GAUCHER'S DISEASE

from the Clinical Point of View.

By BERNARD MYERS, C.M.G., M.D., F.R.C.P.

(Physician, Royal Waterloo Hospital.)

Gaucher's Disease was first described by Ernest Gaucher in 1882. It is of distinct interest at the present time on account of its varied clinical aspects.

Gaucher's Disease is comparatively rare and certain forms of it, such as affection of the lung, still more rare. The disease has been described as a non-hereditary, congenital, familial disease due to changed lipid metabolism, which produces an abnormal substance called kersin. More cases occur in females than in males. It is believed that certain cells of the reticulo-endothelial system store the kersin to form what are called typical Gaucher cells. These cells are chiefly found in the spleen, liver, lymph glands, and bone marrow. I have, however, described a case of Gaucher's disease of the lungs and I rather feel that it will be found in due time to affect the brain also to some extent, or the membranes covering it.

In this affection there are clinically distinct enlargement of the spleen and liver, the pinguecula-like thickenings of the conjunctivæ, a light yellowish-brown pigmentation of the skin and sclera, various changes in the bones, leucopenia, thrombocytopenia, and the hæmorrhagic diathesis. Sometimes the lymph glands are enlarged. Ascites is only occasionally seen. The pain experienced over the bones particularly is that of a dull ache, but the pain over the spleen and liver, and I believe also in the lungs, is apt to be even sharper. When the lungs are affected the cough which resembles severe whooping-cough may be accompanied by hæmoptysis and almost excruciating pain in the chest. The disease may be encountered at any time from birth to middle life and has been found in the early weeks of life. An hereditary case of Gaucher's disease was reported by Dr. J. F. Anderson of Cleveland, U.S.A., but such cases must be rare.

The diagnosis is made from the above symptoms, especially the enlarged spleen and liver without ascites, the peculiar tint of the skin, flask-like expansion of the lower ends of the femora accompanied by dull ache or even sharp pain, a raised temperature, leucopenia, and hypochromic anæmia, and is clinched, if necessary, by a splenic puncture and the finding of Gaucher cells, or by finding these cells after biopsy of a gland.

Harry Sabotka, Glick, Reiner and Tuchman (1937) state "at least three pathological entities of generalized 'lipoid storage' disease, or lipoidosis have been distinguished from clinical and pathological evidence and confirmed by chemical investigations: (1) Gaucher's splenomegaly characterized by large deposits of the cerebroside kersin in spleen and liver; (2) Niemann-Pick's disease in which the phosphatide and cholesterol contents of the viscera, the bone marrow and the brain are increased at the expense of neutral fat; (3) Schuller-Christian's Disease with replacement of the bone tissue by cholesterol deposits."

Further information is given in the American Journal of Medical Sciences, July 1934 by Capper, Epstein and Schless, as follows:—

In *Gaucher's Disease* the blood findings were:

1. Hypochromic anæmia.
2. Leukopenia.
3. Thrombopenia.
4. Later hæmorrhagic diathesis.

In Niemann-Pick's Disease:

1. Moderate secondary anæmia.
2. Slight leukocytosis.
3. Vacuolization of non-granulated cells.
4. Excess of lipoids in blood.

In Hand-Schuller-Christian Disease:

1. There may be a hyper-cholesterolemia.

It is further stated that in **Gaucher's Disease** the eye grounds are negative. Spleen markedly enlarged. Liver enlarged. Slight or no lymph-adenopathy. Age—infancy to adult life. Bones mottling and rarefaction with cortical thinning, flask-like appearance, ends of femora.

Pathognomic Features:

1. X-ray appearance of long bones especially femora.
2. Splenic puncture.
3. Bone marrow examination.

Skin:

Subicteric pigmentation of exposed parts in 45 per cent. Yellow thickened pingueculæ in eyes 15 per cent.

Treatment:

Splenectomy (fatal in 20 per cent.) or radiation (both palliative).

Niemann-Pick's Disease.*Eye Grounds:*

Cherry-red spot in macula lutea occasionally found.

Spleen, Liver, Glands:

Spleen and liver very large.
Moderate Lymph-adenopathy.

Age:

Infancy.

Bones:

Any bones or organs may be invaded by the foam cells.

Pathognomic features:

Splenic puncture.

Skin:

Brownish-yellow discoloration.

Treatment:

No treatment, all fatal.

Again in **Hand-Schuller-Christian Disease** there are—

Eye grounds:

Negative.

Spleen, Liver, Glands:

Not enlarged.

Age:

Any age.

Bones:

Membranous bones involved.

Pathognomic features:

1. Defects in membranous bones.
2. Diabetes insipidus.
3. Exophthalmos.
4. Gingivitis and stomatitis.
5. Adiposogenital dystrophy.

Skin:

Negative.

Treatment:

X-ray treatment of the involved area causes prompt local healing but does not stop the progress of the disease.

I have quoted the above details, because I am of opinion that with more experience of these diseases we shall find them to have many similarities, but with certain differences. In my own case of Gaucher's disease I feel fairly sure that had an autopsy of the brain been allowed, we should have found that certain parts were affected by the lipoid, kersasin. The child was fast developing various nervous symptoms during the last four months of life.

My own case was that of a little girl who was admitted to the Royal Waterloo Hospital at the age of two-and-a-half years, suffering from a very distended abdomen due to an enormously enlarged spleen and liver. The child was very anæmic, the red cells being 800,000 per c.mm. on admission and the hæmoglobin 16 per cent. The white blood corpuscles numbered 3,100. Wassermann test was negative, fragility test showed no abnormality and the van den Bergh test was negative, urine normal.

As there was epistaxis and the child's condition was desperate on admission, I asked Mr. Rodney Maingot to perform splenectomy, as I felt sure it was a case of Gaucher's disease. The epistaxis stopped, and in four months the blood count was normal and the child looked remarkably well. Next year, however, the right femur became enlarged and flask-shaped at its lower end and distinctly painful. It proved to be due to Gaucher's disease and Gaucher cells were found by Mr. St. John Buxton. Six months later the left femur was similarly affected but from our previous experience it was not operated on and, like the right femur, became normal except that they both remained flask-shaped.

Later on various glands in the neck and groin became enlarged and a biopsy showed one to be due to Gaucher cells.

When the child was four years old a number of the dorsal vertebræ became affected so that kyphosis resulted. At the age of six years the little patient came back to hospital with a cough resembling severe whooping-cough, with expectoration which was often blood-stained. The temperature was high for two to three weeks and the pain in the chest really excruciating, so that morphia had to be given frequently for a time. X-ray as well as clinical examination showed that the affection of the lungs was spreading from the mediastinum outwards to the axillary regions and upwards to the apices. Some twenty sputum examinations failed to reveal Gaucher cells.

During the next few months the cough remained on and off and the child became very nervous and irritable, without any cause. She developed movements of the eyes, mouth, nose, face and neck, sometimes becoming better but on the

whole getting gradually worse. She died in January, 1937, at the age of seven years and Dr. F. A. Knott did an autopsy which showed that the liver, lungs, glands and bone marrow were simply teeming with Gaucher cells. It would have been very interesting to have examined the brain but this was not allowed.

A case of Gaucher's disease affecting the lungs was published in France by Merklen, Waitz and Warter (1933) on the "maladie de Gaucher," in which typical Gaucher cells were found in the sputum, but the patient was an adult and had suffered from a certain degree of pulmonary tuberculosis which probably allowed certain of the Gaucher cells to be loosened and found in the sputum.

R. H. S. Thompson and G. Payling Wright (1937) in Guy's Hospital Reports state that the essential pathological change is specific storage of kersasin. Concerning the origin of this kersasin or its mode of accumulation in the reticulo-endothelial cells throughout the body nothing at present is known, although they offered several suggestions.

Those interested in these diseases should read Dr. F. R. B. Atkinson's article on the subject.

I have drawn attention to the clinical features of Gaucher's disease because I have seen it mistaken for severe rickets. We must remember that a case of enlarged abdomen may be due to markedly enlarged spleen and liver, with Gaucher cells. Also severe anæmia may be due to Gaucher's disease. Similarly, epistaxis may be caused by it. Again flask-like enlargement of the femora, and possible spontaneous fracture, has occurred in several cases. The effect on the vertebræ, causing kyphosis, must also be remembered. Then there are the enlarged glands. The lung condition with a cough like severe whooping-cough, high temperature and great pain may occur. Finally, I am suspicious that the possibility of certain nervous symptoms must also not be forgotten.

REFERENCES.

- ATKINSON, F. R. B. (1937), *Med. Press & Circ.* 195.
CAPPER, EPSTEIN & SCHLESS (1934) *Amer. J. Med. Science* (July).
MERKLEN, WAITZ & WARTER (1933) *Ann de Méd.* 33, 97.
SABOTKA, GLICK, REINER & TUCHMAN (1933) *J. Biol. Chem.* 2, 2, 2031.
THOMPSON, R. H. S. & WRIGHT, G. PAYLING, (1937) *Guy's Hospital Reports.* 87, 30