

Pernicious Anaemia and Pregnancy.

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THE association of anaemia and pregnancy has been frequently noted, but, as a rule, the anaemia takes the form of a secondary, chlorotic, or microcytic type with low colour index; it is not proposed to consider these cases further. Less commonly, a very severe degree of anaemia is observed, and is usually of the primary or megaloblastic type with high colour index. This latter has been termed the "pernicious" or haemolytic anaemia of pregnancy.

The association of pernicious anaemia and pregnancy may be conveniently considered according to the following scheme:—

Pernicious anaemia of pregnancy.

An anaemia of the pernicious type directly due to the pregnant state arising during:

1. The period of gestation.
2. The puerperium.

Primary (pernicious) anaemia with pregnancy.

A megaloblastic anaemia not primarily due to the pregnancy but associated with it.

1. Pernicious anaemia present before the pregnancy.
2. True primary (pernicious) anaemia first observed during or after pregnancy (*a*) through the activation of a latent pernicious anaemia—under the increased strain produced upon the haemopoietic tissues by the gravid state; (*b*) arising in predisposed women.

"PERNICIOUS" ANAEMIA OF PREGNANCY.

The anaemia may arise during any month of pregnancy, or in the puerperium, but there is not any difference in the character of the anaemia so observed; both are directly due to the gravid state, although when it commences during the puerperium the condition appears to be more severe.

The earliest cases of "pernicious" anaemia of pregnancy were recorded by Channing in 1842,¹² Lebert,³¹ and Gusserow.²⁴

A large number of cases of pernicious anaemia of pregnancy have been described in the literature from time to time since then, but it is difficult to discuss these owing to the inadequacy of the reports and especially antenatal observations.

According to Osler⁴¹: "Though progressive and often pernicious, the anaemia differs in one all-important particular from that which causes the anaemia of Addison. When recovery takes place it is permanent and the woman may escape in subsequent pregnancies. The second patient in my series (whom I knew well) had an attack of extreme gravity, recovered, bore two children subsequently, and was alive 30 years after the attack. Recovery from the Addisonian form may last 10, 15, or even 17 (McPhedran) years, but such instances are exceptional, and in the cases of reported permanent recovery there is always the question of a mistake in the diagnosis."

Essentially the same views have been expressed by other workers,^{3, 22, 45, 47, 49}, thus Allan² observed that: "Pernicious anaemia of pregnancy is an acute haemolytic anaemia occurring in females under 35 years of age, due to pregnancy, progressing steadily without remissions to death or recovery, and curable by blood transfusions as contrasted with Addisonian pernicious anaemia, an essentially chronic disease occurring after 35 years of age, predominantly in men, of unknown aetiology, running a course characterized by remissions and not curable by blood transfusion."

Alder¹ distinguished pernicious anaemia from pernicious anaemia of pregnancy and considered that they were distinct conditions, true primary pernicious anaemia very rarely, if ever, occurring in the pregnant female. He cited three cases of pernicious anaemia of pregnancy, and went on to say: "Ich fasse daher die Graviditätsanämie nicht als eine durch Schwangerschaftstoxine bedingte echte perniziöse Anämie auf, sondern sehe in ihr nur eine Reaktionsform eines funktionell geschädigten Knochenmarkes auf pathologische vielleicht auch schon physiologische Einwirkungen der Gravidität."

Esch,⁴⁹ however, found that only 35 per cent of 48 cases showed the presence of functionally injured bone-marrow.

Other cases of so-called "pernicious" anaemia of pregnancy have been described,⁶⁵ particularly by Continental workers.

On the other hand, several observers in India^{5, 33, 36, 63, 64} have more commonly seen severe degrees of anaemia, often fatal, in pregnant native women. This "pernicious" anaemia of pregnancy

is considered to be due to a chronic insufficiency of vitamins A and C in the diet,^{23, 63, 64} but a very high percentage of positive Wassermann reactions was also obtained in these cases, and syphilis may therefore be an important aetiological factor.

Symptoms.

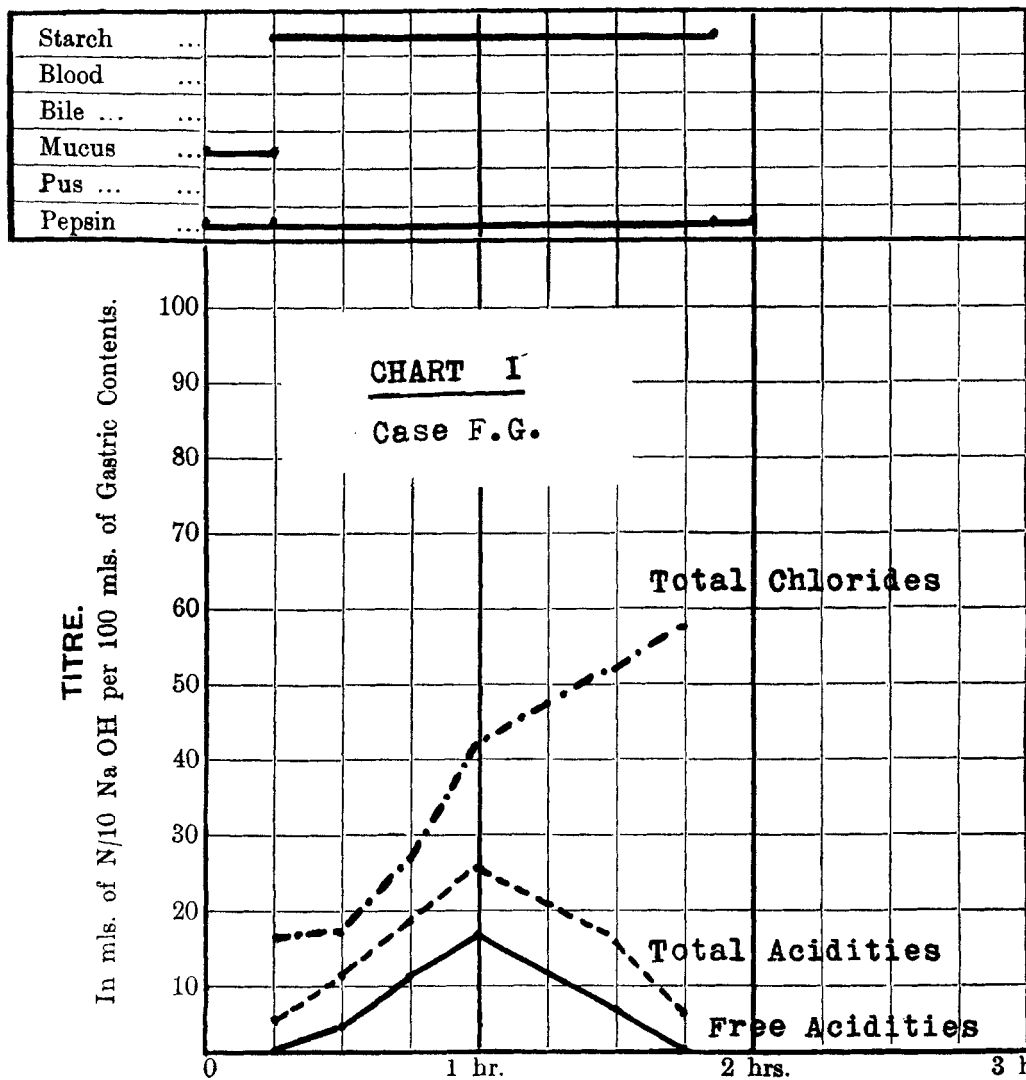
The condition is characterized by extreme pallor, a yellowish tint of the skin, weakness, dyspnoea, nausea, often vomiting; less frequently, sore tongue and diarrhoea. Oedema of the limbs and face is very common and is frequently associated with albuminuria. For this reason confusion may arise with nephritis⁶² and toxæmia of pregnancy, but the blood-pressure, the blood-urea, the renal function tests, and the blood picture distinguish this. There is a profound reduction in the red blood-cells but less marked lowering of the haemoglobin percentage, so that the colour index is, as a rule, greater than unity; the size of the red cells is frequently normal or a little less;²¹ the white cells usually show a slight or moderate leucocytosis rather than the leucopenia of primary pernicious anaemia. Anisocytosis is often found, but platelets are not reduced to the same extent. Abnormal staining, normoblasts, and megaloblasts may all be present. There is an increased amount of bilirubin in the blood and usually a normal gastric secretion (in contradistinction to true pernicious anaemia), although achlorhydria has occasionally been found.^{28, 46, 51, 55} Spinal cord involvement or peripheral neuritis (paraesthesiae) are not present. Remission takes place rapidly after blood transfusion in most cases after the puerperium or abortion, and is usually permanent (*vide infra*); some workers state that recurrences have been noted in subsequent pregnancies,^{2, 21, 25, 33, 37, 40, 44, 56} while others have not observed it.^{9, 19, 30, 38, 41, 55}

Prognosis.

The prognosis, as judged by the literature, was very variable, running up to 87 per cent maternal mortality⁶⁶ before the introduction of blood transfusion.

The use of adequate blood transfusions completely changed this outlook, so that as many as 90 per cent of the patients were cured.⁶⁷

The foetal mortality was also high, death frequently occurring *in utero* at the sixth to the eighth month.^{2, 5} Thus in 122 cases Auberton³ observed 17 macerated foetûs and 66 stillbirths; of the 39 children born alive 13 died in 15 days and the remainder were underweight or underdeveloped; he had, however, seen many normal full-time children born. Similar high mortalities have been noted by other observers.



Recent therapeutic advances, however, would indicate still better lines of treatment in the use of liver or stomach, and the prognosis now appears to be very good.

The following two cases belong to this group.

CASE F. G. A married woman, aged 39 years, admitted to the Manchester Royal Infirmary suffering from a severe degree of anaemia, weakness, loss of appetite, and slight flatulence, had been quite well until April, 1929, when she became pregnant for the second time; she commenced with sickness, pallor, and weakness of increasing severity, but there was never any history of diarrhoea, sore tongue, or indigestion.

In November of the same year her condition was much worse and she commenced to have considerable oedema of the legs and feet. In the following month a therapeutic abortion was induced and she was subsequently admitted to the Manchester Royal Infirmary on account of her profound anaemia.

There was neither a family history of pernicious anaemia nor a suggestion of familial achlorhydria (cp. 61); her one child was well. The previous medical history disclosed only rheumatic fever and scarlet fever.

On admission to hospital she presented a marked lemon-yellow colour of the skin, she was slightly wasted, had artificial teeth but glossitis and oral sepsis were absent. Her liver and spleen were not palpable and there was nothing else abnormal to be found. The reflexes were normal.

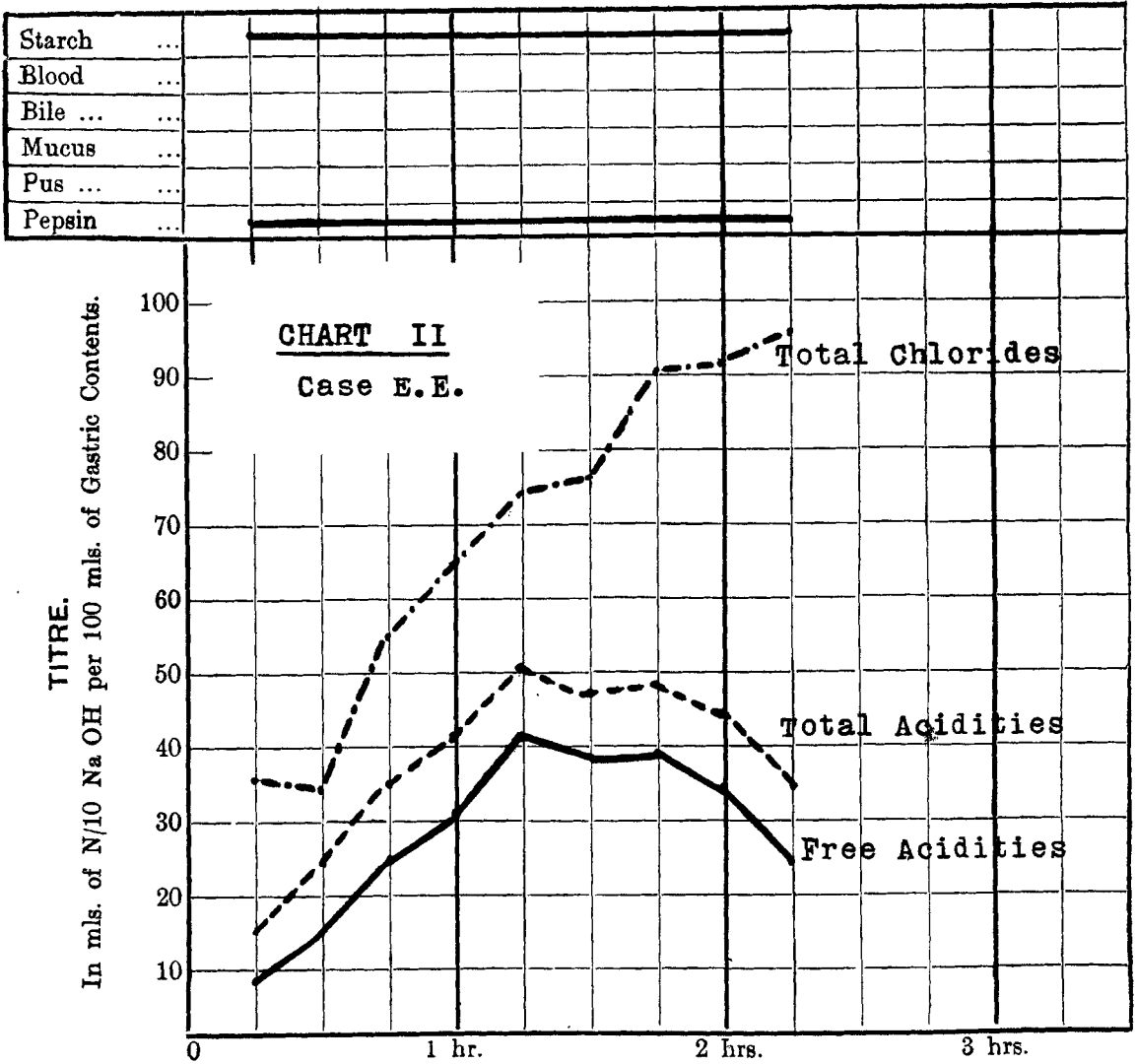
Blood count: red blood-cells, 1,290,000; white blood-cells, 2,700; haemoglobin, 28 per cent; colour index, 1.12; polymorphonuclears, 67.5; lymphocytes, 23.0; large mononuclears, 4.0; eosinophils, 5.5; basophils, 0.0; platelets diminished; anisocytosis and poikilocytosis marked; nucleated red cells present.

Free hydrochloric acid (Chart I) was found on fractional gastric analysis. The patient was given one ounce, by weight, of desiccated hog's stomach daily, and was discharged from hospital five weeks later with a blood count of red blood-cells, 3,704,000; white blood-cells, 4,200; haemoglobin, 60 per cent; colour index, 0.8; abundant platelets; slight anisocytosis and poikilocytosis; no nucleated red-cells.

She continued to take one ounce of the desiccated stomach daily for four weeks only and then discontinued it. When seen 12 months later she had remained perfectly well without any symptoms of the anaemia, and the blood count was: red blood cells, 4,900,000; white blood-cells, 4,400; haemoglobin 90 per cent; colour index, 0.9; abundant platelets and slight anisocytosis only.

CASE E. E. A multipara, aged 30 years, was admitted complaining of anaemia, dyspnoea, palpitation, and oedema of the ankles which became progressively worse after a premature (six weeks) confinement three months previously. There was not any complaint of sore tongue, diarrhoea, indigestion or paraesthesiae. She had had a mastoid operation 16 years previously and the left ear had discharged frequently since then.

There had been four previous normal pregnancies (one child died at six months, one was healthy and the other two had rickets and tuberculous peritonitis respectively), without subsequent complications. There was not any family history of pernicious anaemia or possible achlorhydria



On admission she presented a considerable pallor of yellowish colour; a furred tongue, pyorrhoea, and oedema of her lower limbs; her pupils and discs were normal: she weighed six stones, nine pounds. There was evidence of bronchitis; her liver and spleen were just palpable; the reflexes were present and normal. There was a haemic systolic bruit at the apex of her heart; her blood-pressure was 105/60. Her Wassermann reaction was negative.

Fractional gastric analysis: normal acidities (Chart II). Blood count: red blood-cells, 600,000; white blood-cells, 4,600; haemoglobin, 18 per cent; colour index, 1.5; polymorphonuclears, 37.25; lymphocytes, 56.25; large mononuclears, 0.5; eosinophils, 6.0; basophils, 0.0; platelets scanty; marked anisocytosis and poikilocytosis; nucleated red cells, poichromasia and punctate basophilia present. She was treated with fresh liver (eight ounces daily) and responded rapidly.

After discharge from hospital she was not seen again for 20 months when her blood count was: red blood-cells, 4,300,000; white blood-cells, 5,000; haemoglobin, 86 per cent; colour index, 0.9; normal differential white count, abundant platelets, slight anisocytosis. Normal secretions were still found on fractional gastric analysis. She had not had any treatment and did not complain of any return of anaemia although she had had a full-time normal pregnancy four months previously. After a further five months the blood count showed red blood-cells, 5,225,000; white blood-cells, 6,250; haemoglobin, 95 per cent; colour index, 0.92.

She did not attend again until 12 months later, when a similar history of another normal full-time pregnancy (eight weeks previously) was given without any return of anaemia; treatment had not been given.

The blood count was: red blood-cells, 5,000,000; white blood-cells, 2,620; haemoglobin, 82 per cent; colour index, 0.8; platelets abundant; some anisocytosis; no abnormal cells or staining.

In each of these patients it will be noted that the severe anaemia was directly due to the pregnancy and dated from the commencement of pregnancy and puerperium respectively, while the blood counts were of the typical primary (pernicious) type. On the other hand, the gastric secretions were normal—a condition of extreme rarity in true pernicious anaemia. In both patients previous pregnancies had not produced anaemia, while in the second patient two subsequent pregnancies had failed to cause recurrences.

Both patients are apparently cured completely with normal blood pictures and have not had any treatment for two and four years respectively. These are definite cases of "pernicious" anaemia of pregnancy.

TRUE PRIMARY (PERNICIOUS) ANAEMIA ASSOCIATED WITH PREGNANCY.

In this group are included those cases in which (a) pregnancy has occurred in patients known to have pernicious anaemia and (b) those cases in which true primary (pernicious) anaemia has

been found in pregnant or parturient women. In the first subgroup no doubt arises, since the pregnancy has occurred after the diagnosis of pernicious anaemia, often years previously.

I have found that in a series of 290 cases of pernicious anaemia treated at the Manchester Royal Infirmary during the years 1927 to 1931 the sex proportion was females to males as 1 to 1.07; of the 140 females 23.85 per cent were between 20 and 40 years of age and 50.7 per cent between 20 and 50 years of age when first coming under observation. It is very reasonable to anticipate that pregnancy may occur in some of these patients, particularly when it is realized that the amenorrhoea and diminished fertility frequently associated with pernicious anaemia are much improved in most patients when the anaemia is successfully treated.⁵⁸

Gallupe and O'Hara, in 1924,²¹ observed that: "The occurrence of pernicious anaemia during child-bearing is spoken of in a manner that suggests that there is some cause and effect relationship between the two conditions, but we can find nothing in the literature to suggest that the relation between these two conditions is anything more than one of coincidence." This has been noticed by others.

(a) *Pregnancy following diagnosis of pernicious anaemia.*

The rarity of the association of true primary pernicious anaemia with pregnancy has been stressed (see references 1, 20, 30, and others, *vide supra*), but Heim²⁶ describes a case in which pregnancy occurred during a remission in pernicious anaemia, although the data of the case prior to the pregnancy are lacking.

It is a little difficult to understand why such dogmatic statements should be made unless we assume that prior to 1926 and 1927 the majority of cases of pernicious anaemia died within six months to two years of diagnosis, the general condition or diminished fertility preventing pregnancy. During the last five or six years, however, the successful treatment of pernicious anaemia, first by liver³⁴ and later by hog's stomach,⁵⁸ has entirely changed the prognosis, so that these previously invariably fatal cases now regain and maintain normal health on adequate treatment. In consequence it is to be expected that at least some women who have had pernicious anaemia will become pregnant.

I have had the opportunity of observing such occurrence in three cases of definite and typical primary pernicious anaemia which have been under regular observation and treatment for from one to three years prior to the first pregnancies.

The following case illustrates the small group of individuals with true primary pernicious anaemia associated with subsequent pregnancy.

CASE A. B. A married woman, aged 29 years, had been quite well until January, 1927, when she was in bed for three weeks suffering from marked jaundice, nausea, vomiting, and pyrexia associated with dark urine and clay-coloured stools. She recovered, and was well until recurrences took place in January and June, 1929, when she complained for the first time of marked weakness in the arms and legs, numbness and increased attacks of vomiting. She lost weight and had slight flatulent dyspepsia and amenorrhoea. Her appetite was good and the bowels were regular. There was not any history of sore tongue or diarrhoea. There was nothing relevant in the previous medical or family histories.

On admission to hospital in August, 1929, she had a marked yellow colour with anaemia, her tonsils and spleen were enlarged, there was an upper denture, her lower teeth were good, her liver was normal, bilateral retinal haemorrhages, she weighed six stones five pounds. Her heart was enlarged and systolic bruit was present over the praecordium, her blood-pressure was 115/54. Fractional gastric analysis showed achylia gastrica.

Blood count: red blood-cells, 860,000; white blood-cells, 3,300; haemoglobin, 18 per cent; colour index, 1.1; scanty platelets; marked anisocytosis and poikilocytosis; polychromasia, punctate basophilia, normoblasts, and megaloblasts present. Haemolysis commenced 0.42 per cent, complete 0.32 per cent, saline.

She was given a blood transfusion (400 c.c.) and put on to one ounce daily of desiccated hog's stomach. The clinical condition rapidly improved, and she was discharged from hospital with a blood count of red blood-cells, 3,270,000; white blood-cells, 5,200; haemoglobin, 65 per cent; colour index, 1.01; platelets abundant; some anisocytosis and slight poikilocytosis, no abnormal cells on staining. She was seen regularly at monthly intervals and, eight weeks later, her red blood-cells were estimated to be 5,290,000, and the haemoglobin, 90 per cent. Her menstrual periods returned but became irregular and scanty in March, 1929, when she was found to be about three months' pregnant. The dose of desiccated hog's stomach, which had been reduced to half an ounce, was increased to three-quarters of an ounce and, later, to one ounce daily. Monthly blood counts were made. At no time during the period of gestation did the count fall below red blood-cells, 4,200,000; and haemoglobin, 78 per cent. Two weeks before the parturition the count was: red blood-cells, 4,260,000; haemoglobin, 90 per cent; white blood-cells, 5,900; and colour index, 1.05. Parturition was normal, rapid, and a full-time male child (six pounds, 12 ounces) was delivered. Three weeks later the blood count showed: red blood-cells, 4,440,000; haemoglobin, 78 per cent; white blood-cells, 4,800; colour index, 0.9

Fourteen days later the count was: red blood-cells, 5,180,000; white blood-cells, 4,800; haemoglobin, 86 per cent; colour index, 0.85. She has continued to take half an ounce of desiccated hog's stomach daily, and after 12 months the blood picture is: red blood-cells, 4,300,000; white blood-cells, 5,000; haemoglobin, 80 per cent; and colour index, 0.98.

The blood counts of the child were, at the age of three weeks: red blood-cells, 4,056,000; white blood-cells, 4,000; haemoglobin, 96 per cent; colour index, 1.2; marked anisocytosis and poikilocytosis; abundant platelets. At the end of 12 months the blood count was: red blood-cells, 4,480,000; white blood-cells, 9,300; haemoglobin, 72 per cent; colour index, 0.8; slight anisocytosis and poikilocytosis; abundant platelets.

It is interesting to observe in this connexion that both Heim²⁸ and Offergeld³⁹ state that newborn children of women suffering from pernicious anaemia have anaemia; on the other hand, those from women with pernicious anaemia of pregnancy do not.^{5, 15, 42}

(b) *True pernicious anaemia in pregnancy.*

In this smaller sub-group the differential diagnosis of pernicious anaemia with pregnancy from "pernicious" anaemia of pregnancy requires more care, and is more easily confirmed after prolonged observation following parturition. This includes cases of pernicious anaemia arising during pregnancy or the puerperium not previously diagnosed but probably occurring in women either predisposed to develop pernicious anaemia or else already in a condition of latent pernicious anaemia.

While the proof of a correct diagnosis is not easy, there is not any doubt at all about this in several of the cases which have been under investigation prior to the pregnancies.

I have already shown that heredity is a very important factor in the aetiology of pernicious anaemia, while in an examination of a large number of patients with pernicious anaemia and their relatives it was found that at least 24 per cent had gastric impairment—achylia or achlorhydria.⁶¹ This latter is of considerable significance and indicates the advisability of periodical examinations of such relatives, especially females during the child-bearing period. It has been my custom to carry out regular investigations on as many as possible of the relatives of patients with pernicious anaemia. In consequence of this it has been possible to keep under observation several women who are the subjects of gastric achylia with blood pictures of normal appearance, but who occasionally complained of varying symptoms such as vague dyspepsia. Eventually pregnancy has occurred, and in two patients typical pernicious anaemia has developed subsequently.

The following cases illustrate this point. The father of the first woman had pernicious anaemia and she had achlorhydria, thus suggesting a strong liability to develop pernicious anaemia under suitable conditions of strain on the haemopoietic tissues.

The second woman had a vague history of anaemia and disturbed menstrual functions for 14 years, but she had not come under my observation during that time and no blood or other investigations had been carried out. Pregnancy, however, broke down the residual haemopoietic resistance and the latent anaemia became a definite pernicious anaemia.

CASE I. O. A married woman, aged 31, was seen by me on July 16th, 1930, in the course of an investigation into the relatives of patients with pernicious anaemia. Her father suffered from this condition and she

complained of flatulent dyspepsia, "nerves" and occasional cramps in the right foot. She had always been subject to "biliousness and sick headaches," but there was not any history of sore tongue, diarrhoea or anaemia. She had one child which was quite well, and parturition had been normal four years previously.

Examination did not disclose anything abnormal except achylia gastrica on fractional gastric investigation. The blood count was : red blood-cells, 4,400,000; white blood-cells, 6,700; haemoglobin, 85 per cent; colour index, 0.97; slight anisocytosis, abundant platelets, no abnormal staining.

She was treated with a mixture containing half a drachm of hydrochloric acid and pepsin, gaining much relief. She was kept under regular observation, during which time she became pregnant, having an occasional return of the sickness and headaches. Blood counts showed a slowly increasing degree of anaemia until parturition (Oct. 9th, 1931), which was normal and rapid. She was not seen until three weeks later when the blood count was typical for a moderate pernicious anaemia; showing red blood-cells, 3,420,000; white blood cells, 6,600; haemoglobin, 76 per cent; colour index, 1.12; anisocytosis and poikilocytosis present; platelets reduced, but no abnormal staining reactions observed.

She complained of considerable flatulence, indigestion, paraesthesiae in legs and feet, and nervousness. She was put on to the acid and pepsin mixture again together with half an ounce daily of desiccated hog's stomach (Boots). At the present time her blood count is : red blood-cells, 4,500,000; white blood-cells, 7,400; haemoglobin, 90 per cent; colour index, 1.0.

The child (male) weighed 10 pounds and had a blood count of : red blood-cells, 4,340,000; white blood-cells, 8,600; haemoglobin, 94 per cent; colour index, 1.1; slight anisocytosis; platelets present.

CASE E. M. A married woman, aged 32 years, was admitted to hospital complaining of dyspnoea on the slightest exertion, frequent attacks of dizziness and fainting, increasing pallor, progressive anaemia, nausea, pain in the left side of the abdomen and paraesthesiae in the lower limbs. There had not been any vomiting, diarrhoea, indigestion or sore tongue. The menses had always been irregular and scanty, commencing at 18 years of age. She had a miscarriage at 19 years of age and had never been well since, being "always anaemic." She first noticed the increasing pallor and dyspnoea during the puerperium following a full-time pregnancy seven months previously. There was nothing relevant in the family or previous medical history.

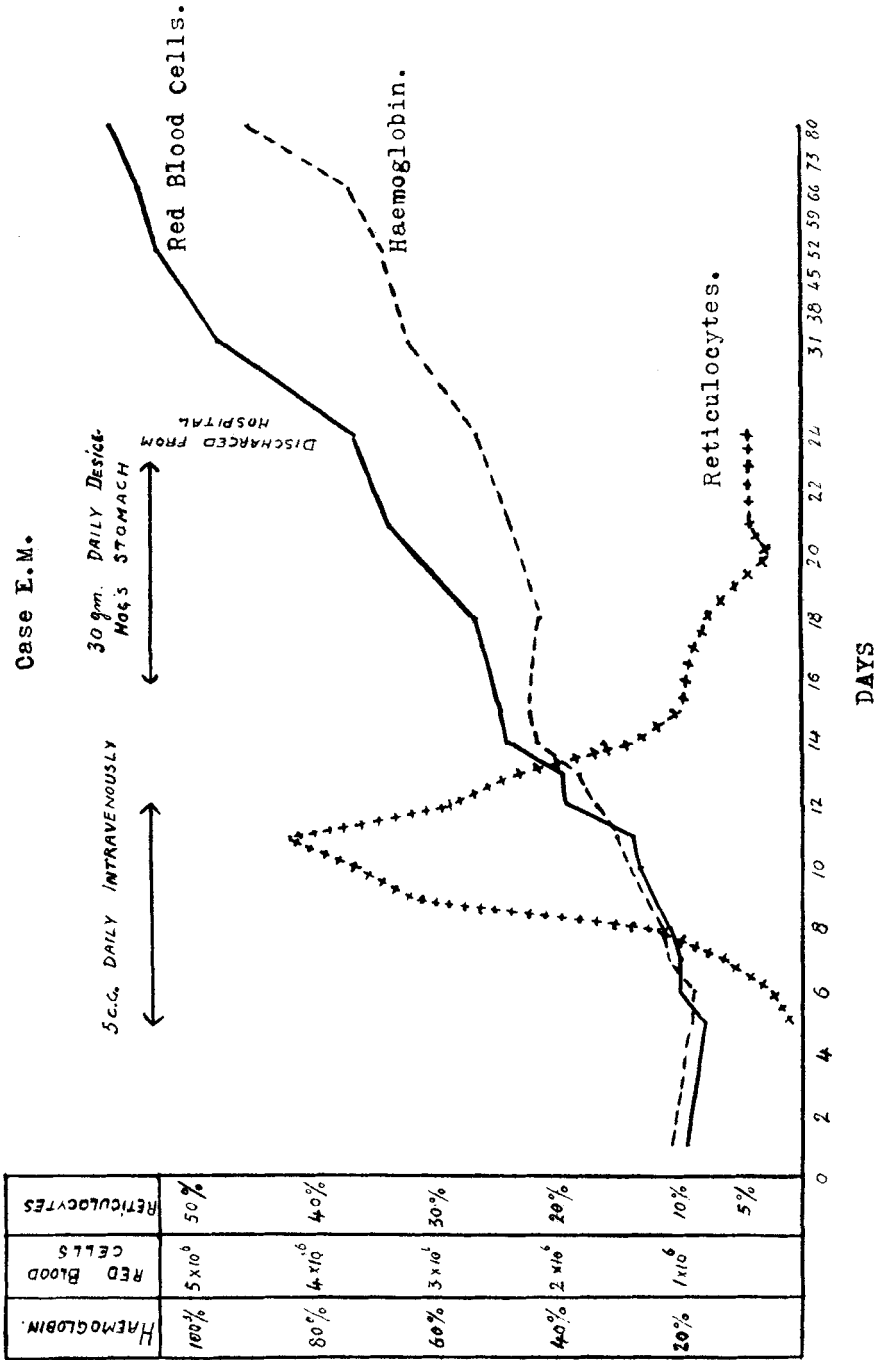
On admission to hospital the patient presented an extreme yellowish pallor of the skin and mucous membranes. Her tongue was fairly clean; there was not any glossitis; she had artificial teeth. There was a haemic systolic murmur over the praecordium. Her spleen was enlarged, normal reflex responses were present but she had an impaired sensation to "pin-prick," "hot and cold," "light touch" in the lower limbs from the lower third of the thighs distally.

Test meal : achylia gastrica.

Blood count (May 14th, 1930) : red blood-cells, 650,000, white blood-cells, 4,100; haemoglobin, 17 per cent; colour index, 1.4; polymorphonuclears, 61.0; lymphocytes, 34.0; large mononuclears, 3.5; eosinophils, 1.5; basophils, 0.0; platelets very scanty; very marked anisocytosis and poikilo-

CHART III.

Case E.M.



cytosis; polychromasia and punctate basophilia; normoblasts and megalocytes present in large numbers.

She was given a blood transfusion (20 ounces; group IV) and put on to eight ounces of fresh liver daily. She responded immediately and six weeks later (June 4th, 1930) was discharged from hospital with a blood count of: red blood-cells, 4,650,000; white blood-cells, 5,300; haemoglobin, 72 per cent; colour index, 0.8; platelets abundant; no anisocytosis or poikilocytosis or abnormal staining.

She was not seen again for six months, during which time she had discontinued all treatment. She was re-admitted to hospital in a severe relapse, with paraesthesiae of the hands and feet, diarrhoea, and indigestion. Her blood count was: red blood-cells, 900,000; white blood-cells, 1,400; haemoglobin, 21 per cent; colour index, 1.1.

Her condition was very grave, blood transfusion being impossible owing to a very strong auto-haemagglutination. She was given, therefore, an intravenous injection of five cubic centimetres daily of a highly concentrated liver preparation, Hepatex P.A.F. (kindly supplied by Evans's Biological Institute, Runcorn), with a remarkable response (Chart III). She received in all 40 cubic centimetres (equivalent to 800 grammes of fresh liver) during eight days with a rapid and satisfactory increase in the reticulocytes to 41.8 per cent. Her condition began to improve within 24 hours of the commencement of this therapy and progressed steadily, with concurrent rise in the red blood-cells and haemoglobin. After an interval of four days without treatment she was put on to desiccated hog's stomach (30 grammes daily) and the improvement continued steadily and progressively. She was discharged from hospital nine days later.

On November 14th, 1931, her red blood-cells numbered 5,290,000; her white blood-cells, 7,900; the percentage of haemoglobin was 96 and the colour index 0.9. This has been maintained by a daily dose of half an ounce of desiccated hog's stomach (Boots).

TREATMENT.

Until relatively recently the different methods of treatment recommended for "pernicious" anaemia of pregnancy were as varied and uncertain as those for pernicious anaemia. That the uterus should be emptied was generally agreed, but further therapy consisted in arsenic, with or without iron, in various forms, colloidal antimony trisulphide,¹⁴ serum, vaccines,^{3, 56} repeated intramuscular or subcutaneous injections of whole, defibrinated or citrated blood in small quantities of 30 to 100 c.c.^{4a, 6, 7, 15, 19, 22} or massive doses of 500 c.c. (Schmidt,⁵¹ Voron and Pigeaud,⁵⁷ and others).

The results of such treatment have already been discussed (*vide supra*). Recurrence was prevented in two patients by artificial sterilization, but this is hardly justified.^{25, 40, pp. 190}

With the introduction of the liver treatment for pernicious anaemia³⁴ in 1926, a new era began with a complete reversal

of the prognosis. Relatively few cases have as yet been recorded following the application of this therapy for pernicious anaemia of pregnancy,^{4, 7b, 10, 17, 43} but the results, as a rule, have been fairly good, especially in association with blood transfusion. One patient who did not respond had a positive Wassermann reaction.⁵⁷

More recently, hog's stomach⁵⁸ was introduced for the treatment of pernicious anaemia, and in this paper the first cases to be treated with this substance in association with pregnancy are described. The results are extremely satisfactory and the prognosis, so far, appears to be excellent.

It is essential that adequate amounts of desiccated hog's stomach should be used (as a rule, this implies one ounce by weight daily in cold milk or water). It is also essential that an active preparation should be employed.⁶⁰

Thus for both "pernicious" anaemia of pregnancy and true primary pernicious anaemia with pregnancy liver and stomach constitute suitable forms of treatment, the latter being more active, palatable, and cheaper besides offering a smaller protein intake for these cases.

It happens occasionally that extremely severe cases of pernicious anaemia are encountered exhibiting auto-haemagglutination: blood transfusion in such cases is strongly contra-indicated. A rapid and suitable therapy is available in the intravenous or intramuscular use of the highly concentrated *protein-free* preparation, Hepatex P.A.F.⁵⁹

It is essential, however, that the anaemia should be of the pernicious type with high colour index for these forms of treatment to be of outstanding benefit.

Ordinary "secondary" anaemia and post-haemorrhagic anaemia respond better to large doses of iron (such as iron and ammonium citrate or Blaud's pills—60 to 90 grains daily).

SUMMARY.

1. The association of pernicious anaemia with pregnancy has been considered.
2. Several cases of true primary pernicious anaemia have been described in association with, but not due to, pregnancy. The patients have been under observation and treatment for several years and have kept in normal health.
3. One patient with familial achlorhydria (and related to a patient with pernicious anaemia) and two with latent pernicious anaemia have been observed to develop frank primary pernicious anaemia as a result of the gravid state.

4. Two cases of "pernicious" anaemia of pregnancy have been described. They had typical blood counts for a primary anaemia, but had normal gastric secretions. Both were cured by suitable treatment and relapses have not occurred following discontinuance of this, although subsequent pregnancies have been observed in one of them.

5. A rapid and suitable form of treatment for both forms of pernicious anaemia consists of the administration of one ounce daily of desiccated hog's stomach. Patients with true primary pernicious anaemia must continue this treatment indefinitely on adequate maintenance doses; patients with "pernicious" anaemia of pregnancy are able to discontinue it after the blood count has returned to normal.

6. A very rapid and safe method of treating extremely severe cases of pernicious anaemia associated with pregnancy, using highly potent liver preparations intravenously, is also described; it is particularly applicable when auto-haemagglutination is present.

7. Relapses have not occurred during pregnancy in a series of three women receiving adequate treatment for primary pernicious anaemia. This suggests that pregnancy can therefore be permitted in such women with pernicious anaemia provided that *suitable* treatment is continued throughout.

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