on pulse or blood pressure were seen. Two patients showed a transient fall in systolic and diastolic pressures of about 10 mm Hg after the first injection, but this returned to the resting level and was not repeated on subsequent instillations. Temperature remained within normal limits throughout and no cases of infection occurred.

Discussion

With the intrauterine route of administration termination of pregnancy was effected in 14 out of 15 cases. In this small series no obvious differences were seen between patients in the first and those in the second trimester of pregnancy. There was a wide range of 7½ to 34 hours in the induction-abortion interval in the successful cases, with a mean time of 18 hours. The total dose in patients receiving PGE_2 varied from 350 to 2,500 μg, with a mean dose of 1,177 μg. This is considerably less than the total dose required by intravenous infusion, which in our own series was from 270 to 6,750 μg, with an average of 3,500 μg.

We have not found the side effects of vomiting and diarrhoea a serious problem with intravenous infusions of PGE_2. Vomiting may occur with the higher doses but is rarely persistent and diarrhoea is practically never seen. It might be expected that these subjective symptoms would be less with intrauterine instillation but in fact most patients in this study vomited on one or two occasions. In contrast, diarrhoea and vomiting commonly accompany infusions of high concentrations of $PGF_{2\alpha}$ intravenously. Karim and Filshie (1970b) reported diarrhoea in 50% of patients receiving 50 μg of $PGF_{2\alpha}$ a minute. With intrauterine administration of $PGF_{2\alpha}$ these symptoms are probably much reduced (Wiqvist and Bygdeman, 1970) and the two patients in this study receiving $PGF_{2\alpha}$ were symptom-free.

The only data with which we can compare the results of this study are those reported by Wiqvist and Bygdeman (1970). They recorded complete or "partial" abortion in 12 out of 13 patients given prostaglandins. All their patients, however, were in the first trimester, while most of ours were in the second, and only three were given PGE_2 (in amounts up to 1,050 μg) the rest receiving $PGF_{2\alpha}$ (maximum total dose 5,400 μg). Induction-abortion intervals were not stated but the interval between first and last injection was up to 9·3 hours in the successful cases and 36 hours in the unsuccessful.

While the two series are not strictly comparable, our experience confirms Wiqvist and Bygdeman's view that the clinical effectiveness of local intrauterine administration of prostaglandins compares favourably with that of intravenous infusion. In one respect our experience appears to differ. Using $PGF_{2\alpha}$ by the intravenous route they found the uterus in the early weeks of pregnancy very susceptible to the abortifacient action of prostaglandins but succeeded in inducing abortion in only one-third of patients in the middle trimester. In contrast we have found PGE_2 by both the intravenous and the intrauterine route an effective abortifacient in the second trimester. It might well be that these results reflect a varying sensitivity of the uterus to a particular prostaglandin at different periods of gestation.

We wish to thank Dr. D. A. van Dorp, of the Unilever Research Laboratory, for gifts of prostaglandins.

References

Beazley, J. M., Dewhurst, C. J., and Gillespie, A. (1970). *Journal of Obstetrics and Gynaecology of the British Commonwealth*, 77, 193.
Embrey, M. P. (1969). *Journal of Obstetrics and Gynaecology of the British Commonwealth*, 76, 783.
Embrey, M. P. (1970a). *British Medical Journal*, 2, 256.
Embrey, M. P. (1970b). *British Medical Journal*, 2, 258.
Karim, S. M. M. (1971). In press.
Karim, S. M. M., and Filshie, G. M. (1970a). *British Medical Journal*, 3, 198.
Karim, S. M. M., and Filshie, G. M. (1970b). *Lancet*, 1, 157.
Karim, S. M. M., Hillier, K., Trussell, R. R., Patel, R. C., and Tamusange, S. (1970). *Journal of Obstetrics and Gynaecology of the British Commonwealth*, 77, 200.
Karim, S. M. M., Trussell, R. R., Hillier, K., and Patel, R. C. (1969). *Journal of Obstetrics and Gynaecology of the British Commonwealth*, 76, 769.
Roth-Brandel, U., and Adams, M. (1970). *Acta Obstetricia et Gynecologica Scandinavica*, 49, Suppl. No. 5, p. 9.
Wiqvist, N., and Bygdeman, M. (1970). *Lancet*, 2, 716.

MEDICAL MEMORANDA

Gaucher's Disease in Mother and Daughter

USHA SOOD, J. FIELDING

British Medical Journal, 1971, 1, 590–591

Gaucher's disease is a rare familial disorder of sphingolipid metabolism characterized by abnormal storage of cerebroside in reticuloendothelial cells. It is caused by a deficiency of the enzyme glucocerebrosidase. The commoner childhood form usually runs an acute course. In the adult it is protracted with progressive splenomegaly, hepatomegaly, skeletal lesions, pigmentation, and often evidence of hypersplenism (Medoff and Bayrd, 1954). Both types occur in the same families. Most cases occur in Ashkenasi Jews though other racial groups are affected. The familial pattern shows a "horizontal spread" involving brothers, sisters, and cousins, but only occasionally parents or grandparents.

The presence of Gaucher cells was considered pathognomonic of this hereditary disorder until Kattlove *et al.* (1969) described chronic myeloid leukaemia with typical Gaucher cells in the bone marrow. They suggest that while the congenital form is due to deficiency of the enzyme with accumulation of its substrate in reticuloendothelial cells, the acquired form in myeloid leukaemia is due to the grossly increased sphingolipid turnover in granulocytes beyond the capacity of the naturally occurring enzyme to catabolize.

We report here adult Gaucher's disease in mother and daughter with some unusual features.

Department of Haematology, St. Mary's Hospital, London W.9
USHA SOOD, M.B., CH.B., S.H.O., Pathology
J. FIELDING, M.R.C.P., F.R.C.PATH., Consultant Haematologist

Case Report

A married woman aged 42 was seen in November 1967 with a six months' history of easy bruising and bleeding from the gums. She had no other complaints. Haemoglobin concentration was 15·4 g/100 ml and platelets 151,000/mm.^{3} Bleeding time, clotting time, cephalin time, prothrombin time, euglobulin lysis time, throm-

boplastin generation, and serum fibrinogen were normal. Clot retraction was slightly defective. No drug history other than occasional A.P.C. tablets was obtained. She was given ascorbic acid 400 mg/day. On follow-up she showed a mild intermittent thrombocytopenia. The lowest value was 62,000/mm.^{3} She still bruised occasionally and the gums continued to bleed easily.

Her history was given with reluctance and two points emerged later. Firstly, she had taken two double whiskies (or more) at midday for some years and additional alcohol later in the day. She was advised to discontinue alcohol. Bruising and gum bleeding subsequently ceased, and the platelet count has remained in the normal range. Secondly, her mother was said to have a chronic anaemia and to bruise easily. The mother was also investigated (see below) and found to have Gaucher's disease. Sternal marrow puncture was therefore carried out on the daughter and a very occasional Gaucher cell found. Megakaryocytes appeared normal in number.

A widow aged 72, mother of the above patient, was seen in November 1968 with a 10-year history of bruising and bleeding gums. She had undergone hysterectomy for menorrhagia 20 years previously. For the past three years bilateral arthritis of the hips impaired her mobility. On examination she had obvious pingueculae on both eyes and yellowish-brown skin pigmentation. A firm spleen was palpable three fingerbreadths below the costal margin. Haemoglobin concentration was 10·1 g/100 ml; W.B.C. 3,200/mm^3; platelets 42,000/mm^3; serum vitamin B_{12}, folate, and iron were in the normal range. Sternal marrow puncture showed numerous clusters of Gaucher cells. Erythropoiesis was normoblastic; haemoglobinization was defective. There was a considerable increase in haemosiderin, mainly in Gaucher cells, some of which showed pronounced erythrophagocytosis. Many "ring" sideroblasts were seen. She was treated with pyridoxine, 100 mg twice daily, without response.

Nine months later she was admitted to hospital with increasingly severe pain in both hips and progressive disability. She was then unable to walk more than 100 yards (90 m) with the aid of sticks. Haemoglobin was 9·4 g/100 ml, W.B.C. 6,100/mm^3 with normal differential, and platelets 33,000/mm^3. The prothrombin, bleeding, and cephalin times were normal. Radiographs of both hips showed severe arthritic changes.

A left McKee arthroplasty was performed three days after admission (Mr. Nigel Harris). Management included fresh blood and platelet concentrate transfusion. She developed mild jaundice, serum bilirubin 4·1 mg/100 ml, which persisted for 10 days. Platelets fluctuated from 30,000 to 153,000/mm.^{3} Histology of the left femoral head showed foci of Gaucher cells but no osteolytic destruction. The articular surface and underlying bone showed extensive changes of osteoarthritis.

A right McKee arthroplasty was performed a month later. She had an uneventful postoperative course.

Comment

Adult Gaucher's disease can be relatively benign. The elder of the two patients was aged 72 and had well-established disease, yet underwent bilateral McKee arthroplasty with good functional results. She was found to have sideroblastic anaemia with many typical "ring" sideroblasts in the marrow, unresponsive to pyridoxine. Gaucher's disease joins the growing list of disorders which may give rise to a failure of haem synthesis whose visible expression is the "ring" sideroblast in the marrow and a dimorphic anaemia (Mollin, 1965). She had persistent thrombocytopenia, and operative management included transfusion of platelet concentrates. She had well-marked skin pigmentation. Haemosiderosis in Gaucher's disease is well documented (Brill and Mandelbaum, 1913). Its cause is not discussed in previous case descriptions. The observation, in this case, of erythrophagocytosis with excess haemosiderin in Gaucher cells, combined with the features of sideroblastic anaemia, links this form of pigmentation with that well recognized in other sideroblastic anaemias.

The daughter was shown to have an early or a mild form of the disease when Gaucher cells were specifically looked for, after diagnosis in the mother. Her complaint had been easy bruising and gum bleeding associated with intermittent thrombocytopenia. In her case, however, the presence of Gaucher cells did not seem to be related to the thrombocytopenia. She had been accustomed to taking significant amounts of alcohol every day. Ethanol is now recognized as a potent depressor of marrow function: megaloblastic anaemia with folate deficiency may occur; spontaneous reticulocytosis after discontinuing alcohol has been known for some time (Sullivan and Herbert, 1964).

There is recent evidence that alcohol may cause thrombocytopenia without affecting other blood elements and without folate deficiency (*Journal of the American Medical Association*, 1970). The effect on platelet production is reversible, as it was in the present case.

References

Brill, N. E., and Mandelbaum, F. S. (1913). *American Journal of the Medical Sciences*, **146**, 863.
Journal of the American Medical Association, 1970, **211**, 1692.
Kattlove, H. E., *et al.* (1969). *Blood*, **33**, 379.
Medoff, A. S., and Bayrd, E. I. (1954). *Annals of Internal Medicine*, **40**, 481.
Mollin, D. L. (1965). *British Journal of Haematology*, **11**, 41.
Sullivan, L. W., and Herbert, V. (1964). *Journal of Clinical Investigation*, **43**, 2048.

Primary Clostridium welchii Meningitis

N. N. S. MACKAY, R. N. GRÜNEBERG
B. J. HARRIES, P. K. THOMAS

British Medical Journal, 1971, **1**, 591–592

A case of *Clostridium welchii* meningitis unassociated with head injury or brain abscess is reported. The illness began with a perforated duodenal ulcer.

University College Hospital, London W.C.1

N. N. S. MACKAY, M.B., B.S., Surgical Registrar
R. N. GRÜNEBERG, M.B., M.R.C.PATH., Consultant Bacteriologist
B. J. HARRIES, M.B., F.R.C.S., Consultant Neurosurgeon
P. K. THOMAS, M.D., F.R.C.P., Honorary Lecturer in Neurology

Case Report

A 38-year-old Chinese waiter, resident in Britain for 12 years, was well until May 1969, when he was admitted elsewhere with a perforated duodenal ulcer. The perforation was oversewn and covered with omentum. Postoperatively he had a low fever, which responded initially to antibiotics. After two weeks, however, he developed a small sterile right-sided pleural effusion and his fever had returned. At laparotomy no pus or other abnormality was found, apart from a possibly oedematous liver. The fever continued, and nine days later jaundice appeared. Biochemically this was of the hepatocellular-damage type and was attributed, on the basis of time intervals, to toxicity to halothane, which had been used at both operations. The jaundice became severe and hepatic coma supervened. Supportive therapy was given and he gradually became less jaundiced, though fever up to 100°F (37·8°C) persisted. He had by now lost a great deal of weight. A white cell count showed a neutrophil leucocytosis (18,500/mm^3). Three months after the first operation a further laparotomy was performed, but no pus or other abnormality was found, though an operative liver biopsy was subsequently reported to show changes compatible with halothane toxicity.

After the third operation the fever continued but the jaundice cleared. Numerous courses of chemotherapy virtually throughout his illness included penicillin, streptomycin, kanamycin, ampicillin, tetracycline, carbenicillin, cephaloridine, and cloxacillin. Four