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Observations

ON

THE SEVERE ANAEMIAS OF PREGNANCY AND THE POST-PARTUM STATE.

BY

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THOSE of us whose professional careers coincide with its modern study will remember how important was the part played by these conditions in severe anaemia. Channing (1842), Lebert (1853), and Gusserow (1871) dealt with this aspect of the subject. Many of Biermer's original cases were in pregnant women, and a large proportion of the cases forming the basis of the monographs of Müller (1877) and of Eichhorst (1878) were in this class. After 1885 the literature shows a striking reduction in the references, and Ehrlich and Lazarus, in Notlmagel's *System*, suggested that local influences in the cantons were responsible for the frequency of this association in the cases reported by the Swiss clinicians. So experienced a teacher as Ahlfeld, they state, had never met with a case. Considering how much has been written by British physicians on the various forms the literature on the anaemia of pregnancy and the post-partum state is very scanty—only one of nineteen in the *Index Catalogue* of the Surgeon-General's Library, both series. In Allbutt and Rolleston's *System* French makes only a passing remark on the association. With few exceptions the textbooks in obstetrics have very little to say, and the gloomy prognosis is an echo of the unfortunate experiences of the older writers. Among recent works Edgar's has the best section. That cases are rare in this country is shown by the absence of reference in the writings of so experienced workers as Byrom Bramwell and William Hunter. In the United States Channing's really remarkable study seems to have aroused an interest in the subject, and five American papers are quoted in Vol. I of the *Index Catalogue* before the appearance of Gusserow's in 1871. In Cabot's¹ series of 1,200 cases of progressive pernicious anaemia, in 35 the disease began during pregnancy or shortly after parturition, 18 during the former. This proportion—about one in thirty-five—is probably the average for the United States. Davis,² in reporting a case, gives a very good summary of the older American literature; and Findley,³ who deals with the subject more recently, concludes that "in all well established cases the disease has proved fatal." In the discussion on this paper Richard Norris stated that there had only been one case among three thousand women at the Preston Retreat. Of the first twenty-three cases of "progressive pernicious" anaemia of which I have notes, all but one seen in Montreal, five were *post partum*. I saw two in Philadelphia, and there were a few at my Johns Hopkins clinic, but I have not the figures. The theses of Decroix,⁴ Husson,⁵ and Robert⁶ indicate that the association is not very common in France. The recent German and Swiss literature is given in Naegli's well known monograph on the blood. Possibly the existing conditions of under-feeding, etc., have led to an increase of cases during pregnancy, and the intense wave of streptococcus infection may have increased the cases of acute septic anaemia *post partum*.

The cases may be divided into four groups:

I. ANAEMIA FROM POST PARTUM HAEMORRHAGE.

(a) The bleeding may be profuse and rapidly fatal. The physician sees fatal haemorrhage in aneurysm, in typhoid

fever, in peptic ulcer, and in ruptured oesophageal varix, none of which conditions present the tragedy of the *post-partum* case. Only once has it been my misfortune to witness this peculiarly pathetic accident. Peace and quiet reign in the lying-in chamber and happiness in the household, for all has gone well, and the young mother is just beginning to realize the joy that "a child is born into the world." The doctor may have left, feeling safe and satisfied. The attention of the nurse is attracted by a sudden restlessness of her patient, whose face shows a beginning pallor, and she finds the dressings soaked with blood. Very soon the symptoms are those of acute anaemia—a rapid, jerky pulse, extreme restlessness, yawning, sweating, sighing respiration, increasing pallor, and with muscular twitchings, convulsions, or a sudden collapse all is over. This was what I saw one afternoon, called hurriedly to the house of a neighbour—a strong, healthy young woman *in articulo mortis*, after a normal delivery, as bloodless as if the carotids had been cut. No wonder that novelists have made such a tragedy the climax of a story. Hitchins, in *The Fruitful Vine*,⁷ makes Dolores die in this way; and it is possible that Walter Savage Landor had in mind this type of death in his beautiful little poem in *Pericles and Aspasia*:

Artemidora! God's invisible,
While thou art lying faint along the couch,
Have tied the sandal to thy veined feet;
And stand beside thee, ready to convey
Thy weary steps where other rivers flow

* * * * *
Fate's shears were over her dark hair unseen
While thus Elpenor spoke.

(b) *The Anaemia Following Repeated Small Haemorrhages*.—This not infrequently follows abortion, more rarely the repeated bleeding after a delivery at term. The following is a good illustrative case:

Mrs. B., aged 45; admitted October 8th, 1918, having had an abortion in the fourth month of her seventh pregnancy, one month previously. She had been losing blood intermittingly, not any large amount, but every few days a clot or two would come away. There had been slight irregular fever, and a progressive anaemia. At times there was a slight purulent discharge. She was cured, and with douches the discharges soon ceased. She looked profoundly anaemic, and with a sallow brown tint of the skin. The blood count was: Red blood corpuscles 2,106,000 per c.mm.; leucocytes 12,800. Ten days later the red blood count was 1,800,000 and the leucocytes 12,000. On the 21st thrombosis of the left femoral vein with swelling of the leg. The blood films showed the red cells irregular in shape and size, many normoblasts, and numerous platelets. In the open air with plenty of good food, iron and arsenic, she improved rapidly, and left the infirmary on December 3rd with a nearly normal blood count.

As in many cases, the anaemia here was due to a combination of repeated small haemorrhages and a mild sepsis. The general appearance was that of an ordinary Addisonian anaemia, for which any casual observer would have mistaken the case. In III and IV of my Montreal series the profound anaemia followed many small haemorrhages after abortion.

II. THE SEVERE ANAEMIA OF PREGNANCY.

The blood of the pregnant woman shows in the early months a diminution of red corpuscles, a low haemoglobin, and a slight leucocytosis (as is well shown in the composite chart in W. L. Thompson's⁸ study from Williams's clinic), to be followed by a rise to or near normal in the ninth month. A slight pallor in the early months is common, and is often associated with the morning vomiting or dyspepsia. That this so-called chloro-anaemia of pregnancy might pass on to a grave and fatal form was recognized by Channing and Lebert, but it was the full report by Gusserow⁹ of five fatal cases that roused the attention of the profession to the seriousness of severe anaemia in pregnancy. The following is a typical case:

On April 13th, 1917, I saw with Dr. Arthur F. Stabb and her husband Mrs. A., the wife of an army surgeon, a primipara of good previous health, though she had had a "tendency to anaemia." The pregnancy, which began in September, 1916, was uneventful until March, when anaemia began and increased rapidly, so that by April 1st she had dyspnoea and swelling of the feet. On April 3rd albumin appeared in the urine in large amounts. On April 10th the blood count was: Red blood corpuscles 864,000 per c.mm.; leucocytes 13,360; haemoglobin 20; colour index 1.12. The lymphocytes were increased 30 per cent., and the normoblasts were 6 per 100 leucocytes. There was the usual extreme irregularity in size and shape of the red cells. Labour began on the 9th, and on the 11th she was delivered of a stillborn child of normal appearance for the seventh month. There was very little haemorrhage, and she stood the strain very well. When seen on the 13th she was well nourished, but with all the objective features of profound anaemia. There were no internal haemorrhages. The case was regarded as a typical example of the so-called toxic or haemolytic anaemia of pregnancy, and, based on an unusually fortunate experience, I ventured to give a favourable prognosis. The recovery was rapid and uninterrupted, as the blood counts show: April 18th, red blood corpuscles 1,036,000; April 26th, 2,368,000; May 3rd, 2,592,000; June 17th, 3,250,000; and December 4th, a practically normal count. The leucocytes rose on April 18th to 45,000 per c.mm., and fell to 3,360 on May 3rd. On April 26th the normoblasts rose to 16 per 100 leucocytes, after which date they disappeared.

III. POST-PARTUM ANAEMIA.

In this, the common form, after a normal delivery without excessive loss of blood, the patient begins to get pale, and within a few weeks the blood count may fall below 2,000,000 per c.mm., and the anaemia may progress and prove fatal in from eight to twelve weeks. How serious this type may be is seen from the high mortality in the series of Channing and of the Zurich clinicians. On the other hand, the experience elsewhere has been more favourable. Dr. Palmer Howard, one of the earliest and most careful students of the subject, insisted that the large percentage of recoveries in the *post-partum* cases, and the absence of recurrence distinguished this form from the true Addisonian anaemia, though clinically the cases appear to be identical. The five *post-partum* cases in my first series all recovered. One was alive more than thirty years after and had passed through two subsequent pregnancies without trouble. The following case gives a good picture of the disease:

Amelia T., aged 35; admitted February 2nd, 1888. In the October previous she had been delivered of her fourth child; no complications. She had begun to nurse the baby, but gradually got pale and weak and had frequent fainting fits and much shortness of breath. On admission the anaemia was so extreme that she could not sit up in bed without feeling faint. The red blood corpuscles were 1,170,000 per c.mm., with extreme irregularity in form and size and many nucleated red cells. The haemoglobin was 15 to 18 per cent. With rest in bed, good food, iron and arsenic, she improved rapidly and left the hospital with a normal blood count.

Not infrequently in severe anaemia there is a continuous fever, which may lead to error in diagnosis, even suggesting typhoid fever, a point to which Cabot refers. The fever may be more irregular, and even associated with chills, which in the following case led to the diagnosis of malaria.

L. T., primipara, aged 24, seen with Dr. Jenkins, October 6th, 1898. Though a difficult labour there were no complications, and for ten days everything was normal. Then she began to get pale and grew rapidly worse, and in the sixth week after confinement, when I saw her, the red blood cell count was 1,200,000 per c.mm., leucocytes 15,000, haemoglobin 15 per cent. Every fourth or fifth day the patient had a chill in which the temperature rose to 103-104°, after which she sweated profusely. There was no discharge, no evidence of sepsis, other than the fever and the chills. The spleen enlarged, and as she lived in a region in which parturition was recognized as one of the factors determining recurrence of malaria this had been

suggested in explanation of the chills. The blood was negative during a chill and after. The red cell count fell to 800,000 per c.mm. and her condition for weeks was critical, but she gradually improved, and four months later she had a nearly normal blood count.

IV. THE ACUTE ANAEMIA OF POST-PARTUM SEPSIS.

In certain types of sepsis there is rapid blood destruction. In acute endocarditis the anaemia with a large spleen may completely mask the clinical picture, as in cases which I reported a few years ago in the *Interstate Medical Journal* (1913). In no condition do we see such rapid haemolysis as in *post-partum* sepsis—a form of anaemia not sufficiently recognized or studied.

In 1882 I saw with Dr. Alloway, on the seventh day after delivery, a young woman in a state of profound anaemia. The blood loss had not been severe, but for some days there had been an unusually foul though slight discharge. The red blood cells were just 1,000,000 per c.mm., the leucocytes 20,000. I never saw the objective features of anaemia more pronounced, and her chief complaint was the painful throbbing of the abdominal aorta, which pulsated with extraordinary violence. She died on the twelfth day. There was "diphtheritic" endometritis, septic thrombi in the pelvic veins; no endocarditis.

Such extremely rapid cases are not common, but Cabot¹⁰ refers to one with identical features, in which the acute sepsis was not suspected. The red blood count was 800,000 per c.mm. "Diphtheritic" endometritis was found at the *post-mortem* examination, without which, as Cabot remarks, the case would have gone into the category of puerperal pernicious anaemia. While every patient with puerperal fever has some grade of anaemia, only in a few does the blood loss dominate the picture. In many of the best textbooks on obstetrics—for example, Edgar (1903)—the condition is not referred to. An excellent account is given by Lea,¹¹ who states that the loss of red cells may be at the rate of from 200,000 to 1,000,000 per c.mm. a week, and that the count may fall to 300,000 per c.mm. Three cases of puerperal sepsis recently in the Radcliffe Infirmary illustrate the condition very well.

Mrs. C., aged 24, admitted under Colonel Collier August 31st, 1918, had a miscarriage late in her second pregnancy. Fragments of retained placenta were removed. She had the typical sallow, pale yellow (not the brown-yellow) tint of skin, and the usual features of moderate anaemia. The red blood cells were 2,700,000 per c.mm., leucocytes 8,600, haemoglobin 46. She improved rapidly, and left the infirmary on September 21st, 1918.

Mrs. M., aged 49, admitted August 8th, 1918, under Colonel Brooks. Since the delivery of her eleventh child, July 16th, she had had severe sepsis with high irregular fever and a progressive anaemia. The blood cultures were negative. The blood count was: Red blood cells 1,580,000 per c.mm., leucocytes 13,400, haemoglobin 16 per cent., colour index 48. Nothing special in the differential count other than a high percentage of lymphocytes. The irregularity in size and shape of the red cells was extreme, and there were many normoblasts. She died on September 8th in a state of profound anaemia.*

Mrs. W., aged 31, primipara, admitted under Colonel Collier, November 30th, 1918, having been delivered a week before. No complications. Acute sepsis developed with high fever and a very offensive discharge. When admitted the patient was very anaemic, with a sallow, sub-icteroid tint and all the symptoms of a severe infection. St. *ptococci* were isolated from the blood, and she was given antistreptococcal serum on December 1st and 3rd. The red blood count was 2,250,000 per c.mm., leucocytes 9,600, haemoglobin 40. The differential count showed nothing special; normoblasts were present in moderate numbers. The anaemia progressed rapidly, the fever remained high, and she died on December 7th.

With an increased frequency of streptococcus infections and an unusual virulence of at least some strains in respiratory affections, it would be interesting to learn if puerperal fever has been more prevalent throughout the country. So far as I know, the *post-partum* sepsis cases have not shown a special tendency to haemorrhage, as have so many of the streptococcal infections of the past six months.

REMARKS.

To the nature of the haemolytic agent in the pregnancy and *post-partum* cases there is as yet no clue, any more

* There may have been septic endocarditis in this case, as a few days before death there was a soft diastolic murmur along the left sternal border. The dancing, vibrating pulsation of the peripheral arteries was extreme and the pistol-shot sound unusually loud. In connexion with the production of this in the arteries, about which so much has been written recently, the following note, dictated September 2nd, 1918, is of interest: "A loud systolic bruit is heard over the abdominal aorta without pressure; but neither heart sound. Over the femoral, without the slightest pressure, two sounds are heard, quality and intensity about equal, and almost as loud as the sounds heard over the heart itself. With pressure both increase in intensity, then a loud systolic murmur develops, and on pressure to obliteration, a loud single pistol shot remains."

than we have to the cause of that most baffling of all blood diseases, Addison's anaemia. The progress and the blood picture suggest the haemolytic type, which can be produced experimentally and which is caused by the poisons of the *Bothriocephalus*. In the profoundly changed metabolism of pregnancy and in the intensely katabolic metabolism of the *post-partum* states we assume the production of haemolytic agents—toxins—but, as French remarks, "the use of the word toxin almost connotes ignorance." Though progressive and often pernicious, the anaemia is caused by an agent which differs in one 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 thirty years after the attack. Recovery from the Addisonian form may last ten, fifteen, or even seventeen (McPhedran) years, but such instances are exceptional, and in the cases of reported permanent recovery there is always the question of mistaken diagnosis.

The blood picture may be of value in estimating the outlook. Signs of active regeneration may be present, as in Mrs. A.'s case, indicated by blood crises and a large proportion of red cells with signs of recent formation, and the basophilic granulation described by Boggs and Morris and by Milne, the mitochondria (Sappington) and the reticulation described by Robertson and Bock.¹² The number may rise from 1 per cent., the normal, to 20 or 25 per cent. with marked bone-marrow stimulation. A high colour index is the rule in the pregnancy and *post-partum* cases. The blood condition is uncertain, however, as well shown in two exceptionally well studied cases in Meyer's clinic, reported by Jungermann,¹³ in which the contrast was striking, the one with low colour index and features of an aplastic anaemia, the other the characteristic Addisonian picture. Both were pregnancy cases, and both had normal deliveries and recovered completely. The absence of platelets is a feature of the common idiopathic anaemia, contrasting, in this respect, with the post-haemorrhagic and septic forms. In the hands of skilful students the criteria offered by the blood examination should, as a rule, be of great value in the prognosis.

My individual experience is exceptional and much more hopeful than indicated in the literature, and particularly in works on obstetrics. The seven cases seen in Montreal and Philadelphia recovered. I have not at hand our large material from the Johns Hopkins Hospital; but I do not remember a fatal pregnancy or *post-partum* case. The later appear to be the more fatal, and the cases reported by Elder and Mathews¹⁴ show that a fatal termination may follow in spite of the most careful treatment.

Acute haemorrhage *post partum* may be rapidly fatal from reduction in blood volume; very large amounts may be lost extending over several days, and yet recovery takes place.

The report of Robertson and Bock, just mentioned, contains much information of value in estimating the blood loss in haemorrhage and the means of treatment. From what is recorded, and from personal experience, I should say the danger of a grave anaemia progressive in character is not great after a fairly profuse haemorrhage. Once the bleeding stops, recovery is progressive and often surprisingly rapid. On the other hand, repeated small losses of blood after abortion or a normal delivery may be followed by an anaemia out of all proportion to the quantity of blood lost. The starting point, indeed, of a few cases of Addison's anaemia appears to be repeated epistaxis or bleeding piles.

The treatment of the cases is that of the severer forms—fresh air, rest, food, iron, and arsenic (in which I still have faith); and if the blood count is very low, 20 per cent. of corpuscles and haemoglobin, transfusion may be employed. The newer technique has many advantages, but the results do not, in Addison's anaemia at any rate, appear to be more favourable than those we had with the old Aveling or Roussel apparatus.

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Observations

ON

INFLUENZA AND ITS COMPLICATIONS.

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THE following observations were made during a severe epidemic of influenza amongst patients of the 3rd and 4th Scottish General Hospitals a few weeks ago. The majority of cases were amongst American troops, and most of the patients were ill on arrival at Glasgow by transport. Others were amongst British troops, and there was no essential difference between the two groups of cases except that pneumonia was more frequent amongst the former. At the outset we were struck by the prevalence of mixed infections, as has been found by various observers elsewhere, and we have endeavoured to trace the part played by the various organisms concerned, as regards both the complications which occurred and the manner in which a fatal result took place. The facts recorded refer chiefly to the results of *post-mortem* examinations, and we bring them forward, as it is desirable to have as many records as possible of the features of the epidemic in different localities. To speak generally, we may say that the symptoms were essentially those of severe influenza, with a preponderance of pulmonary affections, which may be roughly classified under the headings of bronchitis attended with marked irritation, bronchopneumonia, and lobar pneumonia. Amongst the pneumonia cases the mortality was very high.

The epidemic was essentially associated with the presence of the *Bacillus influenzae* (Pfeiffer). Owing to lack of sufficient time at our disposal we were unable to undertake so extensive an examination of sputa as we would have wished, but the organism could usually be found without difficulty, and was often present in enormous numbers. In a small proportion of cases it could not be found, but with regard to these latter it must be recognized that, whilst the microscopic picture is often characteristic, the identification of the organism by microscopic means, when it is scanty, is impossible; and, of course, it is in such cases that the isolation by culture is attended by special difficulty. In over a dozen cases where the organism was present in considerable numbers it was cultivated from the sputum without difficulty, and in many instances the number of colonies obtained exceeded those of other organisms. Cultures were obtained also at *post-mortem* examinations from the bronchial mucosa, the pneumonic patches, abscesses, etc.; in fact, from all the lesions with which it was found associated. The characters of the bacilli isolated agreed in all essentials with those described by Pfeiffer and recently by C. J. Martin, and it is accordingly unnecessary to say anything under this heading. Blood cultures were made in fifteen severe cases, but with negative result in all as regards the influenza bacillus. In five of these cases pure cultures of the pneumococcus were obtained, to which further reference is made below.

The medium which we used throughout was a mixture of defibrinated human blood and tryptic agar, in the proportion of about one to eight; and we have not yet made any systematic examination of other media recommended. The agar being melted, and its temperature being brought to 55°C., the blood is added and mixed, and the mixture is poured into small Petri dishes. For inoculation, a drop or two of bouillon or sterile saline solution is placed on the surface of the medium. This is inoculated from the sputum or other material, and then spread over the surface in the usual way with a bent glass rod. Colonies on this medium remain small, but appear to come up in large numbers; they are practically invisible by transmitted light, there being no alteration of the medium around, but are readily distinguished on examination with a lens by obliquely reflected light. On this medium, however, the bacilli undergo involution at an early stage, and we do not regard the medium as an optimum one. For staining the bacilli in sections we found Giemsa's stain most suitable. The ordinary solution is diluted with fifteen parts of water, and the sections are stained overnight. The process of dehydration with alcohol gives the necessary differentiation.

Post-mortem examinations were performed in 26 cases, and in all a pneumonic lesion was present. In 17 the