Medical Memoranda

Addison's Disease and Pregnancy

Pregnancy in patients with Addison's disease is unusual, and before the introduction of "eucortone" and "doca" it was almost invariably fatal (Perkins, 1932). More recently cases successfully managed through pregnancy have been described (Thom *et al.*, 1941, 1942; Sheldon, 1945; Zwanenberg, 1945; Simpson, 1946; Knowlton *et al.*, 1949). Crises may occur in the early stages due to vomiting, but, once these have passed, the patients usually remain well until after delivery. In the first few days of the puerperium, however, crises of acute adrenal insufficiency are frequent. Hypoglycaemia may also be a serious complication, and irreversible coma may occur. Knowlton *et al.* (1949) recommend stabilization throughout the pregnancy with daily injections of intramuscular doca to allow for requirements which vary in the different stages. Little extra salt is advised, to give a wider margin of safety should vomiting occur and salt ingestion be discontinued. After delivery, intravenous glucose saline, 1 to 2 litres, and additional eucortone, 20 to 40 ml., are given daily.

CASE REPORT

A woman aged 35 was diagnosed as a case of Addison's disease in 1945. The diagnosis was based on the presence of typical pigmentation, including generalized brown discoloration of the whole skin, slaty-coloured patches in her mouth, a deep brown areola around each nipple, and pigmentation of scars. Her blood pressure at this time was 100/68 mm. Hg, and she was complaining of tiredness and of attacks of vomiting. A Kepler test was not performed, but serum sodium and potassium levels were estimated at times when she was thought to show signs of increasing adrenal insufficiency, and in 1949 these showed levels of 215 mg. and 32 mg. per 100 ml., respectively. She was maintained on implants of doca, 200 mg. being inserted every three to six months as she became deficient.

She was maintained in fairly good health until December, 1949. Then, in spite of an implant of 200 mg. on November 12, she noticed increasing weakness and vomiting. At the beginning of January, 1950, she was thought to be pregnant, because of amenorrhoea since November 4, and was admitted to hospital because of severe vomiting. In spite of her dehydration, a rapid pulse, and a blood pressure of 70/40 mm. Hg, her urine contained 14 g. of salt per litre (measured by Fantus's method). Intravenous saline was given, her daily salt intake was increased to 15 g. a day, and eucortone, 20 ml. daily, was given for three days.

After discharge from hospital in January she felt tired and unwell, and vomiting continued to be troublesome. The doca was therefore supplemented by intramuscular injections of an oily solution of doca, 5 mg. twice a week. At the 14th week of her pregnancy there was slight blood loss per vaginam, and she was thought to have a threatened miscarriage. This was treated by rest in bed, and at the same time she was stabilized on a daily maintenance dose of doca intramuscularly. This was increased to 10 mg. a day gradually, and her salt was reduced to 3 g. a day, her blood pressure remaining about 105/70. After discharge from hospital she was maintained fairly well on twice-weekly injections of 30 mg. of doca.

On June 8 she was admitted to hospital because of abdominal pains. From the size of the fundus twins had been suspected, and their presence was confirmed radiologically. On June 9 spontaneous delivery of male twins occurred. Delivery was premature at the 34th week, the infants being very underweight. One, weighing 2 lb. 12 oz. (1.2 kg.) at birth, has survived, the other died of asphyxia.

After delivery a 5% glucose saline drip was set up, 2 to 3 litres being given daily for four days. Doca intramuscu-

larly, 10 mg. a day, was continued, and supplementary eucortone to guard against a crisis. The blood pressure, however, was well maintained at a higher level than before delivery, and on the fourth day signs of electrolyte and fluid retention occurred, with the development of a lumbar pad. Eucortone and salt were therefore discontinued and doca was stopped for 24 hours. She was re-stabilized on doca, and was found to need 5 mg. a day. On July 19 400 mg. of doca was implanted in the erector spini muscles. Lactation began after delivery, but was rapidly inhibited by oestrogen.

Since delivery the mother and the surviving infant have remained well. The patient has, however, had three mild hypoglycaemic attacks, with faintness associated with hunger; each occurred while she was working before dinner. An oral glucose-tolerance test showed a normal curve, but an intravenous glucose-tolerance test showed marked hypoglycaemia three hours after the injection. She has been taking more frequent small carbohydrate meals since this time, and has been free from attacks for three months.

Comment.—Thorn *et al.* (1940) have shown that most patients with hypoglycaemic symptoms have a normal oral glucose-tolerance curve. Many, however, react abnormally to an intravenous glucose-tolerance test in which 0.5 g. of glucose per kg. is given during half an hour; hypoglycaemia develops three to four hours later.

I wish to thank Dr. D. H. G. MacQuaide for his assistance in preparing this paper and also Mr. G. Sturtridge, who undertook the obstetric management of the patient.

T. A. RICHARDS, M.D., M.R.C.P.,
Medical Registrar, Northampton General Hospital.

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A Case of Interstitial Tubal Pregnancy

Individual cases of interstitial pregnancy are of sufficient interest and rarity to deserve attention. When such a case is associated with symptoms and signs even more puzzling than usual, it serves to re-emphasize the difficulty in diagnosis; when, in addition, a study of the case reveals an almost astonishing recurrence of ectopic implantation the details would appear to merit publication.

All writers agree on the rarity of the condition. Bethel Solomons (1949) described a case, the third in his own experience, and quotes Grusetz and Polayes (1944), who collected a total of 199 cases from the literature up to the year 1943. Wynne, in 1918, collected 1,547 cases of ectopic pregnancy and found that there were 18 cases of the interstitial variety, an incidence of 1.16%. MacFarlane and Sparling (1946) found seven cases in a series of 106. MacVine and Lees (1949) stated that at least two of the more severe forms of ectopic pregnancy were interstitial in a series of 107 cases extending over a 10-year period. Thus the incidence would appear to be in the region of 1% to 2% of all ectopic pregnancies reported, and this figure is in agreement with that quoted by Keenan (1944). This figure, however, seems very high and is probably an exaggeration, for, as Johnstone (1928) has pointed out, there must be many series of tubal pregnancies numbering 100 or more but containing no example of the interstitial variety.

CASE REPORT

A 3-gravida 2-para aged 29 was admitted as an emergency case on June 13, 1949. She gave a history of three normal menses following cessation of lactation of her second child, born March 26, 1948. After her last period on March 23,

1949, there had been amenorrhoea until May 24, when a brown offensive vaginal discharge suddenly began without antecedent pain or apparent cause. Two days later there occurred a very profuse vaginal haemorrhage with the passage of many clots. After 24 hours she was able to get up and carry on her household duties, but the loss continued "like the first day of the period" until her admission to hospital three weeks later. Five days before admission she experienced her first attack of abdominal pain. It was central in distribution and a continuous ache in character, being exacerbated by sudden movement, defaecation, and micturition. There had previously been no bowel or micturition symptoms.

The patient's menstruation was normally regular, with a cycle of 30 days and loss of seven days. The menarche had occurred at 16. There had been two normal deliveries, in 1938 and 1948.

The letter from her private doctor contained an outline of the relevant past medical history, and the details were later supplemented by the previous case notes and by correspondence with the hospital concerned. In 1939 appendicectomy was performed in the Bristol General Hospital and convalescence was delayed by peritonitis and wound sepsis. In 1943 right salpingo-oophorectomy was carried out at the Radcliffe Infirmary, Oxford, for chronic salpingo-oophoritis. In November, 1946, she was again operated upon in Bristol for a right ectopic pregnancy. Unfortunately, detailed clinical notes cannot be traced, but there is definite evidence that a right ectopic pregnancy had apparently ruptured into the broad ligament and was densely adherent to the right wall of the uterus, to bowel, and to omentum. The available notes made no mention of the right salpingo-oophorectomy performed three years previously.

Examination on admission revealed a tired, flushed, ill-looking woman. Her temperature was 99° F. (37.2° C.), pulse 90, respirations 20, and blood pressure 125/80. General examination and urinalysis were negative. Her breasts showed equivocal signs of pregnancy. The haemoglobin was 92%. The abdomen was scarred by previous laparotomies. No tumour was palpable, and there was no definite tenderness. There were no signs of free fluid. On vaginal examination the vulva and vagina and their mucosal colouring were normal. The cervix was softened and the os closed; movement was painless, and there was slight bleeding. The uterus was bulky and retroverted, and there was an extremely tender pulsating mass in the pouch of Douglas.

In spite of the unusual history the examination suggested that in the main the most likely diagnosis was that of ectopic pregnancy, but the differential diagnosis was a wide one. The patient was prepared for laparotomy.

Examination under anaesthesia after catheterization confirmed the pre-operative findings. The uterus was anteverted and the pulsating mass could then no longer be felt. After dilatation of the cervix, curettage revealed exuberant endometrium and a sensation of fullness in the region of the right cornu. A large-bore needle was passed through the posterior fornix and frank blood in quantity was readily aspirated. At laparotomy there was a moderate amount of old and recent blood in the peritoneal cavity. The uterus was slightly enlarged and blood was spurting from the site of a ruptured right interstitial pregnancy. The ragged bleeding cavity measured 4 by 3 cm. The anatomy of the right round ligament was normal, but the Fallopian tube and ovary were absent on that side. The left tube was normal, and the ovary contained a corpus luteum. The affected area of the fundus was excised by a V-shaped incision and the uterus refashioned with catgut sutures. The scar was peritonized by a loop of the round ligament. It was particularly noticed that there was no communication between the gestation sac and the cavity of the uterus.

Convalescence was stormy, being interrupted by episodes of paralytic ileus on the second day, wound sepsis on the seventh day, and a discharge of watery purulent material

from the vagina on the seventeenth day after operation. Vaginal examination at this time revealed no abnormality. With sulphonamide and penicillin the temperature settled and the abdominal wound healed soundly. The ileus responded to the usual treatment. The patient was finally discharged 24 days after operation.

The pathologist reported that the specimen, on section, showed a haemorrhagic cavity lined in places by pale clear cells of decidual appearance. No chorionic villi were demonstrated in the sections taken. There was deposition of calcium in the myometrium, and also evidence of myometritis and a salpingitis in the remaining portion of the interstitial segment of the tube.

COMMENT

The difficulty of diagnosing with any certainty an interstitial ectopic pregnancy before operation is well known, and this case was no exception. It is presumed that embryo death and a curiously asymptomatic intraperitoneal rupture took place about May 26—facts compatible with the size of the cavity found at operation. The fresh haemorrhage from the cavity seen on inspecting the uterus was probably occasioned by the preliminary anteversion. The microscopical appearance of a myometritis and interstitial salpingitis was an interesting feature of this case and explained the purulent discharge per vaginam, the wound sepsis, and, partly at least, the post-operative pyrexia.

But perhaps, above all, the case described is exceptional because it demonstrates clearly that on two separate occasions the fertilized ovum transmigrated across the pelvis to become ectopically implanted each time in that portion of the tube remaining after two separate salpingectomies. In Keenan's paper on interstitial pregnancy is mentioned the finding by D'errico of 23 cases of such pregnancy occurring in the stump following the removal of the extrauterine portion of the tube. Such behaviour is an eloquent testimony to the bizarre insistence and persistence of the reproductive function in woman, and it is a reminder of the pitfalls attendant on any operative procedure on the tube devised for the purpose of sterilization.

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JEFFERY SPRY LEVERTON, M.D., M.R.C.O.G.,
Gynaecological Registrar, Bristol General Hospital.

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The West Middlesex Hospital has for many years been helped by a considerable body of voluntary workers in a great variety of ways (*Third Annual Review*, July, 1950–October, 1951, South-west Middlesex Hospital Management Committee). To co-ordinate the work of these helpers and to give formal recognition to their services a League of Friends of West Middlesex Hospital has been formed. Activities of its members include the sewing on of buttons and tapes in wards, singing and playing to elderly patients, visiting patients without relatives or friends, and help with preparations for special occasions such as Christmas festivities. Members of the Women's Voluntary Services have continued to provide a trolley-shop service in the wards, and they also run a canteen trolley for out-patients. Help of this kind is very much appreciated both by patients and hospital staff, says the report, and the value of the work done by these voluntary workers cannot be over-emphasized. It is hoped that they will continue to give their services and enrol their friends.