

ADDISON'S DISEASE COMPLICATING PREGNANCY, LABOR, OR THE PUERPERIUM

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ADDISON'S disease is defined by Osler as a disease characterized by muscular and vascular asthenia, irritation of the stomach, and pigmentation of the skin, due either to tuberculosis or atrophy of the adrenals, or to degenerative changes in the chromaffin system generally.

The disease is fairly rare; it occurs less frequently in women than in men, in the proportion of 1 to 9. Only a few reports are found in literature of cases of Addison's disease complicating pregnancy or the puerperium, and in American medical literature I do not find the record of a single case. Altogether in the literature, there are reports of 11 cases, of which short histories are given below. To these I add a case recently observed by myself.

CASES OBSERVED DURING PREGNANCY

CASE 1. Reported by Barlow, *Lancet*, Lond., 1885, i, 251. Patient, age 42, had suffered with the disease for ten months during which time she was pregnant and gave birth to a dead fœtus. The patient had lues of the suprarenals, verified at autopsy.

CASE 2. Reported by Jacquet, in *Brouardel's Traite de médecine*, 1897, iii, 617, refers to a personal case of pregnancy occurring in the course of Addison's disease. Jacquet confines himself to saying that the child was born in good condition at term. During pregnancy pigmentation and other symptoms of Addison's disease were much accentuated, and after labor the points of election of gravidic melanoderma remained intensified. The further course of the disease in this patient is not known.

CASE 3. Reported by Miller and Fleming, *Brit. M. J.*, 1900, i, 1014. This was apparently a case of familial Addison's disease. The mother and five children all showed symptoms of the disease. The children in the order of their ages demonstrated all the clinical features in decreasing severity and distinctness. The woman stated that bronzing began after her first pregnancy and became intensified in successive pregnancies. She showed great weakness and prostration, giddiness, diarrhœa, vomiting, pain in the back shooting to the shoulders, palpitation, pain over heart and breathlessness, in addition to the pigmentation and the occurrence of dark moles all over the body.

CASES 4 and 5. Reported by French, *Lancet*, Lond., 1908, i, 1398. In French's first case the wom-

an was 40 years old and a XI-para. The symptoms of Addison's disease commenced about 6 months before she last became pregnant. There was nothing of note during the early months of pregnancy, but from the fourth month there was weakness of high grade, vomiting, and syncope. As these symptoms showed no signs of abatement the pregnancy was ended at the sixth month. After abortion the pulse rose rapidly, the heart weakened, there were convulsions, and the patient died the second day of the puerperium. Autopsy showed typical caseation of the suprarenal glands.

The second case was very similar according to French but he does not give any details. This patient died also.

CASE 6. Reported by Vogt, *Verhandl. d. Gesellsch. f. Gynaek.*, 1913, xv, 115; 249. Woman aged 21 years, primipara. Onset of disease unknown. Course of pregnancy normal. Labor began in thirty-fifth week and it lasted 21 hours, one hour of which was due to the secundines. The fœtus was well developed as an 8-months fœtus, 47 centimeters long and weighing 2,250 grams. The child was living at time of report, being then 14 years old and showed no symptoms of the maternal disease. Like the pregnancy, the birth was without incident, and uterine and abdominal contractions left nothing to be desired. The secundines were discharged normally one hour after birth. No uterine inertia was observed either during or after birth. The puerperium proceeded well for the first 2 days, there was then a sudden thermal elevation the third day, which continued. On the eleventh day vomiting began and could not be controlled, causing collapse and death of the patient on the twelfth day. Autopsy showed both suprarenal capsules caseous, with general anæmia, atrophy of the heart, hyperplasia of the aorta, etc.

CASE 7. Reported by Seitz, *Inneren Sekretionen und Schwangerschaft*, 1913, Barth, p. 191. Woman, age 30, on account of great weakness and augmented pigmentation was suspected of disturbance of the suprarenal glands. In her first pregnancy this woman had shown intense pigmentation of all the body, especially of the genital regions, and this did not quite disappear after the birth. In a new pregnancy, 9 months afterward, the intense pigmentation spread to the arms, trunk, and legs. The bronze color was unaltered a year after the birth.

CASE 8. Reported by Guisti, *Rassegna d'ostet. e ginec.*, 1914, xxiii, 465. Primipara; tubercular; 4 months pregnant. The first two months of pregnancy had a normal course. Toward the end of second month mucous and alimentary vomiting, intense gastric crises and general asthenia; face

dark colored; intense pigmentation; asthenia progressively increased. The patient could not stand even for a short time. Blood pressure 100 millimeters. Slight albumin in urine. Diagnosed as pregnancy complicated by Addison's disease. Tubercular reaction positive. Spontaneous abortion at sixth month with dead foetus weighing 850 grams. Secundines normal. The patient's condition was very grave at the beginning of the abortion, rapidly grew worse, and she died a few days later. No autopsy. The Addison's disease, the author believes, began during pregnancy and he ascribes the suprarenal lesions to tuberculosis.

CASE 9. Reported by Falco, *Rassegna d'ostet. e ginec.*, 1915, xxiii, 434. Age 26 years, XI-para. History of disturbed and scanty menstruation. The cephalæa, gastric crises, lumbar and epigastric pains commonly observed in Addison's disease were frequent in this patient. Abnormal pigmentation. Blood examination: red blood cells, 3,800,000; white blood cells, 6,700; polynuclear neutrophiles, 60 per cent; eosinophiles, 1 per cent; basophiles, absent; small lymphocytes, 32 per cent; large mononuclears, 7 per cent. These findings are similar to those commonly observed in Addison patients. There was constant headache. Pulse 80 to 90; apyretic. Adrenalin was administered without result. The patient gave birth at term to a slightly asphyxiated child. The secundines came 5 minutes later and were normal. No inertia. Uterine and abdominal muscular contractions good. Foetus weighed 2,820 grams. Lochiæ normal. First days of puerperium, temperature 38.5°, pulse 110-115. The woman nursed her child and left the hospital after 20 days with all the symptoms gone or improved, but 8 days later she died suddenly. There was no autopsy nor could any particulars be obtained of the symptoms before death occurred. The cuti-reaction for tuberculosis in this case was positive and the author thinks that the Addisonian symptoms were due to a tubercular lesion of the suprarenals. Syphilis may be ruled out.

CASE 10. Reported by Roten, *Gynæcol. helvet.*, Genève, 1915, xv, 113, says that one case of Addison's disease complicating pregnancy was observed at the Basle clinic, but does not give any particulars.

CASES OBSERVED IN THE PUERPERIUM

CASE 11. Reported by Wilkin, *Lancet*, 1883, i, 498. Age 32; married 3 years; one child which died 3 weeks after birth. Patient has been ailing since birth of child. Examination showed severe epigastric pains, deeply bronzed skin with well-defined chocolate-colored spots about arms and neck, mucous discoloration of lips and cheeks, large dark patch on dorsum of tongue with smaller ones like ink stains. Alteration in her color only became apparent soon after birth of her child. No abdominal pains; great lassitude; and weakness, nausea and vomiting which became aggravated. Died after 3 weeks in bed. No autopsy.

My personal case is as follows:

Mrs. H., white; housekeeper; age 28; I-para; admitted to Maternity Ward, Hahnemann Hospital, Chicago, June 4, 1921. Patient had usual children's diseases; malaria. The family history is negative.

State on admission. At term. Labor began about 11 hours after admission and lasted 4½ hours. The pains were regular and the course and delivery normal. Hæmorrhage was moderate; first degree perineal laceration which was repaired with silk gut. Placenta expelled intact. Uterus contracted and involuted well. Lochiæ normal.

Condition remained good until about 20 hours postpartum. The temperature then rose suddenly from 99° to 102° and continued to rise very irregularly on the days following, reaching 105° on June 10. The condition was thought to be a septic endometritis, secondary to labor.

I saw the patient for the first time June 12. On examining her then the prominent symptoms, besides the high temperature, were: (1) deep bronze color of the exposed skin on arms, chest, and forehead, and especially noticeable over both cheeks; bulging eyes; pupils reacting sluggishly; (2) the speech was only a slow drawl, with very slow grasp of ideas in replying to questions; (3) dullness and sensitiveness over right kidney region; (4) area of dullness over the heart small; (5) abdomen, tympanitic, soft, irregular and sensitive.

The patient showed a systolic pressure of 66; diastolic of 52; pulse pressure 14, pulse 90; temperature 102; respirations 26; respiratory suspensions 25 seconds.

The clinical history showed nausea, continued severe headache, aching feeling over body, severe leg pains, weakness, restlessness, nervousness, giddiness, and inability to sleep; also marked lumbar region sensitiveness and pains.

From the bronze color, the manifest hyposuprarenalism and hypothyroidism, and the clinical history I diagnosed the case as puerperal septic absorption with Addison's disease. Adrenal and thyroid extracts were prescribed.

The temperature variations are shown in accompanying chart.

The administration of thyroid extract was discontinued June 18. Blood cultures were negative for bacteria. Vaginal smears and catheter urine gave some streptococci on culture. Wassermann reaction negative. Blood count showed 17,500 white blood cells; lymphocytes 5 per cent; large mononuclears 1 per cent; neutrophiles 94 per cent.

The study of Addison's disease in pregnancy has an interest first on account of the connection of the suprarenal glands to the sexual apparatus. Disturbances in the glandular secretions cause irregularities or inhibition of menstruation, or sterility. The exact mechanism of the suprarenal secretion on the ovarian

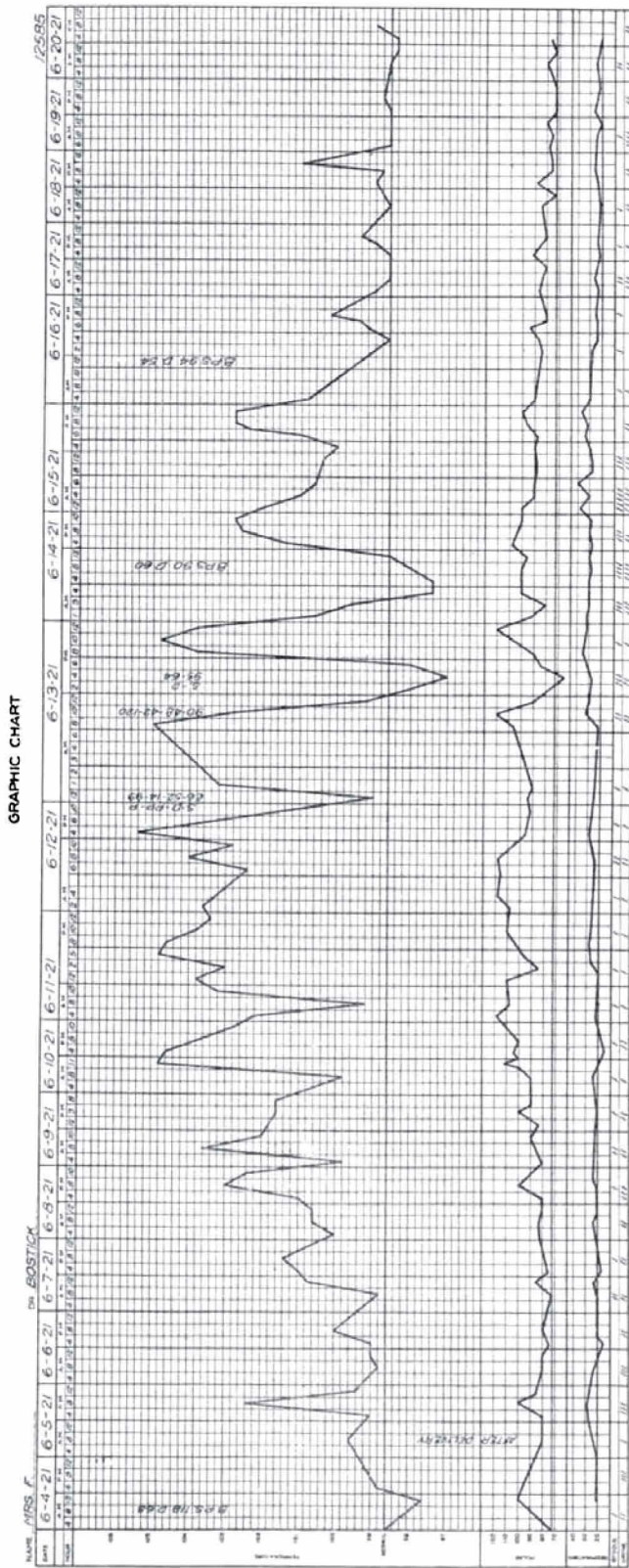


Chart showing temperature variations in author's case.

or other sexual function is not, however, well known. The matter is summarized in Novak's article in Nothnagel's *Specielle Pathologie*, 1912, Supp. vol. 1. Physiopathology of the suprarenals has, furthermore, a special interest during pregnancy and the puerperium not only on account of the direct effects of the glandular functioning in these states, but on account of the reciprocal action of the gravid state upon the suprarenal functions. There seems to be little doubt that gravidity demands and effects superfunctioning of the suprarenals as of other glands connected with sexual activity in the cortical zone, though opinions are divided as to whether there is an increased or reduced secretive activity in the medullary zone. Some investigators have found an increased quantity of adrenalin in the blood of the gravid in all periods and attaining its maximum during labor. Others have not been able to substantiate such findings. Whether, in the case of atrophy of the suprarenals, other internal secretory glands act in a compensatory way to supply their particular secretion or to what extent is not known.

We will now consider the reciprocal effects of Addison's disease and pregnancy, labor, and the puerperium.

As regards pregnancy complicated by Addison's disease, cases may be divided into two groups, the first group comprising cases in which the pregnancy occurs in a woman already affected by the disease and the second group those cases in which the Addison's disease appears only in the course of the pregnancy. Guisti's case belongs to the latter type and those of Seitz, Miller and Fleming and the author are doubtful cases. Although the material on which to formulate an opinion is extremely scant, still from what is known and from the theoretical considerations, it would seem safe to assume that pregnancy does not of itself predispose to Addison's disease in a patient whose suprarenals are normal, but that where there is already existing some alteration in the glands pregnancy acts as a stimulus to render a latent Addison's disease manifest; or at least that the effects of faulty functioning of the glands at a time when they are expected to

do even extra work are more manifest in the organism of a pregnant than in a non-pregnant woman. This also applies to cases where pregnancy occurs in the course of Addison's disease, and the intensification of pigmentation and other symptoms during this period, as noted in several cases in the series, supports the view.

The toxins of pregnancy to which are added those produced by the changes in metabolism due to the lack of suprarenal secretion create an unfavorable state of things, debilitating or impeding the normal powers of defense of the organism and consequently accelerating any morbid process, such as a latent Addison's disease.

The influence which pregnancy, labor, and the puerperium exercise on Addison's disease is frankly bad if we judge by the effects in the series of cases quoted. In the 11 cases, 5 of the mothers died before they had reached term. All of these deaths apparently occurred within a short number of days after labor. In the fourth fatal case, the woman went to term but died suddenly 28 days after the birth. The results are evidently grave for the mother and the eventual history of some of the patients in this series is not known.

As regards the child: in Barlow's case the foetus was dead; French's two cases were induced abortions with dead foetus; in Vogt's case the child was prematurely born; Guisti's case was a spontaneous abortion with a dead foetus. If the child lives to term, however, the prognosis is good.

In those who survived the gravid state there were intensifications of the symptoms in the puerperium. In Miller and Fleming's, Jacquet's and Seitz's cases intensification of pigmentation is distinctly mentioned.

From the series of recorded cases it may be deduced that Addison's disease already existing or becoming manifest in the course of pregnancy or of the puerperium has its already bad prognosis aggravated, and its symptomatology intensified.

It is not easy to estimate exactly the effects of Addison's disease on the course of pregnancy, labor, and the puerperium. Experiments on animals have shown that capsulectomy was followed by early abortion in gravid

animals. Clinical observations, as in this series of cases, are too few to enable a definite opinion to be formed. While French's, Vogt's, and Guisti's cases ended in abortion, spontaneous or induced, all other cases apparently went to term. An unfavorable influence of Addison's disease on the course of pregnancy need only be anticipated if the disease is very advanced and the patient's general condition poor. In such cases, abortion or premature labor must be the rule, due rather to the general state than to the alteration in the suprarenal glands.

As regards the influence of Addison's disease during labor, in none of the recorded cases was there any noted disturbance during the birth. The uterine and abdominal muscular contractions were noted always as good and sufficient. There was no inertia. If adrenalin plays any important part in the mechanism of labor, the loss of suprarenal adrenalin during labor must have been compensated for in some other way.

The disease seems also to have had very little effect upon the course of the puerperium. The uterus involuted well and the lochiæ were normal in all cases where noted. But it is questionable how far the process of lactation was affected by the disease or how far lactation may have been a factor in the death of the mother, soon after the birth in cases where it occurred. Whatever may be the causes, the puerperal state and lactation seems to have a very damaging effect on the course of Addison's disease. I wish to draw particular attention to one symptom which I observed in my own case and which I do not find mentioned in other case reports. I refer to the drawling, slow speech and decreased mentality. The decreased power of the patient to grasp ideas was very marked.

In my own case the feature that at once struck me when I first saw the patient was the very typical bronze discoloration. The persistent headaches, nausea, and vomiting and the aching all over the body with the feeling of very great weakness, were all in keeping with a diagnosis of Addison's disease, and the subsequent rapid recovery from the symptoms after administration of adrenalin and thyroid extracts confirmed me in my

view. The slow mentality and drawling answers might be considered as due to general asthenia.

Another point which greatly interested me was the abnormal nature of the temperature curve. A study of the temperature charts during the pyretic condition of the patient will show at once that it was not comparable to the ordinary temperature findings in cases of streptococcal or similar puerperal infections but that there was some abnormal factor in this patient's case.

In only 3 of the cases was Addison's disease verified by the anatomical findings on autopsy, viz., in the cases of Barlow, Vogt, and French (first case).

As a practical conclusion, we might seek to know what should be the obstetrical conduct to follow in a case of pregnancy complicated by Addison's disease. As stated already, the disease itself has apparently very little influence on pregnancy, labor, or the puerperium, and when the general state of the patient is good, no interruption need be feared. But if the disease has already affected the general state in an advanced degree, the asthenia may be so great as to bring about a spontaneous abortion or to justify an induced one. The few cases on record do not permit any judgment to be formed as to the necessity for interruption of pregnancy. The maternal prognosis is in any case bad on account of the Addison disease itself which will presumably run its inevitable course. But the foetal prognosis is good if the child lives to term or nearly so. The child of an Addisonian patient may be born prematurely or at term without showing any of the symptoms which threaten the life of its mother, and in Vogt's case the child has lived 14 years and is well. The obstetrical conduct in ordinary cases should be limited to the medical treatment justified and only to intervene when circumstances absolutely demand it. In the puerperium especially the obstetrician should seek to remove all possible causes which may render it pathological. Lactation ought to be forbidden, as it renders the patient weaker.

The patient has been followed since she left the hospital. The bronze coloration is still evident, especially in the facial region, less marked in the thoracic region, and with one particular spot on the abdomen.

There is epigastric pain easily elicited on pressure but which disappears when the manipulation is continued. In the lumbar region there is an exaggerated tendency to pain over the kidneys especially on deep respiration, and the patient is exquisitely sensitive to pressure over the lower lumbar area. There is some muscular and vascular asthenia.

I may add that the regional pains are not felt even on strong passive exercises of any kind made on the lower limbs. This points to the fact that the pains are dependent upon some deep-seated, rather than on a local, cause.

While any discussion in regard to the etiological factors connected with Addison's disease is outside the scope of this paper, I wish to say that the von Pirquet and complement-fixation tests for tuberculosis have so far given negative results.

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NOTE.—On June 8, 1922, the family physician, Dr. I. M. Bostick, reports the condition of my patient as follows: Blood pressure systolic, 124; diastolic 84. The bronzing is still well in evidence upon the face and forehead. At times she complains of giddiness with some muscle asthenia and backache. She has steadily gained in weight. She had an attack of influenza in February, 1922, but has apparently recovered without any aggravation of her previous condition.