HÆMOLYTIC ANÆMIA IN PREGNANCY[1]

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THE pernicious anæmia of pregnancy is an acute hæmolytic anæmia, which occurs in women under 35 years of age, is due to pregnancy, progresses steadily without remissions to death or recovery, and is curable by blood transfusion. Thus, it differs from Addisonian pernicious anæmia, which is essentially a chronic disease of unknown etiology, occurring after 35 years of age, predominantly in men, is not curable by blood transfusion, and runs a course characterized by remissions.

About 3 per cent of the cases listed as pernicious anæmia (4) occur during or shortly after pregnancy. In the British Isles, this anæmia is seen once in every 2,000 to 10,000 pregnancies. Hoskins (11) considers the condition common in Northern India and McSwinney (14) finds an incidence of 1.69 per cent in one of the Calcutta hospitals. McSwinney's cases were chiefly among Hindus, while in Bombay, Balfour (2) found this anæmia proportionally much more common among Mohammedans, a fact which she attributes to their confined life during pregnancy. There are no figures for the United States, but from the reports of Smith (24) of Rocky Mount and my own observations in Charlotte, I suspect that this condition is not very infrequent in North Carolina.

Balfour says that in Bombay this anæmia is more prevalent during the last half of the year because of the great number of diarrhœal cases at that time.

Of 500 cases taken from the literature (2, 7, 8, 11, 12, 14, 15, 16, 21, 22, 23, 24) 75 per cent occurred in patients under 30 years of age and 29 per cent occurred in primiparæ.

The appearance of the patient is that seen in any severe anæmia. There is a lemon tint to the skin in half the cases (22). Puffiness of the face and feet is common. The symptoms are those of any severe anæmia: weakness, vertigo, dyspnœa, palpitation, poor vision, and, especially, sore mouth, diarrhœa, and vomiting. There is generally fever (Schmidt reports fever in 97 per cent) starting a day or two after delivery and frequently leading to the mistaken diagnosis of sepsis.

The physical findings include blanched mucous membranes, retinal hæmorrhages (1, 11, 21, 22), sore tongue, a great variety of heart murmurs, enlargement of the spleen (Balfour, 18 per cent; Larrabee, 70 per cent; Schmidt, 30 per cent; McSwinney 16 per cent) and less often enlargement of the liver (Balfour 8 per cent, Larrabee 16 per cent) with slight œdema often limited to the face. Probably because of the short duration of the anæmia, cord lesions have not been demonstrated though pain and paræsthesias are common (21, 22). The blood pressure may be low as in anæmia generally or it may rise as in other toxæmias of pregnancy (21).

About one-half of the cases show a variable amount of albumin in the urine with urobilinogen and occasional casts. Hoskins has reported bile in the urine. There are no other urinary findings of interest.

The gastric juice may show diminished or absent free hydrochloric acid (21, 22), but achlorhydria is not the invariable rule here as in chronic pernicious anæmia.

The blood picture is very much like that of ordinary pernicious anæmia with greatly diminished hæmoglobin and red cells, a high color index, and the usual variation in size, shape, and staining reactions of the red cells. The diameter of the red cells is decreased (8, 15, 22) rather than increased. Nucleated red cells are present, but in the majority of cases these are normoblasts. The platelets have been reported as diminished (1, 8) or normal (15). The bile pigments in the blood are increased. Minot reports increased fragility of the red blood cells with 16 per cent reticulocytes in one case before delivery, both of these factors promptly returning to normal after delivery. There is some discrepancy of opinion about the number of white cells. Aubertin says that there are generally more than 15,000 and in 53 cases he has never seen less than 4,000; Schmidt reports 10,000 or more leucocytes in 68 per cent of cases and

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less than 6,000 in 28 per cent; Rowland says "there may be a leucocytosis regularly during the rapid hæmogenesis of convalescence, as well as in the early so-called physiologic stage of the anæmia," and cites one of Osler's (19) cases in which there were 45,000 leucocytes; other observers report leucopænia frequently as low as 2,500 (12, 24).

A tabulation of some of the cases recently reported (1, 2, 3, 6, 7, 8, 11, 12, 14, 15, 16, 19, 21, 22, 23, 24) shows an average hæmoglobin of 30.1 per cent in 101 cases and an average red cell count of 1,467,000 in 137 cases giving an average color index slightly above 1; in 55 cases the leucocytes averaged 6,746 with polynuclears 58.2 per cent, lymphocytes 36.3 per cent, large mononuclears 4 per cent, and eosinophiles 1.5 per cent.

The anæmia comes on insidiously during the later months of pregnancy and is generally discovered shortly after delivery. Miscarriage or premature labor is the rule. The loss of blood during labor is less than normal. The child fortunately does not share the mother's anæmia (1, 18). The course may be rapidly downward to death within a week or recovery may ensue after several months of illness.

After the uterus is empty, blood transfusion stops hæmolysis and leads to prompt recovery in 90 per cent of the cases (3, 8, 10, 11, 12, 13, 16, 17, 20, 21, 22, 24). I can find no record of recovery before delivery and Aubertin says recovery is unknown except after the uterus has been emptied. Rowland recommends that this measure be carried out promptly. Without transfusion 84 out of 211 patients or 40 per cent have died (2, 9, 12, 14, 15, 16, 19, 21, 23, 24, 25); Gallupe and O'Hara place the maternal mortality at 50 per cent, Larrabee at 75 per cent, and Delmen (5) at 87 per cent. McSwinney had a mortality of 35 per cent in 43 hospital patients in Calcutta and Balfour reports a mortality of 42 per cent among 150 patients seen by her in Bombay.

The changes found at autopsy as described by Schmidt and by Balfour are similar to those found in chronic pernicious anæmia. That this anæmia is due in some way to pregnancy seems obvious, but speculation as to how pregnancy produces it does not seem profitable in the present state of our knowledge. As emphasized 10 years ago by Schmidt, blood transfusion is a life-saving measure, but this fact is not as well known as it might be.

As was to be expected following the work of Minot and Murphy, the feeding of liver has been recommended in mild types of hæmolytic anæmia by Murdock (16), but in a large percentage of instances the process is too acute to warrant the institution of a dietary therapy. It may be that liver feeding after transfusion will be beneficial and it will be very interesting to see what liver feeding during pregnancy may accomplish in preventing this anæmia. However, when one of these cases is recognized, prompt transfusion is certainly the safest therapeutic measure.

CASE 1. In 1910, I saw with Dr. F. D. Austin a young primipara 3 months after normal delivery at term. She had developed diarrhœa a month or so before labor and this had continued during the 3 months since labor. Examination of the blood showed hæmoglobin 35 per cent, red count 940,000, color index 1.8, white count 6,000, with a normal differential count. There were 420 nucleated red cells per cubic millimeter. The patient recovered completely on symptomatic treatment.

CASE 2. In April, 1924, Dr. J. A. Anderson of Gastonia referred to me a young married woman, 19 years old, with a rather well marked secondary anæmia. The previous January she had had a miscarriage at the end of the seventh month, and a week later had œdema, a greenish yellow color, and went into collapse but gradually improved under symptomatic treatment. The next year she went through normal pregnancy and labor without anæmia.

CASE 3. In July, 1925, I saw with Dr. Vann Matthews a woman of 30 years, 5 weeks after her third pregnancy had terminated at term by normal labor. She had fever beginning the day after labor and at the end of 3 weeks had a greenish look. A week before I saw her, Dr. Matthews had given her a transfusion. The hæmoglobin was then 35 per cent, and there were 1,108,000 red cells and 2,400 white cells. During the week after her transfusion she had suffered from an infected arm and violent herpes labialis, so that when I saw her, the hæmoglobin was 25 per cent, red cells 832,000, color index 1.5, white count 2,700 with polynuclears 55 per cent, lymphocytes 44 per cent, and eosinophiles 1 per cent. The red cells showed considerable variation in size, shape, and staining reaction and a few normoblasts were seen. After another transfusion, this patient made an uneventful recovery and is well today.

CASE 4. In March, 1926, Dr. James Davis, of Wadesboro, brought me a young married woman of 24 years. Six weeks before she had had normal labor following a 9 months' pregnancy. During the puerperium she had fever daily and had become steadily paler and weaker, but had refused to go to the hospital until it became evident that she would die. She was seen at midnight. Temperature was 101 degrees, pulse 125, respiration 46 with marked air hunger. The patient was comatose and restless. Her skin was very pale with a strong lemon tint. There was some œdema of the face, but none elsewhere. The examination of the blood showed hæmoglobin 25 per cent, red count 742,000, color index 1.8, white count 6,600 with polynuclears 66 per cent, lymphocytes 33 per cent, basophiles 1 per cent; the red cells showed marked variation in size, shape and staining reaction and many nucleated reds were present including typical megaloblasts. The urine showed only a trace of albumin but was positive for urobilinogen. The patient was at once given a citrate transfusion by Dr. Barret and a second one the next day. At the end of 10 days she was sent home with a hæmoglobin of 50 per cent and a red count of 3,472,000.

On August 31, 1927, Dr. Barret and I were called to Wadesboro to see this patient again. Her third pregnancy had ended at term with a normal labor 19 days before. A week before delivery the hæmoglobin had been 50 per cent and the red count 2,500,000. The day before delivery, her blood pressure reached 160. Urine showed albumin and casts in abundance. For 2 weeks after delivery she was apparently holding her own but then developed an abscessed breast. The hæmoglobin dropped to 30 per cent and the red cells to 1,292,000. The color index was 1.1. She had had fever ever since delivery. When the patient was seen on August 31, the hæmoglobin was 10 per cent and the red count was 960,000 with great variation of size, shape, and staining reaction of the red cells. Many normoblasts were seen but no megaloblasts. The white count was only 2,500 with 70 per cent polynuclears. She was given 800 cubic centimeters of blood by direct transfusion by Dr. Barret. On September 28 Dr. Davis reported that the hæmoglobin was 65 per cent, the red blood cell count 2,800,000, and the white cell count 5,000. The patient was steadily improving.

There have been some reports of the recurrence of this anæmia in subsequent pregnancies. Murdock thinks there is a strong probability of recurrence and thought it likely that his second patient had suffered with hæmolytic anæmia following labor 6 years previously. In the second case reported by Gallupe and O'Hara there was a history of anæmia in each of the 3 preceding pregnancies severe enough in the next preceding pregnancy to have kept the patient in bed for a few weeks.

Halir (9) reports the case of a woman, age 21 years, who presented a picture of pernicious anæmia in 1920, 8 weeks after delivery. In the spring of 1923, she returned, 3 months' pregnant, and again presented a picture of pernicious anæmia. She died the next year with Hodgkin's disease.

Oettingen (17) reports the case of a woman with hæmolytic anæmia following her third pregnancy, who had had severe anæmia of some sort with her first pregnancies. To prevent recurrence she was sterilized. Reist (20) reports the case of a woman who had been chlorotic from her fifteenth to nineteenth years. She was anæmic during the first and second pregnancies and after her third pregnancy presented a picture of pernicious anæmia. She was sterilized to prevent further recurrence.

Vermelin and Vigneul (25) report the case of a woman whose first pregnancy was normal; in the fifth month of her second pregnancy she showed pernicious anæmia and miscarried during the eighth month with fetus stillborn. She was clinically normal the next year, but aborted during the second month of her third pregnancy. Three months later she again became pregnant and in the seventh month of this fourth pregnancy showed the picture of pernicious anæmia. Premature delivery was induced. The patient died 2 days later.

McSwinney saw a woman during her sixth pregnancy with hæmoglobin 40 per cent, white blood count 3,000,000, color index .66. A year later at the time of her seventh labor the hæmoglobin was 35 per cent, with red count 2,000,000, color index .88. The patient grew rapidly worse and died 5 days after labor.

These reports on recurrence show that the patient seen in two succeeding pregnancies by Halir died a year later of Hodgkin's disease. The patient seen in two succeeding pregnancies by McSwinney died within a week after the second labor. The others all saw women who gave a clinical history of anæmia with previous pregnancies. The fourth case reported was seen in two succeeding preg-

nancies, each time with less than 1,000,000 red cells, and in each incidence recovered promptly after transfusion.

Because of the rarity of recurrence and the promptness with which this anæmia can be controlled by transfusion, sterilization of these patients to prevent possible recurrence seems to me entirely unwarranted.

SUMMARY

The hæmolytic anæmia of pregnancy is an acute condition and should no longer be classified as pernicious anæmia.

It responds promptly to blood transfusion after the uterus has been emptied.

The danger of recurrence need not be a contra-indication to pregnancy and calls for nothing more radical than proper supervision of the patient during subsequent pregnancies.

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