TABLE IV.—*Parallel Changes in the Haemoglobin Percentage, Erythrocyte Count, and Serum Iron During the Menstrual Cycle of Four Hundred Women*

No. of Days After Last Menses	No. 1			No. 2			No. 3			No. 4		
	Hb%	Erythrocytes in Millions	Serum Iron in γ/100 ml.	Hb%	Erythrocytes in Millions	Serum Iron in γ/100 ml.	Hb%	Erythrocytes in Millions	Serum Iron in γ/100 ml.	Hb%	Erythrocytes in Millions	Serum Iron in γ/100 ml.
During	84	4·61	98	88	4·41	88	82	4·02	80	79	4·00	78
6	85	4·45	78	90	4·50	102	84	4·16	83	82	4·04	86
13	89	4·34	93	87	5·32	93	96	4·46	88	89	4·20	80
20	94	4·28	126	92	4·45	105	94	4·74	102	90	4·38	87
27	89	4·04	155	95	4·51	112	100	4·96	106	90	4·41	94
During	80	3·89	69	92	4·39	96	90	4·29	87	85	4·13	83

TABLE V.—*Serum-iron Values in Relation to the Menstrual Cycle*

Days of Cycle	Serum Iron in γ/100 ml.	Days of Cycle	Serum Iron in γ/100 ml.
During	95·3	16–18	112·3
1– 3	88·3	19–21	100·6
4– 6	98·6	22–24	114·8
7– 9	112·3	25–27	130·5
10–12	108·7	28–30	122·5
13–15	99·2	31–33	139·0

(Table III). The average values for girls and elderly women were 111 and 113 γ per 100 ml. respectively, while the average for menstruating women was 105 γ. This indicates that the serum-iron concentration is somewhat lower in menstruating women than in the non-menstruating.

It has been asserted that this lower value in menstruating women is due to the loss of iron month after month. The work here reported indicates that this theory is correct. In order to obtain further corroboration four perfectly normal women were examined throughout a menstrual cycle (Table IV). The examination showed that the serum iron reached its highest value immediately before the menstruation, while the lowest values were found during and immediately after.

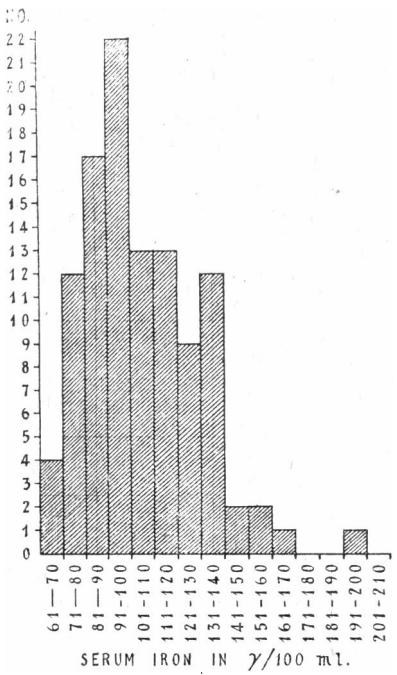

Chart showing amount of serum iron in normal non-pregnant women.

In Table V the 63 serum-iron values obtained in menstruating women (from Table II) are grouped after the menstrual cycle. Here, too, we find higher values shortly before the expected menstruation.

The Chart illustrates the distribution of the serum-iron values obtained in the present series. It shows how the normal limits—70 and 140 γ per 100 ml.—are arrived at.

Summary

Determination of the serum iron has been carried out on 92 healthy females receiving an adequate diet. The five highest values were 194, 166, 154, 146, and 143 γ per 100 ml.; while the three lowest values were 68 γ.

The serum-iron concentration was found to be lower in menstruating women than in those not menstruating.

The theory that the lower serum-iron value in menstruating women was due to loss of iron month after month is considered to be proved by the results obtained.

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REFRACTORY IRON-DEFICIENCY ANAEMIA TREATED WITH INTRAVENOUS SACCHARATED OXIDE OF IRON

BY

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In a recent article by Nissim (1947) the use of saccharated oxide of iron for intravenous injection is described. The following case is reported because the patient responded dramatically to parenteral iron therapy subsequent to the failure of the oral administration of iron in large amounts for long periods, supplemented at various times with ascorbic acid, thyroid extract, molybdenized ferrous sulphate, parenteral liver extract, and folic acid.

Case History

The patient, a woman aged 29, was first admitted to hospital on June 13, 1945, with a three-months history of breathlessness and fatigue. Her appetite and diet had always been satisfactory, she had never suffered from dyspepsia or diarrhoea, her periods were not excessive, and there was no evidence of any other source of blood loss. On examination there was no oedema. The nails, although brittle, were not flattened. Some atrophy of the papillae of the tongue was present. The liver, spleen, and lymphatic glands were not enlarged. Physical examination of the cardiovascular, respiratory, renal, alimentary, and central nervous systems revealed no pathological features. The patient's intelligence was below average.

A test meal showed that free hydrochloric acid was present in the gastric juice. There was no excess of urobilinogen in the urine, and the stool benzidine test was negative. Radiological examination of the alimentary tract revealed no abnormality. The haemoglobin was 30%; erythrocytes, 2,850,000 per c.mm.; colour index, 0.53; white cells, 2,800 per c.mm.; reticulocytes <1%. The sternal marrow contained numerous late normoblasts of the type seen in iron-deficiency anaemia.

There was no response to ferrous sulphate, 3 gr. (0.2 g.) thrice daily for 24 days, followed by 6 gr. (0.4 g.) thrice daily for 20 days. Supplements of ascorbic acid, thyroid extract, and liver extract were given in turn, with no beneficial results. Accord-

ingly she was given a transfusion of 3 pints (1.7 litres) of blood, which raised the haemoglobin level to 68%. She was discharged on Aug. 7, and continued to take ferrous sulphate, 3 gr. three times a day, as an out-patient.

She was readmitted on May 1, 1946, with a haemoglobin level of 51%. Physical examination again revealed no explanation for the anaemia. The possibility existed that the anaemia was dependent on some failure of absorption, although neither clinical nor radiological examination of the alimentary tract had revealed any abnormality. Accordingly a fat-balance test was done, and absorption of fat was found to be normal. A liver biopsy showed no pathological change. Sternal puncture was repeated and a normoblastic marrow again demonstrated, although this time it was somewhat hypoplastic. As no response occurred to continued iron therapy, a further 2 pints (1.14 litres) of blood was given, and this raised the haemoglobin level to 68%. The patient was discharged from hospital on May 14 with instructions to continue taking ferrous sulphate, 6 gr. (0.4 g.) thrice daily.

She was admitted to hospital for the third time on May 5, 1947, with a haemoglobin reading of 38%; erythrocytes, 3,180,000 per c.mm.; colour index, 0.6; white cells, 2,000 per c.mm.; P.C.V., 23%; M.C.V., 72.3 c.μ.; M.C.H.C., 22.8%. A histamine-fast achlorhydria was found. Radiological examination of the skeleton showed no abnormalities. The stool benzidine test was repeatedly negative. A third sternal puncture showed numerous late normoblasts. Folic acid and molybdenized ferrous sulphate were in turn given a trial, but produced no haematological or clinical benefit.

It was now decided to try saccharated oxide of iron intravenously. The preparation was made up according to the method described by Nissim (1947). She was first given 10 mg. of elemental iron as saccharated iron oxide in 1 ml. of solution, the dose being increased to 20 mg., 25 mg., and 50 mg. on successive days. Thereafter she received 14 injections of 100 mg. in 10 ml. of solution over a period of approximately 50 days. During this period the haemoglobin rose from 36% to 90% and the red cells from 2,860,000 to 4,650,000 per c.mm.

Her general clinical state was now excellent. All therapy was stopped, and when the patient was seen again a month later her haemoglobin was 94%; erythrocytes, 4,690,000 per c.mm.; colour index, 1.

The maximal reticulocyte count of 3.2% was on the tenth day after the first intravenous injection of iron. The patient had marked reactions (sickness and rigors) with the last three injections, all of which were given very slowly.

Severe reactions have also occurred in several other cases of iron-deficiency anaemia which we have treated with a solution of saccharated iron oxide given intravenously. We would therefore suggest that further work is required on the preparation of solutions of iron for intravenous injection before parenteral iron treatment is used by general practitioners.

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Medical Memoranda

Bilateral Tubal Gestation

The following case of bilateral tubal pregnancy encountered in Iraq is of particular interest as it occurred in a patient known to have salpingitis.

CASE REPORT

The patient, an Arab married woman aged 30, had had two children, aged 10 and 4. Following the birth of the second child she developed a discharge and was found to have a gonococcal cervicitis and salpingitis. Until her admission she did not conceive again. Her periods had been moderately regular, but the accuracy of this statement is open to doubt. She had been in hospital on several occasions during this time with lower abdominal pain and vaginal discharge, diagnosed as salpingitis, the last admission having been eight weeks before her present illness. Again gonococci were found in the cervical smear. She returned complaining of an attack of left-sided abdominal pain and discharge, but in addition stated she had missed two periods.

On admission she was in no distress. The pulse was 90 and the temperature normal. There was tenderness in the left iliac fossa, and vaginal examination showed a little bloody discharge, normal uterus and cervix, and a tender, rather indefinite swelling connected with the left tube. A diagnosis of salpingitis, but with the reservation that an ectopic gestation might be present, was made, and she was kept in bed in Fowler's position and given sulphathiazole. The pain subsided, but four days later she had a sudden attack of severe right lower abdominal pain, with a rise in pulse rate and abdominal distension, associated with tenderness and fullness in the right fornix. A blood count showed: red cells, 4,000,000; white cells, 11,000 (75% polymorphs). She was not severely ill or distressed in spite of this, and laparotomy was not performed. The distension and pain decreased steadily, and it was not until fourteen days after this attack that laparotomy was undertaken. Then the physical signs had altered radically. The swelling on the left was more definite, and was a mobile mass in the left iliac fossa, not felt from the pelvis at all. The uterus was raised and displaced to the left, and there was a semi-cystic swelling in the right fornix extending up into the right iliac fossa.

Operation.—A lower midline incision was made under general anaesthesia. There was a typical left tubal pregnancy occupying the distal half of the tube, with no sign of leaking of blood into the peritoneum. This was removed. On the right there was a haematoma walled off by adhesions extending into the pouch of Douglas and up into the right iliac fossa. The blood clot was removed. There was no sign of a bleeding point, but the uterine end of the right tube was eroded completely through for about an inch (2.5 cm.), the ends being friable. There did not seem to be any doubt that the haematoma had originated from here and could only have been from a tubal gestation. The ends of the tube were ligated and the abdomen closed. Search for embryonic remnants in the clot was not successful, but considering the probable original size of the gestation this was not surprising. Section confirmed that the tumour removed was a tubal gestation, chorionic tissue being seen in the sections. Recovery was entirely uneventful.

COMMENT

Bilateral tubal pregnancy is rare, the last report of a case in the *British Medical Journal* being in 1937 by McIlrath. Cox and Steinberg (1942), in reporting a case, state that 80 cases are on record in readily available literature, but I cannot be certain whether McIlrath's case is included among these. A further case was reported by Tractenberg (1944).

The question whether the foetuses would have been simultaneously viable or not is a point of great interest in these cases, and is raised by Fishback (1939) in a general review of this subject; but, there being no visible remnants of the products of conception on the right side in the present case, no good comparison can be made. However, it is probable that the right foetus was younger than the left, as the latter gave symptoms only while the patient was in hospital, and it was not palpable on admission.

It will be noted that laparotomy was delayed in this patient, and a word of explanation might be of interest. In this part of Iraq non-urgent abdominal operations can be undertaken with complete safety, but operations for acute abdominal conditions carry an abnormally high liability to complications, most commonly an intractable ileus. I can offer no explanation of this, but it has been the experience of several surgeons serving in this area.

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The Royal College of Nursing has arranged, with the approval of the Ministry of Health, a course for nurses on venereal diseases to be held on May 31 to June 26. It will be open to trained nurses who have been employed for at least six months in a venereal-diseases department. An examination will be held at the end of the course and a certificate awarded to successful candidates. Information may be obtained from: Director in the Education Department, Royal College of Nursing, Henrietta Place, Cavendish Square, London, W.1.