Observations on the Severe Anaemias of Pregnancy and the Post-Partum State.

By Sir William Osler, Bt., M.D., F.R.S., Regius Professor of Medicine, Oxford.

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 (1855), and Guissarov (1871) dealt with this subject. The works of Biermer’s original cases were in pregnant women, and a large proportion of the cases forming the basis of the monographs of Muller (1877) and of Ichihorst (1878) were in this class. After 1885 the literature showed a striking reduction in the references, and Ehrlich and Lazarus, in Notthage’s System, suggested that local influences in the intestines were responsible for the frequency of this association in the cases reported by the Swiss clinicians. So experienced a teacher as Allbutt, 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 a worker as Byrom Bravwell 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 Guissarov’s in 1871. In Cabel’s series of 1,000 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, in reporting a case, gives a very good summary of the older American literature; and Fmdley, 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 Dr. 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 cases of Decornor’s,1 and Robert’s2 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 underfeeding, 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 puerperal, and in ruptured cesocephalic varix, none of which conditions present 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, but 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 respire, very rapid, 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 artesia morbus, 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:

Artemisidia! God’s invisible.
While thou art lying tear along the couch,
Have tied the sash’d 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 intermittently, 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 sure she was in a bad way. She had been cut. At the Preston Retreat, the red count was 1,300,000, and the leucocytes 15,000. 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 increasing pallor, and the patient anaemic, for which any casual observer would have mistaken the case. In III and IV of my Montreal series the repeated small anaemia followed many small haemorrhages after abortion.
THE SEVERE ANAEMIA OF PREGNANCY.

[Jan. 4, 1919]

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 accompanying chart in W. Thompson’s study of William’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. That this so-called chloro-anaemia of pregnancy might pass on to a grave and fatal form was recognized by Channing and Lebort, but it was the full report by Gussarov 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 and well up 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 constant observers in 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 were indistinguishable from those. I have had a number of 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 example of the disease:

Amelia T., aged 35; admitted February 3rd, 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 fainting. The red bloodcorpuscles were 1,170,000 per c.mm., with extreme irregularity of shape, and size and many nucleated red cells. The haemoglobin was 15 per cent. With rest in bed, good food, iron and arsenic, she improved rapidly and left the hospital without residual 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 chillies, which is following on the dia
gnosis of the disease.

J. T. primipara, aged 24, seen with Dr. Jenkins, October 6th, 1888. She had delivered three times with 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 she saw me, the red blood cell count being 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 104°, after which she sweated profusely.

There was no discharge, no evidence of sepsis, other than the fever, and the patient was able to go about 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 chill. The blood was negative during a chill and after. The red cell count fell to 200,000 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 complicate the clinical picture, as in cases which I reported a few years ago in the *Jour, of Laryngology and 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 1832 I saw with Dr. Allaway, 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 septicemia, her chief complaint was the painful throbbing of the abdominal aorta, which pulsed with extraordinary violence. She died on the twelfth day. There was “diphtheritic” endomtitis, septic thrombi in the pelvic veins; no endocarditis.

Such extremely rapid cases are not common, but Cabot refers to ones with identical features, in which the acute sepsis was not suspected. The red blood was 1,800,000 per c.mm. “Diphtheritic” endomtitis was found at the post-mortem examination, without which, as Cabot has shown, there is little to be gained on the subject.

The case I have now to describe had a profound pernicious anaemia. While every patient with purpural fever has some grade of anaemia, only in a few does the blood loss dominate the picture. In many of the cases of sepsis for example, the condition is not referred to. An excellent account is given by Lea,[12] who states that the loss of red cells may be 300,000 per c.mm. per week, and that the count may fall to 1,800,000 per c.mm.

Three cases of purpural 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 low blood pressure, pale yellow (not the brown) urine, and the usual features of moderate anaemia. The red blood cells were 2,700,000 per c.mm., leucocytes 1,500, haemoglobin 48. She improved rapidly, and left the infirmary on September 24th, 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 15,400, haemoglobin 15 per cent. 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 reticulated cells. She died on September 8th in a state of profound anaemia.

Mrs. W., aged 31, presented post-partum trophoblastic disease 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 severely anaemic, with a sallow, sub-interior tint and all the symptoms of severe infection. Stools were dark. The blood was taken from the blood, and she was given antiseptic colloid serum on December 1st and 3rd. The red blood count was 2,250,000 per c.mm., leucocytes 2,000, 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 purpural fever has been prevalent throughout the country. So far as I know, the post-partum sepsis cases have not shown a special tendency to haemorrhage, as 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 little, if any, more

[12] There have been septic endocarditis in this case.

[13] Before death there was a soft diastolic murmur along the left sternal border. The rigors, paroxysms, and delirium were not so marked and for ten days everything was normal. Then she began to get pale and grew rapidly worse, in the sixth week after confinement she saw me, 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 104°, after which she sweated profusely.

There was no discharge, no evidence of sepsis, other than the fever, and the patient was able to go about in a region in which parturition was recognized as one of the factors determining recurrence of malaria this had been...
than we have to the cause of that baffling of all blood diseases, Addison's anaemia. The progress and the bloody patch suggest the haemolytic type, which cases, produced experimentally and which is caused by the poisons of the Botriochopepaeus. In the profoundly changed 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 of the gradual and often progressive nature of the anaemia is caused by an agent which differs in one all-important particular from that which causes the anaemia of Addison. When recovery takes place it is permanent, and no further bleeding 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 proclivity to small hemorrhages and the complication of necrosis. The basophilic granulation described by Boggs and Morris, and by Milne, the purple blood (Sappington) and the reticulation described by Robertson and Bock 14 the number may reach 15-20 per cent. in the normal, and 25 per cent. as a normal marrow bone narrowing. 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 cases: we have not studied in Mayo's series; in the first reported by Jungermann, 15 in which the contrast was striking, the one with low colur index and features of an aplastic anaemia, the other the characteristic Addisonian picture in pregnancy cases, both had no further deliveries and recovered completely. The absence of platelets is a feature of the common idiopathic anaemia, contrasting, in this respect, with post-partum anaemia.

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 pregnancy 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 after a fairly prompt 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. These cases, in many instances, 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 favorable than those we had with the old Avellin or Roussel apparatus.

Obseruations
ON INFLUENZA AND ITS COMPLICATIONS.

BY ROBERT MUIR, F.R.S., LIEUT.-COLONEL R.A.M.C.(T.F.),
PROFESSOR OF PATHOLOGY,
AND R. HASWELL WILSON, M.R.,
LECTURER ON BACTERIOLOGY, UNIVERSITY OF GLASGOW.

The following observations were made during a severe epidemic of influenza amongst patients and staff of the 4th Scottish General Hospital 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 and German. 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 the amount of cases in which a single or multiple infection produced a fatal result. We have examined the following organisms 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 divided into those in which the heart was 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 the lack of sufficient time at our disposal we were unable to make an examination of sputum as we would have wished, but the organism was 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 a dozen cases where the organism was present in considerable numbers it was cultivated from the sputum without difficulty, and in many cases only one or two weeks elapsed between the first and last observations, which were obtained before those of other organisms. Cultures were obtained also at post-mortem examinations from the bronchial mucosa, the necrotic mucous patches, abscesses, etc.; in fact, from all the lesions with which it was found associated, and it was found that the bacilli isolated agreed in all essentials with those described by Pfeiffer and recently by C. J. Martin, and it is in such cases that the isolation by culture is attended by special difficulty. In a dozen cases where the organism was present in considerable numbers it was cultivated from the sputum without difficulty, and in many cases only one or two weeks elapsed between the first and last observations, which were obtained before those of other organisms. Cultures were obtained also at post-mortem examinations from the bronchial mucosa, the necrotic mucous patches, abscesses, etc.; in fact, from all the lesions with which it was found associated, and it was found that the bacilli isolated agreed in all essentials with those described by Pfeiffer and recently by C. J. Martin, and it is in such cases that the isolation by culture is attended by special difficulty. In a dozen cases where the organism was present in considerable numbers it was cultivated from the sputum without difficulty, and in many cases only one or two weeks elapsed between the first and last observations, which were obtained before those of other organisms. Cultures were obtained also at post-mortem examinations from the bronchial mucosa, the necrotic mucous patches, abscesses, etc.; in fact, from all the lesions with which it was found associated, and it was found that the bacilli isolated agreed in all essentials with those described by Pfeiffer and recently by C. J. Martin, and it is in such cases that the isolation by culture is attended by special difficulty.

The medium which we used throughout was a mixture of denitrified human blood and tryptase, in the proportion of one to eight; and we have used it in many cases of acute pneumonia. A careful 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 nicely outlined in large numbers; they are practically inviable 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 evolution we do not regard it as an optimum one. For staining the bacilli in sections we use the method of Gilman's stain of Russell and Jenney. The ordinary solution is diluted with fifteen parts of water, and the solutions 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 pneumatic lesion was present. In 17 the