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Etiology and treatment of eclampsia

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INTRODUCTION

Obstetrics has as its status a progressive branch of medicine. The progress in the past has blended with its environments and the progress of civilization. This branch of medicine deals with the physiological as well as the pathological state of pregnancy. There has always been aid given to the child bearing mother, if not from others in her surroundings, then by herself. The women trained themselves in some places to take care of their fellow friends and visa versa. Though help was needed in practically every case, there was no advancement in this line of medicine for nearly two thousand years.

Since women took care of women, it was thought to be a woman's duty. Those who made it their work to take care of pregnant women were of a low cast, and had no desire to make it a progressive medicine. When a difficult case was encountered, a priest was called in, but he did not get into the sick room, nor did any other man. Consequently the practice remained in a state of rigidity. The title of meutai-man-grand-mother was given by the Greeks at Hippocrates' time to a man who was called in on the difficult cases.

Then there came the great man of the age, Hippocrates, a Greek, who advanced this line of medicine and started it on the
incline to to-days standing. Hippocrates mentioned in his writings that convulsions were found in women who often complained of headache, and who had a tendency to sleep. Hippocrates coined the word "Eclampsia" from the Greek word meaning a shining forth or a flash, and to denote a fever of sudden onset.

Chamberlain invented his forceps in about the year 1600, but they were not widely used.

As time went on the women became more educated, and conditions in general improved. The men became more skilled, and more experimental medicine was started. As the men became more educated, the women gradually withdrew from this line of medicine, and now it is thought to be a man's job to deliver a baby. Though at present, among the lower class of people the primitive condition can often be found still existing. Here we find the antiseptic midwife, perfected caesarian, and the axis traction forceps, which all belong to the empirical period.

Many writers classify the history of obstetrics into periods, the first called the empirical obstetrics, which takes the practice from the earliest time to the middle of the sixteenth century; the latter period called the scientific state, which begins with the discovery of podalic version in 1550.
Gehler, a German writer, and a student of obstetrics in the eighteenth century, used the word "Eklampsia" to distinguish the convulsions that were sometimes found in the practice of obstetrics as a specific disease. At present the word is used to call attention to a disease of acute toxemia of pregnancy, which is characterized by clonic and tonic convulsions, followed by varying degrees of coma. It would probably be more fitting to define "Eclampsia" as a symptom-complex, resulting from pregnancy, and having cerebral phenomena as the outstanding characteristic.

Throughout the literature of the eighteenth century, many excellent descriptions of the disease can be found. Amberg wrote a splendid description of the convulsion in about 1713, with the treatment with nervous powders and phlebotomy.

The text-book on midwifery during the latter part of the eighteenth century and early part of the nineteenth century contained considerable information about "the epileptic fits" occurring in the last few months of pregnancy. At this time they considered the "fits" caused by fetal irritation to the uterus, sudden emotions of the mind, or a blood plethora, and epilepsy.

In Alexander Hamilton's publication on the elements of the practice of mid-wifery, which was published in 1775, he states that the disease was noted in people having plethoric sanguine habits, and that it could only be cured by the bold
use of the lancet, by an open belly, a cool regimen, and spare diet. He noted that when the toxémia occurred in the latter months of pregnancy, it was to be feared much more than when seen in the early part of pregnancy. Hamilton states here that toxemia was generally preceded by the irritation caused by distention of the uterine fibers, by pressure on surrounding viscera causing visceral congestion. Hence there was an altered function of the organs in general.

The scope of this paper does not permit a discussion of the various interesting historical developments and controversies that followed these descriptions, except insofar as they enter the subsequent presentation.

Before proceeding it should be stated that the etiology and treatment of eclampsia are the subjects that will be dealt with mainly. The other phases, symptomatology, clinical and laboratory findings, differential diagnosis and diagnosing will be mentioned only briefly, merely to give unity to the description of the disease.

Perhaps before going farther, we should take this opportunity to call a distinction between pré-eclampsia and eclampsia. Pré-eclampsia taken in those cases presenting the signs, symptoms, and laboratory findings of eclampsia without the state of convulsions. After the woman has a convolution, she then goes into the eclamptic classification. Since pré-eclampsia and
Eclampsia are so closely related, we will give the symptoms and signs of both together.

Symptoms taken from "Principles and Practice of O.B." De Lee.

1. 1. Has predisposition to last three months of pregnancy.

2. Primeparity, multiple pregnancy, and hydramnions, predispose to disease.

3. General dibility, a tendency to sleep.


5. Anorexia for certain foods.

6. Then following we note, headache of frontal in type, disturbance of the senses.

1. Black spots before the eyes.

2. Bright light often effects the eyes.

3. Often note hemiaopsia, or complete blindness.

4. Tinnitus, and often deafness.

2 Physical.

1. Edema of feet, eyelids and often general.

2. Pasty skin and coated tongue.

3. Feted breath.

4. Tenderness over stomach.

5. High blood pressure, pulse pressure low, because diastolisis has increased over other.

3. Laboratory.

1. Urine.

2. **Albumen.**

3. **Hyalin casts, granular cast, with low urea output.**

2. **Combining power low for carbon dioxide.**

3. **Blood.**

   1. Red cells have increased fragility.
   2. Coagulation time is decreased.

4. **Symptoms just before a convulsion.**

   1. Twitching about the eyes, cheeks and legs.
   2. Eyes dilated, before fixed and turned up.
   3. Then go into convulsions.
ETIOLOGY OF ECLAMPSIA

Zweifel has called eclampsia the "Disease of Theories," and to-day this is still true. In the latter part of the seventeenth and the early part of the eighteenth centuries the disease was thought to be due to disorders of the nervous system.

Merriman in 1820 regarded it due to an overloaded state. Willson in 1833 called attention to the increased urea of the blood as the etiological factor. Then by the finding of albuminuria a few years later led to the uremia theory.

1. Bouchard in 1887 thought this disease was due to the accumulation of some auto-intoxication substance in the blood of an eclamptic person. While her blood increased in toxicity, the urine decreased. This he said was due to the failure of the kidneys to secrete the poisonous products formed within the body. Tash took rats and injected some with normal pregnant blood, some with eclamptic blood, and in neither did he find any effect. But in general we may look for two types of toxins, that which is already present, but has increased in amount, and that which is abnormal and gets into the blood system. Those of the first group are sodium, calcium, potassium, magnesium, etc. Those of the latter are foreign protein as tyramine, histamine, etc.

2. In the first group, bio-chemistry study has thrown little light upon eclampsia. With a disease of such severity, with such fulminating clinical manifestations, it is of great interest
to know that chemistry has given us little knowledge about metabolic changes.

There has been found a decrease of calcium in the blood during the state of eclampsia, but the symptoms are much different from disease which is caused by calcium deficiency.

It must be remembered that the calcium is divided into ionized and non-ionized divisions, and that there must be a definite ratio of these to each other. Samson and his co-workers found a group of eclamptic, acute liver damage cases, which had constant changes. They found an increase of quanidine in the blood with a decrease of blood sugar, with unaltered calcium. Now if calcium in some form was injected intravenously, the calcium level would keep the same and accompanying it the sugar content of the blood returned to normal, with the decrease of eclamptic symptoms. But when glucose was given by mouth the symptoms were not relieved. Therefore the significant factor must be the increased quantity of quanidine in the blood, showing that there is a disturbed metabolic process taking place.

3. The second group of foreign products will be discussed under pathological changes.

In 1902 Veit advanced the theory that toxemia was due to the chorionic villi and fetal ectoderm entering the maternal circulation. It then underwent protein degeneration with the formation of a toxic which he chose to call syncyto-toxic. He said that under normal conditions the maternal blood contained sufficient anti-bodies to neutralize this, but if it
kept piling up, in time the decompensation products would exceed the other, which would end in eclamptic symptoms in proportion to the excess toxin. This he proved by injecting an emulsion of human placenta into the peritoneal cavity of a rat, and it caused death. He states the product found here was leucin which injured the hepatic vessels which hindered the capillary circulation and resulted in thrombosis, cloudy swelling, necrosis and even autolysis of the substance of the liver.

Since the above could not be proved definitely, McQuarrie (I suggested that the cause of this disease is an accidental transfusion of incompatible blood between mother and child, as a result of opening of placenta sinuses between the two circulations. He also found in 180 cases that the condition increased in those cases where the fetal and the mother's blood were incompatible. He arrived at the conclusion by injecting methylene blue into the umbilical artery, and found that the mother secreted it in her urine. This they thought had to be explained on the base of a direct communication between the two circulations.

In a series of 118 cases the mother's blood was examined for agglutination power when mixed with blood of their own children. In 24 cases the mother's serum agglutinated, or laked the red cells of the child. Of these 24, 15 had perfect placentas, and not one of these showed a sign of eclampsia. In the other 24, those having incompatible blood, nine showed blue urine. Of these seven had actual eclampsia and two had albuminuria.
An autopsy was performed on one patient, and the dye was injected into the umbilical vein, and was seen to pass out of the uterus through its veins. Therefore McQuarrie says that eclampsia is nothing but a communication between the two circulations. He says it can be produced by injecting foreign blood into animals, resulting in exactly similar symptoms.

In this condition if maternal blood passes to the fetus, this will cause a similar condition in the child, which explains why a fetus of a toxic mother generally causes such high mortality.

This theory explains the rapid lightning onset of the disease, and why it occurs more frequently in women who have a small pelvis, an enlarged uterus, and in those having twins. This, McQuarrie says, is due to the fact that since the uterus is much enlarged, the contractions are much stronger in proportion to the size of the uterus, and have more of a tendency to separate the two circulations and cause an interchange of blood.

Liepman later came out with evidence against the methylene blue injection. He states that the normal placenta is not entirely impervious to the dye. Because if injected subcutaneously into the mother before parturation, it may appear in the child's urine. A few years following, the above theory was retracted, because it was found that the mother's blood would not agglutinate her child's blood. He then changed his idea and
substituted another in which he said that due to the increased fibrinogen and fibrin ferment in the blood of the mother, there was an increased coagulation of the blood. Here he foregoted that the child's blood serum might agglutinate, or lake its mother's red cells and cause a great disturbance.

Cathola and Rasle were of the opinion that interagglutination of maternal and fetal blood may be a factor in the cause of this condition. Out of some ninety two cases of pregnancy, in twenty five of the cases, the blood of the mother and that of the offspring were of a different type. This showed a blood incompatibility in fourteen per cent. In twenty per cent. of twenty nine cases tested, the blood of the mother and that of the fetus was different. Blood incompatibility was found in three women showing albumin in the urine. But after this work on this condition they came to the conclusion that since there was no iso-agglutination, this condition of incompatibility of maternal and fetal blood was not the etiological factor of eclampsia.

In the early study of eclampsia, it was known that the death of the fetus caused recovery in the majority of cases. This led to the idea that this disease was probably an end result of fetal metabolic products. But it seemed strange then why the mother would recover from this if she was properly treated. Then Folk advanced the theory that the disease was probably caused by the fetal products. But again this was disproven by the fact that eclampsia does occur with hydatidiform mole. Wigger in 1928 reported eight cases of hydatidiform mole with eclampsia, which seems to rule out fetal products as
the cause. He then advanced the theory that it was due to an altered function and secretion of the chorionic epithelium of the placenta which is found in both conditions. But this still remains a question to be settled.

Cheinesse attributes the cause of eclampsia to the toxin coming from the placenta. Many experiments since have been worked out to find the toxic factor, but all have been in vain.

Young states that the toxin is formed by placenta infarcts which form decomposed products between the infarct and the uterus. This product they thought went to the liver and here produced degeneration of the liver, resulting in eclampsia.

In going back into the history of placenta disturbances it was noted that Williams in 1886 noticed the presence of many infarcts in the placenta. In trying to find the cause, he never associated it with toxemia. He found them present in sixty three per cent. of his cases, and of all grades and varieties.

Then Young in 1914 connected the large incidents and numbers of infarcts with the cause of toxemia. It is without doubt that some of the infarcts are the result of physiologic endarteritis which would undoubtedly be greater towards the end of pregnancy. But by this process there is a gradual shutting off of the blood supply to the part. The products of necrosis are not in high enough concentration to cause coagulation of blood on the maternal side, thereby making the villus undergo hyalin changes. If there had been rapid shutting off of the blood, the intervillous
maternal blood would undergo necrosis with formation of toxic products.

In the slow forming infarcts, it is thought that the patient is protected from the autolysis of the placental proteins by the formation of a protective zone of hyaline-like material around the placental villi, thus preventing the absorption of necrotic substances. This then gives us an explanation as to why the large firm infarcts give no toxic symptoms. Again, similar infarcts may be produced by the result of trauma of the fetus, causing a rupture of placental vessels on the fetal side, resulting in the formation of an infarct.

Williams and De Lee have stated that abruptio placentae may occur unexpectedly in toxemia, and that cases of toxemia may develop abruptio placentae. Since these two occur quite often in the same patient and under similar conditions, one might think that they are due to similar causes and condition. If one examines the placenta, the only difference found is in the location of the infarct. If it lies in the central portion, the toxic products from the necrotic tissues diffuse through a wider area of placental tissue, and do not become concentrated enough to cause further destruction of the basal portion of the placenta. In this case they may be one that develops the toxic symptoms rather than abruptio placentae. While in a case, if the infarct is close to the maternal surface, the concentration of the toxic substance may be sufficient to
cause dilation and rupture of the sinuses, with extravasation of blood and separation of the placenta. If the above be so, then animal experiment should help confirm the above statements.

In the first experiment, an extract was made by a placenta, and 1 c c. was injected into a rabbit for ten days. Then a necropsy was performed, and a hemorrhage was found in the tubes and glomerule with marked congestion of the kidney. The liver and fallopian tubes were all congested. In the second experiment, normal placenta was used to make an extract, and a pig was used. It was injected intravenously and subcutaneously. Three days after the last injection, the pig developed convulsions, which lasted two hours, and resulted in death. At autopsy a large liver with cloudy swelling, fatty degeneration and necrotic areas were found. The kidneys showed about the same as the other organs.

In another experiment, normal and infarct placentas were used to make extracts. Here the same effects were found as in the two preceding cases.

Therefore the protein split-products of placental autolysis when injected into a rabbit and a pig produced poisonous effects, which both clinically and pathologically, are very similar to those of eclampsia.

Williams states that same results can be obtained by making an extract of other organs as well as of the placental. But Bartholomew and Kroche think that this is no objection to the cause of eclampsia from the products of pl-acental autolysis,
because they think that we are dealing with a protein split-product common to all tissues. We know that if necrosis takes place either in body or in test tube, that there is yielded a highly toxic protein split-product. We also know that the liver, kidneys and spleen are organs that yield readily to the toxic agent, when the detoxifying agents are overpowered. They also undergo autolyses much more readily than muscle, and when they do they in turn produce an increase in the toxic agent within the body. A similar condition can be seen with burns of severe nature, acute yellow atrophy of the liver, and many other diseases.

Gessnu states that women are the only species having eclampsia, and that there are many species of animals having a similar circulation and placenta. So it seems improbable to have the condition in one and not in the other. He states that it is probably caused by some toxic agent from the placenta. In other cases there can be a large quantity of toxic substance from the placenta and the disease will not develop. Therefore Seletzky states that the disease must be of toxic nature coming from internal secretions, and particularly from the placenta.

Zweifel injected albumin from the placenta and the fetus into another animal, and produced no hypersensitiveness as one would expect, so he concluded that this is not due to an anaphylaxis as it was thought to be.

Stern and others found that colloids and crystaloids do
not pass through the placenta; while if the carbon dioxide content of the blood is increased, there is a greater permeability to these substances, and may let toxic substances into the maternal blood. But the placenta is regarded as a protective mechanism to both mother and the fetus. Its function is similar to that of the liver. It decreases in size as the fetus develops, enough so that it can take care of its own carbohydrates storage. Many think that the placenta acts as a semipermeable membrane and it determines what shall pass it. Fats and lipoids cannot pass while amino acids and carbohydrates can pass readily.

The bacterial origin was mentioned in 1884 by Delore as the etiological factor of eclampsia, but from that time on many have thought about it, but haven't been able to decide anything very definite about it. Talbot believed that all of the toxemias are closely associated with some foci of infection, but that no definite bacteria can be found as the cause. They all agreed that some chronic infection within the body may lower the function of the liver and kidneys and thus predispose to some abnormal function of the body organs.

Lawrence found in a series of cases from the St. Mary's hospital, that there was an increase of incidences of eclampsia following certain types of diseases. He had 1708 cases which he divided into two portions. The first contained 907 cases and the second 801. In the first group 280 cases became toxic, 186 mild toxic stage, 89 very toxic, and 5 had convulsions.
To this group he gave prenatal care and cleared up all signs of foci of infection, and any other disturbances found were treated. In the second group which received none of this prenatal care, 28 cases had convulsions, and many of the other stages were found.

Then from going over the history of each patient, and knowing the type of prenatal case she had, he found that the incidence of eclampsia bore a close relation to disease contracted previously to pregnancy. He also found that certain diseases preceded eclampsia more than others, such as general infections, influenza, pneumonia, acute inflammatory rheumatism, scarlet fever, furunculosis and typhoid. It was found also that the mortality increased if the patient contracted some chronic organic defect preceding pregnancy or during it. Those organic functions vary in importance as to the order given, functional defects of the intestinal apparatus, renal defects, cardiac defects.

In the 1927 State Medical convention, attention was drawn to the finding of tyramine in the blood, vomitus, gastric contents, and the urine from an eclamptic patient. A theory was put forth trying to explain the findings. They said that the presence of bacteria or their products acting on amino acids, circulating in the vascular system of eclamptic women led to the formation of the poisonous products found. The amino acids are found in increased quantity in cases of resent placental infarcts or ingestion of large quantity of meat, or from retention of certain products. Then with the presence of some foci in the body, amines may be formed in sufficient
quantity to produce toxic effects. In this theory stress was placed on the following: That the placenta was the most possible source of toxin; that infection must be present for the production of amines; and that kidney dysfunction and the circulatory handicaps of pregnancy make for a more probable development of the toxemia. An examination was made on ninety cases and none showed any sign of histomin. From this the opinion was drawn that facial infection of the teeth, tonsils, and so forth, acted only to lower the general resistance, thus giving the colon bacillus a better chance to work in the organism. This explains why a pregnant woman has lowered resistance to coli bacillus. The bi products from these bacteria are known as antagonistics to the normal functions of the body. To help confirm this idea Johnson reported many cases showing how frequent were breast abscesses, pyelites, hemorrhage, miscarriages and so forth.

Kellogg states that toxemic patients are very prone to develop infections during puerperium.

La Vaile states that the primary cause of thrombosis of the uterine vessels, is due to the presence of bacteria. But we should not be alarmed about infection being the cause, for it was cited back in 1884 that this was probably the cause. But to-day we are no closer than we were then to a definite answer.

From this work on infection it would be advisable to treat every case of pregnancy not only as such, but from the standpoint of infection as well.
to explain some of the facts found in eclampsia, many have attributed it to some altered condition of the blood. In normal pregnancy there is an increase in blood volume, with resultant changes in hemoglobin, hematocrit and serum protein. There is also a change in the cholesterol, lipoids, surface tension and so forth.

In eclampsia we note a further concentration, as this may be relative or absolute. The hemoglobin, hematocrit, and serum protein are not all increased in proportion. There is also an alteration in blood volume, thought to be due to the altered protein of the blood. These are all accompanied with retention of water and salt.

Frank states from his experience that there must be a definite toxin in the blood that produces destruction of liver cells, as is found in the pathological study of that organ. If products are injected into the blood of a toxic nature we get similar pathological effects. If a test, such as the Rosenthal, be run on the liver, we will readily find impaired function. From this result we get altered sugar metabolism. The blood sugar is lowered. The carbon dioxide combining power is lowered, which moves the patient towards the state of acidosis, because the fats are not undergoing complete combustion.

In examining the blood of fifty cases, Walters found there was a marked decrease in the blood sugar content, and lowered carbon dioxide power, while the nitrogen products of the blood remained at the same level. It has been found if the liver
is removed that sugar in the blood rapidly falls, because it has no place to draw from. Therefore it alters the blood sugar, and indirectly alters the protein control.

In 1926 the Maryland Medical School came out with a report on a series of seven cases having from one convulsion to eight, in which the blood sugar was checked every so often. It was found that there was a great fluctuation of blood sugar in this condition. Just before a convulsion was to come on, there was a drop in the blood sugar, and a rise of blood sugar following the attack. The fall of blood sugar did not stay in normal limit, but fell into the hypoglycemic state. Then following the convulsion the blood sugar rapidly went into a hyperglycemic state, rather than coming back only to the normal blood sugar level.

From the nineteen cases studied by Titus, he states that he has conclusive evidence of the great frequency and preponderance of low normal or subnormal blood sugar level in pre-eclampsia.

In the majority of patients, there was an increase of the red cells. The average is a little above normal to 9,500,000, but this is not a definite level, as it varies from hour to hour. This was first thought to be due to the convulsions causing an increased number of red cells, but after some time it was found to be due to the serum migrating from the blood vessels into the tissues, and vica versa. In a normal pregnancy you never see a flexation of the red cells over 1,200,000, and in general is about constant.
If a woman suffering with chronic nephritis becomes pregnant, she may abort, or later on have accidental hemorrhage, or go into an eclamptic state, or she may develop a hemorrhage, then develop albuminuria and finally go into eclampsia, though the hemorrhage is not the cause of the eclampsia, or the renal insufficiency, it is attributed to some other cause. In eclampsia renal lesions are found, but they are far out of proportion to the severity of the attack. Therefore it is thought that the renal state has no direct relation with the toxemia, and if so the renal lesions should commensurate with clinical picture. It is true that the kidneys are involved in eclampsia, because we always have preceding the convulsion, oliguria and anuria, and this functional disturbance precedes the disease.

Eclampsia and diuresis are incompatible with eclampsia. Then for our treatment, elimination of fluid should be produced. Then we run into the snag that chronic nephritis patients when becoming pregnant, rarely become eclamptic. Therefore we can conclude that eclampsia depends on other factors than inefficient kidneys, inefficient liver, or other causes not known about. On the other hand, if one kidney, or both are removed we do not get the state of eclampsia. But if we get a poison from the intestines into the blood stream unchanged, we readily get eclampsia.

The noxious non-protein arises mainly from the gut, and then after absorption takes place, is transformed by the liver to harmless substances such as urea. There is also some peripheral tissues that have the power of destroying the toxic
substance. In the frog the waste products from the action of the posterior legs has three channels of choice to become detoxicated, as in the lung, kidney and liver.

In pre-eclampsia, it has been found that the liver is not up to par in function, so that noxious products get into the systemic blood supply.

Lund believes that eclampsia is a state of uremia, and by uremia he means a rise of some nitrogenous waste product in the blood, due to impairment of liver or kidney function or both. In a pregnant woman, there is a diminution in the output of urine, which would indicate uremia. Now, if the liver be active it will care for the waste products, but if it be inactive then noxious substances enter the blood stream. The impairment of functions of the liver is thought to be due to the fact that the liver is compressed, has a disturbed blood supply due to the increasing size of the uterus, and in some is aided by the tension of muscle tone, and accumulation of fat in the pelvis and abdomen. Then we can say for those having convulsions after delivery that it is due to labor upsetting the viscera, and especially the liver. This was shown in one of Lund's cases in which a post partem woman was fed and the case resulted in a disaster. Then he said that after labor a woman needs rest and not food, and especially if she has had some intestinal upset.

It has been generally found that the fat of the amenum and pelvis, disappears during pregnancy from impaired circulation through it.
It is well known that an impaired heart can produce a toxemia, by hindering the body circulation, especially through the liver and kidneys, thus producing functional inadequacy. Then we can say that the obstruction of blood through the viscera by pressure can precipitate toxemia. The heart case can eat, while the other cannot; and if she does in the second case it is often liable to precipitate a convulsion, because the organs are working to full capacity. Then Duncan, in his criticism said: "Why wouldn't we get the same results in ovarian tumors and fibroids of the uterus?" Then by observing the pressure on the rectum, the condition of the abdominal wall, and the manner of living in each case, he found that they were entirely different. Women with ovarian cysts are not very active and have no other toxins thrown into the blood stream.

Another question of great importance was, the difference in blood pressure in ovarian tumor and eclampsia. The early doctors noticed that during eclamptic states, the carotid arteries were throbbing greatly, showing that there was an increased supply of blood to the head, and attributing the excess blood to the brain as the precipitating factor.

It was found by an experiment on a dog by Lund, that if the aorta was compressed, convulsions resulted; but if the dog was bled and the aorta compressed, no convulsions resulted, showing that rise of pressure and excess blood to the brain may be the precipitating factor. It has been found that hot baths, morphine, chloroform, starvation and purgation act to lower the blood pressure. It also has been found that if the
membranes are ruptured the blood pressure is lowered.

Thus it was concluded that a rise of non-protein nitrogen in the blood of a pregnant woman only produced harm if the blood pressure were high. The rise of blood pressure was then said to be caused by the compression of the abdominal visceral mass, rise of waste products in the blood, and an increase in volume of blood. With the production of pressure on the abdominal viscera and blood vessels, the blood flows in the direction of least resistance, so it chose the limbs and the brain, therefore making the cerebral cells impregnated with a vitiated blood, and under greater pressure than normal, convulsions will result. Then by relieving the volume of blood to the brain by any of the above methods, the convulsions will stop. It relieves because it lets blood pass through the abdominal viscera and the excretory organs. It has been shown that the sole control of blood through a blood vessel is not that of vasomotor control. If a person stands at attention, there is an increase of blood supply to the brain, caused by the tightening up of all the muscles of the body, the limbs and of the abdomen.

In the abdomen the blood only has three channels, one to the liver, one by way of the kidneys, and one by way of the uterus. Then the volume of blood flowing through each is governed by the resistance in the liver, kidney and uterus, all of which are conditioned not only by the caliber of the corresponding supplying arterioles, but also by the compression of capillaries or sinuses into which these arterioles open. If we lessen the abdominal pressure there is a greater
flow of blood through abdominal viscera, which is governed by resistance in other organs.

In eclampsia, the block of blood flow is not complete through the kidneys, so there is hope of recovery if the patient is given the least chance, and the manner of recovery depends upon the state of her cells. The liver has rapid power of regeneration, and the kidneys the same.

Paramore states that since the incidents of eclampsia are on the increase, he does not see how any other factor except physical factors can be of any importance. His conception is that during pregnancy there is at first an increased pressure in the pelvis from the growing uterus. Then as time advances the uterus increases in size taking up the greater part of the abdomen, and then being held in by the back, and the abdominal muscles, so that it must increase the abdominal pressure, and especially in a primigravidae where the abdominal muscles are quite tense and do not give as rapidly. He has noticed that those having eclampsia have an exaggerated intra-abdominal pressure, causing a pathological compression of the abdominal viscera. It also was noticed that in large, muscular, healthy women this condition developed. Therefore it would seem unlikely that these would be the ones that would develop a toxic condition of pregnancy. Through the increased abdominal pressure there is an altered circulation of the abdominal organs and pelvis. The kidney function is impaired, the liver manifestly disordered. In the post-mortem the excretory organs are the ones generally shown to be effected.
Those of the liver are regarded as pathognomonic of the disease. Even when lesions are slight, it is thought that other changes are so slight that they may not be detected by the human eye, but are sufficient to prevent the liver from functioning properly.

There is no definite poison found by Paramore that when injected will produce similar effects to those of intra-abdominal pressure.

It is also known that the eclampsia has an increased tendency to appear in connection with twin pregnancies, acute hydramnios, rapid growing hydatidiform moles and concealed accidental hemorrhages. In each the uterine content is different, but in each we may note eclampsia coming on. From this Paramore thought that the abdominal pressure caused pressure on the organs, and interferred with the capillary circulation, resulting in necrotic changes generally in the periphery of the organ.

There are only three modes of circulation through the abdomen, as before stated through the kidneys, liver and uterus. If pressure effects one organ, it then alters the circulation of the others. If the circulation of the uterus be decreased, the decreased size of the child would be explained. If the pressure in the abdomen be sufficient to change the pressure in the above organs, it is without doubt that the same factor could produce pressure through the uterine wall to alter placental circulation, thereby producing the pathological picture.
The explanation of the rise of blood pressure in pre-eclampsia, can be based on the altered circulation through the liver and kidneys. It has been noted that the rise of blood pressure takes place before the albumin shows in the urine, also before headaches, edema, or malaise, and that this preceding rise is of renal origin. This would indicate a renal difficulty in circulation. This then postulates that there must be an increased flow of blood through the liver, which is a necessary factor in the blood pressure rise. It is interesting to know that if the portal vein was tied off, a fall of blood pressure would be caused, while if the blood flow was increased through the liver an increased rise of blood pressure would be the result. The rise is not due to peripheral arterial contraction, because in shock we have this condition with a low blood pressure existing. If the flow of blood through the liver be hastened, the periportal capillaries may be out of working order, because of the pressure from without. This accelerates the blood flow through the rest of the liver with a consequent disturbance of metabolism, because the liver cells do not have time to function properly. Thus it would be obvious that it would not be the area of necrosis, but the rate of flow of the blood through the liver that predisposes to eclampsia.

The hepatic lesions were first referred to by Schwarz. He states that he found marked widening of the liver veins and capillaries, with marked cell changes. These cells showed marked difference in staining quality. This was all associated with necroses of the liver. Later Hofbauer found
peripheral necrosis of the liver both enemic and hemorrhagic in type, associated with formation of thrombi and bile stasis. Dieckman interpreted the condition due to syncytium tissue and chorionic villi entering the blood stream. These elements being protein must then be broken up by certain neutralizing substances which are probably of the proteolytic enzymes of the blood. By further study these hepatic lesions were found to be specific and were formed primarily as a result of thrombosis of the small end arteries of the portal system. Since these lesions are found in such quantity, they must be in great concentration in the portal system. Then later investigation discovered that if the protein intake was cut down to minimum and a higher concentration of carbohydrates was given, that eclampsia very seldom developed.

A few years before Dieckman came out with his article about Abate's findings that if the serum from a normal person was incubated with saline extract of fresh placenta, the latter was not toxic to mice if injected intravenously. The serum obtained from an eclamptic patient during or soon following a convolution, did not possess this power. Sometime after the convolution, the serum had full neutralizing power. From this we would think that the neutralizing substance of the blood of an eclamptic was used up or bound. Then the latter substance of proteins coming from the intestines was not broken up or neutralized, and therefore had the power of shortening the clotting time of the blood, thus resulting in the formation
of thrombi in the portal veins. To support the above, Wells found that the clotting time of the blood was longest in the morning before breakfast, and shortest about an hour after each meal, and gradually lengthening till the following meal. The intake of carbohydrates had no effect on the clotting time, but if eggs or any protein was taken, the typical curve was obtained. Another factor supporting the above is that during pregnancy there is an increased content of fibrinogen in the blood, and in eclampsia a very high figure is obtained. From this we can say that it would be possible that substances entering the intestines and from them to the liver, may be the cause of the lesions of eclampsia. Under normal conditions the substances entering from intestines were broken up or neutralized. But since the neutralizing agent was used up, by the constant entering protein products from the intestines, there was none left for the latter amount, which could cause a great increase of fibrinogen or the like, and form the thrombos in the portal capillaries. To confirm the above Dieckman took several dogs and injected fibrinogen into the portal circulation, obtaining results identical with those found from an eclamptic patient. If it could be proved that the fibrinogen taken by mouth could produce the same effect as that injected into the portal system, there would be sufficient evidence to explain the lesion of eclampsia in the liver. Also the question of preventive treatment of eclampsia, namely, that of limiting protein diet in the last months of pregnancy, would be answered.
The dietary factor in the case of eclampsia has caused much interest among the obstetricians, but they have not known what food to avoid.

Tweedy states that if foods are eaten, there has to be in the blood antibodies of sufficient quantity to combine with the incoming products. This works well so long as not too large a quantity is taken to deplete the supply of antibodies. Then if these antibodies are used up by the fetal products, the taking of food and the products entering the blood have no antibodies to join with, therefore resulting in toxemia. Many have thought that eclampsia was due to eating of excess fat along with the protein. But in the work of Harding and Wych, not a single case was attributed to this factor. Those who state that the withdrawal of protein or fat has caused a diminution in pre-eclamptic symptoms must show carefully the absence of other changes, not only in the diet, but in environmental factors, likely to act favorably. It is not justifiable to say that if we take these pre-eclamptic patients off diets of solids containing fat and protein and put them on a milk diet, that we are getting better results. Because sufficient milk to equal other foods in calories, equals the other diets in fat and proteins.

If we go back to the fluids such as milk, we are reducing other substances such as sodium, chloride, and the fluid acts as a diuretic which causes no edema, but lowers the osmotic pressure of the blood and tissues, thus causing a reduction of fluid content of the body. This did not prove that the protein and fat are the etiological factors of eclampsia.
Harding and Wych found through a series of experiments on normally pregnant women and eclamptic women, that normal pregnant women could tolerate high quantities of protein and fat, with salt in a minimum amount, and give no serious results. The same results were obtained when a pre-eclamptic patient was fed the same diet. Then a normal pregnant woman was fed a diet high in salt content, and she immediately showed a rise of fluid intake, increase of her weight, and a decreased output of urine, showing that there was considerable urine retention, with considerable dilution of the blood. But she had the ability to adjust her osmotic pressure of the blood and tissues, and to eliminate salt in high concentration. It is this failure of adjusting mechanism which differentiates the toxemic from the normal. If a high salt diet is fed to a toxic woman, the symptoms are readily intensified to such a degree that it endangers the mother.

Then arises the question that if toxemia is a result of brain edema, why does not a hypertonic salt solution intravenously relieve it as does glucose? This can probably be explained from the fact that sodium is held by all tissues of the body, has a high osmotic pressure, and has a toxic effect. While glucose is held and stored readily by the liver, has a non-toxic effect, and has a lower osmotic pressure. Glucose is also readily used in the body, while the sodium concentration is already at normal, and the excess has to be eliminated. Therefore some state that the dietetic factor in the production
of toxemia of late pregnancy is neither protein or fat, but salt, and especially the sodium ion.

Harding found in a few cases of his that if a definite history was taken in those patients becoming toxic over night, that their condition could be traced back to the day or so before, when they had taken a large quantity of salt, usually taken with meat, and the protein of the meat was blamed and not the salt. He said that if you took a woman in the proper state, and administered to her a quantity of salt, that convulsions could be produced in her as a result. He also noticed one case of toxemia coming on after a large dose of sodium bicarbonate had been taken. Some of his cases were given salt, and he found that the albumin and edema increased greatly over the previous day. This was also associated with a high rise of blood pressure, with symptoms becoming so severe that the tests had to be stopped.

From this work he concluded that it was the sodium ion that was the chief factor in causing eclampsia through its great osmotic power. Then this in turn caused cerebral edema and pressure on the vital centers of the brain, causing cerebral anemia with it.

A few years ago the chemistry of the amniotic fluid was determined by Williams and Bargen, which at that time was stated to have a high concentration of uric acid over that of normal blood. This then suggested that the increased concentration of uric acid in the blood of a toxic woman might then be obtained from the amniotic fluid which she had. Then rose the question
just how this uric acid would get into the maternal blood. A few suggestions were as follows: There might and could be a slight separation of the placental edges causing communication to the uterine veins, and the contraction of the uterine musculature might force fluid into the veins. If this condition was so, then many incidents of the disease might be explained, as, for example, why there is a greater number of incidents in primigravidae, and why the rupturing of the membranes is such a valuable procedure and often stops convulsions. It might explain the continuation of the disease when some dilator is used in the cervix, hindering free drainage of the fluid.

To confirm a few of the above ideas, amniotic fluid from a pregnant rabbit was collected, and injected into a young female rabbit, and the injected rabbit promptly died. Then amniotic fluid was obtained from a gravid guinea pig, and injected into the heart of two other pigs, and no effect was obtained. In another series of rabbits injected with amniotic fluid which contained many epithelial cells; death was caused probably from pulmonary embolism. De Lee states in his pathological report of eclampsia, that many thrombi and emboli were found in the lung, liver, brain and skin. From this it is suggested that human amniotic fluid may contain something capable of causing embolism if the amniotic fluid can escape from normal sight to the blood stream.

In the past five years the study of medicine has gone into another field for the etiological factor of eclampsia. This has
been possible because of the delicate machinery, our increased knowledge of chemistry, and our gradual understanding of the glandular activity of the body, with their relation to each other.

It has been found that during pregnancy the thyroid gland undergoes hypertrophic, while there is no change to be found in the other organs. Many have suggested that the failure on the part of the thyroid to hypertrophie may be a cause of this disease.

Williams and Wallis state that the corpus luteum hypertrophies during pregnancy, and if this increases over that of normal pregnancy, it enters the blood stream of the mother and causes vomiting of pregnancy. He also states that cholesterol is highest about four months after coitus, when the luteum cells are most active within the body. He states if luteum product is injected that there is an increase of cholesterol in the body, and that its function is that of a neutralizing agent of the corpus luteum product. Williams and Wallis found that if luteum is injected into an animal, the kidney and liver lesions produced were very similar to that of eclampsia. They concluded that eclampsia was due to an over production of luteum products that were not neutralized.

Kennedy-Hoffman, and Anselmino have isolated two substances from the blood which they have called antihypertensives, and pressor substance from the posterior portion of the pituitary gland. They have taken these substances and by injecting them
into animals have produced similar symptoms to that of eclampsia. They have also found that the amount of concentration of these two materials in the blood varied as to the severity of the symptoms.

The findings in animals were hyperglycemic, increased lactic acid, lowered carbon dioxide, combining power, increased inorganic phosphates. Similar findings were also found in eclampsia by Kennedy and Hoffman. They have also found by further study that there was some interference with the utilization of the oxygen by the tissues, which likewise is seen in eclampsia. From the depression of tissue oxidation an effect comparable to anoxemia represents essential factors of the metabolic derangement in the eclamptic and pre-eclamptic states. Therefore they state that eclampsia is a result of internal asphyxia. When this glandular secretion was injected, it was found that the sodium ion left the blood and went into the body tissue, thus increasing the tendency to edema.

During this disease there is also a polycythemia produced which shifts the blood calcium to lower level, and increases that of the blood, thus causing the striated muscles to be stimulated much easier.

It has been noted that posterior lobe extract has a constrictor effect on the coronary vessels, thus causing an inhibition of the oxidative processes in the heart, leading to dulation with peripheral vasod constriction. This would cause serious effect, but we have drugs to counteract this such as morphine and hypertonic solution of glucose.
From Warburg's experiment he has shown that through this anoxemia there is inhibited oxidation which causes destruction to the liver cells, and that it has an affinity for the peripheral cells of the liver lobules, with production of histamine-like substances. The pressor substance causes constriction of the liver vessels, and thus these two keep increasing the necroses of the liver, thereby setting up a vicious cycle. The constriction of the ramifications of the hepatic artery and the portal vein occurs as a response to pituitary and the constriction of the hepatic vein in the response to the histamine-like substances and to tyramin.

It is also stated that the pressor substance or the histomin will produce a spasm of the umbilical vessels, and cause altered circulation, which may lead to thrombolis or placental infarcts, as it has been shown before that there is an increased tendency for the blood to coagulate in eclampsia. Then with necrosis of this area we get the toxic materials which effect the other organs as shown in the following diagram.

Taken from Hofbauer's article in Am.Jour.of Obst. and Gyn. September 1933, p p 311.
Placenta (Syncytiotrophoblast) ferments.

Impairs functions of

Liver
Capillaries

Resulting in

Hyperactivity of posterior pituitary (Adrenal and thyroid.)

Derangement of inner oxidation
Derangement of water metabolism

Arteriolar spasms in vital organs. (Heart, brain, kidneys, liver.)
CONCLUSION - ETIOLOGY

It is interesting to note that from the very earliest record of this disease there have been many theories advanced as to the etiological factor of eclampsia. In the 17th century eclampsia was called "The disease of theories", and to-day we have many more names to be added, and yet we are no closer than they were to the specific cause.

One of the earliest etiological factors brought forth was a disordered condition of the nervous system. This held for some time, but was later given over to the uremic theory, and on and on each theory being replaced by another.

Some advanced the theory that eclampsia was caused by some toxic substance in the maternal blood. As yet chemistry has failed to reveal any such pathological product, but it has revealed minor shifts of the normal products of the human blood.

In 1902 Veit advanced the theory that eclampsia was caused from a result of chorionic villi and fetal octoderm entering the maternal circulation, and then undergoing protein destruction to form a toxic product resulting in toxic signs.

McQuarrie, through his experimental work, has found in a few cases, that there has been a partial separation of the placenta, causing interchange of fetal blood into the maternal circulation, which in turn caused an anaphylactic reaction. He also found that there may be an interagglutination of the two bloods that result in eclampsia.

Young, through study of the placentas found many infarcts throughout them. He found that those with either a large infarct
or many small ones were more subject to eclampsia, and he states that these infarcts undergo degeneration with the formation of a toxic product, which as yet has not been found.

Delore noticed that there was a greater number of incidents of eclampsia in women who were subject to prolonged, and upper respiratory infection of all kinds. He states that the presence of bacteria in the body produces a chemical substance called tyramine, and that this produces destruction of the body organs which results in eclampsia.

Lund believes that there is an altered function of the liver, intestines, and kidneys, which is brought on through the increased intraabdominal pressure, causing an altered circulation through the body organs. These body organs then produce pathological products causing great disturbances within the body. Some advocate that this also brings a rise of blood pressure, causing impregnation of the cerebral cells, resulting in convulsions.

The dietary factor has caused much dispute in early studies, but at present the problem has been settled that it is not the protein in the food that causes the retention of water, but the sodium ion, and through the feeding of it, the water balance can be maintained. Formerly the cause was thought to be due to the protein.

Borgan found a higher concentration of uric acid in his chemical analysis of the amniotic fluid than in the blood, and through some misfortune the amniotic fluid would get into the blood, making the uric acid sufficiently concentrated to cause convulsions.
Kennedy and Hoffman in recent years have isolated two substances from the blood called antidiuretic and pressor substance, which they say originates in the posterior portion of the pituitary gland. With the production of these two chemicals in the body they state that they have a controlling factor over the blood pressure and the edema through their maintaining factor of controlling the migration of the sodium ion. They also have the controlling factor of the amount of blood each organ of the body shall receive.

I have tried to include in this paper the main theories in the etiology of this disease, though I have not exhausted it by any means. Then I will close the etiology by stating that there is probably not one specific factor, but a multiple of factors that lead to the manifestation of cerebral irritation.
In the vast majority of cases, eclampsia is preceded by premonitory symptoms. Its prophylaxis is in many ways more important than its cure, and is identical with that recommended for pre-eclampsia.

Davis and Edgar claim that this disease is unnecessary if the matter has proper prenatal care. De Lee states that in his practice, he has cut the incidents of eclampsia to zero by proper prenatal care.

Lowering of the present mortality due to eclampsia will be slow, because it depends primarily upon the education of the medical student and the physician as to what prenatal care is good and what is not. The expecting mother likewise has to be educated to follow instructions properly.

To have good prenatal care these rules should be followed. The expecting mother should visit the doctor early in her pregnancy.

(1) At this visit the doctor must get a good history, and pay special attention to previous acute infections. There should be a complete physical examination and foci of infection should be looked for. Blood pressure should be recorded, urine examined, and instructions given as to diet, exercise, etc. Then she should report every three weeks, and bring with her a morning specimen of urine. At every subsequent call the doctor and should examine the urine, note blood pressure. He should ask her about headache, disturbance of vision, swelling of feet,
hands or face, dizziness and constipation. If she should note any of these any other time, she should collect a sample of urine and see a doctor at once.

(2) If, on subsequent call the doctor finds the blood pressure of 160 systolic, with a trace of albumin, with edema, she should then be put on a milk and carbohydrate diet with magnesium sulphate every morning. If there is no improvement, she should then be put to bed with the same treatment. If her condition remains about the same with a blood pressure 160/100, then the doctor should try to carry her to the time that the child is viable. However, if her condition seems worse with rise of blood pressure, twitching, disturbed vision, pain in epigastric region and vomiting, then regardless of the time she should be terminated, provided she does not respond to the general medical treatment. The choice of induction depends on the severity of the case. The doctor can use castor oil and quinine, rectal tube with packing, or a vorhees bag, he can rupture membranes, or do a cesarian.

In the small doctor practice, it is unlikely that he will see a case of eclampsia, but when he is called out on such a case and the symptoms point towards eclampsia, there are three things he should think of:

(1) Is this a case of eclampsia?
(2) What is the gravity of the case?
(3) What treatment should be instigated?

The diagnosis should be obtained from the history and physical examination, and considered serious till improvement has been
made, and delivery has been accomplished. Eclampsia should be considered as one of the obstetrical's greatest problem to control without loss of mother or child.

To absolutely confirm the diagnosis, the urine should be checked, circulatory system studied, as well as the digestion system and the nervous system. This is for a patient in the pre-eclampsia state, while if the doctor is there when the patient is having a convulsion and it is very characteristic, a diagnosis is easily made of eclampsia.

Farmer states that eclampsia is a very serious accident, a "malady of surprise," and a surprise of a disagreeable order. From the time of onset, by the number of seizures, coma, the urine, hypertention, the temperature, and the complications, one can estimate the outcome. The earlier the disease comes on in pregnancy, the more grave is the disease. When the patient is in coma, the gravity is in proportion to its length. The amount of albumin means nothing as to the severity. The complications which increase the severity of the disease are pictures and cerebral hemorrhage. The psychosis that develops means little as to the severity of the disease.

Ieannine states that as soon as albumin appears in the urine, the physician should be on the outlook for eclampsia, and the patient should report to him every other day. He should keep a record of her blood pressure, weight, and fluid intake and output. Then if any of the other symptoms of the disease appear she should be put on treatment at once.
The Stroganoff method of treatment was devised by Prof. V.V. Stroganoff, in Leningrad in 1897. But this treatment did not become widely used in America till Stander made a visit to Stroganoff's hospital in 1925.

The treatment of eclampsia by the Stroganoff method has aroused much thought and criticism. In order that his work may be sure to get the exact detail, I will duplicate it here from the American Jour. of Obst. & Gyn. 1925, 9:327.

(1) Upon admission: (a) Place patient in dark room with minimum of noise. (b) Special nurse. (c) Examination or disturbance of patient only when absolutely necessary, and then usually under chloroform. (d) .02 gm. of morphine hyperdermally, while under chloroform narcosis; usually about 10 to 15 grams of chloroform being employed.

(2) One hour after admission: 2 grams of chloral per rectum with 100 c.c. normal salt solution and 1000 c.c. of milk. should the patient be conscious the chloral hydrate can be administered by mouth with 100 c.c. of milk.

(3) Three hours after admission: .015 grams of morphine hyperdermically under 10 to 15 grams of chloroform.

(4) Several hours after admission: 2 grms of chloral hydrate, as above.

(5) Thirteen hours after admission: 1.5 grms. of chloral hydrate, as above.

(6) Twenty-one hours after admission: 1.5 grms of chloral hydrate, as above.
(7) After each convulsion, oxygen is administered as quickly as possible. This is kept up till the breathing improves, usually about five minutes.

(8) After each convulsion in the clinic, venesection of not more than 400 cc. is resorted to.

(9) In case of frequent convulsions, chloroform and chloral hydrate to be used more energetically than outlined above.

(10) No convulsion for thirty-four hours: If patient has been free from fits for twenty-four hours, or longer, after admission, and has not yet been delivered, she should be given about .5 gm of chloral hydrate every eight hours for about three days.

(11) Child. Operative delivery is resorted to only when intervention becomes absolutely necessary for the sake of the child.

In view of the fact that Stroganoff ran two clinics; in one he had 168 cases, from 1915 to 1924, with a maternal death of six. In the other, he had 78 cases with one death, with a gross mortality of 2.84%. In checking over his work it will be found that 70% of his cases had no convulsions before they entered the hospital, 50% had only one convolution; so the conclusion was drawn that probably all these cases were not true eclampsia.

The treatment of Stroganoff was known to the German, but was not used in any of the other European countries. Many
have tried his line of treatment, but have not followed it closely enough to give it a specific trial. Parts of his line of treatment seem to be very good and some not so good. Stander states that the dose of chloroform is so small that it cannot produce a satisfactory narcosis. Here in our etiology it was stated that chloroform was not to be used because of its specific toxic effect upon the liver. In the second place Stander states that such a small quantity of blood being withdrawn in the venesection would have no effect, and he advises that if blood be withdrawn that about 750 to 1000 cc. should be drawn off at one time, then normal saline or some other physiological solution should be injected to bring the volume back to normal.

The early treatment of eclampsia in the United States, was to cause delivery to take place as soon as possible. Hot packs were used upon the abdomen and legs, diuresis was stimulated, salt solution was injected under the breast, and venesection was performed. The sweating process was abandoned because on examination the doctors found only water and none of the toxic material, and that the presence of the edema was caused by some protective mechanism. The subcutaneous salt was stopped because a retention of sodium was found in the body, and glucose worked just as effectually or more so in producing diuresis, and in being easily assimilated into food for the body.

Hot packs are now used for other purposes than that above. There has been considerable controversy as to the use of methods
producing sweating. Some state that the process of sweating eliminates the fluids of the body, but that the toxins remain within, thus increasing the concentration. Sweating is not brought on with the idea of diaphoretic effect, but it has a great comforting and relaxing effect on the patient.

Venesection has been employed in the treatment of eclampsia from time immemorial. We are indebted to Lechtenstein for placing it upon an intelligent basis. In his work he reduced mortality of his patients from 16.7 to 9.4% through a period of ten years. He advocated that for venesection to be efficacious, it must be in considerable amount, to be more specific, about 1000 c.c. Some think that this increases the toxins in the body, although some toxins have been eliminated in the volume of blood withdrawn. The other opponents state that venesection causes cardiac depression, shock and cerebral anemia. But if the patient has a very high blood pressure, this is a very satisfactory means of reducing it down to 150 M.M. of Hg. Williams advocates it in all cases regardless of the condition of the heart, and states that it should be kept up till the blood pressure falls to 100 M.M. of Hg. This may require the withdrawal of one liter or thereabouts. Many are opposed to this, since it may result in pulmonary edema, and because, since in the normal delivery there is loss of considerable blood, this may all tend to weaken the recovery mechanism of the patient.

For some time, saline and Ringer's solution were injected following venesection. It would seem inadvisable to inject a normal saline or any other of similar nature back into the cir-
cular system, because of the fact that past studies have shown us that it is the sodium that acts as the osmotic governor. Then it would seem more advisable to inject a 10% sugar solution. We are fortunate in having a sugar solution that acts probably better than the saline, because it has a diuretic effect, and it is easily assimilated into a food. It also acts as a detoxicating effect, and helps retain the normal function of the liver cells.

It was often noted that following venesection there was produced edema of the lungs. This was thought to be due to the rapid fall of blood pressure, but later in the use of morphine and when no venesection was performed, the same condition was found. To counteract this condition, many advocated the use of veratrum viride, which was first introduced into the treatment of eclampsia by Stroganoff. Beckman states that at some time or other nearly every well known obstetrician had gone through a period of advocacy of this drug, but at the present time it is being championed by no one.

Irving has lowered his mortality by 1/3 by using venesection in all his cases. He thinks that since there is a toxin in the blood a plasmopaeresis is better than a venesection, in that this reduces the concentration of the toxic material in the circulating blood, but yet retains the active principles of the blood, and retains the fighting resistance of the mother.

Plasmopaeresis was first tried out on a dog. Here the animal was bled into a container containing some anti-coagul-
ant, and then the blood was centrifuged till the serum and cells separated, then the red cells were washed and reinjected into the animal. This was done till all the serum of the dog was completely replaced, with no harmful results. This also had a beneficial effect upon humans in eclampsia, in that it does not lower the resistance of the patient by having a venesection upon her, and it does not lower her resistance to infection, does not produce secondary anemia, and drains off the toxic material in the blood if there is any.

In a series of cases reported by Irving and Taylor in the American Jour. of Obst. and Gyn., 1929, they had very beneficial results from plasmapaeresis in one case especially who entered with headache, vomiting, swelling of feet and ankles, blurring of vision, blood pressure 140/110, and a large quantity of albumin. No fetal movements had been noted for one week previously. She entered with shortness of breath, and fluid in base of the lungs. Membranes ruptured spontaneously, and she started in labor. She had an intrapartum convulsion, and the edema of the lungs became worse. A plasmopheresis was then performed during the second convulsion, soon following reinjection, the edema cleared up, and the urine became negative, and she was soon discharged with a negative urine and normal blood pressure. This shows that if venesection has to be performed, this method is much more desirable in that the patient retains the corpuscles to keep up her resistance to infection.
In eclampsia, we note a further concentration, as this may be relative or absolute. The hemoglobin, hematocrit, and serum protein are not all increased in proportion. There is also an alteration of the blood volume, thought to be due to the altered protein of the blood. These are all accompanied with retention of water and salt. Following a convulsion there is produced an acidosis which again alters the condition of proteins of the blood. Since the blood is increased in concentration, the treatment seems advisable to dilute it, and this is accomplished by venesection, plasmophersis, intravenous glucose, bicarbonate solution, hypnotics, sedatives, eliminations, &c.

Directly following the dilution of the blood, there is an improvement clinically, though if the treatment is not kept up it will reoccur.

Dold in 1911 found that an extract of any viscera contains a toxic substance when injected into a mouse, but that this toxic substance could be completely neutralized by normal blood serum. Then later, when working on this same subject, he found that when he made an extract of fresh human placenta and injected this into a mouse, that symptoms like eclampsia developed. He also found that there was no difference in the toxicity of a normal placenta and that of an eclamptic patient when injected into a mouse. But he found that there was a difference in the ability of the normal serum and that of an eclamptic to neutralize the effects of the placental extract of a normal or eclamptic
placenta. He observed that blood serum from a normal person neutralized the toxic products from a placenta of a normal or an eclamptic patient, but that the serum of an eclamptic would have no neutralizing effect upon the placental extract of either.

This led him to believe that there was some substance in the normal blood that had the power of neutralizing the toxic placental products. This then led him to use transfusion in eclamptic patients, and he reports splendid results if the transfusion was given early in the case.

Many writers state that the patient should be in a dark room, free from noise and excitement, have no visitors, and seldom be disturbed by anyone. Her ears should be plugged with cotton. Then again, other authors state that our patient should be in a light room when the first sign of cyanosis or respiratory changes can be detected by the nurse, since in an eclamptic patient fluid in the lungs accumulates with very few external signs, and if detected early can be checked. Therefore the best thing would be to compromise on the two and get a fairly light room, free from noise and excitement, with everything ready if any disturbance should be encountered.

Gastric Lavage is advocated by many obstetricians because it is useful for certain procedure, as the administration of purgative in a comatosed patient. In the etiology it was found that eclampsia was often precipitated following the administration of certain foods, with the effect of cerebral irritation.
Then by the use of the tube, the stomach can be cleaned out, thus relieving the patient of further toxic substances. Many have brought up the idea that the administration of the tube may predispose to an attack, but if given with an anesthesia should have no bad effect. As soon as the signs of pre-eclampsia are noticed, most of the obstetricians advocate the placing of the patient on a milk diet. If a patient was placed on a milk diet it would seem that she would be on very much of a starvation diet. About all the ordinary woman would take would be about two liters, which would only amount to about 1300 calories. This would not be sufficient to keep the smallest woman alive. It has been found that a liter of milk contains 35 gm. of proteins, 50 gm. of carbohydrates, and 35 gm. of fat. We also know that during pregnancy the caloric requirement increases as pregnancy advances. From further study it has been found that a resting caloric diet for a pregnant person is somewhere near 30 per kilo. Therefore a 132 pound woman should require 1800 calories.

During the world war it was noted that the incidents of eclampsia decreased. On going over the diet in Germany, it was found that it fell short in protein and fat. But nothing was known as to how much the caloric intake was decreased.

If a woman is placed on a starvation diet, it has been noted that beneficial results are produced. This may be due to the depletion of products in the body or to the stopping of the action
of the toxic organ and the opportunity to repair itself, or to a depletion of the sodium intake. Here again if a person is placed on this type of diet the production of ketoses will be controlled, since they surely must be formed. This would have the effect of eliminating water from the cells of the body but toxicating it in another line. If a person is placed on a high fat diet, there is an increased elimination of fluid. Benedict showed that when 67% of the caloric requirement was obtained in fat, there was an increased elimination of water. He also showed that if the diet has been free from salt, and then the person is placed on high fat, there will still be an increased elimination of water from the body, showing that a mild degree of ketoses might be of advantage. It has been shown that the effect of mild ketoses in normal pregnancy is not bad, but the effect of ketoses in toxemia has not yet been worked out. It is known that a ketose producing diet will lower the level of the plasma bicarbonate, thus producing acidosis. Then since the pressor substance as it is called is stable in alkalies and unstable in acids, this shift may be advantageous to the patient. But again it has been noted that depletion in bicarbonate of the blood increases edema.

It has been found that 90% of the total base of the blood is made up of sodium. The other 10% is made up of potassium and calcium and other elements of minor degree. It has been noted that 6 grams of sodium will hold about one liter of water in the body. Then on a diet of variable salt, the edema can
be almost controlled. The chloride acts solely as a vehicle.

The mechanism of control of the acid base may be stated as follows: the body acts as a physio-chemical system in which acid and base are held in equilibrium as a mutual salt. The equilibrium is delicately maintained, and if one factor is altered, the entire group is likewise altered. The total base concentration is the major immediate factor which controls the state of hydration. In short, base holds water. Then if one is given products that shift the equilibrium to the acid side there is then a loss of base and with it a loss of water. If base in maintained and increased, there is water retention. Therefore, to eliminate edema we must supply a food that contains acid radicals and one low in base products. Therefore, an improper diet during the latter months of pregnancy can be of primary importance in causing edema. Normally there is found a certain amount of fluid in the intercellular spaces of the body tissue, and when it is increased above this normal quantity, it is called edema. We may have fluid also collecting in the serous cavities with like mechanism to that of tissue edema. Although edema is seen in many conditions, it is without a doubt that the mechanism is different. There are probably many factors acting together such as increased hydrastatic pressure, increased capillary permeability, disturbed osmotic pressure, variations in acid base equilibrium of the serum and of the body tissues, and probably others not yet discovered.
The early workers in this field found that blood letting increased the edema in nephritis, and that in certain types of edema, if salt was withheld there was a decrease in the body edema.

If the kidney be damaged so that its ability of secreting the excess sodium and water is limited, it would play a great part in the mechanism of edema. The restriction of water intake does not materially contribute to the relief of edema, as edema occurs independently of water intake. From past experience, it has been found that water is a definite agent in increasing diuresis.

If there be pressure intra-abdominally above that of normal embarrassment to the heart and pressure upon the veins, pressure upon the veins and arteries may be caused. We note that there is produced stasis which interferes with the oxygen and carbon dioxide exchange, and as an end result through this mechanical embarrassment we get edema.

If a person be deprived of protein intake for some time, there is a serum protein depletion in the blood. Since it is a well established fact that the concentration of the electrolytes of the serum varies inversely with the concentration of the proteins, and that a depletion of the serum protein automatically raises the concentration of the total base, and when the serum protein falls below 3 to 4 grams %, we may then look for edema. If all this be so and if there be a depletion of
serum protein, it would be inadvisable to do a venesection. In the past, many people have examined the blood of patients with toxemia of pregnancy and have not been able to discover any great pathological substance that might be the cause.

Stander in his works states that the blood is in a state of hydremia. Then later Dieckman working on the globin, cell volume, and serum protein, was able to show that there was either an absolute or a relative decrease in the blood volume. From this he states that since the products of the blood are present in concentrated form, there is a decreased flow of blood through the vessels due to the increased viscosity of the blood. From this he states that if the blood flow is decreased, there is not sufficient food for the cells, and there is a piling up of toxic material at the end capillaries and in the organs which produce destruction to the cells. He states also that there is a resulting acidosis in the tissues, and an accumulation of material in the blood because of the decreased flow of blood through the kidneys. Then, if these materials keep piling up to sufficient concentration, a convulsion is brought on, and in time, if the toxic material is not relieved, death will be the final result. Since the blood is in concentrated form, its clotting time is much increased, which would lead to thrombosis in the vessels where the circulation is much hindered. As the protein decreases in the blood, fibrin is increased, except where gum acasia is given.
It is accepted that in a normal pregnancy there is a true hydremia, and that in pre-eclampsia this hydremia is much more marked. Through Dieckmann's studies, the products of the blood were found much more concentrated than in a normal pregnancy. It was found that in some with the injection of glucose intravenously the dilution of the blood could be retained, if the injections be frequent enough. Then some few months later on a patient was obtained in which the dilution of the blood could not be retained at normal dilution. To this one gum acacia was injected, and since this is of a colloidal nature, and has great power of holding water, and quite hard to be eliminated by the kidney, it was found that the dilution of the blood could be maintained. Thus it would dilute the blood and increase the viscosity, causing good circulation through the organs of the body. This was tried on a patient with convulsions in whom the blood volume could not be obtained, and a great improvement resulted, finally restoring her to normal. The explanation of the fact that the blood volume could not be maintained was thought to be an altered condition of the blood colloids to a state in which they lost their colloidal properties of holding water.

Since in eclampsia, there is a shift of albumin-globulin ratio from the normal 1.2 to 2, then from the fact that the osmotic pressure of serum albumin is almost four times that of globulin, it is evident that the osmotic pressure will be altered. Many state that the edema in eclampsia is caused by
the low serum protein. But Dieckmann has found that in eclampsia with edema the diuresis is greatest during the time that blood protein is at its lowest concentration.

Since good results have been obtained, it is advisable to use 500 to 1000 c.c. of 6% gum acacia solution, as a prophylactic means in checking osmotic alteration in the blood to prevent it from becoming stagnated in the body organs, and from becoming thrombosed there.

If the practicing physician will keep a recorded weight of every patient for every time she returns, the slightest gain in weight, or the first sign of a pathological state developing will be noticed, even though the blood pressure may still be normal or thereabouts. The gain can be taken as the index of oncoming toxemia. Water retention evidently plays a part, or at least accompanies toxemic signs other than edema. In other words the patient can have water retention without signs of edema.

The gain in weight of a pregnant woman has factors influencing it, such as age, dietetics, habits, exercise, and the presence of infection. There is considerable dispute as to how much a patient is supposed to gain per month. The general increase in weight per month is about 2½ to 5 lbs. In Kerwins cases, of 127 he found that the average gain was only 2 lbs per month. Davis states that a gain of over 7 to 7½ lbs per month is pathological. Bengham states that anything over 4 lbs. is pathological. If at some time we should note a constant
weight, and if we eliminate all foci of infection, and the fetus is alive, we can assume the gain of weight of the mother is kept constant by the loss of water sufficient to equal gain of weight.

When we encounter a pathological gain in weight, since the liver function is impaired, we know that glycogen storage is altered, and since glucose has a great detoxicating power, it would seem advisable to inject this intravenously. When this procedure was tried by Titus, it was found to have a very beneficial effect. He states that the convulsions are based upon a hypoglycemic condition of the blood. Then by injecting glucose either by itself or in a sterile solution, or with insulin, the further production of acidosis is hindered. Rather than acting just as a neutralizing agent, the sugar solution has another effect in that it also dehydrates the tissues and promotes diuresis.

Through recent investigation the theory has been supported that there is some underlying factor which causes toxemia of pregnancy. The majority of the investigators state that the pathological picture found in the liver and other organs is a result and not the primary factor. Through laboratory and other experimental work of giving glucose with such beneficial results obtained, would lead one to think that it was some metabolic factor that was the seat of the disease. Then with the use of glucose and insulin, experimentors here obtained much better results, still supporting the metabolic idea.
From the past pathological reports of the liver, there was found fatty necroses, with hemorrhagic areas throughout, but with the administration of glucose these findings have not been further supported.

It is known that the liver has tremendous power of recovery, and if the necroses has not gone too far, the easily assimilated glucose will allow healing to take place. But if the toxic product has caused too much destruction, repair will not take place, as is shown pathologically.

Since glucose had such a beneficial effect, many theories were advanced to explain it. It has been states that since the fetus and placenta require large amounts of sugar, and if the intake is not sufficient, the liver is depleted of its quantity. When the sugar is completely gone, fatty infiltration replaces it, and in time fatty necroses is the end result. Then as stated above if glucose is given, this entire process is stopped and repair takes place. Then it would seem incorrect to place these patients on a starvation diet if glucose has such an effect. We know that starvation produces acidosis, and this, with the lack of glucose might be enough to increase the toxemia by causing destruction of the liver cells. In ordinary pregnancy, we have been wondering if there is a deficiency of glucose or an altered glucose metabolism that causes the changes, and so far, this has not been answered. It is not definitely known as yet just how the glucose and insulin help toxemia of pregnancy, but if this treatment is started
early the toxic state can be warded off, and it seems to have much more activity if given intravenously together. But its use is not adopted by all as yet, and is not without danger, especially when there is no absolute laboratory blood sugar control. But it has been found that the none diabetic patient readily metabolizes 50 gm. of glucose. Beckman advocates intravenous administration of hypertonic glucose solution in single doses of 75 gm. in 300 c.c. of water, (25 per cent. solution) at the rate of not more than 1 gm. per minute, or from an hour and a quarter to an hour and a half for the entire injection. This injection should be repeated within four or five hours during the attack, and for some time following the cessation of the convulsions.

The immediately noticeable effects are diuresis, lowering of blood pressure, cessation of the convulsions and prompt regaining of consciousness. The odor of acetone quickly disappears from the breath, and edema lessens rapidly after the injections.

Beckman states since we have found a disturbance in the carbohydrate metabolism, with hypoglycemia, the addition of insulin to the glucose that is injected becomes very dangerous, and that every subsequent injection of glucose stimulates the endogenous insulin production to further and further activity, so that the addition of insulin to subsequent injection becomes increasingly dangerous.

Layard in 1925 brought forth the treatment of pre-eclampsia and eclampsia with the use of magnesium sulphate. From the use
of magnesium sulphate in pre-eclampsia in his series of 350 cases, there was a gross mortality of 1.6%. Of this 350 cases there were twelve pairs of twins, 270 living babies, 14 babies who died after delivery, and 58 stillborn.

In eclampsia Layard has found magnesium very helpful in the treatment. This has also been used in combination with glucose, intravenously. Through this means of treatment the mortality has been reduced greatly. Through a series of 91 eclamptic cases, there was a mortality of 7.8%. As to the babies in Layard's treatment with magnesium sulphate of the 91 cases, there were 58 living babies discharged from the hospitals, 5 premature babies who died after delivery, 28 stillborn babies. Layard's present day treatment is as follows, taken from the Jour. of Obst. and Gyn., November, 1933, pp.655:

1. Pre-eclamptic.
   1. Usual sedatives and eliminative treatment and dietary regulations.
   2. Blood pressure 150 systolic, or higher, 20 c.c. magnesium sulphate, 10% solution intravenously, blood pressure to be taken twice daily, and the intravenous magnesium sulphate repeated if blood pressure does not go down.
   3. Surgical interruption of pregnancy only to be with the consent of senior attending obstetrician.

2. Eclamptic.
   1. Twenty c.c. of 10% solution of magnesium sulphate, intravenously as soon after first convulsion as possible.
   2. Repeated injection of magnesium sulphate every hour until convulsions are controlled.
3. Blood pressure to be taken every hour after convulsions are controlled, and if it begins to rise again nearing its height at time of convulsion, repeat magnesium sulphate; also repeat if convulsions recur.

4. Intravenous glucose, either 1000 c.c. of 10% solution for patients with little edema, or 50 c.c. of 50% solution in those with marked edema, as indicated for scanty urinary output and for patients with low CO2 combining power, especially if delivery or operation is to be done.

5. If patient is comatos, or very restless in a semi-comatous delirium, and blood pressure is falling, give chloral gr XX and Na Bi L X per rectum.

6. All patients to be prepared for delivery as soon as they are quiet enough to do so.

7. Utmost quiet to be observed, and nurse to be constantly with patient until coma has cleared.

8. Oxygen inhalations after each convulsion until breathing is normal.

9. If patient is in labor, nitrous oxide for pain.

10. If in second stage labor and proper progress is not being made, low forceps extraction or version may be done with consent of attending obstetrician.

11. Cesarean section only to be done for absolute obstetric indications and with consent of senior obstetrician.

In experiments marked out by Stander, he found that in a chemical analysis of the blood before injection and after injection of the magnesium sulphate, there were only minor changes noted. He found an increase of blood sugar to minor degree, with a slight elevation of the carbon dioxide, combining power. The non-protein nitrogen, blood urea nitrogen and uric acid remained unchanged.
Whole blood contains about 440 to 500 mg. % of sodium chloride. There is undoubtedly a relation between the distribution and movement of sodium chloride and of water, and also a relation between the movement of salts, particularly the sodium ion, and the development of edema. It is not through this retention of the sodium ion in the tissue that edema is produced.

In certain manifestations, it has been found that some alteration in the hormones of the body have a great influence on the migration of fluid in the body tissues. But from the fact that magnesium sulphate reduces cerebral edema, it must be due to the fact that sodium and water migrate from the body tissues to the blood, and from the latter to the kidneys. Here we find an increased secretion of water containing an increased concentration of sodium. But on checking over the blood, no increase of sodium could be detected of any great amount.

Stander reports in going through the pathological study of a couple of dogs after intravenous injections of magnesium sulphate, that there was found central necroses of the liver, with alterations in the kidney glomeruli. Meltzer reports that if the drug is injected quickly, 1 c.c. will kill a dog, while if it is injected slowly, 1.5 c.c. of 50% can be injected, showing that it is toxic, when injected slowly, the detoxicating factors of the body can overcome its toxic effects.

From the effect on the blood and liver, Stander objects to its use from a clinical and pathological study of the effects on dogs.
Then following the above comes the experimental work of Layard, Irvin and Vruwink, who had 45 cases of pre-eclamptic mothers who received injection of magnesium sulphate, with only six having convulsions. One patient received 24 injections of 2 c.c. of 50% magnesium sulphate in a period of twenty three days, and delivered a boy in the end. It would therefore seem probable that since she was already toxic with the injection of another toxic substance, if any deleterious effect would come from it she surely would have felt it.

These men found that in therapeutic doses, magnesium sulphate had no deleterious action on the blood, nor produced any pathological changes in the liver, but in active eclampsia by a relief of toxemia, it had a beneficial effect on the blood. Its second action was to dehydrate the brain. It has lowered the mortality below 10% by its use in eclampsia.

From another report of 17 cases by Layard, it was found that the use of magnesium sulphate intravenously had considerable quieting effect on these toxic patients. The type of patient used was just as they came into the hospital. Ten were in convulsions as they entered the hospital, and some had anywhere from 1 to 10 convulsions before entrance. All of these patients were given the same treatment. It was found that with some, 1 injection of magnesium sulphate was sufficient to carry them through the rest of the pregnancy, while with those who were more toxic, anywhere from 1 to 4 injections after the first were received. In none were the convulsions continuous till after the magnesium sulphate had worn off. There was one maternal
death, but in no cases were the fetuses affected. From this group of cases it was found that the convulsions could be definitely controlled, but the difficulty that Layard encountered was to find the dose that would completely cure the patient. He also found that as long as he used the magnesium sulphate intravenously that other treatments could be practically stopped.

In the past there has been no definite dose used in the treatment of eclampsia conditions. It 1907 Einer reports two cases treated with 250 c.c. of 2% magnesium sulphate. Loomis and Sherrick, and McNeile, all of California, use a 2% solution with 7 gm. of calcium chloride to the liter, the dose varying with the patient from 250 to 300 c.c. Davis and Harrar have injected 4 c.c. of 50% solution very slowly into the veins. The majority of obstetricians at the present time are using magnesium sulphate for its anesthetic and inhibiting properties, and its ability to relieve tissue edema, particularly of the brain, in the form of a 10% solution given in doses of 10 to 25 c.c. intravenously, the method introduced by Bogen in 1924.

Einer in about 1925 reports several cases of eclampsia treated with intraspinal injections of magnesium sulphate. From this angle of treatment we find the dose of magnesium sulphate was 1 c.c. of 25% for every twenty pounds of body weight. He states its effect on controlling convulsions is due to its penetration into the spaces between the terminal processes of the neuromes, whereby the contact is cut off. He also found that if too large a dose of magnesium sulphate was administered, a
depressing action was put upon the respiratory center. This could be eliminated by injecting intravenously 10 c.c. of a 25% solution of calcium chloride.

Perhaps the action of magnesium sulphate by the intraspinal method can be better understood if a case report is given from E.H. Alton's article in American Jour. of OBst. & Gyn. Feb. 1925, p.p. 167.

A patient, 28 years of age, with ruptured membranes, entered the hospital in the 8th month of pregnancy. Soon after her entrance she had a series of convulsions, one following right after the other. Several treatments were tried, producing no specific effect. Then a spinal was performed, and 5½ c.c. of a 25% solution of magnesium sulphate was injected. Directly following the convulsions stopped. Then after some time they came again, and another 5½ c.c. were given, with complete recovery from the attack, and she went on to recovery, and delivered a normal child for the length of time pregnant.

Through a series of experiments by Dorsett in 1926, he has found that the toxic effect of the magnesium sulphate was reduced considerably through intramuscular injections. Many have thought that this drug would produce a sluff, but this is probably prohibited by the fact that the gluteal muscle fibers are quite large, and rapid absorption is produced. Through these experiments, it was found that the convulsions of eclampsia could be prevented, but that this treatment did
not cure the disease. Dorsett states that the mode of activity of this drug is mainly through its ability to release cerebral and general edema, and to stimulate diuresis. Through this method of treatment it was found that no other treatment was necessary as long as the convulsions were controlled, and through it the patient could be allowed to go nearer to full term or to full term without other intervention.

McNeile and Vruwink in 1926 have described their employment of magnesium sulphate method at the Los Angeles General Hospital as follows: Beckman - 723.

(A) Treatment of pre-eclamptic toxemia.

(1) The patient is placed on non-protein-salt free diet.
(2) Pushing of all fluids.
(3) Patient is to have one half ounce daily of magnesium sulphate by mouth.
(4) The daily output of urine is to be collected and examined chemically and microscopically, also keep an accurate record as to volume per day.
(5) The blood pressure is to be taken twice daily.
(6) Whenever the systolic blood pressure rises to over 150 mm of hg, the patient is to receive 20 c.c. of 10% solution of magnesium sulphate. This is to be repeated if indicated.
(7) Termination of pregnancy is indicated only when symptoms persistently recur and do not respond to treatment.

(B) Their treatment for eclampsia with magnesium sulphate as follows:

(1) The patient is to have 20 c.c. of a 10% solution of magnesium sulphate intravenously as soon after the 1st convolution as possible, and this is to be repeated in one hour from first, and so on until the convulsions are under control.
The blood pressure is to be taken every hour, and if it starts to rise back to danger zone, she is then to have another injection of magnesium sulphate, and this is to be kept up till condition is controlled.

Patients who are comatose or very restless in a semicomatose delirium, and whose blood pressure is falling, should receive chloral hydrate, 20 grains, and sodium bromide, 60 grains by rectum.

The patient is to be in a quiet room, and a nurse is to be constantly with the patient till she is out of coma.

Following each convulsion the patient is to receive oxygen till her breathing is back to normal.

All patients to be prepared for delivery as soon as they are quiet enough to do so.

Nitrous oxide is to be given to the patient when she is in labor.

If in second stage of labor and proper progress is not being made, low forceps extraction or version is to be used.

No cesarean section is to be used unless you have absolute obstetrical demands.

In 105 eclamptic cases, eighty-nine patients recovered, and fourteen died from all causes, giving a gross mortality of 13.6 per cent. The mortality rate at the Los Angeles General Hospital in the preceding five years was 36 per cent. With magnesium sulphate this was reduced to 14.8 per cent., a reduction of 60 per cent.

We can go back as far as civilization and find many procedures and means of trying to stop pain in the practice of medicine, as one of the main theories of treatment.

Previous to 1929 in obstetric work, there was very little use of sodium amytal in the United States, but it was used quite extensively in foreign countries. It was first used to produce surgical anesthesia, and finally it became quite popular in
France in about 1923. Here they injected it intravenously when the cervix was two to three fingers dilated, and obtained perfect anæsthesia for the rest of labor. They stated it had no effect upon the mother and child after delivery. To be able to understand its use in pathological cases, we should first know its effects in normal labor, which is as follows:

Delmas and Roume tried sodium amytal, and stated that the child was sleepy and unable to feed for two days following its use. The mother was quite restless, and following delivery she slept for two to three days, and that the progress of labor was markedly impaired.

Little was then done with the drug till Robbins and his associates experimented with it on 100 cases, to abolish the pain of labor. They found no slowing in the progress of labor, except in four cases, in which labor was prolonged by one hour, the power of uterine contraction was not impaired. But in the first stage of labor they found that voluntary power was markedly diminished, and that the patient did not respond to uterine contraction. Voluntary power in the second stage was about normal. In obstetric anæsthesia, some patients continued powerful expulsive efforts. They found that 1/3 grain per Kilo could be given within two hours of each other, and produce no pathological effects on fetus or mother.

In most cases of eclampsia, sodium amythal seemed to hasten the delivery, and was given when the pain became regular and at every four minutes, they found that out of the 100 cases, 28 delivered within three hours after the injection.
In 80 cases 1/3 were very restless, 1/3 moderately so, and 1/3 not effected at all. With those who were restless and seemed in pain, if asked about the delivery after some time, remembered nothing about it. In those patients who were restless following delivery, when placed in a comfortable position, showed no sign of restlessness. Of the 80 babies, three were asphyxiated, and breathing started with difficulty, two were apneic, while the rest showed no effect.

Many investigators find that intravenously and intramuscular injections, vary greatly in their effects. The intravenous route acts quicker, but the effect does not last so long, and is not quite so outstanding. While the latter starts a little later, but its effect lasts twice as long and produces much deeper effects from the drug.

The use of sodium amytal in the control of convulsions, has been found to be very satisfactory. Perhaps if a case were recited, its effect could be understood much better.

By More in American Jour. of Obst. and Gyn. 1930. Mrs. I.S. gravida III para II age 36, who was brought a distance of 36 miles in a car, had a convulsion on the road to the hospital. She was given .033 gm. of morphine before sent into the hospital. On admission the blood pressure was 232/136, generalized edema, moderate stupor, twitching about the mouth, face and arms, with a uremic breath. Urine boiled solid, contained coarse and fine granular casts, moderate pus, numerous red cells, Ht 87%, R.B.C. 5,200,000, W.B.C. 15,000, blood urea 33 mg., creatinine 4.7 mg. She was given .5 gm of sodium amytal intravenously
and her blood pressure went down to 190/124. Then glucose was given intravenously, and following this she slept most of the day and night. On the second day the blood pressure was 226/124, but she felt fine. The next morning at 3 A.M. she complained of epigastric pain, and her blood pressure was 230/140. She was then given .325 gm. of sodium amyotal, and she slept the rest of the night. At 7 A.M. she had to be aroused for the taking of castor oil and quinine, and labor began at 2.30 P.M. Sodium amytal .325 gm. was given by mouth twice in the afternoon, and in addition scopalamine .00066 gm., which was given in two doses of .00033 gm. by hypo. She delivered that evening with no trouble, and the baby cried spontaneously. After she came to, her blood pressure was 194/112, and she remembered nothing about her troubles. She was discharged from the hospital in normal length of time, and she and the baby were normal in all respects.

King, Mayer and Ayo have reported very satisfactory results with the use of sodium amytal in the treatment of eclampsia. They tell us that the solution prepared should be allowed to stand for five minutes, and if it gets cloudy it is not to be used, but that we should prepare another solution. It should not be injected faster than 1 c.c. per minute. The effect of the drug takes place in a few minutes, and when .3 gm. has been given the patient falls off in a normal sleep. Following this we note a rapid lowering of the blood pressure, which causes no disturbing effects. They have noted it falling from 216 to 126, within a few hours. The respiratory rate is slightly decreased, with a slight rise of heart rate. The carbon dioxide combining power
and the base metabolism remains normal. Sodium amytal action seems to be through the thalamic centers of the brain.

In a total of thirty cases of convulsions, they reported that only two had further convulsions after the 11th injection of sodium amytal, and that these were checked by further injections. They lost three patients of the thirty, and these were beyond hope before reaching the hospital. In these patients the sodium amytal was used as the chief sedative. Morphine was first given only on entrance to the hospital. Eliminations were hastened by gastric lavage, purgatives, and enemas.

Glucose intravenously is highly advocated, and radical procedure should be limited to forceps, breech extraction, and version. Some will say that the effects produced in these cases might be due to the morphine, but no such striking effects can be obtained when morphine is used alone.

Many users of the drug state that there is no definite dose to be given, but should be given till results are obtained. The intravenous route has many advantages over the other methods, in that the drug has to be injected slowly, and while doing this the effect can be noted, and the dose given more accurately to meet the demands of the patient. In most cases, a dose of $6\frac{1}{2}$ to 9 gr. is sufficient to produce the effect desired from the drug. When the patient becomes sleepy, respiration slows up, and becomes more like in a deep sleep, the color improves, the blood pressure falls, and the heart rate increases. When twitching stops, the proper dosage has been given. In some cases the doctor
may have to repeat the dose in a few hours, and it has been reported that some have given as high as 48\(\frac{1}{2}\) gr. in 12 hours, without any bad effect on the mother or the child. Therefore it should be given until results are obtained.

Van Del states that he has had better results by using sodium amytal by oral administration. He states that the dose can be more accurately controlled. He advocates giving 15 gr. by mouth, then 5 gr. each time thereafter till results are obtained. He also states that this method produces no idiosyncrasy. He also states that since sodium amytal is not a complete analgesic by itself, he advocates giving morphine with it as it produces a much more valuable result.

In about 1889 Halbertsma first suggested cesarean section for the treatment of eclampsia. Then in the nineties Dukressen proposed the use of vaginal hysterectomy for the treatment. From then on some of the great obstetricians still prefer this treatment. It has been stated that the reason it is still in use is because it is more spectacular, easier and quicker as a cure.

Keller states that it does not seem reasonable that any established form of treatment could give uniformly constant results, leaving nothing further to be desired, when the etiology of the condition still remains unknown. Therefore since the etiology is unknown, it seems rather strange that when once cesarean was proposed in the treatment, that it should be kept in use for so many years. It seems unjust to the patient to do a vaginal hysterectomy if there be bacteria in the urin and
the vagina. If this is done it is just laying the mother open for infection. If it is performed, then nature must come into play in such cases to preserve the life of the mother.

It does not seem justifiable that an already toxic mother should be placed under the burden of an anesthetic to increase her toxic state. Williams states that it is probably the operation that is harmful to the mother through the effects of the anesthesia, and that the only way the mortality of cesarian section can be cut down would be to find a non-toxic anesthetic.

But there will always be found a few cases where cesarian will have to be used, such as in dystocia, deformity of the pelvis, and the like. The only advantage of cesarian when it has to be used, is that there are no lacerations to the female parts, no introduction of foreign bodies into the uterus, no overloading of the kidneys, conserving of the mother's strength, no useless bleeding, and the removing of the great cause of eclampsia.

Peterson in 1914 reported 500 cases of cesarians. He divided those into 198 cases before 1908, and 283 cases after 1913. In the five year period from 1908 to 1913 he had a mortality of 48% and 26%, and in the 500 cases a mortality of 35%. At John Hopkins, of 247 cases of mild eclampsia, the mortality was 14.2% by radical treatment, and by the conservative, on the same number of cases was 2.3%. In the severe eclamptics, there was a mortality of 33.8% by the radical methods. By using the conservative treatment on like cases, it was found to be reduced
to 19.4% mortality. These figures run about the same for other practitioners doing this type of work.

Du Bose states that with a suspected case of pre-eclampsia that is in the hospital under medical treatment and studied for a week or ten days on dietetic measures, intestinal hygiene is maintained, and the patient is kept at rest by use of morphine. Then if eclampsia is impending, a section under a local or a spinal should be performed, the abdominal section being the attack of choice. These cases are operated upon under a spinal, as it causes a reduction in the blood pressure, which does no harm in these toxic patients. Du Bose states that prolonged conservative treatment in pre-eclampsia is a dangerous procedure, for when the eclamptic procedure has started, the mortality ratio for both mother and child has greatly increased.

Most of the obstetricians since the intravenous injections of magnesium sulphate have been discovered, have dropped the use of the cesarian, and have come to the conclusion that it is to be used either early in pre-eclampsia, or not at all, except in those with pelvic deformity and obstruction of some type. Then we can conclude that this operation should not be used for spectacular results or quickness, but only when the condition is advancing in severity under medical treatment, or when we have pelvic abnormalities.

In the year of 1848, the reports of autopsies after the intrapartum convulsions, showed the brain to be water logged. But the workers at that time thought the edema was not sufficient enough to cause these symptoms. When the cerebral vessels became
sufficiently congested a pathological picture is formed that can produce the symptoms.

McDonald in 1878 states that eclamptic convulsions are due to extreme anemia of the cerebraspinal centers, and coincident with extreme meningeal engorgement. These are probably the result of each other. Rosenstein says that the toxemia is not caused by any poison in the blood, but is the result of cerebral anemia which in turn produces cerebral edema.

Hurst in 1918 states, as the elimination of the kidneys becomes decreased in quantity, the eclamptic condition becomes worse, and visa versa. De Lee in 1928 states that cerebral edema is probably the cause of the convulsion. Here the edema causes an increased intra-cranial pressure, with pressure upon the brain. Stroganoff in 1930 states that there is a vascular spasm, and that this is the basis of the hypertention, which with cerebral edema is sufficient to produce a brain anemia. If there was a generalized cerebral vascular spasm, there would be produced a permanent paralysis, as is evident where this does occur.

There are many practitioners who think that eclampsia is due to congestion of the brain, and from this belief Arnold and Fay have worked out a treatment for this condition. They have divided the patients into three classes as to the condition of the kidneys, and state of sickness:

(1) Moderate pre-eclampsia.
(2) Threatening eclampsia (without nephritis
(3) Active eclampsia.
Then their treatment for the moderate pre-eclampsia is as follows:

1. The total output of urine for the first 24 hours is measured and charted.

2. Total fluid intake is not to exceed the amount of urine output for the twenty four hours preceding.

3. Then on subsequent days, the fluid intake is to equal that for the previous day's output. Therefore one has to keep an accurate chart of urine output per day, intake per day, and an accurate chart of the patient's weight, to determine, if there is an increasing edema or excess evaporation.

4. Magnesium sulphate in small doses is to be given daily to still further dehydrate the body.

5. The patient is to have moderate feedings, proteins sufficient to keep and maintain body metabolism, and a diet low in salt.

6. Patient is to have food and a drink every three hours of the day, and nothing between feedings. Through this procedure the body fluid level is to be maintained, and there will be a loss of fluid over that of the intake.

Since the threatening eclampsia is similar to the active eclampsia in treatment, I will include them both together:

Treatment of active eclampsia:

1. Patient is given 2 or 3 gr. of sodium luminal. If the patient becomes worse, then she is given 1/4 to 1/2 gr. of morphine, which should come after spinal drainage and glucose intravenously.
(2) 50 c.c. of 50% glucose is to be given intravenously, and given early.

(3) The spinal fluid should be drained off as completely as can be done, with the head raised at a angle of 30°.

(4) The glucose injection should be repeated in four hours, and a spinal in four to six hours, if no improvement is noticed.

(5) Saturated solution of magnesium sulphate should be given by mouth to produce a watery discharge.

(6) When the patient comes in she is to have no fluid intake for the first 24 hours, and the urin is to be measured and charted with the temperature, pulse and respiration.

(7) If dehydration has been thorough and effective, labor need not be started.

From this line of treatment, sedative control is produced. The hypertonic solution dehydrates the body tissues, and increases diuresis. The spinal produces rapid dehydration of the brain.

To note the effect of this line of treatment and the rapidity with which a patient recovers, the following case report was taken from surgery, Gyn. and Obst. - Vol. 55-1933-pp 129.

A woman, age 32, para III, was admitted to the hospital on September 24th, 1930, and was discharged on October 4th, 1930. She was brought in on a stretcher after having a few convulsions at home. She was semi-concious. Widely restless, apparently blind and deaf. She had complained of a head ache, vomiting and blindness. She was then seven months pregnant. Three years before she had a therapeutic abortion from a prolonged attack.
of eclampsia, and another one and a half years before. From her second month she had complained of head ache, vomiting and viscera disturbances. She gave a history of excessive eating and drinking throughout her sickness. On examination, the uterus was half way above the umbilicus. The fetal heart was not heard. She had slight external edema. Blood pressure was 174/105. Urine was scanty, Sp. gr. 1.031, slight amount of albumin, fine hyaline casts, and granular casts. Many pus cells, and a few red cells were present. Soon after entering a venesection was performed, and the blood pressure was brought down to 150/90. This was followed with 50% glucose injection, followed in two hours by 20 c.c. of 10% magnesium sulphate intravenously. This was all accomplished by withholding food and fluid for the first twenty four hours. The output of urine for the first 24 hours was 17 ounces, and her fluid intake for the next day was 15 ounces. At the end of the week a fluid balance of 30 ounces had been established. Through this treatment she was brought back to normal and was discharged on the 10th day. It is important here to note the rapidity of recovery in this pregnancy, and in the first two she had to have a therapeutic abortion, as the case could not be controlled. In her former pregnancies she was treated by Arnold, but at that time he was using the method of pushing fluids, which shows a contrast of the two methods.

The mechanism of action of the above procedure is as follows:

Fluid balance is the ratio of water taken in to that excreted,
regardless of form taken in, and in a normal person the output should always equal the intake. Then in eclampsia we find a disturbance of this balance, which results in the formation of edema and other manifestations. Then we can say that disturbed fluid balance is a definite syndrome, and regardless of the cause, the end results are always the same. It has been a much disputed subject in eclampsia, but now the majority say that it is due to faulty metabolism. Regardless of the specific cause of the edema, the effect on the brain is the same. There is first an increase of fluid in the blood, then as this increases, there is a shift of the fluid into the body tissues to form an equal osmotic pressure. As the blood with its excess fluid passes through the choroid plexus, this in turn secretes more fluid into the ventricles. If the blood fluid was low, the excess would in turn be reabsorbed by the pacchionian bodies, to keep the spinal fluid pressure down. Since this cannot absorb any more, and since the brain is enclosed in a solid case, the brain cannot expand from the edema, thus compressing the blood vessels, and hindering the blood circulation. If this lasts for some time the end result is brain atrophy.

Then the treatment by common reasoning would be to withdraw all excess fluid from the blood, by spinal taps, hypertonic solution of magnesium sulphate and glucose, and to limit the fluid balance so that they equal each other.
CONCLUSION - TREATMENT

In the early history of eclampsia the treatment was of the operative nature to relieve the mother of the foci of generation of the toxic material. From the fact that the radical treatment was the first line of treatment, it has taken a long time to abandon it. The change has only taken place through further education of all older practitioners and medical students. The shift of treatment from the radical to the conservative was brought about by further and better pathological study, which has revealed the liver and kidney damages, edema of the general body and more of the brain, and by considerable experimental work with animals.

From our gradual shift of treatment from the radical to the conservative, we have noticed a gradual reduction of mortality to almost half of that of the former treatment.

We cannot state any definite type of medical treatment for every case of eclampsia that we encounter, for we know that our treatment may vary for every case, and must meet the demand of each specific case. If we consider that eclampsia is caused by a complex toxemia, and that there is no one single etiological factor, then we must abandon the hope of ever obtaining a specific cure. Our treatment must then be directed on the results of the toxemia rather than on the cause of the disease.

We may then divide our treatment into three parts.

1st: Proper supervision of the pregnant woman.
2nd: Treatment of pre-eclamptic conditions.
3rd: Treatment of the eclamptic attack.
1st: Patient is to be placed in a moderately dark room.

2nd: Prevent the patient from biting her tongue, as by placing something between the teeth.

3rd: Prevent her from falling off of her bed.

4th: Morphine, 1/4 to 1/2 gr. hyperdermically, if convulsion continues repeat in 30 minutes.

5th: Catheterize patient and examine urine.

6th: 2 gr. of chloral in 100 c.c. of milk by mouth or rectally 1 hour later.

7th: The morphine is to be repeated 2 hours later, and followed in 5 hours by chloral.

8th: Fluid by mouth if conscious, or glucose intravenously.

9th: If she improves from this treatment, then let her go to full term.

10th: Many advocate inducing labor here with a large bougie, without anesthesia, then deliver child when cervix fuller dilated.

11th: If the condition becomes worse, some advocate doing a cesarian under local.

12th: If the blood pressure is about 165 or higher, with general edema, then do a venesectomy and let the blood pressure fall 20 to 30 mm of Hg.

13th: Injection of 20 c.c. of 10% solution of magnesium sulphate to cause diuresis. This is to be given every hour till the convulsions have ceased.

14th: Give sodium amytal gr. X intravenously or by rectum. This can be repeated in 4 to 6 hours if convulsions continue.

15th: Gastric lavage with soda bi carbonate.

16th: Force fluids. They should be given the best way for the patient, as (Hypodermoclysis (Intravenously (By mouth.

17th: In delivery one should avoid general anesthesia.

1st: If cervix is dilated can use forceps or version.  
2nd: If cervix is not dilated, use bag.
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