chromosome. It appears that monosomic zygotes fail to survive, probably because the loss of genetic material is too great to permit development. Another reason may be that the autosome carries a lethal recessive gene which is expressed or has its effect when it appears alone.

These honest doubts about exact chromosome identification in some cases are not meant to cast doubt on the reliability of published reports. In most cases the authors state that the extra chromosome is *probably* a certain chromosome, but that it *definitely* belongs to a certain group. Until more is known about human chromosome structure, it really matters little which chromosome is extra or is missing; for the present, knowing its group and its probable chromosome number is sufficient. When diagnostic characters make it possible to identify all chromosomes with certainty, these cases may be reviewed.

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CASE REPORTS

Hemochromatosis in a Menstruating Woman

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HEMOCHROMATOSIS is a disease of iron storage in which excessive amounts of iron are found in certain organs, mainly the liver, pancreas and heart. This accounts for such varied clinical manifestations as hepatic dysfunction, pigmentation of the skin, diabetes mellitus and myocardial failure. The disease may be classified as congenital or acquired. The congenital type is called idiopathic hemochromatosis and is the result of an inherited intestinal mucosal defect leading to increased iron absorption in subjects on a normal diet. The acquired type can be due to excessive iron intake, parenteral administration of iron or blood transfusions. Hemosiderosis differs from hemochromatosis only in the tissue damage that accompanies the excess iron in the latter disorder.[1]

This uncommon disease is even more uncommon in women (less than 10%) and rarer still in those under the age of 40. Finch and Finch[1] reviewed 787 cases and found only eight in women under the age of 40 years. In most of these there is a history of diminished or absent menses for several years and fulminating cardiac symptoms. Males lack an adequate means of eliminating iron while females lose an average of 40 mg. each month via menstruation, as well as additional amounts during pregnancy and lactation. These factors account for most of the discrepancy in sex incidence. Over 90% of all patients are over the age of 40, which emphasizes the time required for the excessive iron deposits to accumulate and give rise to symptomatology.

The first case to be reported in a menstruating woman was that described by Roth and Gordon in 1959.[2] This patient was a 39-year-old woman who had even experienced menorrhagia 18 months prior to the diagnosis of this disorder. She had a serum iron level of 348 μg. %, and complete saturation was present. Liver biopsy examination, presence of pigmentation, etc., confirmed the diagnosis.

Two recent communications each reported an additional case. King[3] described a 44-year-old woman with normal menses and two previous pregnancies. Her serum level was 164 μg. % and the iron-binding capacity 230 μg., with a saturation of 71%. Needle biopsy of the liver confirmed the diagnosis of hemochromatosis. The electrocardiogram in this case showed myocardial involvement. Weekly phlebotomies of 500 ml. for eight months removed 13,000 ml. of blood. Her hemoglobin level

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remained normal. Her progressive weakness, her state of being easily fatigued, muscle aching, nausea and intermittent periumbilical pain all but vanished.

Wasi and Block[4] reported the case of a 41-year-old woman with normal menses and four pregnancies. She had taken oral iron for two months, several years earlier. Her serum iron was 153 μg. % and the saturation was 65%. Weekly phlebotomies totalling 32,500 ml. finally caused anemia but improved the liver size and decreased the skin pigmentation.

Our patient was 40 years of age when first diagnosed in 1959. She is the fourth such patient to be reported.

A 40-year-old housewife presented complaining of non-specific back and abdominal pains and chest tightness of nine months' duration. In addition, her appetite was poor and she had nausea and indigestion. This produced a weight loss of 25-30 lb. in a year. The last of her nine pregnancies was in 1954. Since then her menses were regular with a normal flow. In 1951, following a postpartum hemorrhage and stillbirth, she received three bottles of blood, which raised her hemoglobin from 9 g. % to 12 g. %. Again in 1954 four bottles of blood were required because of abruptio placentae. At this time her hemoglobin level of 7 g. % was raised to 11 g. % at the time of discharge from hospital. On one of these occasions she was given 100 tablets of ferrous gluconate to take one thrice daily. She denied taking the medication after this supply was depleted.

She has 11 siblings, all of whom are well. One brother died of meningitis and one sister of tuberculosis. There was no family history of liver disease, diabetes or pigmentation of the skin.

Physical examination revealed a chronically ill, pigmented, grey-skinned woman who looked older than her 40 years. Pigmentation was most marked on the face, palms and legs. Her teeth were in poor repair. A firm, tender liver extended at least three fingerbreadths below the right costal margin in the midclavicular line. The tip of the spleen was easily palpable below the left costal margin on deep inspiration. There was no demonstrable shifting dullness, but an umbilical hernia was noted. The generalized greyish-brown pigmentation of her skin changed to a thickened, dry, bluish type of pigmentation above both ankles.

Laboratory studies revealed the following. Her urinalysis was negative. The hemoglobin was 12.9 g. %; hematocrit, 41%; erythrocyte count, 4,740,000 per c.mm. and her sedimentation rate, 20 mm. in one hour. The white blood cell count was 5900 per c.mm. with a normal differential smear. Her blood urea nitrogen (BUN) was 14.5 mg. %; cephalin-cholesterol flocculation, 3+; thymol turbidity, 3.2 units; albumin/globulin ratio, 3.6/3.15. Her bromsulphalein retention was 14% in 45 minutes. The platelet count, bleeding time, prothrombin time and coagulation time were normal. Serum alkaline phosphatase was 0.3 unit; total bilirubin, 0.4 mg. %; serum glutamic oxaloacetic transaminase, 64 and 89 units; two-hour post-prandial blood sugar, 137 mg. %; and serum iron, 218 μg. %.

A radiograph of her chest showed a normal-sized heart; the cardio-thoracic ratio was 14/29.5. Radiographs of the gallbladder enabled faint visualization of the organ and were suggestive of impaired gallbladder function. Radiological studies of the esophagus, stomach and duodenum revealed a small sliding hiatus hernia, which reduced to a position below the diaphragm when the patient was upright. A constant deformity in the prepyloric area on the lesser curvature that suggested an ulcer crater was noted. Radiographs of the colon were normal. Splenic enlargement was noted. An electrocardiogram revealed a sinus rhythm at a rate of 70 per minute with a semi-vertical heart position. There were some non-specific changes in that the T waves were low in Leads I, II, V5 and V6, with a diphasic T wave in V4.

On admission the diagnosis of hemochromatosis was considered but thought to be unlikely in view of the patient's sex and age. Because of the elevated blood sugar and serum iron level, a liver biopsy was performed. It was reported as diagnostic of hemochromatosis. Subsequently a laparotomy was carried out. No lesion was found in the stomach or duodenum, but the gallbladder was distended and drained. Another liver biopsy at that time confirmed the diagnosis of hemochromatosis. During the hospitalization, two venesections of 500 ml. were carried out. Arrangements were made for this procedure to be continued on an outpatient basis every two weeks.

The patient was readmitted to hospital one week later with a strangulated umbilical hernia. At that time she had obvious ascites. Hence, arrangements were made to restore the plasma that had been removed with each venesection. By November 1960, 10 l. of blood had been removed and her serum iron level was then reported as 280 μg. %. She complained of weakness and dizzy spells following the fortnightly venesections. Her hemoglobin level remained at 12.4 g. % and her hematocrit at 40.5%; a red blood cell count was 4,100,000 per c.mm.

She was readmitted to hospital in 1961, some 14 months after the original diagnosis was made. At that time her liver was not quite as large as previously. Liver biopsy was unsuccessful. Her serum iron level was 257 μg. %. A glucose tolerance test revealed a peak level of 191 mg. % in one hour and 176 mg. % in two hours. Ten months later her bromsulphalein retention test was reported as showing 4% retention in 45 minutes, and the two-hour post-prandial blood sugar was normal at 88 mg. %.

Following this she had three or four additional venesections but then failed to return for follow-up examination until admitted to hospital on September 20 for a trial period on a new iron chelating agent, desferrioxamine.[5] Her pigmentation was still evident, and her liver was enlarged two fingerbreadths below the right costal margin. The tip of the spleen was just palpable. The routine hemogram and urinalysis were normal. Her prothrombin time, fasting and postprandial blood sugars and serum electrophoresis were all normal. A bromsulphalein test revealed retention of 8.5% of the dye in 45 minutes. Her serum iron level of 296 μg. % on admission had fallen to 205 μg. % at the conclusion of a week's treatment. Her urine iron level for three days preceding treatment averaged 0.63 mg. per day (Kennedy method[6, 7]). She then received 800 mg. of desferrioxamine daily in 1 litre of 5% glucose in water, given slowly intravenously over a period of five to seven hours. For the next seven days her total urine iron levels were 6.0, 4.6, 5.1, 5.1, 5.9, 6.6 and 5.8 mg. daily. The patient refused a liver biopsy and was dis-

charged pending arrangements for possible further administration of desferrioxamine either orally or intramuscularly.

Attempts were made to examine various members of her family. Only four of the 11 siblings were examined. All of these had normal serum iron values and no findings to suggest hemochromatosis. The remaining members of the family refused to appear for examination.

The diagnosis of this disorder rests on liver biopsy. A serum iron level greater than 200 μg. % or a saturation value of over 70% is suggestive. These values may also be high in the presence of acute hepatitis, aplastic or hemolytic anemias and transfusion hemosiderosis. Since anemia may rarely occur in patients with hemochromatosis, the serum iron value may be confusing. Liver biopsy is therefore essential for definite diagnosis.

Treatment has been by means of weekly phlebotomies. Despite the development of new chelating agents such as desferrioxamine,[5] phlebotomy still remains the simplest, least expensive and most effective form of therapy. It is possible that the oral administration of desferrioxamine may totally prevent absorption of iron from the gut. This would be a welcome addition to current therapy. Some patients do not co-operate in the phlebotomy program and thus may fail to benefit from having the disease diagnosed. By using desferrioxamine orally it would be possible to prevent the development of hemochromatosis in the members of the family who have elevated serum iron levels and excess iron storage. It is hoped that earlier diagnosis and treatment will cure most of these patients in the future.

SUMMARY

The fourth case of hemochromatosis occurring in a menstruating woman is reported. The diagnosis in this 40-year-old woman seems well established. The use of desferrioxamine intravenously produced only a tenfold increase in the urine iron excretion from 0.6 to approximately 6 mg. daily. Examination of other members of the family was hindered by their refusal to co-operate; at least four of them appeared to have normal serum iron levels and no evidence of hemochromatosis on physical examination.

The desferrioxamine (Ciba 29837-Ba) was obtained through the generosity of Dr. R. W. Shepherd, Medical Adviser, Ciba Company Limited, Dorval, Quebec.

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Listeria Monocytogenes Meningitis in an Adult, with Survival

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IN 1954, the first case of *Listeria monocytogenes* meningitis in an adult in Canada was reported.[1] Recently a second case has been described[2] and, as in the first case, the patient did not survive. The following communication is concerned with the first Canadian case of *Listeria monocytogenes* meningitis in an adult who recovered.

A 52-year-old woman was admitted to hospital complaining of shaking chills, vomiting and increasing drowsiness of four days' duration. There was also a history of mild occipital headaches dating back several months, and more severe during the four days preceding her admission to hospital. No history of previous significant illnesses or recent contact with domesticated or wild animals was obtained. The patient had not left her city of residence in the previous six months.

On physical examination, the patient appeared subacutely ill. Her rectal temperature was 105° F., the pulse rate only 66 per minute, and the blood pressure 124/80 mm. Hg. Although stuporous, she could be aroused and was oriented. Her response to repeated questions and commands was accurate but very slow. Except for a slight resistance to flexion of the neck, the neurological and, indeed, the entire physical examination was negative.

Her hemoglobin was normal. The white blood cell count was 18,200 per c.mm. with a differential count of 67% polymorphonuclear leukocytes, 9% juvenile neutrophils, 1% myelocytes, 5% monocytes, and 18% lymphocytes. The sedimentation rate was 38 mm. in one hour. Urinalysis showed 3+ albumin and a few white blood cells.

Lumbar puncture was performed immediately and revealed a clear, colourless cerebrospinal fluid which was at normal pressures. However, the fluid contained 230 red blood cells and 380 leukocytes per c.mm. (62 polymorphonuclear leukocytes and 318 lymphocytes). The cerebrospinal fluid protein concentration was 70 mg. %. No organisms were seen on Gram stain.

Because of the severity of the illness, treatment was instituted immediately and consisted of administration of intramuscular chloramphenicol, 1 g. every eight hours, and intravenous fluids. The next day the culture

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