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Diagnosis and treatment of pre-eclampsia

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Of
Pre-eclampsia

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The aim of this work is to produce, in a volume of convenient size, an up-to-date discussion of Pre-eclampsia, sufficiently full for the varied requirements of all classes of medical men.

In those instances in which there is a difference of opinion, neither view is meant to be emphasized, opposing facts being stated only for what value they may have. To avoid favoring an opinion or theory any conclusions which are to be drawn are left to the experience and observations of the reader.

Preeclampsia is essentially eclampsia before the outbreak of convulsions and the onset of coma. (9) It is a mild form of eclampsia which is regarded as a definite toxemia, characterized by an acidosis and a relative hypoglycemia. (15)

The term eclampsia has been applied for years to a more or less definite acute toxemia of pregnancy, usually manifesting itself in the latter half of the gestational period. The most characteristic manifestation of eclampsia is convulsions, and the term is naturally associated with their occurrence. Closely allied to the actual eclamptic state is preeclampsia which, from every viewpoint, is eclampsia minus its most characteristic phenomena, convulsions. (15)

History

J.C.W. Lever in 1843 entered the paper "Cases of Puerperal Convulsions, with Remarks" in Guys Hospital Reports, London. It was he who first noted the similarity presented of patients laboring under anasarca with Morbus Brightii, which led to the examination of the urine. At first he thought this was a pregnancy in a female with a granular degeneration of the kidneys but due to the slow disappearance of

albumin he decided it was some transient state probably connected with gestation itself. At this time he noted that in those cases in which albumin was wanting, inflammation of the brain and meninges was detected after death. By use of a catheter he removed the urine and found no albumin except in those who had had convulsions, or in those who had presented symptoms and who were easily recognized as precursers of puerperal fits.

By his observations he divided his cases into two groups: (1) Albumin found in the urine during pregnancy and having extreme evidences as shown in the edema of the hands and face. In such cases he noted that the convulsions would be more severe and last longer after delivery. The urine retains albumin longer than the second type. (2) In this group the albumin, fits are less violent and seldom reappear after delivery.

His conclusions were that any condition producing passive congestion of the kidney produces albuminous urine and believed pregnancy to be a cause. He also believed the size and shape of the uterus to be important and was aware of the fact that the condition may not be excited until the onset of labor.

In 1886 it was noted that certain cases of eclampsia were associated with hemorrhagic hepatitis, by Jurgens and Klebs, but Pilliet in 1888 first detected the characteristic hemorrhagic lesion. (42)

Also about this time Vincent reported a case of eclampsia with icterus with a meningeal hemorrhage, capillary hemorrhage of the liver and a slight nephritis. He described liver changes as we see them to-day and finds nothing which suggests a septic infection. He termed the lesion a peripheral necrosis of the lobule. (42)

Pre-natal care was probably first introduced by Vassili Vassilievich Stroganoff in 1897. He said, "By far the most striking advance if preventative obstetrics is the expectant treatment of eclampsia by means of quietude, isolation in a dark room, and exhibition of sedatives and purges." However pre-natal care was not taken up until the writings of J.W.Ballentyne, on Diseases of the Foetus, had become rather widely read. (14)

Etiology

Preeclampsia and eclampsia is caused by pregnancy and is self limited by delivery.

The true etiology of eclampsia is unknown. (18, 28) Although many theories have put forth as the cause,

none have been proven and none are absolutely accepted by any group. Eleven of the most important theories are listed below.

Eclampsia occurs predominantly in one type of physical habitus, that many of these are an endocrine imbalance is shown by sugar tolerance curves, blood iodine estimates and basal metabolic determinations. (16) The pituitary is not the only type of endocrine dysfunction that will produce toxemias, it is known that hypothyroids are very much benefited by thyroid extract therapy. (9) Parathyroid insufficiency has also been accused of being the cause of preeclampsia because it was found that the blood calcium was low and when parathormone was given the symptoms were much abated. (22) Although the blood sugar of eclampsias is very nearly normal some cases were found to be lower than normal and that investigator believed it to be due to an over functioning pancreas. (25)

It is common knowledge that the pituitary is enlarged during normal pregnancy. Allen (2) believes a relationship exists between the diminishing out-put of urine, as the patient approaches term, and the hypertrophied, hyperfunctioning pituitary. This endocrine disturbance

produces a water imbalance. Furthermore the treatment based on this theory has produced the results expected from many years of observation of patients both clinically and at autopsy. (3)

A disturbance of water metabolism has been mentioned as etiological, and Siegle and Wylie (38) believe it to be a disturbance of carbohydrate metabolism because of the blood sugar changes, but neither say anything about the cause of these so-called etiological factors.

The oxygen content of the blood is important in the development of the severer eclampsia. (40)

It is not known whether the kidney of pregnancy is bacterial or chemical. (26) Many men subscribe to the idea that bacterial infections play an important role in the etiology of eclampsia. The continued infection exhausts the detoxifying power of the liver. No bacteria or toxins have been isolated and proved to be the etiological agent, although a streptococcus has been isolated from the spleen of a young eclamptic and injected intravenously into two rabbits which remained healthy and were killed on the fourth day, their livers were found to present a microscopic picture similar to that presented by the patient. (32) Hayes drained the

kidney pelvis prior to delivery, in this condition and pernicious vomiting, and all patients showed immediate relief.

The source of the supposed toxins, causing eclampsia, concerns nearly every organ and mechanism in the female body. DeLee (21) says- "We assume a toxic element in the causation of these violent motor and cerebral phenomena, and in some cases we think we can discern a pure and complete toxicosis." The fetus is said to excrete a poisonous substance by its metabolism, and certain poisons are said to be squeezed from the placenta by uterine contractions, thus explaining the much greater tendency toward eclampsia a few days before, during and after delivery. (26) Although there probably is a specific toxin the source is as yet unknown. (2) Albuminuria may be due to a changed condition of the placenta, which is an excretory organ, as well as a source of nutrition for the fetus. It is thought to detoxify the excrement of the fetus, and when functioning improperly may allow the mother's circulatory system to be loaded with poisons faster than they can be excreted. (26) Bartholomew and Kracke (6) believe there is a relationship between placental infarction and eclampsia.

It is indicated that hypercholesteremia may be the cause of eclampsia. This is probably due to a hyperpituitary or a hypothyroid activity and is a normal response to pregnancy to meet the demands of rapid cell growth of the fetus and to prepare for lactation. (5)

The dietary history shows inadequate food supply in either quantity, quality or both. Adequate nourishment is conditioned by clinical isgns and symptoms, contributing to a state equivalent of starvation. (16) Whether this is the cause or the result of the toxemia is hard to say, because others say with equal finality that the preeclamptic has an increased appetite. (29)

Eclampsia is under nervous influence and might be called a special form of neurosis. (26)

The theory that increased intra-abdominal pressure is responsible for liver lesions of eclampsia, although an attractive hypothysis, must as yet be considered unproved. (24)

Increased guanidine and lowered blood calcium are thought to be the cause of eclampsia because these two conditions do exist. On the return of these substances to normal by giving calcium or parathormone, the latter

governs calcium metabolism, the symptoms of eclampsia become much improved. The increased guanidine is due to the lowered calcium which in turn is caused by the demand of the fetus. (22)

Predisposing Factors

Predisposing factors are said to be foci of infection, especially the teeth, (from which tyramine is liberated and is said to cause elevated blood pressure and other toxic symptoms, (20) multiple pregnancies, hydramniotic states and previous renal and hepatic diseases, over eating and constipation. Meats in excess putrify in the large intestine and predispose to the disease. During the war in Edinburgh the percentage of eclampsia decreased to two-fifths of the original number, this was thought to be due to a decreased amount of protein in the diet. (13, 28)

Besides those activating factors mentioned above, McIlroy (28) believes acute infectious diseases, especially of the kidney, are important. (28) Porter (32) says that it has long been known that kidney disease increases the incidence of eclampsia. However in direct opposition to this statement Howlett (19) says, "There is no evidence that nephritis predisposes to eclampsia."

Fantus (12) says there is no probable relation between climatological factors (atmospheric pressure, air temperature, and rainfall) and the frequency of the disease. However, it is a known fact that in Siam, where the diet is mostly rice and vegetables, the clothing light and sunshine abundant, toxemias of this type are very rare. (34)

McGoogan (27) reports a series of eclamptics of which 40.9% of the multiparas had had a previous toxemia of pregnancy either of the so-called low reserve kidney type, preeclampsia or eclampsia. Other writers agree with this finding. Scarlet fever, diphtheria, acute rheumatic fever, previous nephritis (27) angina and laryngobronchitis are said to predispose to eclampsia and preeclampsia. (12)

Incidence and Occurrence

The tendency to develop eclampsia increases with age, (27, 12) and is most frequent between the ages of 20 and 30. It is four times as frequent in primipara, where previous nephritis was not a factor in either, and nine times as frequent in cases of multiple as in cases of single pregnancy. (12, 13). Other investigators believe the disease occurs more frequently in the young women under 25 years of age. The same

author (27) reports 9 cases of eclampsia in 1,709 deliveries or an incidence of 1-200. Seven of these were under 20 years of age, one was 20 and the other 28, a negress. Seven of the patients were primagravidae and one was secundagravidae, the other was para six. Two of the patients were in the seventh month of pregnancy and the remaining seven at or near term. Kellogg (20) reports that out of 552 cases in the Boston Lying In Hospital there were 61 cases with evidence of disease independent of pregnancy and 491 cases with no evidence of disease independent of pregnancy. Of this group 414 cases were preeclampsia grade 1; 65 grade 2; and 12 cases of eclampsia. If preeclampsia and eclampsia are to be thought of as a single disease it may be said to have an incidence of from 0.57 to 1.49 per cent. (12, 27)

It occurs ten times as frequently in blondes as in brunettes. (13) It occurs more often in colder climates and in colder seasons, (13) although others do not agree, believing that climatological factors has no relation to its occurrence. (12)

There is undoubtedly a periodicity in the occurrence of eclampsia. In the city of Tammerfors, during the twenty years reviewed, pregnancy, labor,

and the perperium were complicated by eclampsia twice as often in April, May and June as at other times of the year, and the incidence of eclampsia was lowest in the month of March. (12) At the University of Nebraska, during recent years, the month of March was found to be one of the highest incidence.

It occurs predominantly in one type of physical habitus (16), and is not restricted to race or color. (27) It is seen more frequently a few days before, during and after delivery. (26)

Others think that cardio-vascular failure and defects, and anemia, cause the woman to be more susceptible to preeclampsia. (32) One-fourth of all albuminuric cases become eclamptic. (26)

Pathology and Physiology

The toxemias of pregnancy are classified in many ways, all are arbitrary and represent but one man's conception of the disease. According to Arnold (4) patients may be classified into three groups:

1 - The moderately preeclamptic
2 - The Dangerously threatening preeclamptic
    a. Without chronic nephritis
    b. With complicating chronic nephritis
3 - The actively eclamptic or convulsant group.

Another classification is as follows:

1 - Pernicious vomiting
2 - Low reserve kidney
3 - Preeclampsia
4 - Eclampsia
5 - Chronic Nephritis
6 - Acute yellow atrophy

McGoogan's classification is probably a little more descriptive and inclusive, it is as follows:

1 - Pernicious vomiting
2 - Hepatic types
    a. Low reserve kidney (Mild preeclampsia)
    b. Preeclampsia (Severe preeclampsia)
    c. Eclampsia
    d. Acute yellow atrophy
3 - Nephritic types
    a. With chronic nephritis (With or without convulsions)
    b. With chronic nephrosis (With or without convulsions)

It is said that eclamptics must have 2 gms. of albumin per liter of urine and the blood pressure must be 150/100 or above.

Because of the scarcity of pathological material in preeclampsia, it is assumed the pathology will be similar, but to a less degree. There will be no brain hemorrhage and less liver necrosis. The cloudy swelling and granular degeneration of hepatic and renal cells will be less marked, as will the edema of these cells.

As with every thing else concerning this disease,

the pathology also varies. However the most characteristic histologic finding in eclampsia is the so-called hepatic lesion; a perilobular hemorrhage and liver cell necrosis...There are associated renal changes, but the characteristic lesion of eclampsia is hepatic, although even this is not a constant accompaniment. (15)

Autopsies failed to show a single, uniform, unfailing pathological lesion (13), however Porter (32) gives this description of the most typical findings in the liver of an eclamptic: Weight 2,000 gm., the edges are sharp, dark brown blotches, three to five cm. in diameter, are found on all surfaces. The capsule is covered with soft and multiple adhesions, especially on the superior surface. On section the appearance is commonly described as nutmeg. The amount of free blood is less than that found in normal liver. On microscopic examination he describes an irregular distribution of cell necrosis with hemorrhage in these areas, round cell infiltration around blood vessels and bile ducts and a cloudy appearance of other liver cells. He regards this as the chronic stage of acute yellow atrophy. (13)

Studies of the organs of patients dying from

eclampsia show certain typical pathological phenomenon. In the liver there are focal areas of hemorrhagic necrosis and fatty degeneration, predominantly in the periphery of the liver lobule, as a rule...In the kidneys cloudy swelling and fatty degeneration are the rule...There is no doubt that the above changes are the result of eclampsia and not the cause. (9)

Exploration during the terminal stage of eclampsia has shown the brain to be gray-white (anemic), edematous, and often associated with excessive amounts of extra arachnoid and subarachnoid cerebrospinal fluid. Histological study indicates widespread cerebral edema, enlarged perivascular fluid spaces, and frequently punctate hemorrhages as well as occasional focal or extensive recent subarachnoid hemorrhages. (4) Allen (2) believes the sumptoms due to cerebral dysfunction are in turn due to water retention in the cerebrum, with pressure. Pathologically, the eclamptic brain differs little from 'wet brains' or cerebral edema found in other well recognized hydration states such as acute alcoholic wet brain, status lymphaticus, acute toxic hydration states in children, and status epilepticus. (4)

From a clinical standpoint, the biochemical changes associated with eclampsia, are limited to a few abnormalities in the urine and blood. The urine usually shows large amounts of albumin, with hyalin and granular casts; these findings being associated with a definite arterial hypertension.

The blood chemistry changes of note are usually limited to a uric acid increase of from 5 to 9 mg. and a co2 combining power decrease to below 35 volumes per cent. The blood sugar findings are not definite, although Titus and Dodds (15) have demonstrated, what they term 'a relative hypoglycemia' immediately preceeding the convulsive seizures. (38) They state that the general trend of the sugar content is downward; although for years it has been assumed that eclampsia is usually associated with a hyperglycemia. When the blood chemistry presents evidence of nitrogen retention, it is produced either by a primary renal condition or a renal condition directly resulting from the eclamptic toxemia. (15)

Siegle and Wylie (38) also state that there is a relative hyperglycemia following the convulsions. They further state that a normal, subnormal or increased blood sugar may be the case in preeclampsia.

This is further borne out by Allen (1) saying that neither hypo- nor hyperglycemia is characteristic of eclampsia. He believes that the blood sugar level depends on the patients nutritional state, degree of emotional stability, and muscular activity immediately preceeding the taking of the specimen. The blood sugar concentration has no effect on the convulsions except a rapid rise or fall is apt to precipitate them. (1) However most writers agree on a hypoglycemia (22)

Hyperglycemia is caused by asphyxia, increased acidity of the blood and moderate damage to the liver, varying degrees of each factor are found commonly in eclampsia. Carbohydrate intolerance is seen in starvation, essential hypertension, and upon anterior lobe extract administration of the pituitary gland. In this condition the pituitary is hypertrophied, and normally should produce a hypoglycemia, but in eclamptics it does not, presumably because there is hypertrophy of the Islets of Langerhans. (16)

Preeclampsia may show decreased sugar tolerance and hyperglycemia while eclampsia may show increased sugar tolerance and hypoglycemia. The latter has occured while giving hypertonic glucose. Hypoglycemia may indicate overactive insulin production or damaged

liver tissue. (16)

Conterow (22) states that in normal pregnancy and early labor there is general diminution of the total serum calcium 10.61 to 9.61, slight increase in the diffusible calcium 5.08 to 5.55 and a marked decrease in the non-diffusible calcium 5.53 to 3.49. In the late toxemias some men do find a low calcium, others find it to be normal. However a hypocalcemic condition of the body can exist without being indicated by the blood studies because the bones and tissues will be low in calcium before it will show in the blood.

A low calcium index is due to the increased demand and the deficiency in the average American diet is indirectly responsible for the nervous imbalance; as tingling, numbness and tetany. This in turn is due directly to the increased guanidine because of calcium shortage, calcium being needed to render it non-toxic. (22)

Patients with a high inorganic phosphorous have a low co2 combininb power and those patients with ten mgs. per cent, on enterance to the hospital, have not recovered. (16)

Guanidine is a toxic product of volumtary muscle action and of break down of nitrogenous foods $NH_2C(NH)NH_2$. It becomes unable to metabolize carbohydrates and store glycogen. Thus the body becomes depleted, especially the supply in the muscles. Lactic acid, protein wastes and guanidine become proportionally increased. Parathormone governs the mobilization of calcium for after parathyroidectomy the blood calcium falls and there is a marked increase of guanidine compounds in the blood and urine. This must be the explanation of part of the symptoms as Major (22) says, "Guanidine in small doses causes a marked and lasting elevation of blood pressure, and in larger doses causes convulsions and death."

The excessive amount of cholesterol found in the blood is due to one of two things, probably, either a hyperpituitary or a hypothyroid activity, it is further increased by a diet containing much cholesterol. Baratholomew and Kracke (5) believe this to be the fundamental basis for the toxemias of pregnancy. It is probably responsible for the nausea and vomiting until it is stored in the reticulo-endothelial system. Excessive storage in the liver in the first half of

pregnancy produces excessive fatty change in the periphery of the lobules with subsequent central necrosis of the inner zone of the lobules and is persistently found in fatal cases of pernicious vomiting.

In the same way that hypercholesteremia is responsible for sclerosis of blood vessels it is responsible for placental infarction because of the sclerosis found in the vessels leading to the infarction. The affected tissue undergoes autolysis with liberation of peptone, guanidine and histamine as toxic split products of placental protein. The amount and location of the infarction, degree of obstruction, and autolysis determines whether pre-eclampsia, eclampsia, or abruptio placenta will occur. (5)

If hypercholesteremia is the cause of the toxemia it should be prevented by the administration of thyroid extract or iodine, and the restriction of fats and foods containing cholesterol, during pregnancy. (5)

The lowering of the total protein per 100 cc of blood, in normal pregnancy, amounts to about 1 gram of albumin. Each gram of albumin exerts an osmotic pressure of 5.5 mm. Accessory factors in regulating

oncotic pressures are brought into play as - elevation of blood stream fat and globulin content of plasma, alteration in pulse pressure and blood volume, and elevation of blood pressure. All of these changes occur in preeclampsia and eclampsia, but the blood pressure and pulse pressure differs in degree. (16)

Diagnosis

Diagnosis depends upon a correlation of the symptoms, physical findings and laboratory work. One symptom may seem almost negligible, but when associated with any second finding, it always indicates seriousness. Thus patients presenting any two of the major symptoms should be kept under almost constant surveillance or, when possible, hospitalized.

Symptoms-The onset may be abrupt, but premonitory symptoms may be present for a number of weeks before the patient presents herself or considers herself ill. (9) The early symptoms may occur at any time and are preeclamptic in character until the onset of the convulsion or coma. Minor disturbances of the nervous system have been found to be the second most constant sign of incipient toxemia. Manifestations such as slight nervous irritability,

mild and transient headache, occasional dizziness and fleeting specks before the eyes are often complaints of the patient. (33) Headache is probably the earliest and most important symptom. 86% of preeclamptics show headache after the 20th week, usually frontal or occipital, transient blindness in 20%, nausea and vomiting associated with epigastric distress, in 68%. Dyspnea is a common symptom, the percentage of which is not given.

In a review of 30 cases, the predominating symptoms on admission were: edema in 24 instances, headache in 16, dizziness in 7, spots before the eyes in 6, and nausea and vomiting and epigastric pain in 5. (9)

The terminal cerebral symptoms are similar throughout this entire group. Headache, vomiting, irritability, and mental torpor occur early followed by stupor, convulsions, and respiratory failure. These symptoms have constantly arisen in neurosurgical problems dealing with brain tumors, increased intracranial pressure, and cerebral edema. (27)

Physical Findings-The early signs are detected by three instruments; the sphigmomanometer, scales and a test tube. (34) This indicates that the change in blood pressure, edema or gain in weight, and

urinary findings are the three most important physical findings. There is invariably a slight rise in the systolic and diastolic pressures several weeks before albumin appears in the urine. (34) Blood pressure recordings are probably the most common, constant indication of toxemia. However, it is not appreciated generally that the blood pressure is normally lower during pregnancy. The blood pressure in the early trimesters of pregnancy fluctuates between 90/60 and 110/60. Thus a rise in blood pressure to 130/60, which is 40 points above normal, is stressed as a danger signal. (33) However some men believe that a rise in the diastolic pressure is more significant than a systolic rise. (31) Blood pressure above 130/60 to 150/90 is considered potentially eclamptic; and from 150/90 upwards occur the graver toxemias. (33)

Ophthalmoscopic study of the eclamptic reveals spastic vessels, patchy edema of the retina and discs, and at times detachment of the retina. Eye signs of the preeclamptic are much evident, if at all.

An excessive gain in weight (over 400 gm. per week) should be met by recording weight and blood pressure, the first bi-weekly and the last twice daily. (31)

The recording of weight has proven invaluable. A gain of weight of over eight pounds per month, even though not associated with other symptoms, is indicative of impending toxemia. A gain in weight of over twenty-five pounds in the first seven months demands active treatment, for at this period of gestation most toxemias develop. (33) Theedema of eclampsia is generalized and does not disappear with rest. (16) Women who do not gain more than 20 to 25 pounds during pregnancy are rarely subject to toxemia. (34)

Laboratory-It is because of the difference in the findings in the urine that there is so much controversy in the pathology and etiology of this condition.

The presence of albumin in the urine has been accepted as one of the most constant findings and its presence is only of diagnostic value. (33) The urine may show from 860 to 38,600 mg. of quantitative protein in 24 hours. (16) In a series of 30 cases examination of the urine disclosed albumin in varying amounts in 29 cases and absent in one case. Casts were present in 17 cases, a little more than one half of the cases. The specific gravity of the urine was 1.016 or higher in 23 instances and below 1.016 in 7. (9)

In another series of 9 patients albumin and casts were present in the urine of all the cases, and the specific gravity was below 1.016 in only two instances.(9)

Albumin may disappear when the child dies or it may appear for the first time when the child dies, especially when it becomes macerated. (26)

Blood chemistry is an indispensable index of the severity of the disease. The N.P.N. remains within normal limits, except late when it may rise indicating involvement of the kidney. The blood urea nitrogen remains low as in normal pregnancy, with the result that the ratio between urea nitrogen and N.P.N. of the blood is about .4 as compared with .5 in the normal non-pregnant individual. The blood uric acid is increased in this disease indicating a disturbance in its destruction in the liver. The uric acid content of the blood may be regarded as a fairly safe criterion of the severity of the disease. The normal is 3 to 3.5 mg percent, it may go to 8.8 in eclampsia during convulsion or pre-eclampsia before delivery. It is usually highest from 24 days before, to 24 days after delivery.

The blood sugar is not greatly disturbed but may

be decreased. In preeclampsia, ante-partum, the serum albumin is found to be 3.81, the serum globulin 2.77, making a total serum protein of 6.58. The first six months of normal pregnancy are marked by a fall in serum protein to an average of 6.2%. The decrease is principally in the albumin fraction. In the last trimester the serum protein gradually rises to an average level of 6.9%. Normal non-pregnant plasma albumin content is 4.5 to 5.5, globulin is 1.5 to 3.0. (16) In a review of 13 cases McGoogan reports the serum albumin to be 3.0, serum globulin 2.1 and a total serum protein of 5.1. (27)

The alkali reserve is often greatly decreased, sometimes even to a true acidosis level, as determined by the carbon dioxide combining power, average 46%.

The blood chlorides are greatly decreased except in an occasional patient with marked edema. Thioneine and glutathione are within normal limits. The increased uric acid cannot be accounted for by increased thioneine and the hyperglycemia, when it does occur, cannot be accounted for by the increased thioneine or glutathione so it is a true hyperglycemia due to muscular activity. (39)

There are alterations in cholesterol, lipoids, surface tension etc., and are more marked in preeclampsia

than eclampsia. (11)

Differential Diagnosis

The differential diagnosis will be based on McGoogan's classification of the toxemias.

Low Reserve Kidney-Incipient Toxemia-According to Kellogg (20) the term Low Reserve Kidney is misleading, and should be classified Preeclampsia Grade 1. Incipient toxemias comprise the largest number of cases. The most common finding is a slight elevation of blood pressure whose upper limits have been arbitrarily placed at 130/90. Minor nervous manifestations are usually present. Albumin may be present in the urine, but it is more often absent. The eyegrounds are negative; the blood chemical tests negative. Slight edema may be present; and if so, it is associated with a relative gain in weight. (33)

Preeclampsia Grade 2, Kellogg (20)-In moderate toxemias the blood pressure is arbitrarily placed above 130/90. Nervous manifestations are more constant and pronounced. Albumin in the urine is more often present. Renal function tests are normal, but the urinary output is often slightly diminished. Blood chemical tests are negative. The eyegrounds

often show spasticity of blood vessels, but edema is quite the common finding in more advanced cases. Generalized edema with its associated weight gain is noted in the majority of cases. (33)

Acute Yellow Atrophy of Liver-In the early stages of the disease, it may be difficult to distinguish it from pernicious vomiting. Jaundice, as a rule, is an early symptom and nausea and vomiting are not continuous. The rapid autolysis of liver parenchyma results in the liberation of large quantities of amino-nitrogen into general circulation, which appears in large quantities in the urine. (37)

Nephritic Types-The nephritic toxemias are differentiated by the History, which reveals as past acute contagious disease, chronic focus of infection, or past cardio-renal, but more often the History is essentially negative. The history of other cases indicated that repeated and short spaced pregnancies accounted for the presence of cardio-renal disease. Physical examination reveals the hypertension impaired renal function with nitrogen retention in the blood. Renal function tests as urea concentration, creatinine, etc., all show definite decreased kidney function. Quite often

myocardial involvement is present. The eyegrounds show vascular tortuosity, hemorrhage and degenerative retinitis. Degenerative retinitis is not always of long standing. Following the termination of pregnancy, the writers have seen vision and eyegrounds improve beyond belief. Pregnancy is the best physiological test of renal function, thus more consideration should be given this group. The death rate of such cases in a five-year follow-up was greater than in all other acute toxemias. (33)

Preeclampsia is differentiated from the kidney types by not having increased N.P.N. or Creatinine, both diseases have an increased total specific protein (especially the albumin fraction), increased uric acid and a decreased CO2 combining power.

Prognosis

In general the prognosis seems to depend somewhat upon the type of treatment.

The pregnancy following one accompanied by toxemia may not be associated with toxemia but succeeding pregnancies are very apt to be accompanied by toxemias. (43) Succeeding pregnancies may be of lessened severity if of pure hepatic type and without renal pathology. A somewhat higher death rate was noted

among the blacks than the whites. The young woman below the age of twenty and the primipara seemed to have a more favorable prognosis than the woman in the older stages of her child-bearing career or one who had had previous pregnancies. (30) The prognosis for the mother and child is more unfavorable the earlier in pregnancy the condition develops. (12)

Fetal mortality is approximately 24.1 per cent in preeclampsia and 44.4 per cent in eclampsia, due to toxemia alone. 24.1 per cent of preeclamptics deliver prematurely. (43)

The patient who presents heartburn, scotomata, frontal headache, tinnitus, and formication and numbness of the extremities, in the earlier weeks of pregnancy, often carries severe renal damage, marked hypertension and is destined to a premature term of pregnancy or death. (16)

One-fourth of all albuminuric cases become eclamptic (26). However, of the 522 preeclamptics treated by Harden, with the protein stabilization treatment, not one developed coma or convulsions. (16)

Prophylaxis

The prophylaxis of eclampsia is the adequate treatment of the preeclamptic and is an important

part of prenatal care. A rational prophylaxis of eclampsia is only possible, if the first signs of intoxication and the first symptoms of insufficiency of the organs in question are observed and recognized. Pregnant women are to be controlled by rather frequent and careful observation. The gradual introduction of successive therapeutics measures must be based upon the fact that the convulsive phase of eclampsia is always preceeded by preliminary symptoms. If this fact is neglected it will certainly be impossible to decide which method of treatment is the better. (23)

Prevention of eclampsia occupies a more important part in the management of preeclampsia than that of any other obstetrical complication. The prophylaxis of eclampsia is two fold; early recognition of the toxicosis and prevention of the attacks. (7) In twenty years de Snoo (9) observed eclampsia only twice without having recognized the toxicosis previously. (

No hard- and-fast rules can be laid down for the treatment of toxemia, as its manifestations are varied in the case of each individual patient. (27) Prophylaxis requires examination every two weeks, during the last months, of blood pressure, urine and body weight, and for edema. Eradication of foci

of infection, especially by dental care, should be attempted. (31) Every pregnant patient should be treated by a dentist if there is evidence of caries at all, even if only in one tooth. Oral sepsis is a predisposing cause of throat affections, toxemia, and puerperal sepsis, and also of inability to suckling. Extractions do not produce abortions by any means, and in ante-natal care dental treatment is one of the most valuable aids we possess. (28)

Careful attention in every patient to the condition of the teeth and skin, to the diet, and to the absence or presence of vomiting, hypertension headache, and ocular symptoms, will go far in mitigating or eliminating the serious types of toxemia such as acidosis and eclampsia. (27) Sudden or fulminating attacks of toxemia may occur, especially in the later months of pregnancy, and these cannot always be forseen or prevented. They are rare and in most cases when investigated will be found to be due to some gross error in diet. Therefore McIlroy (28) believes the general preventative treatment of eclampsia resolves itself into: 1. The careful avoidance by dieting, of excessive or unsuitable food intake and the adoption of a diet which will make up for

deficiencies resulting from fetal demands upon maternal tissues; -2- The elimination of harmful substances by physiological rest and the suitable stimulation of those organs which are concerned with excretion. Drugs are excellent and in many cases necessary, but one can do more by proper dieting and elimination than by any other means. Sedatives may be necessary but their employment is an indication of ineptitude in stimulating physiological function. (28)

Another important fact also mentioned by McIlroy (28) is the importance of exercise. Reduction of the mothers weight can be brought about not only by dieting but by open air exercise--two or three miles should be walked daily. Many men have said that women should train for the event as an athelete would for competition.

Heartburn is sometimes a sign of grave impending toxemia. Many authors have found good results from advising small dry meals with low fat content. Fluids should be given between meals. This gives the gastric juices an opportunity to act. Dilute hydrochloric acid in 15-30 drop doses during meals gives relief in cases where hypo-acidity is present.

Headache, is persistent, may be due to anxiety, hypertension, eyestrain, or intracranial tension, and should never be overlooked. It is sometimes the first danger signal of the onset of eclamptic convulsions. Rest in bed is necessary in some cases and careful dieting of the carbohydrate type. If it is very severe, lumbar puncture may give relief. Calcium lactate or calcium gluconate have also been given with good results. Pain on the whole is a rare symptom in pregnancy. It is present in severe forms of toxemia in the region of the epigastrium, and is due to tension under the liver capsule owing to small hemorrhages. General treatment beings relief. (27)

Edema is usually accepted as a sign of danger in the future. Rest in bed, regulation of the diet, and general treatment especially with small doses of magnesium sulphate will have a beneficial effect. Restriction of fluids also has a marked effect when balanced equally with the urine output. In edema due to cardiovascular changes the treatment should be on ordinary medical lines.

There is a considerable amount of fairly serious anemia in association with pregnancy and accompanies many cases of toxemia. The anemia is mainly due to

to vitamin and iron deficiency. Sunlight, fresh air, and a generous mixed diet is essential in the prevention and treatment. Green vegetables such as spinach contain iron. As already mentioned, the fetal drain on the maternal iron is considerable.

In the antenetal clinics of some hospitals, yeast and massive doses of ammoniated citrate of iron in powder form were given to a large number of the patients. In the wards each patient received once a day, a routine dose of iron and cod liver oil. Marmite and cooked liver or liver extract were given to some of the anemic patients. Transfusion of blood, as most obstetricians know, is of great benefit in the treatment of severe anemia, toxemia, shock, and sepsis.

In a normal pregnancy a blood urea of 22, or slightly over, reassures us that renal function need not be a source of anxiety. If the urea content indicates renal complications we try treatment by rest in bed and dieting, but if this fails the pregnancy may have to be terminated. Uric acid is, however, a finer test of nitrogen retention than urea if found elevated. The sugar curve of the blood is an indication of the aberrations which take place

in carbohydrate metabolism. In cases in which the blood sugar content is high, insulin may be given with discretion.

Examination of the urine-Albumin is the danger flag throughout pregnancy. When it persists and is considerable in quantity it should never be overlooked. Hence the routine examination of the urine in all cases of pregnancy is a necessity. A considerable amount of albumin in the urine should not be allowed to persist for more than two to three weeks as there is the danger of permanent kidney damage.

Bacteriological examination for the colon bacillus by culture of the urine at the bedside gives many more positive results than those obtained when the urine, after standing, is sent to the laboratory for culture. Pyelitis rarely requires treatment other than rest in bed, dieting, warmth, and urinary sedatives and antiseptics. A very large number of these cases are sent to the hospital for treatment, and in no case has surgical interference been necessary; as a rule, these patients clear up very satisfactorily, and a ketogenic diet is giving good results in some cases. (27) An important indication of renal damage

is the low specific gravity of the urine. The urea concentration test is useful in determining renal function. The presence of casts is also of value. The quantity of urine passed is very important, especially in serious cases of toxemia. The intake and output of fluid should be carefully measured and compared. Scanty or suppressed urine is a grave sign of toxemia and may indicate immediate efforts for the termination of the pregnancy. In renal cases suppression is even more serious, as it indicates a greater degree of concentration than toxemia. Hot packs, electric light baths, and diuretics such as citrate of potash are of benefit. Urea may be used with care.

In addition to those measures cited, Fantus adds the following from the therapy of the Cook County Hospital:

1-A salt poor, low protein and low fat diet. An abundance of fruit and vegetables and carbohydrates, milk (at least three glasses a day), a small amount of protein and fat (one helping of meat and one egg daily), a minimum of salt and of spices, and from six to eight glasses of water daily should be taken.

2-Magnesium sulphate purgation, as required.

3-Skin hyperemia production, with its blood pressure reducing tendency. Profuse or exhausting diaphoesis is not intended. Methods best employed are electric light cradle for from fifteen to twenty minutes daily, or to the point of incipient perspiration, followed by a dry pack; or a warm bath (100°F.) daily for fifteen minutes followed by a dry pack; or general ultraviolet irradiation with a minimal erythema dose, the lamp at 75 cm. distance, for from two to seven minutes according to the intensity of the rays or the sensitiveness of the patient, to different fourths of the body surface every other day, the various surfaces being irradiated again at each next round for possibly one minute longer until pigmentation or constitutional reetion sets the limit, which may be reached with fifteen minutes exposure.

4-General regimen. The patient should avoid chilling and reduce her physical and mental activities. (31)

It is agreed by every one that a weekly examination of the urine blood pressure and weight notations every two weeks are important. If the diastolic pressure reaches 90-100 the blood pressure and urine should be run daily. (20)

Howlett (19) is one of the few who still believes

in the use of Bashams mixture which is iron ammonium acetate. (19)

As one of the most radical preventative proceedures Waldstein (19) of the Rotunda Hospital, advocates induction of labor if albuminuria has not disappeared after three days of intensive treatment.

TREATMENT OF PREECLAMPSIA

Obviously the treatment of preeclampsia must remain empiric and relatively unsatisfactory until the actual cause of the disease is discovered.(30) Preeclampsia has required some rational basis of treatment directed toward certain fundamental physiological disturbances that occur with-in the brain. (4)

The question of the management of preeclampsia is one upon which there still exists a wide difference of opinion. In some clinics every effort is used to remove the products of gestation as speedily as is possible, while in other clinics, of equal standing, the fetus is almost, or entirely, ignored as a factor in the disease. As is usual, in instances of this kind, there is perhaps a midposition that is more logical than either extreme. It is with this in mind that the various methods of therapy are presented, without partiality to any one school of thought.

in general it may be said that there are two main groups, one advocating radical and the other conservative methods, and each possessing certain merits. The radical group subscribes to the belief that since eclampsia occurs only in connection with pregnancy and the convulsions usually cease when the uterus is emptied, the logical way to treat the condition is to terminate pregnancy. The conservative advocates believe that this is unnecessary and is usually harmful. However, it is very evident that the strong tendency today is toward conservatism.

The treatment may be divided into four great plans; sedative; measures to reduce blood pressure; eliminative; and operative. (18)

Results are much better in the hospital than in the home and because of this fact it will be convenient to describe the emergency treatment which is most used when the patient is first admitted. It is believed by Kellogg that the treatment of preeclampsia should be as radical as the treatment of eclampsia should be conservative. (20) In the preeclamptics the objectives of treatment, whether at home or in the hospital, should be first, to antidote as far as possible the effects of the toxemia;

second, to help the crippled emunctories by proper regulation of diet; third, to stimulate the elimination of toxins; to terminate the pregnancy as conservatively as possible before the onset of convulsion, if the results of treatment are not satisfactory. (28)

Hospital Treatment is varied and the intensity of the treatment is modified as to whether the patient is in the preeclamptic stage or the threatened eclamptic stage.

Preeclampsia-When the blood pressure exceeds 140 or when either albuminuria (more than a trace) or edema (especially facial) or both add themselves to the hypertension, the patient should be immediately hospitalized. Nonprotein nitrogen estimations, blood chloride determinations (if edema is present), and carbon dioxide combining power tests along with repeated retinoscopy will furnish an index as to progression or regression of the toxemia. (31) Patients with definite signs of hypertension, albuminuria, edema of the extremities, headache and beginning visual disturbances have been placed in this group. In several of the patients sufficient number of them to arouse apprehension regarding the further progress of the pregnancy. (4) Other measures will include:

1. Absolute rest in bed, which alone will often do wonders in the reduction of blood pressure and the relief of other symptoms. If the patient is restless, potassium bromide (4 gm. daily) and chloral hydrate (from 1 to 2 gm. daily) or phenobarbital (0.10 gm., two or three times a day) will permit sleep and comfort.(31) Ross (35) claims that nembutal given in .1 gm. doses 4 times daily prevents the occurence of convulsion in preeclampsia.

2. Fasting-No feeding should be allowed and moderate drink restriction should be enforced for a day, followed by a salt-poor diet, e.g., oatmeal gruel, and later by a lactovegetarian diet (1,500 calories daily). No tea or coffee should be taken. Edema indicates limitation in fluid intake (to 1,000 cc. a day) until the edema is gone, then gradual increase in the fluid intake, provided the urine elimination increases proportionately. (31) As far as practical, the level of fluid intake is maintained so as to equal and balance with the previous days output. An accurate chart record is made of the intake and output of fluid and the patient is weighed daily. (4)

3. Purgation by magnesium sulphate (30 gm., best given in ice cold effervescent lemonade) every six hours until watery bowel movments are obtained, then 15 gm. daily the first thing in the morning. (31)

4. Food and drink are given at 3 hour intervals throughout the day, no eating or drinking being permitted between these small meals. A diet of solid foods of wide varieties including proteins is given. The patient is fed well but moderately, a salt-low diet, soft and liquid nourishment high in water content being avoided, as are also sweets and desserts. (4)

If the blood pressure goes down and no other symptoms appear, the patient is watched carefully, until term, for recurrence of symptoms. The patient should report at once if disturbance of vision, dizziness or unusual headache should appear. (31) However in moderately preeclamptic group a prompt and beneficial effect is the rule, and normal full term deliveries will occur in nearly all patients. (4)

Threatened Eclampsia-If in spite of these measures, the blood pressure, measured three times daily, continues to rise (systolic 150 mm., diastolic pressure 100 mm., or higher) or if increasing toxemia is revealed by the study of the continuous 24 hours

specimen of urine, the blood tests or other signs or symptoms, such as apathy or restlessness, or the appearance of headache, or when visual disturbances or epigastric pain associate themselves, there is one of two proceedures to be followed. The uterus may be emptied or a more extensive dehydration therapy may be instituted, the latter treatment is usually the one of choice, it consists of the following:

Dehydration Treatment-Arnold and Fay (4) Make careful observations and records of: 1. Blood pressure at least every two to four hours. 2. Urine output. 3. Fluid intake. 4. Record all sigsn and symptoms; number, frequency, duration, a nd degree of severity.

1. Absolute limitation of fluids until the progression of symptoms is stopped (4), making careful observations on pulse pressure, and output of water from bowels and kidneys. (3)

2. Intravenous administration of 50 cc. of 50 per cent glucose every four to six hours as necessary to control progress of symptoms (4) valuable and probably more dangerous, and the former to be used purely for the purpose of, and only to the extent necessary for, the abstracting of water from the tissues into the blood stream, so as to make it

available for early elimination by the bowels, kidneys, etc. (3)

3. Oral administration of saturated solution of magnesium sulphate until watery stools are obtained. (4)

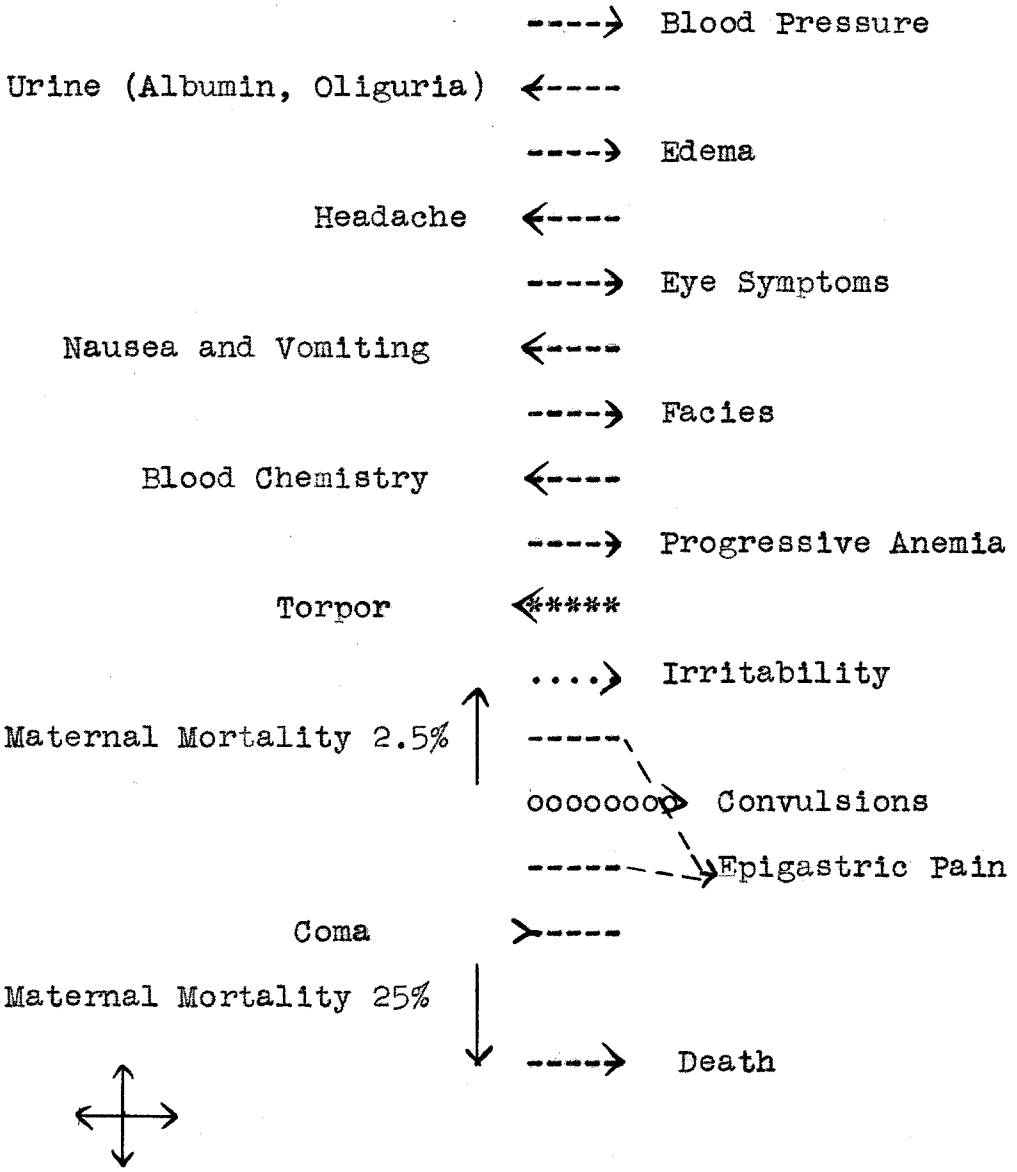
4. If there is no marked improvement in 15 to 30 hours, one or more spinal drainages may be done, at 4 to 6 hour intervals, or when this prodeedure is impractical, venesection is done, using the pressure cuff as a tourniquet in order to check the effect on the pulse pressure. (4) It should be drained until it is impossible to obtain more, also it should be drained at a slow rate of speed to avoid cerebellar herniation which, in this condition, is a very rare accident. (4)

5. A strict balance of fluid and dry solid diet is maintained. When the patient is benefited, and the 24 hour urine output is known, resume the giving of fluids at three hour intervals in daily amount not greater than the previous days output, gradually resuming feeding at these intervals also. (3)

This more intensive method of dehydration permits adjusting treatment to the degree of urgency apparent in the case. Many patients in this group yield promptly and satisfactorily to one or more of the

measures without spinal drainage, if fluid intake is carefully curtailed, but spinal drainage should not be long deferred if headache and other cerebral symptoms have not decidedly abated within a few hours. (4) If there is relief of all symptoms except the hypertension, you may expect the case to go to term, if kept under close observation. (2)

Kellogg offers a slightly different method of controlling preeclamptics, he believes in terminating pregnancy before eclampsia supervenes. By using the chart on the following page, he has found that when the toxemia crosses the convulsion line the mortality rises from 2.5 to 25 %. Torpor and irritability, mental but especially physical, best exemplified by the finger vaguely scratching an itchy nose, index the last point at which one can interfere with a good chance that the patient will never cross the convulsion line. He interferes on the progression of signs and symptoms irrespective of the baby, especially if the signs are preconvulsive or precoma.



Crossed arrow indicates that the signs and symptoms of the patient may remain at, progress or regress from, any stage of the disease shown on the chart.

In his experience there are two kinds of cases, that which arises from neglect and that which develops in spite of intensive treatment. The former can be recovered, the latter is not likely to be recovered.

Every case of eclampsia is an individual problem and the problem of treatment is also individual. (18, 33) The patient moves along the lines of the chart with varying degrees of speed and usually there are noted transitory periods of improvement, in the cases with good care, which may be utilized, as soon as the subsequent down turn begins as a wise moment for interference of whatever type selected. The patient is thus 'peaked' for obstetrical intervention.

Kellogg (20) has certain objections to the treatment as described, and gives these reasons for his objections, they are as follows: Morphine at first produces torpor and may be followed by irritability, thus masking the signs of impending convulsions. Magnesium sulphate in quantity and concentration necessary to produce watery stools, often produces vomiting, also 7-15 watery stools a day is not

conducive to rest. It produces a distended and irritable bowel in case the patient comes to laporotomy, and therefore is more pervious to micro-organisms. Magnesium coma is not uncommon in those with renal insufficiency and these patients are much more sensitive to morphine. Starvation increases the tendency to acidosis but this is controlled by the glucose needle, which is irritating. Stomach and colon tubes are irritating to the point of being responsible for the induction of convulsions.

Kellogg (20) then modifies the above regime by putting the patient in a dark room and keeping everyone out but the nurse and the attending man. Fluids are restricted and a light balanced diet is given, a daily check on the urine and blood pressure is made and bowel movement is aided from above and below. If the patient is not controlled he trusts entirely to interference at the time described, if the patient is near convulsions he believes in palliative treatment until the patient is 'peaked'.

Sometimes forcing the patient to deliver when near the convulsive stage, with the idea of forcing her into the intra- or postpartum group with its lower mortality, prevents eclampsia. Whether it is

the intervention with the subsequent drop in blood pressure that prevents eclampsia is not known. (20)

Treatment of Delivery

1. Indications for the interruption of pregnancy.

As has been mentioned, Kellogg (20) believes in interrupting pregnancy before the onset of eclampsia, he finds that if the pregnancy is interrupted with the onset of torpor and irritability the patient stands a good chance of never crossing the convulsion line.

The single most important indication for the interruption of pregnancy in the preeclamptic is the uncontrollable rise in blood pressure, this measure not only saves the mother's life but also prevents subsequent invalidism from resulting permanent kidney damage, if the pregnancy is allowed to continue. (31) A considerable amount of albumin in the urine should not be allowed to persist for more than two or three weeks as there is the danger of permanent kidney damage. Scanty or suppressed urine is a grave sign of toxemia and is an indication for termination of pregnancy. (27)

With rapid dehydration, emaciation and

jaundice; if the blood pressure is low, the uterus should be emptied without delay. (27)

The eye grounds should be examined and if hemorrhages, separation of the retina or retinitis is present it is an indication for the termination of pregnancy. (27)

2. Methods to be considered.

Labor may be induced or cesarian section practiced. The method to be chosen for the induction of labor will depend on a number of facts, chiefly the proportion between the size of the fetus and the diameter of the birth canal.

Induction of Labor.

This proceedure depends mostly upon the condition of the lower uterine segment, any forcible method of removing this obstruction results in shock to the patient (33), and should not be attempted with anything less than the most favorable cervix. (20) The rapid evacuation of the uterus by the cervical canal is dangerous, especially in late pregnancy, owing to hemorrhage and shock. (27)

If there is no disproportion and the symptoms are not urgent, 60 cc. of castor oil given by mouth or through a stomach tube may suffice to induce labor

within 24 to 48 hours. At this time the dose may be repeated, if the first dose failed, provided the symptoms show that there is no urgency. Quinine sulphate may be given in doses of not more than 20 grains.(34) Rupture of the amniotic sac almost invariably succeeds in initiating labor within 12 to 24 hours. (31, 33) Rupture of the membranes prevents absorption of fluid by the mother and lessens the intra-abdominal pressure. The danger of the cervix being ruptured at the time of delivery is not great. (40) If this possibility is feared it can be preceeded by cervical dilitation, with the finger, and separation of the membranes at the internal os. (27) When the cervix admits two fingers the proceedure has been carried far enough, the use of dilators is unnecessary. (40)

The introduction of a rubber tube or bag is also advised. (27) Bag induction is used only in multipara, at term, with soft and widely dilated cervixes. (33)

Administration of the oxytoxic fraction of the pituitary, posterior lobe, is sometimes effective but is considered a hazardous proceedure. (34)

The toxic patient is more responsive to

medical and surgical induction than the non-toxic patient and usually has a short rapid labor.

Labor should be conducted with all possible freedom from pain or trauma. Obstetric analgesia should be practiced during labor to avert the onset of convulsions by giving, for example, Morphine Sulphate (0.015 Gm.) hypodermically, repeated in four hours if required, and Phenobarbital Sodium (0.10 Gm.) by mouth, repeated in two hours and later every four hours, as required. If, during the second stage, labor becomes very slow or the blood pressure rises, indication for forceps or version is present. (31) Other than this the conduct of labor will not be discussed, in this paper.

Operative proceedures.

The type of surgical management depends mostly upon the condition of the lower uterine segment, (33) With anything less than the most favorable cervix, the uterus is to be emptied by abdominal hysterotomy, which is a wise proceedure only in selected preeclamptics. This proceedure carries a 45% fetal mortality, if the infant is under five pounds, and a maternal mortality of only 5 to 6%. The fetal mortality is much less if the baby is over five pounds, and especially if

pre-operative medication is with held. (20)

The choice of an abdominal or vaginal section depends chiefly upon the period of gestation and the parity of the patient. Abdominal section is the operation of choice in the primigravidae at or near full term or in the multipara with a definitely viable fetus. Vaginal section may be the operation of choice where the fetus is definitely not yet viable. These cases are especially suited for spinal anesthetic. (15)

Cesarian section should be done in rapidly advancing signs of threatened eclampsia; i.e., threatened eclampsia of an alarming nature, and in definite disproportion between the fetus and the birth canal. This treatment seems radical, but it is actually conservative; for many dangers threaten the toxic pregnant woman. (33) Abdominal section has its place for consideration and is reserved for preeclampsia, except in those acute toxemias where there is a definite obstetrical indication necessitating the operation. There are no rules to be followed except those gained by experience. A case of nephritis may require induction or abortion, or preferably abdominal hysterotomy and sterilization. (33)

Anesthetics.

Anesthetics require carefuly consideration in cases of toxemia. Gas-oxygen is safe; chloroform is a hepatic poison; ether may cause pulmonary complications. Acidosis is a common finding in the toxic patient and inhalation anesthesia intensifies this complication. (33)

Spinal Anesthesia is the one most used, and requires due attention to the state of the blood pressure. If low, spinal anesthesia is contraindicated. (27) Reinburger and Russell (33) have long employed local anesthesia for all cesarian sections, and have attempted to substitute local perineal infiltration and nerve blocks for vaginal deliveries. They believe, however, that spinal anesthesia is superior to any other method. In the cases especially suited for surgery, spinal anesthesia is used by a great many men (31,18,27,15,33) with the idea that it in no way increases the toxemia. They show a marked hypertension and the fall in blood pressure usually associated with spinal anesthesia need cause no special concern, this result is one of the objectives of preceeding treatment. Section can be done more rapidly and with greater ease under spinal anesthesia than under either infiltration or

block anesthesia, and in this type of patient operating time is often the deciding factor. (15)

Although spinal anesthetic is considered the anesthetic of choice it has its contraindications. Some of the newer anesthetics, pernocton, sodium amytal, and avertin have been used with considerable success in the treatment of eclampsia and their employment as an anesthetic, combined with a local, may reduce the mortality rate of active intervention to that or the more conservative methods. (9) Luminal and nembutal have been advised by others. (

Sedation

Sedative treatment consists of the promptest possible administration of morphine hypodermically, chloral by rectum, and magnesium sulphate intravenously.

Morphine Sulphate, 0.015 gm. by hypodermic injection, is to be repeated in one hour if required, provided the patient has not been given it before; then not oftener than every four or eight hours. Respirations should not be depressed to less than ten per minute. As soon as it can be made ready, one should also give a Chloral Hydrate enema, giving 2 gm. of chloral for the first dose and a smaller quantity

after two hours, and then at intervals of from four to eight hours as required.

Chloral Enema

RX Chloral hydrate . . . . . 8.00 Gm.
Mucilage of acacia . . . . . .30.00 cc.
Water, to make . . . . . .60.00 cc.

M. Label: Tablespoonful (15cc.) in 150 cc. of water given slowly by rectum. Give 10 cc. dose after two hours, if required. After this not oftener than every four to eight hours. (31)

Fantus (34) says that chloral hydrates has the greatest hypnotic and sleep producing power per price unit and is especially indicated in hypertension. It should be used in 20 to 30 gr. doses.

Bromides, 15 Gr. or Phenobarbital, 1/2- 3/4 Gr., Tid., may be used particularly during periods of restlessness. This also lessens arteriolar spasm. (34)

Magnesium sulphate acts as: 1-a depressant; 2-a dehydrating agent; 3-a diuretic; 4-reduces respiratory rate. Magnesium sulphate is given slowly intravenously in doses of 20 cc. of 10 per cent solution of the crystalline salt every hour until the convulsions are under control, and subsequently at longer intervals as indicated by blood pressure readings taken hourly. It is contraindicated if there is coma or marked acidosis (carbon dioxide combining

power less than 20 volumes per cent.) Calcium chloride solution (5 per cent) should be kept in readiness for slow intravenous injection if alarming respiratory depression should occur; 2.5 cc. may suffice to produce immediate improvement. If facilities for intravenous injection are not available, 10 cc. of 25 per cent magnesium sulphate solution may be given intramuscularly. (31) The intravenous injection is clinically proven to be a safe proceedure. 6 gm. magnesium sulphate is given in 20 cc. doses of 10 per cent solution in 24 hours, this dosage is within the normal limit. However 12 gm. have been given in 10 hours without bad effects on respiration. (29) Tucker (36, 34) has not found it necessary to give more than four doses of magnesium sulphate. Should it fail sodium amytal, 6-12 grains, or nembutal 6-9 grains, can be given intravenously, but these put the patient to sleep and so is not as desirable as magnesium sulphate which awakens them.

Diet in Preeclampsia

In regard to the feeding of patients suffering from considerable loss of albumin due to chronic nephritis, there is some diversity of opinion. If the protein loss is excessive the tissues will be

drained. In the case of a pregnant patient suffering from this condition there is the added drain from her fetus. She will, therefore, suffer from protein starvation unless her intake is supplemented by protein. Physicians not infrequently find that patients suffering from nephritis show signs of rapid improvement when a protein diet is provided. It is desirable to get a patient, suffering from toxemia, onto a mixed diet as soon as possible as much better results have been obtained than when adhering to the rigid rules which practically mean starvation.

To further quote McIlroy (28) on the subject of diet she believes, along with others, that the diet should be, as far as expedient, that to which the patient has been accustomed. It ought to be of a plain mixed variety and should include a supply of green vegetables and fresh fruit. Preserved foods are deficient in vitamines and therefore less nourishing. Cereals contain a considerable quantity of calcium and other minerals, but should be taken with liberal amounts of milk. In the case of well nourished patients, butcher's meat and eggs should be taken sparingly, if at all, in the last three months of pregnancy, in order to relieve the strain of protein excretion:

fish, chicken, and cheese are good substitutes. In addition it is found, as a matter of experience, that there is less rigidity of the fetal head on a reduced protein diet and as a consequence labor is rendered easier. Smaller meals at frequent intervals are advisable in cases of digestive embarrassment; fluids are necessary but should be restricted if there is a tendency to edema of the tissues. A mixed carbohydrate diet with a supply of sugar will prevent the onset of acidoses. (28) However, carbohydrates favor water storage, the cells of the body on carbohydrate metabolism require two-thirds more water than when maintained upon a protein metabolism. (4) If attention is paid to limitation of quantity in the diet of mothers who are overweight or gaining excessive weight in pregnancy it will be found that in addition to the improvement in maternal welfare the fetus derives a marked benefit. The child may be born below the average weight but it will have had an easier passage through the parturient canal and its postnatal loss in weight will be found to be less. (27)

The child does well, the first few years, on a diet approximating the vegetarian order. Probably a diet too high in protein is not well while in utero. (26)

In the study of diabetes it was found that if the patient was allowed to choose his own diet it would approximate carbohydrate 5, protein 1, fat 1.

Howlett (19) believes the milk diet is in many cases effective. He further states that the incipient eclamptic has an abnormal appetitie and although many believe the amount of food should be drastically cut, and especially the protein, he believes that the protein should not be reduced as the kidney is not impaired.

In the prevention of the attacks, a saltless diet is much to be preferred to a milk diet. (7) Under a milk diet eclampsia broke out in more cases, and with much greater vehemence and frequency, than under a saltless diet. Under the latter, the attacks in intercurrent eclampsia never recurred as they did under a milk diet. de Snoo (9) writes that of 1525 women with albuminuria under a saltless diet, only 6 had attacks after the second day and these were few and light, which shows that no more attacks are to be feared after 48 hours. In the cases in which attacks did occur under a saltless diet, investigation showed that mistakes in the diet had been made. The diet must therefore be controlled by quantitative

determinations of the physiologic salt excreted in the urine, which must not exceed 1 to 2 gm. per day. (7) He further argues that milk contains 1.7 gm. per liter and because of its content is contraindicated.

Protein Stabilization Treatment:

Group 1. For those patients whose symptoms do not interfere with the regime. The total caloric intake is adjusted to the 24 hours resting requirement of the mother and the fetus. The protein requirement is calculated on the basal need and determined from the N.P.N. of the urine and the urinary loss of protein. For example the N.P.N. of the urine is 10 Gm., multiplied by the N. factor 6.25, is the amount of protein metabolized or 62.5 Gm. If there is 20 Gm. of albumin lost in the urine this is added, totaling 82.5 Gm. of total protein metabolized and lost. The intake is adjusted to meet the requirements and adjusted by milk, eggs and meat, excluding veal, ham and fresh pork. Also a high carbohydrate, low fat diet is used. The ratio of carbohydrate to fat being 3 1/2 to 1 and is an indirect attempt to reduce blood stream fat. Fluid was not restricted below 2 liters a day and patients were allowed water as

desired, which often is not enough to sweep the nitrogenous wastes from the body. Daily evacuation by milk of magnesia or soap suds enema was found imperative. Morphine was used sparingly for restlessness.

The surface area was calculated on the DuBois chart by height and weight calculations. This figure is used on another table to get the number of calories needed in the resting state. The daily deposit of protein in the fetus at term is .7 gm., or 4 1/2 gm. of animal protein. The calories required by a 3 kilo infant is 6.3 calories per hour. The diet must have adequate calory value for unusualy activity of the fetus.

Group 2. For those patients whose symptoms interferred with the regime just given, as those unconscious or unable to retain or assimilate food by mouth, the following method is given. 10 to 25 per cent glucose is given intravenously at 4 to 6 hour intervals, in quantities approaching the 24 hour chloric requirement. Wasting of tissue protein cannot be prevented by this treatment, but it is minimized. The lower bowel is emptied by colonic irrigation and a retention catheter in the bladder was released hourly. Morphine is given until the respirations

were 15 to 12 per minute. (16)

This treatment is associated with lower levels of blood pressure and pulse pressure, improved urinary elimination, improved red blood counts and hemoglobin content, plasma albumin, and a practical disappearance of marked symptoms of preeclampsia and eclampsia. Eclampsia cases in the hospital show a marked decrease in the average number of convulsions under this treatment. In 4 years 522 patients with late gestation toxemias were treated thus, not one developed convulsions under this treatment. A practical therapeutic test indicates that this treatment has dealt with the fundimental factors in the prevention of eclampsia. (16)

Alkaline Treatment

This treatment is based on the fact that there is a diminution of the total serum calcium in cases of preeclampsia. Calcium is the main custodian of hepatic efficiency during pregnancy. There is also a decrease in plasma bicarbonate throughout gestation.

Ordinary diet is given in all cases.

An alkaline compound tablet is given orally three times a day, or every three hours as necessary. This tablet contains potassium citrate, grains 40;

sodium bicarbonate, grains 20; calcium sodium lactate, grains 7 1/2.

In cases of severe albuminuria for intravenous administration, an ampoule containing 20 cc. of a sterile aqueous solution of sodium bicarbonate, grains 20, and of the diuretic sodium acetate, grains 20,, (Potassium citrate grains 40, as a diuretic may be given orally and it will in no way produce cardiac distress), is mixed with an ampoule containing anhydrous calcium acetate, grains 5 1/2, glacial acetic acid, minium 1, and sterile water sufficient to make 2 cc. The glacial acetic acid develops carbon dioxide on mixing with the bicarbonate solution and insures the solubility of the calcium ions.

For intravenous administration the contents of the alkali ampoule are added to about 140 cc. of sterile water, the 2 cc. of the calcium ampoule are then added, the resulting isotonic solution being introduced by funnel and tube. A slightly hypertonic solution is preferred however. Injections are to be made slowly, sensations of warmth, breathlessness and faintness, which passes off in one to two minutes after the injection, are due to the sudden influx of calcium.

This treatment causes the albumin reading to fall rapidly in all cases and in many cases is clear by the third or fourth day. If the albumin reading rises again another injection is indicated. If it remains at .5 or .25 parts for some days an injection of calcium gluconate alone is often sufficient to cause its disappearance. In cases of orthostatic albuminuria the patients are allowed up and this often causes the albumin to disappear. The blood pressure falls correspondingly, and rises if the albumin rises. On the day before labor it is not unusual for the albumin to reappear in the urine, a rise of 1 to 2 parts Esbach is now regarded as signifying the onset of labor.

Edema, epigastric pain rapidly disappear and do not return, even though the blood pressure rises, and albumin reappears; headache, and occasionally dimness of vision, however, may be complained of on the return of objective signs. This treatment causes increased urinary output, decreased urinary albumin content, decreased blood pressure, edema, and other signs and symptoms. It is also advantageous in that the expense is minimal, making it available to all patients.

Mild cases may be treated by oral administration of the alkaline compound tablets; occasionally a single intravenous dose of calcium alone may be necessary to hasten complete disappearance of signs and symptoms.

More severe cases will respond only to the additional intravenous medication, which should be repeated if improvement is not pronounced or if signs and symptoms recur.

Labor should be induced if treatment fails or when the patient reaches full time, because of exacerbations when labor is delayed.

Only 2% of the cases required induction, in the control series 66% were induced. 11% of births were premature against 63% in the control series. (8)

Another advantage in this method is that the expense is minimal. (8)

Irriadiation Treatment

Ultra-violet light-The use of ultra-violet light in the treatment of preeclampsia is based on the following conclusions:

1. Deamination may be a process of reduction, which is probably the result of either hydrolysis or

oxidation. The latter, or oxiative deamination, is the more likely.

2. There is an absolute defficiency in the blood calcium of the preeclamptic. That calcium is an active antagonist of certain by-products of amino acids and of real hypo-calcemia.

The questions then immediately arise: 1. Is there any means whereby such products can be oxidized on a large scale, in situ? 2. Is there any means by which calcium metabolism can be speeded up, and the calcium mobilized to combat the toxin or toxins?

Ultra-violet light is apparently the answer to both questions. Treatment was given by the use of the mercury vapor lamp and the light from this lamp is one of the most powerful oxidizing agents in existence. That ultra-violet light does oxidize is proven by the fact that within a minute after turning on the light the smell of ozone is apparent. The effect of ultra-violet light has also been repeatedly demonstrated in cases of carbon monoxide poisoning.

The rays between 3,900 and 7,800 Angstrom units are visible and have the power of penetrating the epidermis, they become active in the subcutaneous tissues. The long ultra-violet rays, 3,900 to 2,900 Angstrom units, penetrate as far as the deep layers

of the dermis , where is a rich blood supply bringing systemic blood well under their influence. The short ultra-violet rays are not considered here as they are cut out by the filter. The filter removes all rays below 3,300 Angstrom units.

In regard to calcium it is known that ergosterol is manufactured and stored in the dermis, and changed to vitamin D when irradiated with ultra-violet light; also that utilization of calcium depends in great part on the presence of free, available vitamin D. Irradiation should theoretically raise the low blood calcium and increase the supply available for combating the toxemia.

If the ultimate cause of toxemia is an oxidizable toxin, it would be expected that with the destruction of this toxin the blood pressure would fall, and after a few treatments the patient should look and feel better, which is what happens. In all cases there was an instantaneous fall in blood pressure, as much as 30 mm. systolic and 16 mm. diastolic. By the next day the blood pressure had risen but not to the height that it had been the day before. With continued treatments the patients gradually improved and in two cases the blood pressure fell with an obvious lysis.

In all cases, after two or three treatments, the patients stated they felt much improved, and all symptoms and signs were diminished except the albumin which did not always diminish.

The effect is not due to capillary dilatation because the doses were light and at a great distance, comparatively, from the skin; not enough heat could be generated to cause dilitation. If an erythema dose had been given the erythema would not appear for at least six hours, whereas the fall in blood pressure was instantaneous.

The treatment was given as follows...The patient is put on a strict diet, excluding as far as possible all protein, and absolutely all animal protein. During the treatment the diet may be worked up gradually but is modified at the slightest increase in blood pressure.

The patient strips to the waist and lies on her back, on a couch, for two to three minutes to allow the blood pressure to reach a steady level. The blood pressure reading is then taken, by the same person every day to avoid errors. The patient lies first on one side and then on the other, under the light. After the treatment she turns on her back and lies

quietly for a minute or two and the blood pressure is again taken. The dose of ultra-violet light cannot be given as every machine has its own erythema point, as has every patient.

At first treatment is given every day, as the patient improves it is given every other day, and in the end twice a week until labor set in.

It should be remembered that if this treatment is to be of any use an early diagnosis is absolutely essential. Dickson (10) makes a diagnosis on an increased blood pressure alone, anthing above a 140 mm. of mercury systolic, without waiting for any other signs or symptoms. Treatment is best given for from four to six weeks, at least. It is not a certain cure but a big help in the treatment of the preeclamptic.

Along with the idea of improving circulation, the patient should be instructed to always lie on her side while in bed, as this pressure is less than when lying on her back.

Quartz light-A number of German investigators are using the quartz light on patients suffering from the late toxemias and believe that their good results may be due to the action of the rays on the vessel spasms in the kidney, brain, and skin. (27)

Symptomatic Treatment

Conditions similar to the toxemias of pregnancy are benefited by calcium gluconate. Dextrose alone relieves the condition but it recurrs, calcium gives permanent relief. It is said that calcium neutralizes guanidine regardless of the blood calcium level (2), and it has been explained how a hypocalcemic condition can be present and still have a normal blood calcium. Calcium and dextrose is a logical treatment, calcium neutralizes guanidine which has a toxic effect on the liver, the glucose prevents acidosis and replenishes the glycogen store in the liver. (2)

Also in regard to the calcium level is the parathormone treatment, which is an endeavor to restore the blood level and the balance between the diffusable and non-diffusable calcium. It is particularly useful in prophylaxis. With the first appearance of symptoms, as tingling and cramps, calcium is particularly good treatment. It is used in conjunction with diet and rest. If symptoms are urgent calcium gluconate or dicalcium phosphate are given, the first is given in doses of 60 gr., well diluted, Tid., with viosterol. In severe preeclampsia parathormone is given in 20 unit doses by hypodermic, it raises the blood calcium level

and promotes diuresis. The maximum effect occurs in about six hours and it can be repeated in 8 to 12 hours, and then every 24 hours until symptoms are disappeared. Much getter results have been obtained when calcium and viosterol were given simultaneously. Improvement is claimed to result in 24-48 hours. (22)

If convulsions arise morphine is used for their control. Twenty units of parathormone are given by hypodermic and 10 cc. of 10% calcium gluconate is given intravenously, followed by 50 to 70 grams of dextrose in 10 to 25% solution. (22)

As an emergency treatment lumbar puncture is frequently employed. This proceedure must be carried out very slowly, literally drop by drop, for fear of herniation of the medulla through the great occipital foramen, which would result in sudden death. (31) The spinal fluid should be drained as completely as possible (45 to 100 cc.) preferably with the head raised to an angle of 30°. When spinal fluid drainage is impracticable venesection may be substituted. (3)

There is much discussion concerning the value of phlebotomy. However it is pretty well agreed that it should be reserved and used only as an emergency measure. Blood letting robs the patient of millions

of red blood cells, so necessary as the carriers of oxygen to the tissues. The cerebral tissues require large amounts of oxygen and in the presence of anemia and anoxemia not only is the function of the brain disturbed and reduced, but permeability of the capillaries is increased, causing casts, and hence the red blood cells preserved if possible, as well as sufficient and optimal circulation through the capillaries so that tissue function may be maintained.

As blood volume remains one of the most fixed values in the body, the withdrawal of a pint of blood is followed within a few hours by a re-establishment of the volume in terms of available fluid. Thus, the patient has been but temporarily benefited from the standpoint of fluid volume and reduced arterial pressure only to re-establish subsequently the same volume at the expense of a loss of important oxygen carriers as well as protective white blood cells, removed at the time of blood letting. If blood letting is repeated, a secondary anemia ensues with little actual loss in blood volume,this may be combatted by substituting plasmophoresis.

Phlebotomy has, therefore, been practiced only in emergencies and blood volume has been temporarily

reduced by active purgation associated with intravenous glucose to assist blood volume in obtaining its replenishment from the interstitial storage reservoirs (cerebro-spinal fluid, brain, liver, muscles, etc.) Repetition of purgation again depletes blood volume, requiring it to turn to the tissue reservoirs for its source of readjustment rather than to fluids ingested and thus easily obtained. Hence, the rationale of fluid limitation and even its complete curtailment, during the active period of dehydration, is established in the well advanced type of cases. (4)

According to McPherson (18) venesection is done if the systolic blood pressure is over 175. About 500 cc. of blood may be withdrawn. It is best not to permit too much bleeding for there may be a considerable loss of blood at the time of delivery and shock may ensue. (18) Some men allow the patient to bleed rapidly until the pressure has dropped 20 to 50 mm. of Hg. Okintschitz (30) believes that venesection is of no definite value.

Pulmonary edema is a rather common and formidable complication of eclampsia. It is combated by the general dehydrating measures plus the administration

of digitalis, oxygen intransally or intra-peritoneally, and strophanthin (0.5 mg. intravenously) (33, 31, 30, 36). In this complication atropine sulphate is said to be the most efficacious drug, the dosage must be massive and repeated as the occasion demands. (33)

Acidosis is chiefly combatted by intravenous glucose, with or without insulin (30). The administration of sodium bicarbonate will neutralize the ever-present acidosis of eclampsia. (33) Acidosis and persistent vomiting can also be relieved by gastric lavage. (33) Mention may be made of the Tweedy method in which elimination is stressed He gives no food, employs gastric and bowel lavage with large amounts of sodium bicarbonate; has the patient lie on her side with foot of the bed elevated, and uses only small doses of morphia. (18)

Postpartum Care.

As in any severe case of preeclamptic toxemia convulsions may occur from 24 to 48 hours after delivery, and according to Hoffstrom, (31) as late as a week, Sedatives and other measures as described should be continued for several days. It is well to give as routine, soon after labor, a hypodermic

injection of morphine sulphate 0.015 gm. (31) Hoffstrom (18) has re-emphasized the fact that treatment at this stage should be more radical than conservative, half way measures such as employing morphia timidly in 1/8 gr. doses, and removing little or no blood, invite failure.

Blood pressure readings and the urinary output should be recorded daily. The blood should be examined for nonprotein nitrogen retention. The low protein and salt poor diet should be continued until edema has disappeared. Then fluid may be given freely, provided the kidney can respond to the appeal. If the blood pressure and urine do not return to normal within two weeks after delivery, the therapy of nephritis is indicated. (31)

The patient requires constant supervision, especially if signs of puerperal psychoses develop, for in such cases an attempt may be made to kill herself or baby. All sources of worry and irritation should be removed. Nursing should not be permitted until the patient has regained consciousness for a few days and when her strength justifies it. (18)

After the attack, the patient is closely guarded for at least three years, especial attention being

paid to renal function, and no pregnancy is advised until that time. The woman with eclampsia'does not vaccinate herself' or develop an immunity. Recurrent eclampsia takes place in about 2 to 5 per cent of the cases. Nephritic toxemia is very apt to appear in later pregnancies. (18)

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