kept on troubling her from time to time. In 1943 she was arrested by the Germans and transferred to a concentration camp, from which she returned with a pulmonary tuberculosis.
ADULT GAUCHER’S DISEASE

CASE 6

M. P., a brother of Case 5, a 42-year old married Jewish business man, had no complaints. One year ago he had an attack of sciatica which lasted for only ten days.

On physical examination, the spleen was found to be two fingerbreadths below the costal margin and the liver was one fingerbreadth enlarged. He had myopia and malar flushes exactly similar to those of his sister. These flushes were not presented in the unaffected members of the family. Sternal puncture revealed Gaucher cells. His wife was examined and found to be normal. Two children, 6 and 3 years old, respectively, were apparently normal.

The patient’s condition was followed. He had no complaints when he was seized by the Germans and deported to Poland. He did not return.

CASE 7

A. X., a Jewish girl, born September 15, 1923, was seen for the first time in January, 1939, through the courtesy of Professor Van Creveld.

History. When she was two years old, a swelling of the abdomen was noticed. Professor de Lange, who was the first to make the diagnosis in 1929, found an enlarged spleen and liver, hypochromic anemia, leukopenia and thrombopenia, with marked hemorrhagic diathesis. There were no changes in the bones at that time. Gradually the typical “Gaucher” pigmentation developed on both legs.

The diagnosis of Gaucher’s disease could be made with certainty because in a sister (E. X., Case 8) splenectomy had been performed and Gaucher cells had been found in the spleen.

Since the report in 1931 by de Lange,13 the patient’s illness progressed steadily14 so that when we saw her the liver and spleen had become excessively enlarged. There were also radiologic signs of involvement of the bones. In the sternal marrow many typical Gaucher cells were found.

Course. The condition had become gradually worse when the patient and her parents were deported in 1942 to a German concentration camp from which they never returned.

CASE 8

E. X., a Jewish girl, born March 19, 1927. She is a sister of the patient reported above (Case 7). She was also described in de Lange’s papers. She was first seen in April, 1939, through the courtesy of Professor van Creveld.

History. This child showed an enlargement of the spleen at an early age. Splenectomy was performed in 1930 and Gaucher cells were identified in the spleen. A detailed chemical examination of the spleen was carried out by Westenbrink26 who isolated and identified kerasin.

In 1938, she began to complain of pain in the left leg, and fever. Extensive cystlike rarefications were present in the x-ray pictures of the left femur. Similar attacks of pain recurred regularly.

Physical examination. The patient showed slight generalized swelling of the lymph glands and a very large liver of firm consistency, reaching down to the umbilicus. Both lower legs showed the typical leaden brownish-grey pigmentation. Liver function tests were normal. It is curious to note that in this case (as in Case 1 where splenectomy had also been performed) the typical leukopenia was replaced by a slightly high leukocyte count. The blood picture was as follows: hemoglobin, 80 per cent; erythrocytes, 4,570,000; leukocytes, 10,400; platelets 120,000.

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The blood chemistry findings were essentially normal. Sternal puncture revealed the presence of many typical Gaucher cells.

Course. This girl shared the fate of her sister.

* Cases 7 and 8 have been described by de Lange13-14 and Heilbron.7
CASE 9

The occurrence of Gaucher’s disease in two sisters (Cases 7 and 8) naturally focused our attention to the possible presence of the disease in one of the parents. Both had been examined in 1932 by de Lange and on that occasion had not shown any physical abnormality.

On re-examination, the father (P. X.) had no complaints at all. In addition to a chronic bronchitis, we found pingueculae on both eyes and a few scattered grey spots on the skin of the legs.

The mother (E. X.-C.) gave a history of prolonged bleeding after slight injury and during menstruation. No abnormalities were found on physical examination.

Hematologic examination in both cases yielded normal results.

Sternal puncture was carried out in both parents. No typical Gaucher cells were found but the father’s marrow contained a rather high percentage of “unclassified” cells of the type most authors would call reticulum cells or stem cells. Some of these resembled in appearance Gaucher cells but they were smaller in size. The nuclei of these cells were rather small and in some cells they were shifted to the periphery. The protoplasm stained faintly and was inhomogenous in character. It contained a few irregular vacuoles. Occasionally the cytoplasm resembled its structure compressed tissue paper. Because of the presence of these cells it was felt that the father of cases 7 and 8, who did not show the clinical characteristics of Gaucher’s disease, actually suffered from that disease in a minor degree. Apparently it was he who had transmitted the disease to two of his children where what had been a latent abnormality in his case had given rise to a severe clinical picture at an early age in theirs.

The family tree of Cases 7, 8, and 9 could not be completed. The two girls had three brothers. All were examined clinically and by sternal puncture. In no way was any evidence of Gaucher’s disease obtained in them. Other members of the family on either the father’s or the mother’s side could not be examined. So far as could be ascertained by questioning, there was no case with the clinical features of Gaucher’s disease among them.

CLINICAL SYMPTOMATOLOGY

The cases here presented, together with those earlier described by one of us2 illustrate most of the salient features of the disease. Many clinicians who have not had a wide experience with this rare malady think of Gaucher’s disease as a more or less fixed clinical picture. The reverse is true. There is a remarkable variability in many respects. The disease may make its onset early in infancy, in childhood or early or late in adult life. Its progress may be slow or rapid but it is important to know that its course is always progressive. “Spontaneous remissions” occur during times when the patient may be relatively or entirely symptom-free but the objective findings have never been observed to regress. As a matter of fact it is the rule that patients do not develop any complaints at all until relatively late, when the spleen and liver have already increased to a considerable size. During the “silent” or “subclinical” stage the subject is unaware of his condition until a medical examination happens to take place. In some instances of the present series the disease was discovered only when the relatives of a known case were examined.

Although the disease process seems to be going on continually, the rate of progression varies considerably from patient to patient. The earlier the onset, the more rapid seems to be its course. Cases observed early in infancy almost invariably die within the first year15; persons with Gaucher’s disease in childhood seldom grow older than 50 years; when the disease becomes manifest late in life it does not seem to shorten the lifespan of the individual.

The localization may also show considerable variation. Although spleen and liver are the most prominently involved it is probably safe to say that Gaucher’s disease hardly ever spares the bone marrow. However, the presence of the Gaucher
cells does not necessarily upset the *macroscopic* structure of the bone, and thereby
the disease may escape detection by radiologic examination, even when bone-
marrow puncture or postmortem examination\(^7\) proves that the cells are there. In
the later stages, when massive aggregations of the cells occur, the bones usually
show generalized or local osteoporosis.\(^9\) Even in the advanced cases, however, the
degree of macroscopic affection of the bone is variable and through this we may
encounter considerable variations in the clinical picture. Repeated attacks of low
back ache, radiating along the sciatic nerve, either unilaterally or bilaterally,
may be the first complaint (cases 5 and 6). Or patients suffering these "*osseous
forms*" may enter the hospital with a spontaneous fracture (case 2) or for what seems
a purely orthopedic problem like "arthritis" of the head of the femur (case 3).
Bone abscesses occurred in case 2.\(^{14}\)

Next to localizations in spleen, liver and bones, foci of Gaucher cells have been
found in the lungs,\(^{19}\) the kidney,\(^9\) and the brain,\(^{29}\) but these sites are rare.
Complications are frequent in this disease and they also depend on the varied
localization. Pigmentation of the legs has been referred to\(^3\); it occurs relatively
late in the disease and has been observed to disappear.\(^{14}\) Cachexia supervenes in the
long standing cases. Case 1 died under a clinical picture of cor pulmonale, possibly
due to accumulation of Gaucher cells in the lungs. Other cases we have seen had an
increased second pulmonary sound, as a possible indication of pulmonary hyper-
tension. Most remarkable was the combination of Gaucher's disease with an islet
cell tumor of the pancreas in case 2. The clinical picture in case 3 was dominated
by the successive episodes of splenic infarcts which gave rise to perisplenitis and
adhesions around the spleen. Bleeding from these adhesions after splenectomy
caused the death of this patient. Case 5 suffered mainly from "*symptomatic
sciatica*." She also had gallstones, a combination we have seen in other cases.
She later developed tuberculosis as did Gaucher's original case.\(^6\) In two cases of
this series a splenectomy was carried out successfully. The impression was that
the operation does not significantly alter the course of the disease. It certainly did
not stop its progress. Interestingly enough, these patients' leukopenia changed into
a slight but permanent leukocytosis, whereas the thrombocytopenia and hemor-
rhagic diathesis remained. Our experience confirms the opinion of several authors\(^34\)
that splenectomy should be carried out only if the spleen itself gives rise to local
symptoms which justify its removal. If a patient, as was instanced with case 3,
has had repeated attacks of perisplenitis, the surgeon should be prepared to find
extensive adhesions between the spleen and the diaphragm. This situation combined
with the hemorrhagic tendency caused the death of case 3. Treatment with a
purely vegetarian diet appeared to be just as unsatisfactory as splenectomy. Several
of our cases have been treated with this diet. The assumption was that by cutting
down the exogenous supply of lipoids in the diet, a slowing down in possible
storage of the Gaucher substance could be induced. The results have not borne
out any support for this hypothesis and it is not unlikely that the restricted
diet has hastened the death in case 4.
THE STERNAL MARROW IN GAUCHER'S DISEASE (FIG. 7)

In all our cases, the sternal puncture was carried out in the manubrium. Films were made and stained with the May-Grünwald-Giemsa stain. We recommend that several thin films be made. The cells should be looked for especially at the end of the smear. The best search for the presence of Gaucher cells is made with a low power lens without oil immersion (fig. 5). The typical cells will catch the eye at once by their unusual size, usually 30 or 40μ, although there may be considerable variation in size. The cells possess one or two nuclei that are usually situated eccentrically. In the smaller Gaucher cells, the nucleus is sometimes in the center; in the larger ones it is always displaced toward the periphery. The nuclei are relatively small with a well-stained nuclear membrane. They often contain a nucleolus. The nuclei of the Gaucher cells resemble the nuclei of those cells in the bone marrow which are referred to by some authors as reticulum cells, by others as stem cells, and which are found in a small number in normal bone marrow. As a matter of fact, it is not unusual to find an increased number of these reticulum cells in the marrow smear of patients with Gaucher's disease. Even more commonly one finds cells that are somewhat intermediary in type between the reticulum cell and the Gaucher cell. They have the size of the reticulum cell, or are a little larger, the protoplasm has the faint staining of the reticulum cell but it is more meshy in structure. If they were seen in normal bone marrow one would
call them reticulum cells; in the presence of typical Gaucher cells, one is inclined to regard them as small atypical Gaucher cells. They are probably reticulum cells that have taken up less kerasin and therefore have not changed in type as completely as the typical Gaucher cell. They be might called "early" or "young" Gaucher cells. This view is in accordance with the opinion of most pathologists, who have found similar transitory types between Gaucher cells and reticulum cells in the spleen and therefore regard the Gaucher cells as a transformed reticulum cell (Mandlebaum and Downey
d).

The cytoplasm of the Gaucher cell occupies by far the larger part of the cell body; it stains slightly gray or bluish. In the typical cells it shows a coarse
mesh as if it consisted of compressed tissue paper (fig. 6). Sometimes the protoplasm contains vacuoles so that it resembles foam cells. Erf* by the use of the supravital staining technic has shown that these vacuoles are artefacts produced during the fixation process. The cytoplasm of the Gaucher cell does not stain with any of the known dyes; neither does it take the sudan or Goldman's lipoid stain or oxydase stains. The protoplasm does not show double refraction. All these properties fit in with what we know about the characteristics of the lipoid keratin that has been isolated from organs containing Gaucher cells.

Many authors have reported the finding of Gaucher cells in the bone marrow of living cases. Some have used biopsies of the tibia,21, 1, 25, 16 but the majority have preferred to use sternal puncture.26, 33, 32, 8, 22, 31, 21, 8, 36 Only in a very few cases has the puncture failed to reveal the presence of the typical cells. Indeed, one might

Fig. 7, Case 3. A drawing of the sternal marrow in Gaucher's disease. Three Gaucher cells are drawn separately under high power.
very well call the sternal puncture the only method that will enable the clinician to establish a positive diagnosis of Gaucher’s disease with certainty. The cells distinguish themselves from all normal bone marrow cells with great ease by their size and structure. The only difficulty that might present itself is in differentiating the cells from the large cells that occur in Niemann-Pick’s disease, but the protoplasm in the Gaucher cells is characterized by a fibrillar, meshwork, whereas the Niemann-Pick cells have a foamy appearance.

It is significant that one also finds the Gaucher cells in the marrow in those cases where no gross lesions seem to be present in the bones on x-ray examination. This proves that in most cases the cells are almost universally scattered throughout the bone marrow. It is only in those places where the cells accumulate closely enough to produce atrophy of the bony trabeculae and thinning of the cortex that a “nidus” of some magnitude is formed. It follows that the distinction between visceral types and osseous types of the disease has only a relative, and no absolute, meaning. In fact, cases 7 and 8 were described first as purely visceral in type while marked bony lesions developed later. This happened in two sisters, while splenectomy had been performed in only one of them. Splenectomy apparently was useless as a measure against the progression of the disease in the bones.

The importance of sternal puncture as a diagnostic procedure in Gaucher’s disease manifested itself especially in the elucidation of the hereditary mechanism in cases 7, 8 and 9. Neither father nor mother of the girls showed clinical evidence of the disease; yet the fact that two of their children were affected could only be interpreted by the assumption that one of the parents was a “carrier.” By the detection of atypical reticulum cells, resembling Gaucher cells in the father’s bone marrow, this assumption was substantiated. This, then, appears to be one of the most important advantages of the sternal puncture; viz., the possibility of establishing an early diagnosis in individuals where the clinical picture is not fully developed. In this connection, the cases of Vogel, Erf and Rosenthal, Petit and Schleicher, and Morgans are especially interesting. These patients showed no enlargement of spleen and liver (as yet) but only involvement of the bones. Without sternal puncture the diagnosis would have been impossible.

Emile-Weill, Isch-Wall and Perles have advocated splenic and even hepatic punctures as diagnostic procedures. As a matter of fact, hepatic puncture was used by one of us on a former occasion. However, we feel that the sternal puncture has all the advantages of ease and safety and none of the drawbacks associated with the splenic or hepatic puncture in these patients in whom we know that there is a tendency to bleed.

**Summary**

The authors present nine cases of Gaucher’s disease in which the diagnosis, suspected on clinical grounds, was definitely established by the detection of the Gaucher cells in the smear of the sternal marrow. The authors review the varieties of the clinical picture in this disease. They discuss the importance of sternal puncture with special reference to the possibility of establishing the diagnosis in subclinical cases.
REFERENCES


ADULT GAUCHER’S DISEASE, WITH SPECIAL REFERENCE TO THE VARIATIONS IN ITS CLINICAL COURSE AND THE VALUE OF STERNAL PUNCTURE AS AN AID TO ITS DIAGNOSIS

J. GROEN and A. H. GARRER