PREGNANCY AND GAUCHER'S DISEASE

BY

Y. M. BROMBERG, M.D.

R. TOAFF, M.D.

AND

D. DIENGOTT, M.D.

(From the Obstetric-Gynaecologic Department and Medical Department "A," Hadassah University Hospital, Jerusalem, Israel)

Gaucher's disease is a rare condition affecting the reticulo-endothelial system, which is loaded with a complex lipo-protein (kerasin, a cerebroside) not normally found in the body. Clinically this condition is known to be characterized by an enlargement of the spleen, sometimes reaching to enormous dimensions, a much less marked hepatomegaly, moderate anaemia, leucopenia, and thrombocytopenia, with a tendency to bleeding, skeletal changes, a brownish pigmentation of the skin, and frequently a peculiar yellowish thickening of the conjunctiva (pinguicula). Most of the above manifestations are due to an invasion of the spleen, liver, and bone marrow by large histiocytic elements with a foamy cytoplasm charged with kersin, which are termed Gaucher's cells and are pathognomonic of the disease.

The condition has a familial tendency and may appear in infancy and childhood, but diagnosis is usually arrived at in the adult. Females are more often affected than males, and the disease has a predilection for the Jewish race.

We were repeatedly confronted with the problem of management of pregnancy in Jewish patients affected by Gaucher's disease, and, surprisingly enough, could find no data in the available literature on this subject. Indeed, the only reference to the influence of the disease on the female genital functions concerns the frequent occurrence of menorrhagia (Brill and Mandlebaum, 1913). The haemorrhagic tendencies, the anaemia, the splenomegaly, the destructive changes in the bones, and the poor general condition of these patients may lead obstetricians to consider the interruption of pregnancy. We felt, therefore, that a report of our experience of Gaucher's disease complicated by pregnancy might be helpful for an evaluation of the risks involved.

Material

The present study is that of a group of seven Jewish women of Eastern European extraction affected by Gaucher's disease in whom the course of 13 pregnancies was recorded (Table I). Nine were deliveries at

TABLE I.—Data on Pregnancies in Seven Women Affected by Gaucher's Disease, in Relation to Establishment of the Diagnosis

Case No.	Age at First Examination	Age at Appearance of Symptoms	Age when Disease Diagnosed	Age at Marriage	No. of Pregnancies	Age at Pregnancy				Full-term Delivery	Children Alive	Therapeutic Abortions
						1st	2nd	3rd	4th			
1	34	32	34	21	3	30	34	36	—	2	2	1
2	26	24	26	22	2	23	25	—	—	1	1	—
3	33	18	28	26	1	26	—	—	—	1*	1†	—
4	29	10	24	24	1	24	—	—	—	1	1	—
5	32	31	32	26	1	27	—	—	—	1	1	—
6	25	?	25	19	2	25	27	29	32	2	2	—
7	12	12	16	20	1	21	—	—	—	1	1	—

* Twins. † One was a stillbirth (cerebral haemorrhage).

term, resulting in nine living offspring, and four pregnancies were interrupted. One of the patients had a twin pregnancy, and on delivery bore one living child, the other being stillborn. The pregnancies occurred between the ages of 21 and 36 years. The first pregnancies were preceded by a marriage interval of 0.5–1.5 years in four cases (Cases 2, 3, 5, and 7), whilst in three cases conception was preceded by a period of sterility, involuntary in one case (Case 6) and voluntary in two cases (Cases 1 and 4).

Parity.—Four out of seven patients had only one pregnancy, which ended with a full-term delivery (Cases 3, 4, 5, and 7), while three others had respectively three, two, and four pregnancies (Cases 1, 2, and 6). Case 1 had two full-term deliveries and one artificially induced abortion. Case 2 had one full-term pregnancy and one artificially induced abortion. Case 6 had two full-term pregnancies and two induced abortions (the abortions in all cases having been performed because of Gaucher's disease). The patients who conceived only once had been discouraged by their medical advisers from venturing upon further pregnancies. It should be mentioned that the current medical opinion among the physicians of Israel is that pregnancy involves increased risks for the patient affected by Gaucher's disease, and that the majority of full-term pregnancies reported in the present paper occurred, therefore, before the diagnosis of the disease was established.

In all cases reported (Table I) the diagnosis was based on the absolute criterion of finding Gaucher's cells in the bone marrow or spleen. The clinical manifestations and relevant laboratory findings are given in Table II.

Menstrual History.—In three of the seven cases periods of menorrhagia were recorded (Table II). In none was the increased blood loss during the menstrual periods severe enough to require special treatment. Menstruation occurred regularly during the observation periods of two to seven years. In Case 4 a short period of amenorrhoea occurred, lasting three months. Cases 2 and 6 became pregnant while suffering from menorrhagia, indicating that this increased menstrual flow was not associated with failure to ovulate.

Influence of Gaucher's Disease on Course of Pregnancy

In this series there was no case of spontaneous abortion or premature labour. The course of pregnancy was not complicated by the toxæmias or by haemorrhagic accidents. It should be noted that the enormous spleen typical of the disease does not interfere with the normal increase in size of the gravid uterus. This was our experience with two cases (Nos. 1 and 6) in which no distress resulted from the pressure of the uterus on the enlarged spleen and liver. All the babies delivered at full term were normally developed and their birth weights within normal range. No case of foetal death *in utero* occurred. In Case 3, a twin pregnancy, one foetus died during delivery, and post-mortem examination revealed a cerebral haemorrhage. The course of labour in all cases was uneventful. The third stage was not complicated by haemorrhage of more than an average amount, in spite of the known tendency to bleeding found in these patients. Lactation was normal in all but one case.

Influence of Pregnancy on Gaucher's Disease

It was our experience that pregnancy did not adversely affect the course of Gaucher's disease. On the contrary, in at least two patients there was an increased feeling of well-being during pregnancy (Cases 4 and 6). That in these two cases the diagnosis of Gaucher's disease was made during pregnancy was not due to any deterioration in the condition of the patient but to the finding of splenomegaly on

TABLE II.—*Clinical Symptoms and Relevant Laboratory Findings in Seven Patients Affected by Gaucher's Disease*

Case No.	Spleen	Liver	Bones	Pigmentation	Pin-guicula	Haemorrhages (At Time of First Examination and in Previous History)	Bone Marrow	Splenic Puncture	Blood Picture	Blood Cholesterol (mg./100 ml.)	Remarks
1	Hard. Enlarged to 2 fingers above iliac crest	4 fingers below costal margin	No changes	Dark pigmentation of exposed parts and of oral mucous membranes	Bilateral	Subungual. Ano-rectal. Menorrhagia	Gaucher's cells	—	R.B.C. 3,600,000. W.B.C. 3,600. Hb 10 g./100 ml. Thrombocytes 110,000	150-190	2 weeks after second delivery
2	Hard. Enlarged to 2 fingers below iliac crests	Hard. 3 fingers below costal margin	"Erlenmeyer flasks" in both femurs	Dark pigmentation of face, especially forehead and cheeks	—	Menorrhagia	"	—	R.B.C. 3,400,000. W.B.C. 4,200. Hb 10 g./100 ml. Thrombocytes 90,000	130-160	
3	Hard. Level with iliac crests	Hard. Reaches to iliac crests	"Erlenmeyer flasks" in both femurs*	Pigmentation of face, especially forehead	Bilateral	Subcutaneous	"	Gaucher's cells	R.B.C. 4,200,000. W.B.C. 2,100. Hb 12 g./100 ml. Thrombocytes 280,000	165	
4	Hard. Reaches the symphysis pubis	Hard. 2 fingers below costal margin	No changes	Yellowish, of the face	—	Epistaxis	"	"	R.B.C. 3,200,000. W.B.C. 2,600. Hb 9 g./100 ml. Thrombocytes 60,000	90-100	
5	2 fingers above iliac crests	Not enlarged	"Erlenmeyer flasks" in both femurs	—	—	—	—	"	R.B.C. 4,180,000. W.B.C. 3,800. Hb 12 g./100 ml.	—	
6	Hard. Reaches iliac crest	Hard. Reaches umbilicus	No changes	Yellowish, of the face	Right eye	Menorrhagia. Epistaxis. Dental. Subcutaneous	Gaucher's cells	—	R.B.C. 2,700,000. W.B.C. 3,200. Hb 9.8 g./100 ml. Thrombocytes 85,000	100-138	7 months pregnant
7	Hard. 4 fingers below costal margin	2 fingers below costal margin	No changes	—	—	—	"	—	R.B.C. 3,950,000. W.B.C. 2,800. Hb 14.8 g./100 ml. Thrombocytes 105,000	—	

* Some impairment of movements and muscular atrophy.

routine abdominal examination. The major manifestations of Gaucher's disease did not appear to be aggravated during pregnancy. No changes were noted in the size of the spleen or liver. Despite considerable thrombocytopenia (in Case 4 and in the first and second pregnancies in Case 6) no aggravation of the haemorrhagic tendency was observed. In Case 1 severe bleeding from the anorectal mucosa, a condition antedating the third pregnancy, continued during the first two months and went on unabated after the pregnancy had been interrupted. Severe skeletal changes, accompanied by impairment of function in the lower extremities, preceded pregnancy in Case 3. No further anatomical or functional damage was wrought by the pregnancy. The general impression received during the relatively short period of observation was that pregnancy or repeated pregnancies have no adverse effect upon the disease.

Discussion

The course of Gaucher's disease is a chronic one interrupted by infrequent exacerbations characterized by haemorrhagic episodes, bone pains, and a general deterioration in the patient's condition. Thannhauser (1950) states that "in the interval (between individual flare-ups), which often lasts 10 years or more, there are no complaints and no disturbances of important functions. The patient may lead a normal life and even perform hard work. . . ." Life expectancy of these patients seems to be only slightly affected, especially when symptoms become manifest during or later than the third decade (Thannhauser, 1950).

In our opinion, women affected by the disease should not be deprived of the chance of becoming mothers if a negative answer can be given to the following two questions. (1) Does pregnancy endanger the life of the woman? (2) Does the disease affect the offspring?

This study of nine full-term pregnancies in seven patients leads us to believe that childbirth does not exert any deleteri-

ous effect, either immediate or remote, upon the woman suffering from Gaucher's disease. In fact, in every case in this series there was a comfortable pregnancy, followed by a successful normal full-term delivery. It is especially important to observe that haemorrhagic complications, which could be expected in Gaucher's disease, did not in fact occur. In Case 6 we had the opportunity of studying the patient over a period of seven years, throughout the course of four pregnancies, and no deterioration in her condition was observed.

Concerning the fate of the offspring, our short period of observation allows only limited conclusions. All infants born in our series were normal at birth and subsequently showed normal development. None showed any manifestation of Gaucher's disease. No absolute evidence that the disease is hereditary has been claimed in the literature on the subject, and the chances of the child becoming affected by the same condition are negligible.

It seems justifiable to draw the conclusion that women affected by Gaucher's disease should not be denied motherhood. No justification for the interruption of pregnancy in patients affected by the disease was found in the present study.

Summary

The course of 13 pregnancies in seven patients affected by Gaucher's disease has been studied. Nine pregnancies proceeded to full-term deliveries and four were interrupted during the first trimester.

The course of the nine pregnancies which continued to term was uneventful, and they terminated in normal deliveries of apparently healthy babies.

Four pregnancies were interrupted because of the prevalent opinion that pregnancy involves serious risks for the woman affected by Gaucher's disease.

The effects upon each other of pregnancy and Gaucher's disease are discussed and the conclusions drawn that conception in women affected by the disease should not be discouraged, and that interruption of pregnancy in this condition is not justified.

REFERENCES

- Brill, N. E., and Mandelbaum, F. S. (1913). *Amer. J. med. Sci.*, 146, 863.
Thannhauser, S. J. (1950). *Lipidoses: Diseases of the Cellular Lipid Metabolism*, edited by H. A. Christian, pp. 476, 508. Oxford Univ. Press, New York.

USE OF THE ELECTRODERMATOME, WITH SPECIAL REFERENCE TO ITS VALUE IN SERIOUS BURNS

BY

PATRICK CLARKSON, F.R.C.S.

Senior Plastic Surgeon, Plastic Centre, Basingstoke;
Casualty Surgeon, Guy's Hospital

AND

D. A. CAMPBELL REID, F.R.C.S.

Senior Registrar, Plastic Centre, Basingstoke

This article is based on experience with the electrodermatome during the past year at the Basingstoke Plastic Centre. Our experience in plastic and general surgery confirms the view widely held in America that in ease and reliability of cutting grafts of varying sizes and depth the electrodermatome presents an advance over other graft-cutting instruments. The graft-cutting instruments hitherto available have been the Thiersch razor, the Blair blade, the Humby knife, and the Paget dermatome. Of these the Humby knife has the widest range of general usefulness and needs the least experience for reliable results. The razor is, of course, in all respects inferior to the Blair blade, but even with the Blair blade in the most expert hands it is not possible with certainty to cut areas of graft from the thigh (the most common donor site) of more than 8 to 10 by 3 to 4 in. (20 to 25 by 7.5 to 10 cm.); the graft can be cut of uniform thickness only if it is very thin. Irregularities in thickness leading to poor donor-site scars are common. With the Humby knife grafts of 10 by 4 in. (25 by 10 cm.) can be cut with some practice. It has the added advantage of making possible grafts of medium thickness in depth; but again thickness of graft tends to vary. The Paget dermatome cuts an area of up to 8 by 4 in. (20 by 10 cm.). This instrument has been of great value in certain definitive repairs of the hand and elsewhere, but the donor-site scars are liable to keloid formation; it is a time-consuming method, and there is often trouble with the dermatome cement. Furthermore, in addition to the limitation of length it is not possible to cut thin split-skin grafts reliably with it.

There are many repairs which properly belong to the field of general surgery but which are still often referred to plastic centres simply because of the technical difficulty which current grafting instruments present to surgeons. Early experience in watching the use of the electrodermatome in a general surgical service (at the Brooke Army Hospital, San Antonio, Texas) convinced one of us that the electrodermatome could be of value in this way, as well as being an advance on other grafting instruments in the ease, speed, and reliability with

which extensive reasonably thin split-skin grafts could be cut from a variety of donor sites in patients with serious deep burns.

The Instrument

The electrodermatome was introduced in the United States after the last war. It is an electrically powered instrument in which a rapidly oscillating blade placed horizontally cuts against a lower fixed bar. The thickness of the graft can be regulated by adjusting the two micrometer screws which carry a vertically adjustable bar immediately above the knife edge. Grafts from 0.015 to 0.055 in. (0.038 to 0.138 cm.) can be cut. The maximum width of graft, which is 3 in. (7.5 cm.), can be reduced as required by a third screw which operates a pair of width guides against which the blade cuts. The length of graft is limited only by the extent of the donor area. The small electric motor is encased in metal to ensure its being spark-proof. It is connected to the instrument by means of a flexible drive shaft, and is operated on 10 volts A.C. or D.C. by a foot switch controlled by the surgeon. The knife blade is slotted into the instrument much as a razor blade into a razor, and is held there by three screws which are tightened by a spanner. We have found it possible to get good use out of blades which have been sharpened two or three times, although this is contrary to the manufacturers' experience. One blade will remain sharp during the cutting of skin from most of a thigh.

For sterilization, the dermatome, flexible shaft, and spanner are autoclaved; the blades are cold-sterilized. The motor, which does not enter the sterile field, must not be autoclaved. It is simply cleaned with a damp cloth.

Operation of the Electrodermatome

An adequate or the best available site is selected; it may be thighs, buttocks, legs, arms, chest, abdomen, or back—that is, any area except head, neck, hands, and feet. The skin of the donor site is covered with a thin coating of mineral oil such as sterile liquid paraffin. It is put on a slight stretch by the surgeon's free hand, placed behind the area from which the graft is to be cut. The dermatome is then placed with its undersurface flat against the skin. While firm pressure is maintained on it the instrument is moved slowly and steadily forward. An assistant grasps the cut edge of the skin graft with a pair of haemostats placed on each corner as the graft presents above the cutting blade, and slight tension is maintained by him on the graft. When the necessary length of graft has been cut the front of the instrument is directed upwards to sever the attachment of graft to the donor site.

Applications of the Electrodermatome

1. *In Burns.*—*Graft cutting.*—The special value of the instrument is the ease and speed with which extensive areas of graft can be cut even by those with little experience in its use. This saving of time can be of great importance during an operation in the second week in cases of serious

FIG. 1.—Early excision of sloughs with the electrodermatome. The instrument is run once or twice rapidly over the burnt area (in this case on the fifth day).