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Preeclampsia

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PREECLAMPSIA

by

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To my wife - without whose help
this task would have been doubly
hard.

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INTRODUCTION

Of all the problems confronted in an obstetrical practice, none, in my mind, are more interesting than those involved in the prophylaxis, diagnosis, and treatment of the so-called "toxemias of pregnancy". In spite of greatly improved obstetrical education and prenatal care there are four thousand maternal deaths every year in this country as a result of these "toxemias".

Acknowledging the tremendous field to be covered in order to gain a practical, clinical knowledge of this disorder, the author has undertaken to discuss but one small part of this pathological state, i.e., the present acknowledged term preeclampsia. The writer shall attempt to confine this discussion only to severe preeclampsia, remembering that the dividing line between mild and severe preeclampsia and eclampsia is very fine. Consequently, any deviation from the strict confines of severe preeclampsia into mild preeclampsia or eclampsia should be permissible in order to gain a complete working knowledge of the disease.

Definitions:

"Hippocrates mentions convulsions in pregnant women and knew that they most often occurred in women

who had headache and a tendency to sleep (coma). The word eclampsia means to flash, to shine out, and was introduced by Boissier de Sauvages in 1760, and Gehler in 1776. More properly it should be Eclactisma (Kossman)". (DeLee 1934)

Such was the first recognition of toxemia. Later, when finer definitions of the disorder were worked out a distinction was made between toxemia without fits and the toxemias with fits and the toxemias in which definite previous pathological states existed. Limiting ourselves as much as possible to the state of toxemia without fits, some term properly describing this condition must be used. Bar suggested the word "eclampsism" for this condition of preparedness for convulsions and limited the term to true premary toxemias. (DeLee 1934)

Another authority has advocated the discontinuance of the term "preeclamptic toxemia" and has suggested instead the word "preeclampsia", and furthermore, that its use be limited to the relatively small group of cases in which the patient presents the signs, symptoms and laboratory findings of eclampsia, but has not yet developed convulsions. In other words, preeclampsia is essentially eclampsia before the outbreak

of convulsions and coma. When used in this sense, preeclampsia is relatively rare, not exceeding 5% of all the toxemias of the latter half of gestation, and occurring about fourteen times in every one thousand deliveries. (Stander 1929)

This same opinion has been voiced by McGoogan (1932) and Solomon (1933). The same conclusion is given in the complete definition by Dorland (1936) in which eclampsia is defined as "a condition characterized by convulsions in a pregnant woman, which in some way are dependent on the pregnancy and which would not have occurred had she not been pregnant", and preeclampsia as "threatened eclampsia".

Classification:

In order to facilitate a working knowledge of all toxemias of pregnancy, some classification must be acquired and understood. Hoping to avoid confusion, the following eight classifications are given by way of record only. Conclusions as to the correct classification will be left to the reader.

McGoogan (1932) presented his classification of the toxemias of pregnancy as being:

I. Pernicious vomiting.

II. Hepatic types.

a. Low reserve kidney (mild preeclampsia)
b. Preeclampsia (severe preeclampsia)
c. Eclampsia
d. Acute yellow atrophy

III. Nephritic types.

a. With chronic nephritis (with or without convulsions)
b. With chronic nephrosis (with or without convulsions)

In 1934 DeLee presented the following four groups with the acknowledged etiology:

I. The true toxemia caused by circulating poison.

II. Acute nephritis caused by bacteria or toxins from focal infections or toxins of pregnancy (eclampsism)

III. Chronic nephritis caused by pregnancy in a patient with degenerated kidneys.

IV. Malignant hypertension.

Some prefer the following:

I. Mild preeclampsia (low reserve kidney, mild late toxemia, mild recurring toxemia)

II. Preeclampsia

III. Eclampsia

IV. Nephritic toxemia (Mussey 1934)

Allen (1935) acknowledged the Arnold-Fay classification:

I. The inherently normal

II. The potentially abnormal.

III. The moderately preeclamptic.

IV. The dangerously preeclamptic.

V. The eclamptic or convulsive group.

Continuing the attempt to derive some workable classification Tillman (1935) produced the following:

I. Hypertension

a. Mild
b. Moderate
c. Severe
d. With late albuminuria

II. Nephritis

a. Mild
b. Moderate
c. Severe

III. Preeclampsia

IV. Eclampsia.

On presenting the last classification, objections were raised by Stander, who preferred a classification based on etiology, symptomotology and pathology. Consequently, such was the basis for his own, presented in 1937:

I. Vomiting of pregnancy. (50% of all cases)

a. Reflex vomiting
b. Neurotic vomiting
c. Toxemic vomiting

II. Low reserve kidney (kidney of pregnancy, albuminuria of pregnancy, 35% of all cases)

III. Nephritis complicating pregnancy.

a. Glomerulonephritis (hemorrhagic Bright's Disease)
b. Nephrosclerosis (hypertensive)
c. Nephrosis (degenerative Bright's Disease)

IV. Preeclampsia. (5% of all cases)

V. Eclampsia

VI. Acute yellow atrophy of the liver.

After nineteen years study in 232 cases, Reinberger (1936) produced a classification based on variances in signs and symptoms:

I. Incipient toxemia comparable to low kidney reserve: Blood pressure up to 130/60, + albuminuria, eyes negative, blood chemistry negative, slight edema and gain in weight.

II. Moderate toxemia comparable to preeclampsia: Blood pressure above 130/60, nervousness more pronounced, albuminuria, blood chemistry negative, eye grounds - , blood vessel spasticity, edema +++.

III. Severe toxemia comparable to eclampsia: Blood pressure 150/80 to 200/100, nervousness to convulsions, diminished urine, albuminuria +++, blood chemistry -, nitrogen retention, eye grounds -, blood vessel spasticity and edema, edema and gain in weight +++.

IV. Chronic nephritis with pregnancy superimposed comparable to nephritic toxemia: History, hypertension, nitrogen retention, myocardial involvement, eye grounds, vascular tortuosity, hemorrhaging and degenerative retinitis, death rate in five years follow-up greater than in all other

acute toxemias.

V. Benign hypertension comparable to medical benign hypertension; blood pressure above 160 returning to normal after delivery.

To date one of the most complete and comprehensive classifications has been offered by Kellog (1937). This he divides into group "A", which includes cases in which some evidences of disease independent of pregnancy exists, and group "B", including cases in which there is no evidence of disease independent of pregnancy existing. The complete classification is given in a simplified chart and the remainder of this thesis will be concerned with group "B" and primarily preeclampsia number two.

"TOXEMIAS OF PREGNANCY"
(Kellog 1937)

GROUP "A"
Evidence of Disease Independent of Pregnancy - 61 Cases

I. Nephropathies associated c arterial vascular disease

Essential Hypertension

Benign Form
45 cases
A. Cerebral change
B. Cardiac failure
C. Renal failure
Arteriosclerotic kidney with uremia

Malignant Form
7 cases
A. Endarteritis
Nebrosis
Uremia

II. Inflammatory Nephropathies i.e.Nephritis

Glomerulonephritis

Diffuse

Acute Chronic
4 cases

Focal

Pyelonephritis

Acute

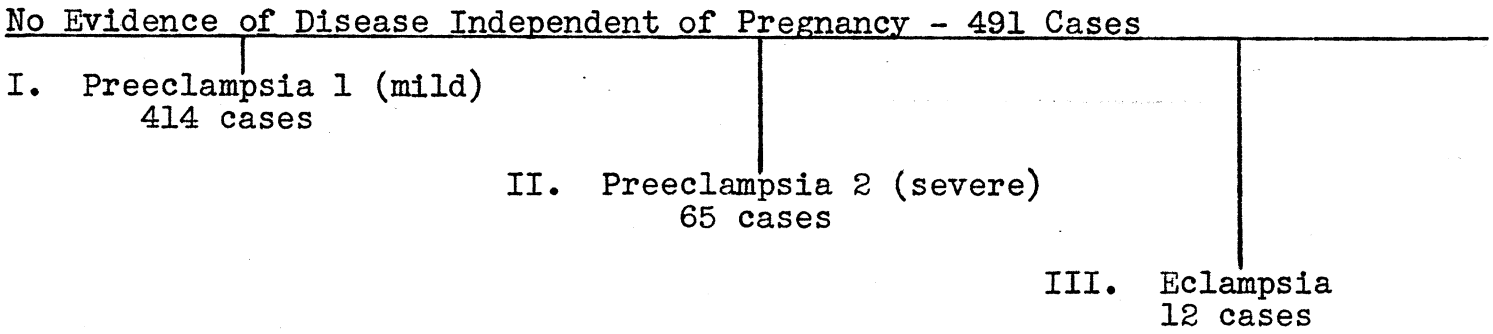
Chronic
5 cases

III. Degenerative Nephropathies i.e.Nephrosis

A. Chemical poisoning
B. Bacterial toxins

Special Types
A. Amyloid
B. Lipoid

GROUP "B"


No Evidence of Disease Independent of Pregnancy - 491 Cases
I. Preeclampsia 1 (mild)
414 cases
II. Preeclampsia 2 (severe)
65 cases
III. Eclampsia
12 cases

In the following discussion the writer hopes to present an historical review of the most important theories and practices concerning the etiology, pathology, symptomotology, diagnosis, course, complications, prognosis and treatment of preeclampsia. Consequently, conclusions as to correctness, and clinical practicability of these theories and practices will not be included, for such is not the purpose of the author.

ETIOLOGY

Incidence:

In an analysis of 801 cases of toxemias of pregnancy Stander (1929) found 74 cases which fell into the group called preeclampsia. These 74 cases constituted 9.2% of the total number of the toxemias. In simpler figures preeclampsia existed in one case out of every 116 cases in total admissions. Consequently, it can be seen that preeclampsia, although it appears fairly infrequently, occurs often enough to forewarn the common practitioner to be prepared to meet this emergency.

Predisposing Factors:

Predisposing factors influencing the occurrence of not only preeclampsia but all the toxemias of pregnancy, are legion in number and are more or less under dispute by the various authorities. According to the report of the Commission of the Obstetrical Society of Philadelphia on the incidence and treatment of the toxemias of late pregnancy in Philadelphia, preeclampsia occurs more in the spring and fall. (Schumann 1931) The same opinion is expressed by Gambrell (1935) for he maintains that the disease occurs more in colder

climates and colder seasons. However, Fantus (1935) maintains that "climatological factors bear no relation to the occurrence".

The age of the pregnant woman has often been discussed as being a factor toward her predisposition to preeclampsia. The Commission of the Obstetrical Society of Philadelphia (Schumann 1931) concludes that age incidence has no bearing on the condition. Most authorities believe that such is not the state and have concluded that the younger woman is more likely to be afflicted with preeclampsia. In his report of 30 cases in the Nebraska University Hospital from 1926 to 1930 inclusive, McGoogan (1932) found 14 of these cases were women under 25 years of age. Likewise, Gambrell (1935) places the greatest incidence between 20 and 30 years.

As to nativity, the Society of Philadelphia reports that no conclusive evidence exists as to its effect. Likewise, McGoogan (1932) says that it is not restricted to race or color. Of interest is the statement by Gambrell (1935) that preeclampsia occurs ten times more frequently in blonds than in brunetts.

The parity of the patient is often connected with her likelihood to develop preeclampsia. Of the 30 cases reported, McGoogan (1932) found 8 cases in primi-

para and 22 in multipara. The Society of Philadelphia considering there are more multipara than primipara, believes this toxemia is more common in primipara. The same conclusion is reached by Gambrell (1935) when he says that it occurs "four times more in primipara than in multipara where previous nephritis is not a factor".

As is the case in studying the etiology of any disease, previous history is always deemed exceedingly important. In an accurate check of 30 cases, McGoogan (1932) records the following: 9 or 40.9% had had previous toxemia, either low reserve kidney, pre-eclampsia or eclampsia; 4 had had scarlet fever; 2 had had diphtheria; 3 had had acute rheumatic fever; 2 had had history of previous nephritis; all of which may have had renal involvement present. All authorities are in agreement with the fact that previous hepatic and renal disease and previous toxemia predisposes the pregnant woman to future occurrences of one of the toxemic states. (Schumann 1931 - Gambrell 1935 - Fantus 1935 - Stander 1929)

Reviewing 111 cases, the Society of Philadelphia (Schumann 1931) finds that adequate prenatal care decreases the incidence of toxemia and the mortality both fetal and maternal.

More or less a waste basket group includes illegitimacy, ectopic pregnancy, multiple pregnancy, hydramniotic states, obesity, malpositions and malpresentations, all influencing the presence of preeclampsia. (Lawrence 1925 - Johnston 1929 - Gambrell 1935 - Schumann 1931 - Allen 1933 - Kellog 1937 - Mathews 1938) Of special interest is Kellog's (1937) statement, "From a practical point of view it is my opinion, based on experience, that obesity is the most important secondary etiological factor in the production of eclampsia. Evidently obesity and faulty elimination, another important factor, can be readily prevented. Exposure to cold, infections, worry, loss of sleep, and overwork and tiredness have repeatedly been the immediate precursors of toxemias". Mathews (1938) has considered the obesity of the patient in influencing the presence of toxemia in a review of 190 pregnant women weighing 200 pounds or more. Of the 190 patients, 44.5% had some type of toxemia. Of this 44.5%, 61% were primipara and 38.3% were multipara. The group of toxemic patients in the 190 was classified as follows: Low reserve kidney 45.3%; preeclampsia 11.3%; eclampsia 5.6%; unclassified hypertension 10%.

McGoogan (1932) has very adequately summarized

the incidence of the first appearance of evidence of the disease when he concludes that 90% of cases appear in the last two months of gestation. The first symptoms appeared prior to the 8th month of gestation in 43-1/3%; during the 8th month in 43-1/3%; and during the 9th month in 13-1/3% of cases.

Exciting Factors:

It was the original intention of the author to omit the general and specific exciting factors in the etiology of preeclampsia. However, prolonged investigation brought forth so many and varied ideas that for purely historical reasons a more or less chronological recording of the various theories will be introduced here to the reader. Too much concentration on the etiology will lead to confusion, so for this reason only the outstanding theories - and these just in brief form - will be given. As so adequately put by Zweifel (1935), the toxemias of pregnancy are "Diseases of Theories".

Generally speaking, foci of infection and subsequent organic defects have been listed as exciting factors in the etiology. "Incidence of disease previous to pregnancy is much higher in toxemic patients than in non-toxemic pregnant patients and it increases

in amount to the severity of the disease." (Lawrance 1925)

I. General infections

a. Influenza
b. Pneumonia
c. Acute inflammatory rheumatism
d. Scarlet fever

II. Chronic organic defects

a. G. I. Functional defects
b. Renal defects
c. Cardiac defects
d. Misc. like anemia, chronic tonsilitis and endometritis

(Lawrance 1925) The same is maintained by Hardin (1935) and Johnston (1929) with the addition of the production of tyramine and its ability to cause convulsions in dogs.

Hardin (1935) maintains that diet inadequacies, improprieties, inabilities in the ingestion, digestion and assimilation of foods may be a factor in the excitation.

One of the outstanding and most often advanced general exciting factors is that of pre-existing cardiovascular renal disease. This theory is most firmly upheld by Corwin (1927), Herrick (1927), Tillman (1934), Peters (1936), and Zimmerman (1937). Porter (1934) states that "an individual who has chronic cardiovascular changes, chronic renal changes, and whose liver has

lost detoxifying powers and is already under considerable load will be particularly susceptible to eclampsia". Peters (1936) reviewed 320 patients and found that 41 of them, or 13%, suffered at one time from pyelitis or pyelonephritis. Zimmerman (1937) found on postmortem examination of 23 patients that 10 had pyelitis or pyelonephritis. On the other hand, Howlett (1935) before the Tennessee Medical Association brings forth the view that "There is no evidence that nephritis predisposes to eclampsia".

So far we have discussed theories advanced to explain the general exciting factors in the etiology of preeclampsia. Greater interest and still greater controversy exists in the theories advanced for the specific exciting factors in the etiology. One of the most interesting theories, because of its historical value, and, to say the least, as correct as any advanced in these modern times, is that of Alexander Hamilton. As early as 1775 he advanced an opinion as to the cause of the convulsions of pregnancy. The growth of the uterus in the abdomin prohibits the flow of blood to the remainder of the abdominal organs and thus an over-engorgement of the brain resulted, and this edema caused the eclamptic state.

(Stander 1929) In 1899 Chas. Jewett summarized in a test, "The Practice of Obstetrics by American Authors", and concluded that toxemias of pregnancy were due either to: (1) uremia, (2) ammonaemia, (3) hydraemia, or (4) toxaemia. He very fittingly closed his discussion on this subject by saying, "The last word has by no means been spoken on this question".

As is usually the case in situations similar to this, the endocrine system was first pointed out as the guilty agent in the production of preeclampsia. Polak (1926) concluded that "The woman who develops a preeclamptic toxemia or an eclampsia is the woman who starts on her pregnancy with defective emunctories or an unbalanced endocrine system". Likewise, Hofbaurer (1933) alleged that there was a definite endocrine basis in the etiology of toxemia. Opponents of this theory are as strongly convinced that there is no pituitary origin of preeclampsia and that technicians are unable to find presser and antidiuretic substances in patients with toxemias of pregnancy. (Huriwitz 1933 - Bullock 1933 - Byron 1934 - Wilson 1934)

Other workers have attacked the endocrines singly in attempting to uncover some specific exciting factor. Reinhoff (1929) noted that guanidine com-

pounds were capable of producing a condition in dogs similar to preeclampsia and eclampsia. (Major 1928) Consequently, he maintained that since parathormone governs the mobilization of the available calcium of the body, and that after a parathyroidectomy blood calcium levels fall and a marked increase in the guanidine compounds in the blood and urine of animals occurred, that lack of parathormone was the etiological factor behind preeclampsia and eclampsia.

G. Van S. Smith and O. W. Smith (1933) have turned their attention toward the presence of an anterior pituitary-like hormone and marked variations in oestrin in the toxemias of late pregnancy. After quite extensive laboratory work they have concluded, "The eclamptic state alone gives abnormally high prolan and abnormally low oestrin curves as compared with those in the normal pregnant woman, the pregnant hypertensive patients and patients with chronic nephritis. The high prolan occurs at least 6 weeks before the clinical diagnosis of preeclampsia can be made".

The studies of the placenta have played their roll in this confusing work and some authorities believe that perhaps placental infarcts may play an important roll. These infarcts are said to be caused by

vascular changes due to an hypercholesteremia. (Bartholemew 1932 - Kracke 1932 - Tenney 1935)

Irving (1936) brought forth the idea that a general arteriolar spasm was a definite cause and Eastman (1934) from studies of retinal arterioles, vessels of nail fold, muscle biopsies, and autopsy findings on kidney, liver, brain, and heart muscle, concludes that the etiological factor is one of arteriolar spasm, the cause of which is unknown and states that this conception is accepted by Volhard, Hynemann, Hinselmann and Fahr of Germany, and Irving, Mussey and Herrick of this country.

Another incidence of interest arises in 1932 when Paramore advanced the theory long ago voiced by Alexander Hamilton, placing the etiology in the rise in abdominal pressure with degenerative liver lesions resulting. However, opponents of this theory also exist, and their disbelief is borne out by an experiment on 11 dogs with the conclusion that, "The theory that the liver lesions of eclampsia are due to increased abdominal pressure, although an attractive hypothesis, must be considered as yet unproven". (Maddock 1935)

After further investigation into the possibilities of some mechanical factor having a roll in

the direct cause of toxemia, Hayes (1936) advanced the theory that urinary back pressure was exceedingly important as a cause of toxemia of pregnancy.

With increased interest of the modern student in blood chemistry changes and increasing improvement in the technique of their studies, it was advanced that perhaps the blood sugar levels were important in causing preeclampsia and eclampsia. Consequently, a thorough study of the blood sugar levels in eclamptic patients was done by Mays and McCord (1935) and the following three conclusions recorded:

(1) Neither hypo nor hyperglycemia is characteristic of eclampsia. The blood sugar concentration probably depends on the patient's nutritional state and the degree of emotional stability and muscular activity immediately preceeding the taking of the specimen.

(2) The absolute blood sugar concentration has no effect whatsoever on the incidence of convulsions.

(3) Convulsions occur during a rapid rise in blood sugar concentration as well as during a rapid decline.

Because of the different degrees of edema pre-

sent in preeclampsia and eclampsia some investigators have felt that perhaps water-imbalance within the organism was at fault. J. O. Arnold began to turn his attention toward this water-imbalance and discarded the old idea that some toxin or poison existed. He however was hardly the originator of this line of thought, for Hugh L. Hodge, called the greatest obstetrician of the 19th century, and professor of Obstetrics of Pennsylvania from 1835 to 1863, voiced the opinion that, "Modern theories consider puerperal convulsions to be the result of a toxemia, or blood poisoning, but the evidence of any poison or malcondition of the blood is exceedingly meagre. Toxemia appears to have been inferred rather than positively proved". Thus Arnold (1933) adequately summarized his belief as follows: "While the immediate or approximate cause of eclampsia has thus been definitely assigned to edema of the brain - to water-imbalance - rather than to any long sought for specific toxin in the blood, we can declare with equal frankness that the remote factor (or factors) involved in the production of this trouble making fluid-imbalance, is not yet known. The hypertensive state of the nervous system produced by pregnancy and aggravated by the pain and excitement incident to

labor is often undoubtedly an important predisposing factor, but we still await further psychochemical revelation that will take us all the way back to the relative genesis of the difference between normal and abnormal water-elimination, water-retention and water-disturbance in the body of the pregnant woman; and of the factors that control these processes". Further agreement along this line of reasoning is found in the beliefs of McGee (1935) for he says, "Of the many theories regarding the etiology of eclampsia, probably the most popular today is that propounded by Zangmeister: That there is a disturbance in the water balance of the body with retention of sodium chloride and water".

By now the reader is well aware of the fact that the etiology of preeclampsia rests purely in the hands of the theorists and this fact is going to influence greatly our treatment of the disease and turn our attention merely to symptomatic relief. Our conclusions will be identical with those of Lazard (1933) who after analyzing 575 cases of eclampsia and preeclampsia, maintains that, "In view of the varied etiological factors which may produce the eclamptic syndrome, it is in all probability impossible ever to obtain a specific cure for eclampsia". The writer has felt,

however, that in spite of the confusion, a brief resume of the various theories should be included in this entire discussion, purely for historical reasons.

PATHOLOGY

A consideration of the pathology of the preeclamptic state is actually a study of the pathology of eclampsia, since few preeclamptics have reached the autopsy table. If a mortality occurs in a pregnant woman who has been diagnosed as a preeclamptic, it usually occurs because she has become an eclamptic through failure or lack of treatment. Likewise, it is impossible to discuss the essential pathology of this condition, for as has been pointed out, the etiology is undetermined and consequently, the investigator cannot determine which of his findings is the essential pathology. Therefore, this discussion will be a summary of the pathology of eclampsia found during diagnosis and by postmortem.

On inspection the generalized edema of the patient is evident, especially noticeable in the feet, ankles, lower limbs, hands and face. As a result of this generalized edema, the patient has a pasty white appearance and on inspection of the nail folds and retina a state of angiospasm will be seen to exist. (DeLee 1934)

Grossly, the kidney appears enlarged and edematous, with the capsule tightly stretched but usually

strippable. It has the gross appearance of the kidney of pregnancy, nephrosis, nephropathia gravidarum, or acute glomerulonephritis. (DeLee 1934) Microscopically can be seen the edema of the glomerular loups, albuminous degeneration of the convoluted tubules, degenerative changes in the arterioles, thrombosis of the capillaries in the glomeruli and hemoglobin cells. (McGee 1925) Also, may be seen a narrowing of the lumina of the glomerular capillaries due to a massive thickening of the capillary basement membrane and to an increase in endothelial cells. (LaVake 1932) Lately, the glomerular epithelium and endothelium are the seat of necrosis and fatty degeneration, while capillary tufts occasionally contain fibrin thrombi, and the convoluted tubules show evidence of fatty and hyalin degeneration. (Kellog 1937)

The liver usually presents the gross appearance of cloudy swelling with a tightly stretched capsule and subcapsular and periportal or portal petechial hemorrhages. (Kellog 1927) The microscopic picture is consistent with every case and considered pathognomonic. This picture includes focal hemorrhagic necrosis, thrombi, lobular degeneration peripherally, acute yellow atrophy, fatty degeneration with clody swelling and small

hemorrhages. (LaVake 1932 - DeLee 1934 - McGee 1935) Kellog (1937) reported some early degenerative lesions in the liver which consisted of fragmented liver columns periportally arranged with the cells containing "birdseye bodies".

The brain presents the typical appearance of edematous congestion with flattening of convolusions, small or large hemorrhages or cerebral softening from thrombosis. (DeLee 1934 - McGee 1935)

The heart is often found with the ventricles contracted and containing blood which does not clot readily. The muscle has many areas of fatty degeneration with tiny hemorrhages, necrosis, thrombi and subpericardial hemorrhages. (DeLee 1934 - McGee 1935)

On inspection the lungs are usually pale in color and found to be greatly congested and increased in weight. Microscopically the picture consists of congestion, pulmonary edema, pleural hemorrhages and many small thrombi. These thrombi are composed of fat, liver cells, decidual cells and syncytium. (DeLee 1934 - McGee 1935)

As has been mentioned, the capillary spasms in the arterioles exist in the circulatory system while several blood changes are demonstrable in the laboratory.

These consist of increased concentration, increased uric acid content, a low pH and lowered carbon dioxide combining power. (McGee 1925)

A resume of all the autopsy findings has been given but the reader must remember that many times all of these findings do not appear in the same patient, and that these findings are those present in eclampsia. We can only surmise, since the concensus of opinion is that the etiology of preeclampsia and eclampsia are the same, that the pathological findings would be identical with the exception that perhaps they may be less severe or less extensive in the preeclamptic.

SIGNS AND SYMPTOMS

In the consideration of preeclampsia agreement is more nearly reached in the viewpoint of the various authorities when an enumeration and discussion of the signs and symptoms is reviewed. Here again some deviation from our original intent into the realm of mild preeclampsia and eclampsia must occur in order to have an understanding of the course of the disease. Generally speaking, the signs and symptoms can be listed under four headings, i.e.: Circulatory, digestive, urinary, and nervous.

Circulatory Findings:

Circulatory findings are often the first to appear and include such varying states as edema with its changes in the various organs and the weight gain associated with it; blood pressure changes; and finally, through laboratory studies, changes in the blood itself. Historically, edema was one of the first signs noted. Chas. D. Meigs (1867) especially stressed the swelling of the feet and legs and stated, "Let the student never fail, when consulted about a pregnant woman's health, to examine first her feet to learn whether they be oedematous or no, and if they be swollen

let him dread eclampsia if she be primipara and particularly if she have a bounding pulse and the slightest cephalalgia". Kellog (1937) and Stander (1937) stress the appearance of edema and its predelection toward appearing first in the face and then the extremities, while McGee (1935) stresses the appearance of edema of the hands and face. It is especially diagnostic when this edema becomes general and does not disappear with rest. (Harden 1935) McGoogan (1932) found edema present in 24 out of 30 preeclamptic patients.

Associated with edema is the rapid gain in weight. McGee (1935) states that this is one of the most important signs. Reinberger (1936) advocates an accurate recording of weight and maintains that a gain of over 8 pounds per month, even though no other signs are present, is indicative of impending toxemia, while a gain of over 25 pounds in the first 7 months demands active treatment for most toxemias develop in this period. A mild preeclamptic gains a trifle more than 1 pound a week in the last trimester, while a moderate preeclamptic has an excess weight gain and a severe preeclamptic undergoes a marked increase in weight. (McGee 1935) Weight gain is stressed by most authorities. (Harden 1935 - Kellog 1937 - Stander 1937 -

McGee 1935 - Reinberger 1936 - DeLee 1934)

Associated with edema are the eye findings. The eyes are involved in 90% of the cases. The findings here constitute edema of the retina with retinal hemorrhages and even detachment of the retina, but no albuminuric retinitis. (Stander 1937) Harden (1935) records blindness in 20% of the cases although he does not say edema was the sole cause. Most authorities stress spasm of the retinal vessels with edema, spots before the eyes, blurring of vision and flashes before the eyes. (DeLee 1934 - McGoogan 1932 - Hardin 1935 - Kellog 1937 - McGee 1935)

In the routine examination of the pregnant woman the blood pressure is occasionally checked and to many men serves as a means of diagnosis and classification of the severity of the existing toxemia. Reinberger (1936) brings forth a view not often mentioned. He believes that it is not appreciated generally that the blood pressure is normally lower during pregnancy, ranging from 90/60 ro 110/60. A rise to 130/60 is stressed as a danger signal, from 130/60 to 150/60 as potentially eclamptic, and above 150/60 a graver toxemia. Other authorities are more interested in the diastolic blood pressure. A mild preeclamptic may have a diasto-

lic blood pressure over 90 while a moderate preeclamptic will have a diastolic over 100 and the severe preeclamptic has a diastolic over 110. (McGee 1935) McGoogan (1932) reviewed 30 preeclamptic patients and found the systolic pressure to be as follows: 140 to 150 - 4 cases; 150 to 170 - 2 cases; 170 to 200 - 7 cases; over 200 - 7 cases. The American Committee on Maternal Welfare reported to the Journal of the American Medical Association in 1935 that a slight rise in both systolic and diastolic blood pressure occurs several weeks before albuminuria. A high blood pressure which is moderate at first and then mounts very fast is especially diagnostic. (DeLee 1934) A reversal of the normal takes place and the blood pressure is usually higher at night. (Harden 1935)

Blood studies reveal an anemia with an average red blood count of 3 or 4 million. (Harden 1935) Further tests show an increase in uric acid content with a lowered CO_2 combining power. NPN and ureaN are normal with normal blood sugar and inorganic elements, such as calcium, magnesium, sodium, potassium and phosphorus. (Stander 1937) DeLee (1934) maintains that a hyperglycemia exists. On the other hand, Reinberger (1935) says, "Blood chemical tests, though run routinely, have proven

of no value either from a diagnostic or prognostic standpoint". A deeper consideration of the blood findings will be taken up in the discussion on diagnosis.

Urinary:

Along with blood pressure checkings and recording of weight gain, the obstetrician routinely searches for albumin in the pregnant woman's urine. The first findings of albuminous urine in connection with puerperal convulsions was by John C. W. Lever of Guy's Hospital in 1843. (Garrison 1924) Since then it is stressed in every article on the subject. Reinberger (1936) believes that the importance of albuminuria is much beneath blood pressure, irritability and weight gain, and that it is rarely found in incipient toxemias and is usually a sign of a more severe type of toxemia. McGee (1935) records his findings in mild preeclampsia as a slight trace of albuminuria and in moderate and severe preeclampsia more than a trace of albuminuria. Mathews (1938) on reviewing 190 pregnant women weighing 200 pounds or more found 45% of them developing some type of toxemia and, of these, 35% had a trace or over of albuminuria. Reviewing 30 patients McGoogan (1932) found albuminuria in varying amounts in 29 and absent in 1.

Of further importance is the decrease in urinary output. The mild preeclamptic has a urinary output of less than 1500 cc in 24 hours. The moderate preeclamptic has a urinary output of less than 1000 cc daily and the severe preeclamptic has a marked oliguria or anuria. (McGee 1935) Further mention is made of scanty, scalding dysuria 4 to 30 times daily. (Harden 1935) The specific gravity in the majority of patients is 1.016 or higher. (McGoogan 1932) DeLee (1934) reports findings which occur and which are quickly ominous. These are oliguria, albuminuria, casts, red blood cells and white blood cells, bile, and indican. Meigs (1867) reports that casts in the urine are exceedingly important diagnostically and prognostically.

Digestive:

Epigastric pain is reported as being an exceedingly common symptom. (McGee 1935 - DeLee 1934 - Stander 1937 - Harden 1935 - McGoogan 1932) This pain occurs in approximately 20% of cases (McGoogan 1932) but may manifest itself as a right upper quadrant pain (Harden 1935) and usually occurs only in the severe preeclamptic and eclamptic (McGee 1935) A more common digestive symptom is the presence of nausea and vomiting in approximately 68% of cases. (Harden 1935) McGoogan

(1932) finds the incidence of nausea and vomiting is nearer 20%. The presence of jaundice is mentioned by McGee (1935) and DeLee (1934) with bilirubinemia in a small percent of cases. Harden (1935) mentions pyrosis after meals as an occasional finding.

Summary:

The whole is summarized by Kellog (1927) and given, in his opinion, in their order of appearance through the entire course of the disease. This resume constitutes first, signs and symptoms relative to hypertension; second, albuminuria and edema (especially of the face) followed by sudden weight gain, blurring of vision, nausea, vomiting, increased respiratory depth, torpor, irritability (either mental or motor) epigastric pain, convulsions, coma, and death. This order varies somewhat in the estimation of other authorities, but is fairly correct in the enumeration of the typical signs and symptoms of mild preeclampsia to severe preeclampsia into eclampsia, in chronological order.

DIAGNOSTIC PROBLEMS

A thorough understanding of the preceeding chapter will be a tremendous help to the student in arriving at a fairly correct diagnosis of the toxemias of pregnancy. However, several problems are confronting the diagnostician and an adequate solution to these problems would be a great aid in accurate diagnosis.

The first problem to be solved is the present more or less inability to predict early in gestation whether or not a toxemic diathesis exists in the pregnant woman. The second problem is the making of an accurate diagnosis from the various signs and symptoms presented by the patient. The third problem is to differentiate the toxemia when it does appear, chiefly from the state of essential hypertension, the acute and chronic nephridities and nephroses. The fourth and last problem is to accurately classify the severity of the disease in order to judge which type of treatment is needed at the moment the patient presents herself. This discussion will attempt to show the work that has been done toward the settlement of these problems.

Early Preduction:

Some workers have turned their research toward the discovery of a test which, if positive, will give

the obstetrician some insight as to the possibility of his patient developing a toxemia late in pregnancy. Principles in this work are W. J. Dieckmann, H. L. Michel and P. W. Woodruff of Chicago. Since 1933 they have used the ice water test for vasomotor lability and they call it the "cold pressor test". Since the blood pressure is so easily affected by external influences, they submit the patients to no other manipulations than those definitely concerned with the blood pressure responses. All extraneous noises and manipulations are reduced to a minimum. Only one person presides over the test. In many instances the self-recording sphygmomanometer is used so that the operator is as far away from the patient as is feasible for the test. Great care is taken in bringing the basin of cold water to the patient's hand and passively emersing and withdrawing the hand from the water. They report that the test seems to be of value in aiding to detect those pregnant patients who have a primary hypertension. 152 normal pregnant patients were subjected to the test in early pregnancy. 90 patients with the test gave an increase in the systolic blood pressure of 30 mm or more and 15 of these subsequently showed evidence of toxemia. 32 gave a rise of from 20 to 29 mm and one of these developed

toxemia. The cold pressor test seems to be of value in enabling one, early in pregnancy, to detect those patients who may develop toxemia. 30% of the patients in the early months of pregnancy who had normal blood pressure at the time of the test and showed excessive responses developed toxemia of pregnancy, whereas of the group that did not give normal responses to the cold pressor test only 2 patients developed toxemia of pregnancy. The diastolic pressure responds in the same manner as the systolic pressure; the rise, however, was rarely as great in actual mm's. It has also been used by them and others as a test to determine whether or not a patient who had toxemia in a previous pregnancy might have a recurrence if she again became pregnant. (Dieckmann 1938)

It would seem that if these findings are true perhaps in the near future some test will be available to the practitioner and warn him to carefully observe those patients having a stronger positive reaction to the test.

Diagnosis:

The second problem is almost as difficult, for in this the signs and symptoms have already presented themselves and the obstetrician must now make the diag-

nosis of toxemia and classify it as to its severity. Diagnosis is made by the signs and symptoms as have been given and by blood chemistry studies. Kellog (1937) has laid down the following routine studies, but concludes that as extensive as their results may be, they are "usually all of little value". He studies accurately the blood pressure, presence of albuminuria, specific gravity, urea clearance, liver function tests, blood vessel changes in the eye grounds, renal function tests, dilution concentration tests and increased blood uric acid and diminished CO_2 combining power. Stander (1934) has great confidence in blood chemistry, for he says, "Blood chemistry is an indispensable index of the severity of the disease and of specific treatment needed". He gives the following blood findings:

(1) NPN normal, except late when it shows the result of the disease on the kidneys.

(2) Blood ureaN low, as in normal pregnancy. The ureaN ratio with NPN equals 0.4 as compared to 0.5 in the normal nonpregnant female.

(3) Blood uric acid increased.

(4) Blood sugar not greatly disturbed.

(5) Alkali reserve is often greatly decreased, sometimes to acidosis, therefore, he advises watching

the CO_2 combining power for the necessity of antiacidotic treatment.

(6) Blood chlorides are not markedly decreased. Many authorities began having great confidence in the finding of hyperglycemia and making a diagnosis on this point. (DeLee 1934) Consequently, I. A. Siegel and H. B. Wylie (1933) made extensive studies on the blood sugar findings in eclampsia and preeclampsia and found blood sugar determination errors ranging from 1.1% to over 20% with variations of 0.5mm on the scale reading in spite of technically correct handling. Consequently, they concluded that the diagnostician cannot depend on blood sugar levels determination to diagnose eclampsia or preeclampsia.

Differential Diagnosis:

The third problem next presents itself. This constitutes differentiating the various states which may resemble the toxemias of pregnancy from the toxemia itself. According to McGee (1935) this group includes epilepsy, hysteria, brain tumor, chemical poisonings, meningitis, acute and chronic nephritis with uremia, gumma of the brain, malignant hypertension, pyelitis, cerebral thrombosis, apoplexy and diabetic coma. Heinz

(1932) adds tubal pregnancy to this list and sites a case where tubal pregnancy occurred with a rise in blood pressure, low abdominal pain, nausea and vomiting. From this list the reader can readily realize that the diagnosis of the toxemias of pregnancy is not a simple one and that confirmation of the diagnosis requires a complete check, in every way, of every region and system in the patient's body. This examination includes a complete physical, complete blood chemistry, complete kidney and liver function tests and may necessitate even xray studies. The most difficult problem in this differential diagnosis occurs between preeclampsia and nephritis. May (1936) states that "too often the differential diagnosis between preeclampsia and nephritis is impossible until a subsequent pregnancy has given the kidneys the best renal function test". He believes that chronic nephritis conforms more closely to the following:

(1) Elevated blood NPN.

(2) Toxemia before the fifth month of pregnancy.

(3) History of previous pregnancy with toxemia.

(4) History of previous predisposing disease

(such as scarlet fever).

(5) Albuminuric retinitis.

(6) Moderate secondary anemia.

(7) Systolic blood pressure over 160 with little or no albuminuria.

(8) Slowness or failure of the blood pressure and urine in returning to normal during the puerperium.

(9) Impaired renal function tests.

Schwarz (1934) believes "the main differential points in the diagnosis of preeclampsia from the low reserve kidney are chiefly in the finding of an increasing uric acid content and a lowered CO_2 combining power".

The cold pressor test and a test involving the injection of a posterior pituitary extract seemed to several as a means in differentiating preeclampsia from essential hypertension or vascular-renal disease. Herbert L. Michel (1938) at the Central Society for Clinical Research in Chicago last November 1937 reports, "With the cold pressor test those patients who already had toxemia of pregnancy gave minor responses to the test, whereas those with essential hypertension and vascular renal disease gave definite responses to the test. Furthermore, patients with a similar history of hyper-

tension but with normal blood pressure at the time of the test gave marked responses to ice water stimulation". As to the test with a solution of posterior pituitary, he says, "We were able to confirm a diagnosis of toxemia of pregnancy in every patient in whom a diagnosis of toxemia of pregnancy had been made. Patients in whom a diagnosis of essential hypertension of vascular-renal disease had been made reacted to injections of solutions of posterior pituitary by a rise in blood pressure of not more than 11 mm, as compared to a rise of 52 mm in the former group, thus the test served to confirm diagnosis rather than predict toxemias of pregnancy".

Classification of Severity:

The final problem to be solved after a definite diagnosis is made is the classification of the severity of the disease. McGee (1935) divides preeclampsia into mild, moderate and severe. The mild preeclamptic has the following symptoms and signs:

(1) Gain of more than 1 pound a week in the last trimester.

(2) Diastolic blood pressure over 90.

(3) Urinary output less than 1500 cc in 24

hours.

(4) Edema of the feet.

(5) Slight trace of albuminuria.

Moderate preeclampsia includes the following signs and symptoms:

(1) Excess weight gain.

(2) Diastolic blood pressure over 100.

(3) Urinary output less than 1000 cc daily.

(4) Edema of the hands and face.

(5) More than a trace of albuminuria.

Severe preeclampsia he lists as having:

(1) Marked increase in weight.

(2) Diastolic blood pressure over 110.

(3) More than a trace of albuminuria with oliguria or anuria, red blood cells and casts.

(4) Generalized edema.

(5) Headache and dizziness.

(6) Eye symptoms or lassitude.

When the preeclamptic closely approaches the eclamptic state a further differentiation is made between the mild and the severe. Thos. Watts Eden (1922) gives a criterion for differentiating the mild and severe by allotting the following findings to the severe type:

(1) Temperature above 103°.

(2) Pulse over 120.

(3) Blood pressure 200 or over.

(4) The urine solidifies on boiling.

(5) Absence of edema.

(6) Persistent coma.

(7) More than 10 convulsions.

With this differentiation he reports a mortality of 2.8% in the mild and 21.05% in the severe.

Peckham (1935) after an analysis of 127 cases moderated this criterion by advocating the following differentiating points:

(1) Temperature over 103°.

(2) Pulse 120 or over.

(3) Blood pressure 180 or over.

(4) No or slight edema.

(5) Deep and persistent coma.

(6) 20 or more convulsions.

With this criterion used in 205 consecutive cases 102 were classified as being mild with no deaths. 103 were classified as severe with 25 deaths or a mortality of 24.27%.

Summary:

Consequently, in the diagnosis of preeclampsia

the obstetrician is confronted with these four problems: First, the prediction early in gestation of the patient's predelection to toxemia; second, accurate recording of signs and symptoms; third, differential diagnosis; and fourth, classification of the toxemia as to mildness, moderation or severity.

THE MANAGEMENT OF PREECLAMPSIA

We now approach the most interesting and most instructive part of our discussion concerning preeclampsia. It is here we see theory put into practice and the clinical results tabulated. By this means, evidence is slowly gathered in the proof of one or more theories concerning the etiology. Treatment of preeclampsia is quite complicated because the etiology is not known. It is divided into four main divisions, i.e.: Prophylaxis, active treatment, delivery and postnatal care with prognosis. The discussion of the management of preeclampsia will be carried out under these four headings. Here again more than in any of the preceeding chapters our discussion will include mild and severe preeclampsia and eclampsia, for our treatment is based on the attempt to alleviate the symptoms and prevent mild forms from developing into severe forms.

Prophylaxis:

"Under no circumstances is the old saying of 'Prevention is better than the cure', so well illustrated as in the prophylactic treatment of puerperal epilepsy." (Rigby 1851)

Since little was understood in 1851 of the

preeclamptic state, the obstetrician was chiefly concerned in preventing the onset of convulsions. Consequently, his treatment consisted of measures to prevent eclampsia. Rigby (1851) outlines his prophylactic measures when he records, "The treatment which we have recommended during the last few weeks of pregnancy, is particularly valuable in keeping off any disposition to these attacks: Regular, and for her condition, even tolerably active exercises and strict attention to the bowels, should be required, especially in primipara. If any distinct symptoms of cerebral congestion make their appearance, such as flushed face, headache or slight wandering; if, more over, the pulse be slow and laboring, we must at once relieve the circulation by bleeding; and by an active dose of calomel and James' powder at night with a warm pediluvium, and a brisk laxative the next morning, endeavor to ward off the dreaded attack."

Such was the prevailing idea and not much change is noted in the prophylactic treatment until that introduced by J. Clifton Edgar in 1903. His treatment is outlined as follows:

I. The amount of nitrogenous food would be diminished to a minimum (a milk diet with fish and white meats).

II. The production and absorption of poisonous materials, in the intestines and body tissues, should be limited and their elimination should be aided by improving the action of:

a. The bowels (diet, doses of colocynth and aloes at bedtime and a saline cathartic in the morning).

b. The kidneys (glonoin).

c. The liver (calomel and soda at bedtime and sulphur water in the morning).

d. The skin (wool or flannel clothing, massage, hot baths and hot air baths).

e. The lungs (oxygen administration).

His routine treatment for diaphoresis and diuresis was the administration of a tablet containing calomel, digitalis, and squill, 1 gr. each and muriate of pilocarpine 1/20 gr., followed the next morning by a full dose of Villacabras water. If no cardiac disease was present he permitted the use of jaborandi.

Our attention is now turned to the modern authorities and their treatment will be discussed by outlining chronologically. Modern treatment uses diet, water intake and output and the administration of minerals and vitamins as a nucleus.

After a detailed discussion concerning food and drink control in the pregnant woman, J. O. Arnold

(1933) before the Medical Society of New Jersey, concluded, "The obstetrician has now, in the control of the intake of food and drink, and in the methodical application of principles of fluid-balance, a very definite and practicable means of preventing the socalled 'toxemias of pregnancy'."

Dame Louise McIlroy (1934) of England is a strong believer in diet management. She proposes a 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 on the maternal tissues. This diet should consist of one or two pints of milk per day, green vegetables once or twice a day, one or two eggs a day, sea fish (iodine) twice weekly, calves liver once a week, plus whatever light foods the patient wants. The patient should also receive two ounces of codliver oil daily. The weight should be carefully watched and the light diet with a moderate diet is given on alternate days. The light diet consists of crackers and a glass of milk every three hours with two oranges. The patient should walk two or three miles daily. Along with this diet management, the elimination of harmful substances by physiological rest and suitable stimulation of those organs

which are concerned with excretion should be accomplished.

Jos. Bear (1934) advocates strict hygiene of pregnancy in prenatal care with regular, frequent urinalysis, blood pressure readings and weight checking. The patient should be on a calcium dietary plan.

The therapy of the Cook County Hospital consists of a routine examination every two weeks. This includes blood pressure recordings, urinalysis, weight checks, appearance of edema and eradication of foci of infection. If a rise in blood pressure of over 130/70 or a gain in weight occurs, the blood pressure is then read twice daily and the patient placed on a salt poor, low protein, low fat diet. In addition to this, magnesium sulphate purgation is started and by means of an electric cradle, a bath, or ultra-violet light, skin hyperemia is maintained. (Fantus 1935)

The American Committee on Maternal Welfare (1935) advanced definite prophylactic measures. These include:

(1) Proper elimination and a general diet. This diet includes protein and vitamin foods with reduction of fats and carbohydrates. Salt is used sparingly and water is limited to three pints daily.

(2) Foci of infection should be removed.

(3) The patient should regularly visit the Doctor, at which time blood pressure, urine and weight gain are checked.

(4) If the blood pressure goes up, diet and physical activity are definitely limited, saline cathartics are administered and sedatives given. These sedatives consist of bromides 15 gr., phenobarbitol 1/2 to 3/4 gr., t.i.d.

After nineteen years study in 232 cases, Reinberger (1936) evolved a logical prophylactic therapy for the incipient toxemia. He advocates simple elimination diet and rest. Elimination is accomplished with magnesium sulphate. The diet consists of high carbohydrate, low protein, and salt free. He eliminates meat, fish, eggs, cheese and salt. Since this diet "may be a factor in the production of the socalled anemia of pregnancy", (Russell 1936) Reinberger also gives these patients iron, liver extract, vitamins, calcium and viosterol in large quantities.

A. A. Landry (1936) places all the prophylactic measures in the administration of calcium and vitamin "D". He says, "In the later months of pregnancy calcium and viosterol (vitamin "D") are used.

This is specific for nervous imbalance, tetany and tingling and numbness, and cramps." DeSnoo (1937) again advocates dietary plan with a minimum of salt and frequent blood pressure checkings. He explains this by saying, "When it is considered that disturbances of gestation but rarely occur in animals, it is obvious that one must look for this cause in the fact that the human being has deviated from nature; i.e., in civilization. I believe that the custom of salting food is in a high degree responsible for these disturbances, especially edema and convulsions."

Consequently, the reader will realize after this review that prophylaxis involves close observation of the patient with blood pressure, urine and weight checkings. Control of the patient is administered through food and water intake and mineral and vitamin administration. As to the correct measure to be used, the writer will draw no conclusions but leave this problem to the clinical judgment and experience of the reader.

Treatment:

Let us now consider the pregnant woman who has definitely become preeclamptic either through failure of the prophylactic treatment, mismanagement by the

obstetrician, or who presents herself for the first time to her Doctor definitely presenting the first signs and symptoms of preeclampsia.

This discussion will include the historical development from 1775 to 1913; a brief resume of the change from radical to conservative treatment, a detailed discussion of the modern conservative treatment with its modifications and more isolated methods of treatment such as the use of calcium, vitamin "D", and parathormone, ultra-violet light and heparmone.

I. History.

It is intensely interesting to read of the early history of the treatment of toxemia and observe the gradual change that has taken place. Alexander Hamilton in 1775 published a book titled, "Elements of the Practice of Midwifery", in which he lays down certain treatment for late toxemia as follows: "Convulsions at an early period of Pregnancy chiefly happened to Young Women of a plethoric, sanguine habit, and can therefore only be removed or palliated by a free and bold use of the Lancet, by an open belly, cool regime, and spare diet. If insensible or comatous, Opium, Musk, and other Antispasmodics should be exhibited by

way of clyster, and the Patient should be aroused by Epipastic and stimulating Cataplasms applied to legs and hands. Convulsions are generally mortal, the Vis Vitae must be supported by replenishing the vessels with the utmost speed: This is done by pouring in nourishing fluids as fast as possible by the mouth and by clyster, warm applications should also be made to the stomach and feet, and nervous cordials given internally along with Opium. When Fits come on with Labor pains, a speedy Delivery, if it can be done with Safety, either by turning the child or extracting with the Forceps when the Head is within reach, will prove the most effectual cure."

In 1849 the accepted treatment consisted of shaving of the head and the use of cupping to relieve the head symptoms. It was reported that cupping gave almost instant relief. Along with this, antispasmodics were administered, bleeding was accomplished, and the woman was delivered as soon as possible. (Gooch 1849)

E. B. Sinclair and G. Johnston in 1858 advanced the use of purgatives - hydragogue cathartics - bleeding, and acupuncturation of the labia majora.

In 1861 Francis H. Ramsbotham in his book, "The Principles and Practice of Obstetrical Medicine

and Surgery", went into great detail as to the accepted treatment of toxemia. He introduced the reason for his treatment by saying: "Believing that the cause most commonly consists in pressure to which the cerebral mass is subjected, the same treatment must be adopted that had been recoursed to under ordinary apoplexy: viz. - the abstraction of blood, and acting briskly on the intestinal canal. 40, 50 or 60 oz. of blood is withdrawn and 10 or 12 gr. of calomel and 1 tablespoon of infusion of senna and jalap administered every one-half hour. If this treatment is not successful a drop or two of croton oil is given by mouth and turpentine and assofoetida by rectum. The head is then shaved and cold packs applied. Cupping glasses applied to the back of the neck or behind the ears or leeches to the temples or blistering the bald head or neck is now considered rather useless. Opium is considered injurious by many present obstetricians today. Emptying the uterus will usually put a stop to the fits."

Chas. Meigs in 1867 advocated bleeding, cupping, and shaving the head. He mentioned that "darkness, repose and silence are essentials. Sinapisms ought to be freely applied to the lower extremities,

and to the abdomen; and the location of them should be changed from time to time, so as to keep up a constant irritation of some distant part with a view of diverting the sanguine mass from the cerebrum".

In addition to the above treatment, Reamy of Cincinnati introduced in 1870 the use of veratrum viride to produce a rapid fall in blood pressure, as well as in the pulse rate. (Stander 1929)

In 1871 Sir James Simpson advanced the belief that no antispasmodics or opiates should be given, but that if sedatives were needed, chloroform should be given. In addition to this, the usual treatment with purgatives and bleeding was carried out. Alfred H. McClintock (1876) further advanced Simpson's treatment. Twenty years later in 1896 E. P. Davis in a "Treatise on Obstetrics" advanced the same treatment.

Of great importance is the year 1897 for Garrison's History of Medicine, 1929, states: "By far the most striking advance in preventive obstetrics is the expectant treatment of eclampsia by means of quietude, isolation in a dark room, and exhibition of sedatives and purgatives as was introduced by Vasseli Vassilievich Stroganoff in 1897, with such recent modifications as the additional use of magnesium sulphate

(E. M. Lazard 1897) or its intramuscular injection (Lee Dorset)."

Chas. Jewett in 1899 advanced three main means of treating the otxemic patient.

I. Sedation - chloroform, morphine, veratrum viride or chloral hydrate with or without sodium bromide.

II. Empty the uterus under deep anesthesia.

a. Caesarian
b. Mechanical dilatation of the cervix.
c. Deep incisions in the cervix
d. Or combined mechanical dilatation and deep incisions of the cervix (accouchement force)

III. Elimination of the poison or poisons - cathartics (croton oil, compound jalap powder, or calomel, followed by salines and high enemata of magnesium sulphate). Diuresis (dry or wet cups over the kidneys followed by hot fomentations). Glonoin or veratum viride as diuretics.

In 1920 kidney decapsulation was introduced by Edebohls. This form of treatment was accepted by Pinard, Lubbert, Cardwell and Brindeau, but had a mortality of 40% and was soon discarded. (Stander 1929)

About this time Lichenstein, believing the cause to be retro-placental hematoma and the formation of insufficiently oxydized protein substances with their absorption, had the patient assume a squatting posture. He believed that intra-abdominal pressure

was three times as great in this position and prevented formation of a retro-placental hematoma by making placental separation more difficult. This position was assumed by raising the patient's head and shoulders and flexing the legs by means of pillow supports. Hammerschlog maintained that this posture was of little value in the treatment of toxemia. (Stander 1929)

The last obstetrician before our accepted modern authorities to make any change in the accepted treatment was Mayer (1913) who used the serum of a normal pregnant woman to treat eclampsia. In his experience recovery followed this treatment.

Such has been the historical development of the treatment of preeclampsia and eclampsia up to 1913. Much has been purposely omitted for the author wishes to take up in greater detail, in the following discussion, the change which has taken place in treatment and show how the radical conception of the past years has slowly changed to the conservative beliefs of today.

II. Radical vs Conservative.

We now approach a most interesting phase in our discussion of the treatment of the preeclamptic patient. Here we wish to show the change that has taken place up to the modern conception of the treatment of

severe preeclampsia or eclampsia. This change begins in 1896 and is concerned chiefly as to when and how the patient should be allowed to be delivered of her child. The development is divided into four periods; first, the radical; second, the transition; third, the conservative; and fourth, the modified Stroganoff. During these four periods the general treatment of the patient has been much the same as that laid down by V. V. Stroganoff in 1897. This included as already described, quietude, isolation in a dark room, exhibition of sedatives and purgatives. This treatment has remained much the same with changes only in the type of sedatives used, methods of purgation and edema control. The great change however, has been in the time and way of relieving the uterus of its burden. This discussion will be concerned with this latter change. The author is deeply indebted to C. H. Peckham (1935) for his results of 384 cases and the facts, figures and ideas presented by them.

The radical period extends from 1896 to 1911, inclusive. During this time the general Stroganoff method of treatment was used and the delivery of the patient was extremely radical. The conception then was

that no matter how ill the patient was she should be delivered. This was done "usually through the cervix, as caesarians were not used". In primipara, in the last month of pregnancy, dialation of the cervix was done. This was extremely serious and was followed in most cases by great shock. Following accouchement force the baby was delivered by version and extraction. Then the patient was sweated and bled. During this period Peckham and Bergland reviewed 110 cases and found a groos maternal mortality of 22.8% and a gross fetal mortality of 57.6%.

A period of transition extended from 1912 to 1918, inclusive. Here the radical treatment was gradually given up and some men delivered by caesarian section, others by vaginal section, and still others by sedatives, opiates and the disregard of the baby, for a time. These latter were approaching the more conservative idea of treatment. A review of 71 patients treated during this time with such treatment gives us the following mortality percentages:

Gross maternal mortality	16.9%
Gross fetal mortality	59.0%

This method consequently lowered the gross maternal mortality but increased the gross fetal mortality, be-

cause of the beginning tendency to disregard the fetus for a time.

We now approach the conservative period of development which extended from 1919 to 1924, inclusive. During this time the treatment was ultra-conservative. The patient was treated by sweats, venesection, and opiates. The baby remained undelivered until the cervix was dilated by the regular processes of labor. This treatment resulted in a further decrease of the gross maternal mortality and a further increase in the gross fetal mortality.

The fourth period extends from 1925 to 1933, inclusive, and is termed the modified Stroganoff period, for the general Stroganoff idea of treatment was used, amended, however, by Stander who excluded the use of chloroform and venesection. The treatment may be outlined as follows:

(1) Using a dark, soundproof room.

(2) 1/4 gr. morphine administered and a small amount of blood drawn for chemical examination.

(3) Administration of large doses of chloral hydrate per rectum and morphine repeated.

(4) Few venesections and no sweats.

(5) Liquid nourishment through a nasal tube.

(6) Induce labor by rupturing the membranes or by bougie and deliver with forceps when well dilated.

Such was the modified Stroganoff method as used by Johns Hopkins University and Hospital. 127 patients were treated during this time by this method and the treatment resulted in a gross maternal mortality of 11.0% and a gross fetal mortality of 51.1%, a definite reduction over the three preceeding periods. (Peckham 1935 - Bergland 1935)

Let us now consider several opinions as to the results of the present treatment and its modifications. In 1925 Carl M. Wilson in a comparison of the results obtained after radical and conservative treatment in the obstetrical department of Johns Hopkins Hospital concluded that the end result was "twice as good under conservative management as under radical". He stated that, "Those cases do best which are subjected to a minimum amount of obstetrical interference". He advanced a belief in the use of free venesection and morphia in moderate doses.

J. W. Williams (1927) in an article "The Toxemias of Pregnancy and the Treatment of Eclampsia" brought forth four definite conclusions:

(1) In mild as well as severe cases of

eclampsia, the results are better under conservative than under radical treatment.

(2) In mild cases a modified Stroganoff technique gives almost ideal results.

(3) In severe cases such treatment gives twice as good results as more radical treatment, but is still followed by a mortality so high as to urgently demand improvement.

(4) It appears that all the generally used anesthesias superimpose an additional toxemia on that associated with the disease.

H. J. Stander's view in 1929 after an analysis if 801 patients with toxemia of pregnancy is, "Pre-eclampsia is to be viewed as the forerunner of eclampsia, and as such is a serious complication. Conservative treatment in most cases, and radical interference under local or spinal anesthesia in exceptional cases, seems to give the best results. In such cases, Stroganoff treatment should be begun while preparations for operation are made, and continued afterwards".

In 1934 L. G. McNeile reviewed the conservative treatment of the late toxemia of pregnancy with special reference to the use of intravenous magnesium sulphate during the period from 1924 to 1934 and the

following are his findings:

Mortality in Preeclamptic Patients Treated by Magnesium Sulphate from 1924 to 1934

	No. of Cases	No. of Deaths	% Mortality
To July 1929	143	4	2.80%
July 1929 to Nov. 1932	228	2	0.80%
Nov. 1932 to April 1934	164	3	1.76%
Total	540	9	1.66%

Preeclamptics with Convulsions Under Magnesium Sulphate

	To July'29	July'29 Nov.'32	Nov.'32 Apr.'34	Tot.
Cases in labor + magnesium sulphate	55	78	77	210
Convulsions	5	1	8	14
Cases in last 2 weeks of pregnancy and magnesium sulphate	88	150	92	330
Convulsions	6	9	6	21

As can be seen, the use of magnesium sulphate in the preeclamptic seems to have diminished the tendency towards development of convulsions.

McNeile also gives the indications of caesarian in preeclampsia in 540 cases reviewed as follows: Previous section 3 cases; abruptio placenta 3 cases; deformed cervix 1 case; primipara aged 41 years 1 case;

toxemia of pregnancy 8 cases.

The report "The Management of Preeclampsia and Eclampsia" of the American Committee on Maternal Welfare in 1935 contains the conclusion that "The toxemia of late pregnancy is a nonsurgical condition which should be treated by medical measure in a vast majority of cases".

The last viewpoint to be included in this discussion is that of F. S. Kellog written in 1937. "I interfere on convulsive signs and symptoms irrespective of the baby, especially if I observe the pre-convulsive and pre-coma signals of irritability and torpor. The treatment of preeclampsia should be as radical as the treatment of eclampsia should be conservative."

This discussion has attempted to show the change in the consideration of the mother and baby throughout four periods from 1896 to 1933. Since 1933 the author has brought forth the opinions of several authorities as to their acceptance of a radical, conservative or combination of the two viewpoints, as to treatment. Experience, and clinical judgment should lead the reader to the correct technique.

In the discussion following, a detailed outline of the conservative treatment will be given, fol-

lowed by several of the special techniques devised.

III. Modifications of the Stroganoff Treatment.

In this part of the discussion the various modifications of the Stroganoff treatment will be brought out in detail. The treatments as outlined will be those used by 14 authorities who constitute a representative crossection of the practicing obstetricians. The purpose of this treatment is to prepare the patient for as safe a delivery as possible from the viewpoint of herself and her baby. Consequently, following this resume another discussion limiting itself to the various methods of delivery will be necessary. Purely for ease of outlining, the various treatments will be given in chronological order from 1931 to 1936 inclusive. All the treatments are built with rest and quietude, sedation and dehydration as a nucleus. Variations of treatment used by different authorities occurs in one or more of these principles as will be noted by the reader as he reviews each treatment outlined.

The first variation in treatment to be discussed is that of J. W. Ross (1931) who is a staunch supporter of the use of nembutal in the treatment of

preeclampsia and eclampsia as a prophylaxis for convulsions. During the three years preceeding his report which was given in 1931, he treated 35 cases of preeclampsia with nembutal 0.1 gm. capsules by mouth. One capsule was given 4 times a day and none of these 35 cases developed convulsions. 3 preeclamptic cases not given nembutal developed convulsions. During this period he also treated 24 cases of eclampsia. 23 had no prenatal care. In these cases nembutal stopped and controlled the convulsions when morphine sulphate failed. 0.2 gm. of nembutal in 4 cc of normal saline was given intravenously, followed by 6 or 8 capsules per rectum. From his experience during these 3 years of treating both preeclamptics and eclamptics he concluded that nembutal was clinically superior to and safer than morphine, chloroform, chloral hydrate and magnesium sulphate.

In 1932 L. S. McGoogan before the Nebraska State Medical Society, outlined his treatment as follows: Rest in bed, copius elimination with magnesium sulphate orally, and sedatives. Sodium amytal was found to be a very satisfactory sedative. The diet should be low in protein (enough to meet basal metabolic requirements) and little or no salt.

W. J. Stevens (1932) before the Canadian Medical Association, outlined nine main points of treatment:

(1) Measure the daily urine output.

(2) Determine daily the blood pressure and albuminuria.

(3) Maintain a water balance.

(4) Dehydrate by glucose and magnesium sulphate.

(5) Check weight daily.

(6) Spinal puncture. 45 cc to 100 cc drawn off at intervals of 4 to 6 hours.

(7) Venesection.

(8) Low salt diet.

(9) Induction or caesarian.

After an analysis of 575 cases of eclampsia and preeclampsia treated by intravenous injections of magnesium sulphate, E. M. Lazard (1933) made the following conclusions as to that method of treatment: Objectives of treatment of preeclampsia should be: (a) Overcome effects of toxemia by sedation and elimination. (b) Remove as much work as possible from the embarrassed emunctories by regulation of diet and balance of fluid intake and output. (c) Terminate pregnancy as conser-

vatively as possible, where not the proper response to treatment has resulted, before the onset of convulsions.

Out of 225 cases of eclampsia and 350 cases of preeclampsia treated by intravenous magnesium sulphate the gross mortality of the whole series was 5.9%. The reader can pause here to compare this figure with the four figures given for the four periods presented in the preceeding discussion and note the marked improvement.

Of special interest is the brief statement by C. N. Ploussard given in 1930 as to the use of magnesium sulphate. He brings forth the view that the reason intravenous magnesium sulphate sometimes fails is because not enough is given. He does not hesitate to give one and sometimes two ampules of a 50% solution every hour.

The treatment of W. J. Dieckmann (1933) is based on the finding of an increase in blood and plasma volume with alterations in the hemoglobin, the hematocrit and serum protein, and retention of water and salt. These findings he believes call for treatment by diluting the blood. This he does by delivery, venesection, plasmapheresis, intravenous glucose or bicarbonate so-

lutions, hypnotics, sedatives and elimination.

In 1934 L. G. McNeile brought forth the routine conservative treatment of the late toxemias of pregnancy. This includes:

(1) Absolute bed rest.

(2) A milk diet.

(3) Fluid balance - if necessary use a retention catheter and also measure the bowel movements.

(4) 1 oz. of magnesium sulphate every 6 hours until watery stools occur and then 1/2 oz. daily.

(5) Urinalysis of a 24 hour specimen daily.

(6) Blood pressure taken 3 times daily.

(7) With a systolic pressure of 150 or higher, 20 cc of a 10% solution of magnesium sulphate is given intravenously and repeated when the blood pressure continues to rise. 60 to 120 cc of this solution can be given in 24 hours.

(8) 300 cc of a 25% solution of dextrose given intravenously 1 to 4 times daily.

(9) For restlessness, chloral hydrate 20 gm. and sodium bromide 60 gm. given per rectum.

(10) If the patient improves a basic diet is added.

(11) If the patient continues toward greater

severity induce labor by rupturing the membranes or by Vorhees bag.

M. P. Rucker before the Virginia Medical Association in 1934 outlined his four main principles of treatment:

(1) Sedation - 20 cc of 10% magnesium sulphate intravenously or sodium amytal and avoid external stimuli, i.e., noise, bright lights, jarring of the bed, or even the prick of a needle.

(2) Rest - if in labor - for the first stage with morphine and hyoscine or sodium anytal and hyoscine; for the second stage - local infiltration of the perineum with 0.5% novocaine.

(3) Promote kidney activity - if conscious give water and weak lemonade. If not conscious give 1 pt. water through a nasal tube every 8 hours. If this is not successful use hypertonic glucose solution intravenously.

(4) For edema of the lungs and cyanosis - digitalis 1/2 cat unit as early as possible, withdraw 500 or 600 cc of blood by venesection, and force oxygen into the peritoneal cavity until tympanitic.

The next treatment is the interesting one brought out by Arnold and Fay as the Temple treatment

in 1934, and centers on the prevention and control of toxemia by fluid limitation and dehydration. It is outlined under the three headings: Potentially abnormal group; the moderately preeclamptic; and the dangerously preeclamptic.

The potentially abnormal group is treated by prophylaxis. This treatment includes 5 small, well-balanced meals per day, low in salt and carbohydrates. Fluid intake and output charts should be kept and balanced. The moderately preeclamptic's treatment is:

(1) Keep water and blood pressure records.

(2) Withhold all fluids until the 24 hour urine output is known.

(3) Chart accurately the fluid intake and output.

(4) Dehydrate daily or every other day with magnesium sulphate 1 or 2 oz. of a saturated solution every 1 or 2 hours until a watery stool occurs.

(5) Small meals every 3 hours with no food or drink in between.

(6) Give varied balanced food low in salt and sugar.

(7) When sufficiently dehydrated balance the fluid intake and output throughout pregnancy.

The dangerously preeclamptic is treated by:

(1) Bed rest, quietude with constant watching.

(2) No food or fluid for 24 hours.

(3) Measure the fluid output during this time.

(4) Spinal drainage consisting of 40 or 80 cc every 3 or 6 hours.

(5) 50% glucose solution or 10% magnesium solution intravenously.

(6) Early magnesium sulphate purging with a saturated solution every hour until effective.

(7) Judge the results by dehydration and not by the blood pressure.

(8) After 24 hours begin feeding every 3 hours.

(9) Control fluid intake and diet the remainder of the pregnancy.

These authorities make special emphasis of the fact that sedation is used only when absolutely necessary, as early consciousness and mental clearing are helpful in further treatment. Out of 116 near convulsive patients and 98 convulsive patients 6 deaths occurred which could be attributed to neglect or some severe

secondary disease.

K. S. Howlett (1935) before the Tennessee Medical Association gave his viewpoint as to treatment. As to diet, he believes in a liberal use of protein - as in nephritis - no salt and a free use of water, unless edema is present. If hypertension, edema, and albuminuria occur the patient is put at bed rest with restricted fluids on a near starvation diet. Glucose is given by mouth to avoid acidosis or hypoglycemia. Magnesium sulphate is given daily with Basham's mixture of iron and ammonium acetate. The severe preeclamptic is treated by bed rest, quietude, purgation and glucose by mouth, rectum or intravenously. For sedation 20 to 30 gr. of chloral hydrate or 6 to 12 gr. sodium amytal is used.

The therapy of the Cook County Hospital is reviewed by Fantus (1935) consists of absolute rest with potassium bromide 4 gm., chloral hydrate 1 to 2 gm., or phenobarbital 0.10 gm. twice or 3 times a day. In addition to this, the patient is placed on a fasting diet with fluids limited to 1000 cc per day and purgation accomplished with magnesium sulphate.

The American Committee on Maternal Welfare in 1935 presented their beliefs as to the correct man-

agement of preeclamptic toxemia and eclampsia. This included:

(1) Bed rest.

(2) Reduced diet - especially meat, protein and salt.

(3) Limit the total fluid intake to the total fluid output.

(4) Sedation by sodium amytal 6 to 12 gr., pentobarbital sodium 6 to 9 gr.

(5) Intravenous magnesium sulphate 20 cc of a 10% solution or intramuscularly 20 cc of a 25% solution.

(6) Intravenous dextrose 250 cc of a 25% solution or 1000 cc of a 10% solution.

(7) Terminate pregnancy if the toxemia can not be controlled.

Before the Minnesota Medical Association in 1935 L. A. Lange outlined a treatment:

(1) Hospitalization in bed.

(2) Quiet, darkened room, no visitors.

(3) Strict milk diet of 1 or more quarts a day depending on the edema. Fluids are not restricted except in the presence of edema.

(4) Sedatives - barbitals, chloral, morphine.

(5) Blood pressure is taken several times a day.

(6) Fluid intake and output carefully checked.

(7) Administration of magnesium sulphate or castor oil.

(8) In the presence of edema - magnesium sulphate intravenously 20 cc of a 10% solution every 4 to 6 hours for 6 doses or a 10 to 20% solution of glucose.

(9) Withdraw 750 to 1000 cc of blood by venesection.

(10) Empty the uterus when a daily output of 5 gm. albumen per liter and a blood pressure of 200 is reached.

McGee (1935) treats his mild preeclamptics with a salt free regular diet. Moderate preeclamptics he places in bed rest and gives 1 oz. magnesium sulphate by mouth. If edema is present fluids are restricted to 1500 cc daily. Blood pressure determinations and urine examinations are done daily. The patient is placed on a preeclamptic diet which he outlines as consisting of (a) no salted foods, (b) very small amounts of meat, eggs, fish, cheese, oysters, oatmeal,

prunes, cranberries, plums and any fatty or greasy foods, (c) eat only well-cooked fresh vegetables. No canned vegetables are allowed, (d) drink no more than 3 glasses of water, milk or buttermilk a day, (e) use sweet salt-free butter, (f) 3 slices of whole wheat bread a day, (g) fruit and fruit juices, (h) desserts - tapioca, cake without salt and eggs, cornstarch pudding, gelatine and fruit ices.

For the severe preeclamptic McGee orders hospitilization with a careful measuring of the intake and output of fluids. Regulation of these is such that the output is 80% of the intake. One dose of 1 oz. of magnesium sulphate is given. If edema is present fluids are limited to 1000 cc a day. The patient is placed on an eclamptic diet and should be on this diet no longer than 5 days. This consists of (a) fruit and fruit juices, (b) water and fruit ices, (c) berries and melons, (d) baked Irish potatoes, asparagras, carrots and lettuce. If the blood pressure is below 140/90 and oliguria is present, ephedrine sulphate 3/8 gr., is administered every 4 hours.

The last author and treatment to be given is the dehydration treatment of M. G. Elliot (1936). Outpatient cases are given printed instructions. They are

told to measure their 24 hour urine accurately. Then the next day their fluid intake should be 1 glass less than this finding. They should keep track of each day in this manner keeping a record of their findings which should be brought to the clinic. 1/2 to 2 tsp. of magnesium sulphate is taken every morning. 4 small meals are eaten daily with no eating or drinking between meals. Meat may be eaten once a day but no salt, sweets, or desserts are allowed. The hospitalized cases are placed on the same type of diet. If these cases are severe no fluids are given the first 24 hours and the amount of catharsis is increased. 100 cc of a 50% glucose solution or 20 cc of a 10% magnesium sulphate solution is given intravenously. Elliot compares his dehydrated group of 20 patients and a non-dehydrated group of 20 cases. This comparison resulted in the following findings: In the dehydrated group no convulsions, abruptio placentae, or macerated fetus appeared. All but 4 of the 40 cases continued to full term. In the non-dehydrated group there was one prepartum convulsive patient, 2 postpartum convulsive patients, one macerated fetus and one stillbirth. 8 of these 20 cases delivered prematurely.

The beliefs and findings of 14 practitioners

have been presented. In the main, these are essentially alike, but each has slight differences in the details of treatment. By way of record, all 14 of these have been presented in as much detail as possible but not by reason of comparison. Whether the treatment is correct or logical only the experienced clinician can judge.

This discussion has dealt with the treatment of the preeclamptic both mild and severe, from the time her symptoms appear up to term, or else to the state where termination of pregnancy is deemed advisable. Before methods of inducing and delivering these patients can be discussed, there are three more or less specialized forms of treatment to be reviewed. These are next in our consideration.

IV. Specialized Form of Treatment.

Besides the more or less generally accepted standardized treatment which we have just outlined, several specialized methods of treatment have been devised. These include methods of using a liver hormone, calcium, vitamin "D", parathormone, and ultraviolet light.

The first method was advanced late in 1927 by H. A. Miller and D. B. Martinez. It involved the use of heparmone, supposedly a liver hormone, in the treat-

ment of toxemia. In 1929 A. M. Mendenhall and L. D. Smith produced clinical evidence that liver extract in the treatment of the toxemia of pregnancy was of little value. They summarized their article by stating, "In summarizing this group of 25 cases, it becomes evident that there was only one in which there was any strong evidence of real benefit from heparmone. It failed to stop convulsions; it failed to prevent convulsions; and it failed to relieve the general preeclamptic symptoms, such as continued high blood pressure and albuminuria. In the one case it failed to benefit the early toxemia of pregnancy."

Consequently, in 1935 Harden, McEllroy, and Huggins, discontinued treatment by heparmone and in its place advanced protein stabilization as the logical treatment. This treatment by diet brings about an adjustment between the protein intake and the nonprotein nitrogen plus protein loss in albuminuria. This diet was high in carbohydrate and low in fat with the ratio of carbohydrate being 4:1 of fat. Clinically, patients seem to improve under such treatment. Such improvement was attributed to the fact that the diet "restores concentrations of the various serum protein fractions and reduces edema". The authors go on to say that, "H. J.

Stander is inclined to agree with the above discussion".

The second specialized form of treatment was developed through the work of Cantarow (1931), Malmejec (1932), Daly (1933), and Landry (1936). This treatment is based on the presence of increased guanidine and decreased calcium in the pregnant woman; the fact that calcium is an antagonist of guanidine; the experimental evidence that guanidine can produce convulsions and clinical evidence derived from the giving of alkaline substances, vitamin "D" and parathormone.

Cantarow (1931) in a discussion on calcium metabolism and calcium therapy, says, "The fundamental importance of the inorganic constituents of the body in the maintenance of normal cellular function, long realized by physiologists, is only now being fully appreciated by clinicians. Unless one is familiar with the significance of calcium metabolism in cellular physiology it is impossible to appreciate the various functional aborations which may result from a disturbance of calcium metabolism."

As to the effect of calcium, Landry (1936), states: "Calcium affects all the tissues of the body. It has a tonic effect on the heart similar to that of digitalis, essential to the normal physiological effect

of the latter: It slows the heart rate, lowers the blood pressure and increases vascular tone. It depresses neuromuscular excitability and increases diuresis in edematous states."

Cantarow (1931) also records: "In normal pregnancy and early labor there is a gradual diminution in the total serum calcium (10.61 to 9.61 mgm), a slight increase in the diffusable calcium (5.08 to 5.55 mgm), and a marked decrease in the non-diffusable calcium (5.53 to 3.49 mgm)."

More experimentation as to the guanidinemia in relation to childbirth was carried out by Malmejec in 1932. He concludes: "There is an increase in the blood guanidine in the late toxemia of pregnancy and this guanidine is neutralized by the administration of calcium regardless of the blood calcium index." Also, Cantarow found (1931): "Guanidine increased in the blood of 8 preeclamptics and 4 true eclamptics". Guanidine administered to dogs on a high protein and low calcium diet gave convulsions, bloody diarrhea, vomiting, stupor, coma and death. When calcium was present in the diet and guanidine was given, the above did not occur.

From these findings it would appear that in

pregnancy there is decreased calcium and increased guanidine. It would also appear that guanidine in the absence of calcium causes many signs and symptoms similar to toxemia and that calcium is its direct antagonist. Consequently, the men interested in this type of treatment experimented on increasing the calcium quantity of the pregnant woman and sought for measures to accomplish this. Landry (1936) found that the metabolism of calcium involved two factors, i.e., the absorption and the utilization. He discovered that absorption involves three factors:

(1) The Hion concentration within the intestines.

(2) The relative proportion of other substances in the diet.

(3) Vitamin "D".

Calcium was found to be absorbed in the upper small intestine and its absorption depended on an acid medium, consequently, calcium was given one to two hours before meals when alkalinity is at its lowest. If the diet contains too much fat the absorption is inhibited for the calcium formed with fatty acids insoluable soaps. Vitamin "D" was found to promote the absorption, assimilation and deposition in the bones of the calcium. Such

were the factors influencing absorption. Utilization, however, was found to depend on parathyroid hormone. This hormone restores and maintains the normal balance between the diffusable and non-diffusable fractions of the serum calcium and elevates the blood calcium.

It remained, then, to clinically utilize this theory involving the administration of calcium or other alkalines, vitamin "D" and parathormone. Cantarow (1931) in 8 preeclamptics and 4 eclamptics gave 10 cc of a 10% solution of calcium gluconate intravenously with prompt and striking relief from the extremely urgent symptoms.

Landry (1936) treated mild preeclamptics with a low protein and fat, and high carbohydrate and calcium diet. The patient was placed in bed rest with frequent sunshine baths. In addition, calcium gluconate, 1 level tsp. (60 gr.) well diluted, was given one hour before meals, three times a day or dicalcium phosphate 1 or 2 tablets taken three times a day. In addition, viosterol 10 to 20 drops twice a day was given. Severe preeclamptics were given parathormone in 20 unit doses by hypodermic and found that such improved the general condition and relieved the immediate symptoms with the maximum effect in about 6 hours. Then in 8 to 12 hours this was repeated with the addition of calcium glucose

and viosterol. Landry found that these patients always improved in 24 or 48 hours.

Another important worker is an Englishman who has based his treatment "on the findings of Cantarow, Montgomery, Bolton, Cameron, Osman, and Close". He is Alexander Daly and in 1930 he published this "Aid in the Treatment of Toxemia of Pregnancy". He also finds that a "diminished total serum calcium exists in normal pregnancy and early labor and is especially low during the preeclamptic state, consequently, the patient should be treated with alkalies, to raise the plasma bicarbonate, to increase the calcium content of the serum, and also, in severe cases, to obtain a relatively rapid action by the introduction of a suitable diuretic by the intravenous route."

In the light of these conclusions, Daly gave all cases of albuminuria and severe and mild preeclampsia the following treatment: 1 tablet every 3 or 4 hours composed of potassium citrate gr. 40, soda bicarbonate gr. 20, and calcium sodium lactate gr. 7½. If the condition was severe he also gave intravenously one ampule of 20 cc of a sterile aqueous solution of soda bicarbonate gr. 20, and the diuretic sodium acetate gr. 20. Also, intravenously, was given one ampule of anhy-

drous calcium acetate gr. 5½, glacial acetic acid 1 minim and sterile distilled water to make 2 cc. Directions for giving these two ampules are as follows: Put the first ampule in 140 cc of water then add the second ampule. Then make the total quantity up to 170 cc with sterile water and give slowly by gravity. This treatment gives a sensation of warmth, temporary breathlessness and a feeling of faintness, all of which pass off in one or two minutes. It causes a cessation of headache, edema and epigastric pain but later a rise in blood pressure, albuminuria and dimness of vision may appear, not as a bad sign, but as a sign of labor. These patients are given a regular normal diet and an increased fluid intake. Daly treated 83 patients in this manner. 2% of these patients required induction and 11% had a premature labor. For control, he had 131 cases not under this treatment. 66% of these required induction and 63% had premature labor.

Such has been the findings of these men in the use of calcium and aiding its absorption and utilization for the purpose of combating a quanidinemia. The results are published here and it is hoped that the experienced reader can draw the correct conclusion from their findings.

The third and last special method of treatment is one which involves the use of ultraviolet light and was brought out in an article, "The Use of Ultra-Violet Light in the Treatment of Preeclamptic Toxemia", by A. T. H. Dixon (1935) of the Edinburgh Obstetrical Society. "This treatment is founded on the belief that in the preeclamptic's blood there are unoxydized by-products of amino-acids and a real hypocalcemia, as brought out by proof furnished by Mitchell, Hamilton, Daykin and Major, and that ultra-violet light is an aid in the utilization of calcium and that calcium is an antagonist of the unoxydized products of amino-acids."

Believing such, the preeclamptic was treated as follows:

(1) Non-protein diet.

(2) The patient strips to the waist and is irradiated on both front and back with ultra-violet light. The dosage is not enough to produce erythema and is first given in daily doses. If the patient improves the doses are decreased to every other day and finally to twice a week until term.

Dixon reports three cases treated in this manner. Blood pressures were taken before and after treatment. Each case had a marked drop in blood pres-

sure following irradiation and an alleviation of symptoms. He concluded that this treatment may not be a sure cure but is an aid in preventing a mild case from becoming a severe one and an aid in carrying the severe case on to viability of the fetus.

This discussion has attempted to bring forth three special forms of treatment which have deviated from the usual form and are presented here by way of interest and in the hope that they may be utilized in all or in part. This concludes the various methods of treating the toxemic patient up to the time when it is deemed advisable to deliver her. Our interest now shifts to the various procedures for carrying out this task.

Methods of Delivery:

When using any of the methods of treatment as previously outlined, the practitioner is ultimately confronted with the problem of delivering the patient, either because she has reached term and gone into labor, or else because she has not responded to treatment and to preserve her life it is deemed advisable to deliver her. Authorities vary also in their beliefs as to the treatment of preeclampsia and eclampsia when they have reached this state. Obstetricians appear to be lined

up in three groups. The first group includes those who believe a caesarian is indicated in every case. The second group includes those men who vary their form of treatment and make it fit the case, consequently, this group permits natural labor to take place in some cases, carry out induction in others, and caesarian section in the remainder. The third group is composed of men believing that caesarian is never necessary and either induce their patients or allow them to go into labor of their own accord.

John M. Bergland (1935) is strongly opposed to any form of delivery other than caesarian, the reason being, "We believe that the ordinary induction of labor takes so long that the patient may have convulsions before delivery". Therefore, "delivery is affected frequently by caesarian section." Caesarian is also most frequently used by R. T. LaVack, although in mild cases he sometimes resorts to medical induction. He says that indications for caesarian are:

(1) Border-line cases and preeclampsia increasing in severity.

(2) Toxemia developing rapidly and a hard cervix.

(3) Late childbearing age.

He goes on to bring out, however, that he does induction and uses a modified Stroganoff with version or forceps at an acession of convulsions if labor is not in progress. For induction he uses morphine and a Vorhees bag, plus a weight. After one hour 20 gr. of sodium bromide is given and then chloral hydrate every two hours. The placenta he expresses manually.

The second group of men vary the method of delivery according to the case. Occasionally the case is delivered via naturalis, at other times the patient is induced with variation in the methods of induction, and occasionally a caesarian is done.

In 1932 McGoogan reported 30 cases with the methods of delivery employed and the results. One patient refused treatment and was dismissed and delivered. 7 were admitted in labor and delivered via naturalis. Two were induced with a Vorhees bag. 10 fell into labor spontaneously and delivered. 10 were delivered by caesarian section. Out of the 29 mothers there were no deaths. 30 infants were born (one pair of twins) with 4 fetal deaths or a mortality of 13.3%.

H. J. Stander and J. F. Cadden (1934) reviewed treatment of 43 preeclamptic patients and presented their findings in the interesting chart included:

Type & Result		No. of Patients
Castor oil and quinine induction	Successful	3
Castor oil and quinine induction	Unsuccessful	0
Castor oil and quinine and nasal pituitary	Successful	5
Castor oil and quinine and nasal pituitary	Unsuccessful	5
Morphine only		1
Insertion of bougie and medical induction		4
Insertion of bougie and medical induction and Stroganoff		1
Modified Stroganoff		3
Modified Stroganoff and medical induction		1
Caesarian section		2
No treatment but rest and toxemic diet		18

Of the total 43 patients treated no mothers died and only 2 fetal deaths occurred.

McGee (1935) says: "It may be possible with careful management to carry a preeclamptic to viability of the fetus, or even to full term", at which time he delivers all multipara from below. Primipara, however, he treats differently. First he determines the state of the cervix. If the cervix is soft he dilates it and strips the membranes at the internal os and starts medical induction. If no labor insues he packs the

cervix with gauze, ruptures the membranes and gives small doses of pituitary or inserts a bag. If this treatment is not successful the case is "nearly always a disproportion of parts". If such is the case, he believes in doing a low cervical caesarian section under local. He includes also the use of forceps and episiotomy under parasacral or local anesthesia.

Stander (1937) uses the bougie for the induction of labor in multipara, allowing labor to proceed to the second stage, at which time he applies forceps. In primipara, the usual treatment is caesarian section under local, spinal or perhaps by an avertin anesthesia. An inhalation anesthesia is never given.

The third group of men believe that caesarian section is never necessary. J. O. Arnold (1932) says: "Caesarian for eclampsia has not been done in five years". His treatment consists of first controlling the toxemia, second re-establishing a safe fluid balance and then interferring with the pregnancy by induction or natural labor.

W. Stroganoff firmly believes in early rupture of the membranes as the logical treatment of toxemia. "In severe cases of severe eclampsism where the patient has not responded to hospital treatment, rup-

ture the membranes if the os will admit one finger." With this treatment, used in 16 cases of severe pre-eclampsia, two had convulsions prior to delivery and four had convulsions after delivery.

K. S. Howlett (1935) outlines a method of induction which he says can be used in the home. This consists of dilating and packing the os, insertion of a rubber catheter, puncturing the membranes, and cautious use of small amounts of pituitary.

L. A. Lange (1935) admits that induction by bougie or bag depends on the condition of the cervix. The second stage he shortens by forceps or version. This treatment depends upon the station of the head. He disbelieves in the use of chloroform and employes nitrous oside as the anesthetic.

The American Committee on Maternal Welfare outlines two methods of induction, one to be used if the need is not urgent, and the other if the need is urgent. The first consists of the use of castor oil and no more than 20 gr. quinine sulphate. With this 5 or 6 doses of one to two minims of posterior pituitary extract, repeated at ½ hour intervals subcutaneously is given. If the need for delivery is urgent, in addition to this the membranes are ruptured.

H. J. Stander (1929) in an analysis of 801 cases of toxemia of pregnancy found 24.3% of the pre-eclamptics were induced. Maternal mortality for pre-eclamptics was zero and fetal mortality was 18.9%.

The treatment used by three groups of men has been reviewed. The first group is radical in the use of caesarian section. The third group is ultra-conservative and the second group is a combination of the two. Results in all three groups from the figures given appear more or less the same. Perhaps the experience of the reader will aid him in selecting the proper type of delivery to be used in these severe pre-eclamptics or eclamptics.

PROGNOSIS AND POST PARTUM CARE

At first sight it would seem that after the patient is delivered the Doctor need not worry as far as the toxemia is concerned. However, recent studies and reviews have brought out the fact that the toxemic patient needs careful watching over a period of many years, in an attempt to discover any harm which the toxemia may have done and forestalling the same occurrence during the next pregnancy.

Mortality:

Figures seem to vary greatly as to the immediate maternal and fetal mortality. McGee (1935), after a study of many preeclamptics and eclamptics, reports that he believes the maternal mortality runs from 10 to 30% and the fetal mortality from 40 to 60%. Schumann (1931) reporting on 111 cases, places the maternal mortality at 5.4% and Tillman (1935) records a fetal mortality of 24.1%. McGoogan (1932) reports 30 cases with a fetal death of 13.3%. H. J. Stander reviewing 43 preeclamptics gets a maternal mortality of 0 and a fetal mortality of 5% and later reviewing 74 cases of preeclamptics had a maternal mortality of 0 and a fetal mortality of 18.9%. DeLee (1934) states: "Recovery is usually complete and the child usually lives."

Postpartum Care and Advice:

Immediately after delivery it is extremely important that the deliverer remain with the patient at least one hour for it is not rare for postpartum convulsions to occur. Consequently, careful watching with sedation should be the immediate postpartum treatment. (American Committee on Maternal Welfare 1935)

McGee (1935) advocates continuous check of the blood pressure and urine and says these should be normal by the end of the lying-in period until the 6th week postpartum examination. The patient should be on a preeclamptic diet. At the end of the six weeks a blood pressure and urine examination is done. Any lacerations of the cervix are repaired and erosions cauterized and all rhetroverted uterii are brought forward and a Smith-Hodge pessary used for one month. Before dismissing, the patient should be instructed in the use of contraceptives and should practice contraception for at least two years "to avoid change to chronic nephritis on subsequent pregnancy". Mussey (1931) also advocates that "a woman who had preeclamptic toxemia should not become pregnant again until one year or more has elapsed and only after examination and extension of the functional ability of the kidneys to stand the

strain of pregnancy has been done".

Complications:

Complications of severe preeclampsia and eclampsia are:

(1) Recurrent toxemia.

(2) Renal damage.

(3) Hypertension.

It is because of these three that the care of the toxemic patient does not stop with her dismissal from the hospital at the end of the lying-in period. Because of these complications she should be constantly watched.

It is well known that the toxemic patient seems to be pre-disposed to further attacks of toxemia. J. D. Peters (1938) kept track of 198 patients who had had one attack of some toxemia of pregnancy. 37 of these had no further pregnancy. Of the 161 remaining only 8 were known to have escaped recurrence of toxemia in later pregnancies. 144 patients had 213 subsequent attacks of toxemias of varying severity. Out of 203 other patients 34% had subsequent attacks of toxemia. Bear (1934) reports recurrent toxemia in 2 to 5% of cases.

The second great complication is the presence of some renal damage following the toxemic attack. C. A. Eldon (1936) reports: "50% of preeclamptic patients

show evidence of renal damage by urea clearance studies three months after delivery". Bear advances the idea that nephritic toxemia is very apt to appear in later pregnancies because of some renal damage occurring during a previous attack. J. D. Peters (1938) observed 203 patients over a long enough period of time to permit deductions concerning the ultimate outcome. He discovered that 49 patients or 24% had died with evidence of renal or vascular disease. 70 patients or 34% were known to have residual renal or vascular disease. 69 patients or 34% had subsequent attacks of toxemia. 15 patients or 8% are alive without residual incapacity one year or more after the most recent attack.

The last complication and one closely linked with the preceeding one is that of hypertension. This has been closely analyzed and well presented in a recent article by J. E. Wood, Jr., and H. Nix (1938). "It is too common to discharge patients from the hospital and say they were all right because their blood pressure is normal. As the records show, there is a sudden drop after pregnancy, lasting about two weeks. This is due to the fact that the patients are in bed during those two weeks and are inactive, and that the recurrence of hypertension afterwards is due to the

fact that they are up and active." In a group of 500 patients with antepartum blood pressure of 140/90 or higher the older the age incidence the greater the tendency toward postpartum elevation in blood pressure. 75% of patients 35 years of age or over leave the hospital with an elevated blood pressure. Their entire findings are given in a complete chart reviewing 500 cases of the late toxemias of pregnancy.

500 CASES OF THE LATE TOXEMIAS OF PREGNANCY

Age Groups	No.of Pts.	Systolic 250	200	170	140	Diastolic 150	130	110	90	B.P. Above 140/60	B.P. Below 140/60	Convul-sions	Albu-min
15-24	240	6	21	89	124	11	44	127	58	106	134	68	204
25-34	149	9	32	50	58	12	29	80	28	94	55	19	117
35-44	105	17	20	44	24	12	26	41	26	77	28	8	80
45-54	6	1	3	--	2	2	--	4	--	5	1	1	4
B.P.on discharge above 140/90	282	30	58	90	104	30	72	131	49	--	--	51	220
B.P.on discharge below 140/90	218	3	18	93	104	7	27	121	63	--	--	48	185
Gravid 1	229	7	24	89	109	11	40	122	56	96	133	68	208
2	51	4	8	15	24	4	10	27	10	28	23	11	43
3	42	2	3	18	19	2	6	25	9	30	12	8	35
4	29	1	13	5	10	3	11	10	5	23	6	3	14
5	27	2	3	11	11	3	5	15	4	18	9	2	21
6	20	3	5	8	4	2	6	10	2	18	2	1	14
7	22	--	4	10	8	2	4	8	8	13	9	2	17
8	9	1	--	6	2	--	2	4	3	5	4	1	6
9	15	2	1	6	6	1	3	6	5	8	7	--	8
10	16	2	4	4	6	3	1	9	3	14	2	--	8
11	13	1	5	3	4	1	4	7	1	9	4	2	7
12+	27	8	6	8	5	5	7	9	6	20	7	1	24
Convulsions	99	4	21	38	36	8	23	60	8	51	48		
Albumin	405	33	67	153	152	35	86	201	83	220	185		

In this section the author has attempted to bring out a few of the figures that have been presented in regard to maternal and fetal mortality. Also, the beliefs of several authorities have been recorded as to postpartum care during the lying-in period and later life of the patient. Three outstanding complications have been reviewed. These include recurrent toxemia, renal damage and hypertension. With this we close what we believe to be the last step in caring for the patient whom we know to be preeclamptic or eclamptic.

SUMMARY

These writings have been chiefly concerned with severe preeclampsia, however, where the author has deemed it advisable to include mild preeclampsia and eclampsia, this has been done. Because there is such a slight difference these three diseases appear to be only three stages of one disease. Consequently, in order to understand what has already occurred to our severe preeclamptic and what may occur, deviation into these two other extremes were considered excusable. Small summaries have been given at the end of each section and since the purpose of this writing was to give no conclusions, but only a presentation of historical and present day concepts, it would be superfluous to reiterate those various summaries here. The author's idea as to correctness and clinical practicability of all the theories and practices reviewed in this record has been omitted because of the lack of clinical experience and judgment on behalf of the writer. By way of summary then, a chart of 59 leading authorities throughout the world has been prepared. This chart in part is taken from H. J. Stander (1929) but has been amended by the author to include the various authorities whose works have been outstanding since 1929. These

authorities and their treatment are given in the hope that it will aid the reader to arrive at a correct conclusion as to the generally accepted, successful treatment used throughout the world.

Arnold	Conservative	plus H_2O balance
Bailey, N. Y.	Conservative	
Bauch	Conservative	
Bear	Conservative	
Bech	Conservative	
Brindeau, Paris	Radical	
Caldwell, N. Y.	Conservative	plus paraldehyde
Cantarow	Conservative	plus calcium
Daly	Conservative	plus alkalis
Danforth, Evanston	Conservative	plus venesection
Davidson	Conservative	
Davis, Milwaukee	Conservative	plus magnesium sulphate
DeLee, Chicago	Radical	
Dickson, Edinburgh		ultra-violet ray
Dieckmann, St. Louis	Conservative	plus magnesium sulphate
Duncan, Montreal	Conservative	
Ehrenfest, St. Louis	Conservative	occasional section
Fantus, Chicago	Conservative	
Foulkrad, Phila.	Conservative	plus induction (by rupturing membranes)
Harden	Conservative	plus protein stabilization
Holmes, Chicago	Conservative	
Howlett, Tenn.	Conservative	plus glucose and late rupture of membranes.
Johnstone, Edinburgh	Conservative	plus colonic lavage

Keller, Phila.		Autogenous vaccines plus middle line therapy.
Kellog	Radical	
King	Conservative	
Landry	Conservative	plus calcium, vitamin "D", parathormone.
Lang, Minn.	Conservative	
Lazard, Los Angeles	Conservative	plus magnesium sulphate
Litzenberg, Minn.	Conservative	plus venesection
Malmejec	Conservative	plus calcium
Martinez		Heparmone
May		Fluid balance
McGee, Alabama	Conservative	
McGoogan, Omaha	Conservative	sodium amytal
McNeile	Conservative	plus bag or rupture of membranes.
McPherson	Conservative	
Miller, New Orleans	Conservative	
Miller, Pittsburgh	Conservative	plus heparmone
Mussey, Rochester	Conservative	
Newell, Boston	Conservative	
Peckham	Conservative	
Piper, Phila.		middle line therapy
Plass, Iowa City	Conservative	
Ploussard		large amounts of magnesium sulphate

Polak, Brooklyn	Conservative	plus magnesium sulphate
Ross		nembutal
Rucker, Richmond	Conservative	plus magnesium sulphate
Schumann, Phila.	Conservative	plus occasional section
Solomons, Dublin	Conservative	plus gastric and colonic lavage.
Spalding, San. F.	Conservative	
Speidel	Conservative	
Stander	Conservative	first, radical late
Stevens	Conservative	and then late caesarian
Titus, Pittsburgh	Conservative	plus glucose
Ward, N. Y.	Conservative	plus bag induction
Williams	Conservative	
Wilson	Conservative	
Zubrzicki	Conservative	

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