

THE COMPLICATION OF PURPURA WITH GESTATION<sup>1</sup>

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**P**URPURA hæmorrhagica is a rare complication of pregnancy. In the literature are 39 cases which have been reported. There is, of course, no method of estimating the number which may have been actually encountered and not recorded. Apparently multiparæ are the more frequently affected, as published observations show that 28 cases were found among women between the second and fifth pregnancies, against five primiparæ and 6 cases after the fifth gestation.

As to age incidence, purpura occurred twenty-two times between the ages of 22 and 35, six times under 22 and eleven times above 35 years.

Purpura seldom appears throughout the gestation; however, there is a marked predominance between the sixth and seventh months. One notes that in 22 cases it appeared before the eighth month, in 12 before the sixth month, and in 5 cases after the eighth month.

It is surprising how little the general condition of the patient in some cases is modified by purpura hæmorrhagica. Often in the most alarming there may be no systematic disturbance whatever, although marked anæmia and a state of asthenia may develop as a result of the continued loss of blood. With this may occur gastro-intestinal upset, thready pulse, and fever. There is often œdema and a trace of albumin in the urine.

Stephen Mackenzie has divided purpura into autotoxic, vascular, mechanical, and neurotic. Doubtless in pregnancy we have a combination of the vascular and toxic groups with a neurotic influence. The case of hæmorrhagic diathesis reported subsequently in this paper belongs, it is believed, to the group described first by Denys and Hayem, and since then has been studied carefully by Bensaude and Rivet, Pratt, Duke, and others.

Duke reported a series in 1910, in which he attempted to prove that both hæmorrhage and purpura in one type of case could be attributed entirely to an almost complete ab-

sence of blood platelets, and in doing this found, after study of normal individuals and patients with numerous diseases, that this type of hæmorrhagic diathesis had invariably a reduced platelet count whenever they had a tendency to bleed. The tendency to bleed was studied by means of the bleeding time—not the coagulation time. This was prolonged in both human subjects and in experimental animals whenever the platelet count was reduced to a certain level (10,000), and this was associated in humans with bleeding from mucous membranes and ecchymoses. In one case, in which the count was reduced below 3000, the patient bled from scratches, pin pricks, minute injuries made on the gums by the chewing of rough food, from acne pustules, hang nails; in fact from any abrasion whatever, either of the skin or tissue. He also found that the condition could be relieved immediately by direct transfusion of blood, which operation caused instant increase in the platelet count. The platelets were found to be short lived, under these circumstances, and disappeared in from 3 to 5 days, at which time the hæmorrhagic diathesis, in all its glory, returned. Hæmorrhagic diathesis was relieved, in some of his cases, by a spontaneous increase in the platelet count. He felt, from a study of a series of cases in 1912, that one group of hæmorrhagic cases could be separated from a variety of other types by a clinical picture which was characterized in every instance, first, by a tendency to bleed into the skin and tissues, and from every abrasion, no matter how made; second, by an enormously reduced platelet count—from one thousand to fifty thousand; third, by a normal coagulation time; fourth, by a prolonged bleeding time—10 minutes to 1½ hours (the normal bleeding time is less than 3 minutes), and, fifth, by a non-retractile blood clot. These cases were analogous, he thought, to those described by Denys, Hayem, Pratt, and others.

This disease was found to be of varying etiology. It was noted complicating diphtheria,

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tuberculosis, nephritis, aplastic anæmia. Similar illnesses were reported in the literature complicating lymphocytic leucæmia, hæmorrhagic small pox, typhoid fever, and pneumonia. The case which is to be reported subsequently was similar to these, it is believed, and occurred as a complication of pregnancy.

In a series of thirty-eight animal experiments in which benzol, diphtheria toxin, and tuberculin were injected into animals, in only those in which the platelet count was markedly reduced was there any abnormal tendency to bleed. In one animal treated with diphtheria toxin, typical purpura hæmorrhagica with a very low platelet count, non-retractile clot, and prolonged bleeding time was produced.

The normal platelet count, as given by different observers, ranges between 200,000 and 400,000. Hayem in his cases of purpura hæmorrhagica made counts of 89,000, 62,000 and 41,000. Bensaude and Rivet studied fresh blood films in 5 cases of purpura hæmorrhagica and noted that the platelets were greatly reduced. In studying purpura hæmorrhagica complicating nephritis, Pratt noted a count of 9,000. Selling, in a case of benzol poisoning with purpura hæmorrhagica, noted a platelet of 3,000.

Hayem, Denys, Bensaude and Rivet, Duke, Minot, and others, all agree in their observation of a striking tendency to bleed in patients with very low platelet counts, and in several instances note an amelioration of symptoms with a rise in the count. Duke, with his patients and animals, noted hæmorrhagic diathesis in mild form whenever the count was below 60,000, and in severe grade when the count was below 10,000.

It is interesting to mention in this connection the origin of blood platelets, since it seems likely that a certain type of purpura hæmorrhagica is due either to a reduced formation, or to an increased rate of destruction of platelets. The most interesting work in this relationship is that of J. H. Wright, who states, on the basis of microscopic examination of the bone marrow, that the source of the blood platelet is the megacariocyte of the marrow, and that platelets are formed by the

budding off of pseudopods which are projected into the capillaries from the megacariocytes. His observations have been corroborated by other observers.

The characteristic symptoms of purpura of the platelet-free type are:

1. Petechia and ecchymosis. The rash may be modified by any co-existing skin lesions, or by mechanical agents, such as that produced by a bruise or by rubbing.
2. Bleeding from mucous membranes. This accompanies the petechia almost always, and ecchymosis usually.
3. Prolonged bleeding time. This was observed in all cases where there was a tendency to bleed with a return to normal immediately if the platelet count rises. This feature is found constant and distinctive, and it is the most reliable guide we have in showing the severity of hæmorrhagic diathesis in this type of trouble.
4. A reduced platelet count. This ranges from 60,000 to nearly nil. Usually the count is so reduced that the platelets can hardly be found in either counting chambers or blood smear. A rise above 10,000 is almost invariably associated with a reduction in the bleeding time, and an improvement in the patient.

5. Normal coagulation time.

6. Non-retractile clot. Retractility of the clot seems to depend on the presence of blood platelets, and returns when the counts rise to a certain limit (40,000).

The fundamental cause of many types of purpura is still unknown. Some evidently occur in connection with infections and with intoxications, and this would seem to point to a relationship of cause and effect. While it is not capable of demonstrable proof this suggestion must be given consideration.

It has been argued that purpura in pregnancy is no different from that in the non-gravid woman. A few observations of Henri Vignes on the changes in the blood of the normal pregnant woman are pertinent and interesting. In normal gestation he finds,

1. The blood mass is augmented by 8 per cent, through superabundance of serum.
2. The number of red blood cells is clearly diminished, as is also the hæmoglobin ratio.

3. The cells have the property of sedimenting with greater rapidity in pregnancy. Following the technique of Lingemeier, it takes 5 to 6 hours to precipitate *in vitro*, completely, the blood cells of a woman not pregnant nor in her menstruation. It requires less than 2 hours to produce the same phenomenon in a woman 7 or 8 months pregnant.

4. There exists as light leucocytosis, more marked in primiparæ. Baer gives the figures as 11,000 for primiparæ, and 6,000 for multiparæ. These figures are increased by 50 per cent during labor, and especially if there be an early rupture of the membranes. The increase is more particularly in the polymorphonuclears.

Consequently, when we consider that the barriers protecting the woman non-pregnant are broken down by the blood change occurring in the sixth or seventh months of pregnancy, there should be reason for her greater danger from purpura.

Ferroni believes in the classic theory which attributes the hæmorrhagic troubles of purpura to a lesion either of the kidney or the liver, under the influence of the nervous system, this applying more distinctly to purpura gravidarum.

The new ideas of E. Frank and Kaznelson, who speculate on the preponderant rôle played by the spleen in the pathology of purpura, are interesting, but they are not as yet confirmed by a long experience.

John Phillips, in an elaborate discussion of purpura in menstruation and pregnancy, says that women with amenorrhœa or irregular menstruation have a disposition to erysipelas of the face, erythema nodosum, purpura simplex, and purpura hæmorrhagica, which he thinks are only degrees of the same hæmorrhagic disorder. He reports 3 cases of purpura in non-pregnant females occurring at the menstrual time, one of whom died of hæmorrhage.

Peusch reports a woman of 21, who, a year after the birth of a child, had a severe headache and petechiæ. In 10 days a normal menstruation of 3 days' duration occurred. Her next period was at the proper time, but excessive. On the fourth day she fainted. Hæmorrhage from the bowel was profuse and a uterine hæmorrhage followed, which con-

tinued for 10 days. After several weeks the rash disappeared and she made a slow recovery.

From the foregoing description two facts are apparent:

1. Purpura may be related to a known disease of which it is a symptom, or it may be a complication showing the violence of the pathogenic germ.

2. It may be only the expression of a state of which the cause is unknown, residing probably in the functional modification brought by the pregnancy into the maternal organism. This last series of cases is denominated idiopathic purpura.

Among the affections which determine purpura in pregnancy is scurvy, which Zangemeister remarked in his case. He argued that the scurvy shows symptoms so slightly at variance with the gastro-intestinal conditions, progressive anæmia, muscular and articular pains, and cutaneous hæmorrhages, which one meets in gestation, that differentiation is difficult and the same form of disturbance is likely responsible.

The evolution of symptoms is similar to those in the cases reported by Bregier and Ferroni, where the general picture resembled scorbutic purpura, but the affection taking a serbious turn may go on in one instance to a fatal termination, while in another the patient recovers her equilibrium with no untoward result.

Well-defined hæmophilia is always easily recognized, but there are in addition instances like that which Grazzani reports of women not hæmophiles who, nevertheless, bleed excessively when they are pregnant and in labor and also postpartum. This circumstance is also noted by Phillips and Rowe, as if pregnancy had reinforced the tendency of the scorbutic cachexia responsible for much disorder in the maternal organism, interfering with its repair, even after the expulsion of the products of conception.

Diehl, in a classification of purpura, includes scorbutic purpura and maintains that the petechiæ are in this case secondary to the scorbutic cachexia. Purpura due to tuberculosis, malaria, and cardiopathies are analogous. He says to differentiate scurvy in pregnancy is

difficult, as the gestation itself is often accompanied by alimentary disturbances reflex in origin.

From a clinical point of view the facts present themselves in the great majority of cases as follows:

The victim is usually a multipara. Her age is from 22 to 35 years. The patient shows at first the appearance of good health, and the family history may be negative. Her former pregnancies have been normal and each one terminated with the birth of a full term, living infant. Her present pregnancy may have been normal or there may have been a complication of metrorrhagia of sufficient importance to attract attention, when the woman finds herself again enciente. The beginning of the pregnancy is not marked by any serious accident. At this time she may have noted a peculiar odor which seems to come from a fermentation of gastro-intestinal origin. To all appearances, however, she is in good health and her gestation shows no untoward symptoms until sometime in the sixth or seventh month she experiences a vague discomfort, loses appetite, and complains of headache; she has palpitation and a gastro-intestinal trouble which becomes more marked. Some time later there appear hæmorrhagic spots on the skin, then petechiæ, which are at first discrete, but later become confluent. These spots usually appear in successive crops. The woman finds that her gums are tumefied and painful and begin to bleed; epistaxis becomes troublesome; she usually has a persistent diarrhœa; she consults a doctor, who finds that the fetus is living, but that the mother has purpura with symptoms of grave character. The patient is usually pale and depressed, short of breath, although no abnormal symptoms can be found in the heart, lungs, or other organs. Blood pressure may be normal, the pulse is rapid, corresponding with that of a light fever. A trace of albumin is usually found. She may improve. The reverse is generally the case. Gastro-intestinal troubles increase. Mucous hæmorrhages are frequent. The patient bleeds from the mouth, the nose, the bladder, and the rectum. She becomes rapidly anæmic and exhausted, is confined to her bed. Hæmorrhages increase from all mu-

cus surfaces, the temperature rises. She goes into rapid labor without great pain. She is delivered normally and may begin to improve. Generally, however, she dies after a few hours or a few days because, for some reason, the organism cannot re-establish itself after expulsion of the products of conception.

#### PROGNOSIS

The prognosis in cases where purpura hæmorrhagica complicates pregnancy becomes very grave. The outcome is generally less serious when an early abortion ensues. Only occasionally a patient goes to term and recovers. Involution is more or less prolonged.

In half of the cases the fetus perishes *in utero*, or dies within a few days following the birth. It presents, usually, however, a normal appearance. Very rarely there develop hæmorrhagic accidents to the fetus, analogous to those of the mother.

A brief list of case reports instructs one on the prognosis.

Phillips, two cases, British Lying-in, 1887. One, age 32, para-VII, recovered, the other died of hæmorrhage the second day following delivery.

Peuch, primipara, sixth month, epistaxis, petechiæ, no external hæmorrhage, died the fifth day.

Peuch, para-V, age 30, eighth month, petechiæ suddenly overspread the entire body, fetus expelled the same night, postpartum hæmorrhage, death.

Budd Van Sweringen, Ft. Wayne, 1905, primipara, sixth month, whose cervix had been thrice cauterized by preceding attendant for pernicious vomiting,—found nose bleeding and gums oozing, bloody urine, profuse vaginal discharge, profound dyspnoea, petechiæ general over body, slight temperature. Symptoms cleared up in a few days. Delivered 3 months later with no purpuric symptoms.

Robert Barnes, Brit. M. J., para-III, sixth month, rheumatic pains, fever, premature fetus lived 3 hours, purpuric spots appeared same day. Prostration, delirium and hæmorrhage were followed by death in a few hours.

Barnes and Byrnes, Brit. M. J., Nov., 1867, patient developed spots of purpura hæmorrhagica, subconjunctival ecchymoses, prostration and delirium, died day after delivery. Two days later her husband developed variola.

Wiener, Arch. Gynaek., 1887, xxi, 281, hæmorrhagic purpura in two sisters: the first dies suddenly after rash appears, the second is taken 14 days later in seventh month with identical symptoms, is delivered next day. During delivery a scarlatiform rash appears on head, neck, and trunk, hæmorrhages of skin present themselves, bloody expectoration, hæm-

aturia, sanguinolent stools. Woman dies third day with no elevation of temperature. At the time an epidemic of small pox prevailed in Breslau.

Ferroni, Rome, 1903, para-IV, age 31, sixth month, discrete petechial rash localized on thorax and lower limbs. After 12 days bloody stools, albuminuria, profound anæmia. Suddenly delivered voluntarily of living baby showing no traces of purpura. Two hours later after declaring she felt better, she suffered profound dyspnœa which was followed by loss of consciousness and death.

Diehl, *Ztschr. f. Geburtsh.*, 1890, p. 218, reports a para-VII, age 36, no history of bleeders, six confinements normal. Patient expelled dead fetus at eighth month, no notable bleeding. Later she developed general purpuric hæmorrhages, uterus at umbilicus became gangrenous and there was a vaginal discharge. Blood examination was negative. Six days later patient suffered violent pain, and petechiæ and ecchymoses succeed in crops; she had no fever, but died on eighth day.

Hanot and Luzet, *Arch. Exp. Med. & Path. Anat.*, 1891, xv, 772. Primipara, age 22, at term suddenly suffered ocular disturbance and coma; petechiæ and ecchymoses appeared, a macerated fetus was expelled. The next day patient went into deep coma, albumin was notable, and woman died. Autopsy showed cerebri spinal meningitis.

Le Clerc, *Lyon médical*, 1908, reports a hæmophilic, age 32, para-V, with three living children, one a hæmophilic. Purpura at third month with epistaxis, bleeding of gums, and conjunctival effusions. Fourteen days later she was delivered with slight loss of blood of a dead child. Blood examination showed polymorphonuclears 86 per cent, mononuclears 13 per cent, non-retractile clot, normal coagulation time. Patient died next day.

#### TREATMENT

As to the treatment of purpura hæmorrhagica little is to be said. The use of drugs, either styptics, general remedies, or serums, has been found futile. Complete rest should be advised, and patient should eat nourishing food, and perhaps be given a tonic.

Transfusion is the only effective means of controlling the hæmorrhage, and may have a prolonged or even permanent effect. The theory suggested by Duke that the increased blood platelet count—above 10,000—results in control of the hæmorrhage, seems a plausible one to account for the favorable result.

Repeated transfusion may be required to tide over a temporary process which caused a platelet deficiency, and this may lead to a cure. At present no other method of treatment has been found worthy of trial.

#### AUTHOR'S CASE

The especial reason for the presentation of this subject at this time is that, during the summer of 1922, the author saw in consultation with a very careful diagnostician an able practitioner, his friend, Dr. John I. Byrne of St. Joseph, Missouri, a case of purpura hæmorrhagica complicating pregnancy, in a patient whose history is appended.

Mrs. A. F. S., age 36, para-VI. She has always been under the care of Dr. Byrne in each of her labors. Her first confinement was perfectly normal. The second child was born without untoward symptoms, but in the third month following the birth the mother developed an acute appendicitis. The appendix was perforated within 12 hours after the onset of pain. Operation was followed by a somewhat stormy convalescence and complete recovery.

The third pregnancy began soon after the recovery from the appendicitis. She became toxic and several convulsions were suffered, but the child was delivered near term and lived. Her fourth and fifth pregnancies were normal in every respect.

The present trouble developed in the sixth month of the last pregnancy with painful purpuric spots on the legs and abdomen, and these gradually affected the whole body. At the end of 3 weeks, hæmorrhage from the gums and nose began. At that time 10 cubic centimeters of normal horse serum was given and this completely controlled the symptoms for 3 weeks. Then followed repeated hæmorrhages from the bowels, nose, and gums. She was desensitized and the horse serum was repeated, but it failed to stop the bleeding. A transfusion of 350 cubic centimeters of citrated blood was given. This partially controlled the hæmorrhage but oozing was still observed. Various styptics, such as calcium lactate and stypticin, were given, but without effect.

Because of fear of more extensive bleeding consultation was called and it was decided, as the patient was becoming more anæmic and consequently weaker, that an induction of labor should be done before the control of the transfusion was exhausted.

Accordingly, in anticipation, another transfusion was done and the Voorhees bag was used to inaugurate labor pains. After 6 hours, a baby girl, weighing 6½ pounds, was delivered and lived 10 hours. The child seemed strong and well developed, but it was noticed in a short time that wherever it had been touched by the hands large ecchymotic spots appeared. The ecchymoses gradually increased although there was no hæmorrhage from mucous membranes. This feature is of especial interest from the viewpoint of heredity, since, in nearly all of the other cases found where purpura developed, there was no evidence of the condition being transmitted to the offspring. The authors quoted, where mention is made of the subject, usually observe that the purpura was not transmitted. This child was

evidently a bleeder, and the source of its disturbance was like that of the mother, probably a toxæmia. In this particular, the case is, so far as we have been able to determine, unique in that both mother and child suffered from an identical condition.

There was no time during this last pregnancy any sign of kidney disturbance, and while the bleeding from other mucous membranes was quite free, no blood was found in the urine. There was no excessive bleeding following the birth, and all other hæmorrhages promptly ceased as soon as the patient was delivered. She was discharged from the hospital at the end of 2 weeks after the birth and is now, apparently, in better health than usual.

#### CONCLUSIONS

1. Purpura is a very rare complication of pregnancy. The literature includes 39 cases previous to this report.

2. Purpura in gestation is most often of the hæmorrhagic form, characterized by these symptoms: hæmorrhages from mucous surfaces; petechiæ and ecchymoses; a remarkably reduced platelet count; prolonged bleeding time; normal coagulation time and non-retractile clot as in the non-gravid woman similarly affected. With the gravid woman, however, there is greater frequency of metrorrhagia.

3. Beside the purpura hæmorrhagica associated with a definite pathological state complicating gestation, there are others more rare, which may be denominated idiopathic purpura of gestation.

4. Idiopathic purpura always manifests a harmful influence in gestation, usually resulting in premature delivery.

5. Multipara between the ages of 22 and 35 are most often affected. Usually the patient is in the sixth or seventh month of her pregnancy.

6. Purpura is frequently complicated by infection, but some cases occur without any

real evidence of infection. Toxæmias appear responsible for a number of cases.

7. The offspring of purpuric mothers are not usually affected by the eruption, although in the present case, the child developed ecchymoses.

8. The fetal mortality is 50 per cent.

9. Nearly all cases of purpura hæmorrhagica which go to term end fatally at the delivery, or soon after the labor, from hæmorrhage.

10. No drug therapy is of the slightest avail. Direct transfusion of blood, keeping the platelet count over 10,000, is the only remedy. Repeated transfusion may be necessary to tide the patient over the period in which her platelet count is reduced.

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