A Lecture ON THE ETIOLOGY AND TREATMENT OF PUERPERAL ECLAMPSIA.

DELIVERED AT THE MEDICAL GRADUATES' COLLEGE
AND POLYCLINIC.

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As the majority of those attending this College are either in private practice or intend entering upon it sooner or later, it is essential that the latest views of any subject considered, especially one of such vital interest as this to any engaged in the practice of obstetrics, should be placed before you; but, as Zweifel has termed eclampsia "the disease of theories," I shall only mention what may be regarded as the more important with reference to the etiology of this disease—so terrible in its onset and course, and so terrifying to those around. It may appear as extraordinary that such an enormous amount of writing—in 1908 alone Eardley Holland states in an admirable review that there were over 100 scientific papers on the eclampsia problem¹—has been devoted to this subject, but this is due to the fascination of the unknown. When the exact cause of a disease is demonstrable it ceases to be of such interest to the pathologist and to those who are searching for light. Until we know exactly the cause of onset of an affection it will be studied as carefully as heretofore, but with the help of modern methods of investigation the task becomes easier than formerly.

Puerperal eclampsia may be defined as a disease peculiar to the pregnant woman, and almost invariably manifesting its presence by convulsions of a tonic or clonic character, accompanied by unconsciousness and followed by coma or sleep. It may occur either during gestation, immediately before, during, or after confinement, and may be extremely slight in the manifest symptoms, or so terrible and grave as to kill immediately or within a few hours of the occurrence of the first convulsion. It is most usual to occur in the latter part of pregnancy, rarely before the fifth month, and very rarely before the fourth month; generally a short time before term, less frequently in labour, and least frequently after labour. Its frequency varies from 1 in 500 cases to 1 in 250, according to various tables. About 70 to 80 per cent. of all cases occur in primiparae. It is very difficult to estimate the incidence exactly, because most figures are taken from clinics to which patients are sent on account of the convulsions, whereas in ordinary private practice they would be treated at home. We know that 80 per cent., or between 75 and 80 per cent., according to various statistics, of those women attacked by the disease recover, and it is important to note that they recover under all kinds of treatment. Therefore there is a mortality of about 20 or 25 per cent.—a terrible mortality in any disease. I shall endeavour to see if there is any method of treatment which will diminish that mortality. In some tables the death-rate has been much higher—as much as 32 per cent. in Schroeder's clinic.

DIAGNOSIS.

There is, as a rule, no difficulty about diagnosis, but it is possible that it may be confounded with:

1. Cholaemic eclampsia, which condition seems to have been established by Braun, Frerichs, and others, and is a rare disease. There are no signs of renal mischief, such as albuminuria, oedema, etc., and symptoms point to the liver, as epigastric tenderness, vomiting, and intense headache, and pain referred to the region of the liver. A state of nervous agitation develops and convulsions follow; the patient sooner or later becomes comatose. In the severe cases jaundice always develops, and the urine may contain biliary matter or remain normal. The condition of the blood favours thrombosis; embolism and haemorrhages and petechiae, as well as purpura, are common.

2. Epileptic convulsions, which may, of course, occur at any time during pregnancy in the epileptic. There may, however, be some doubt about a case seen for the first

time in the "status epilepticus," when the patient passes from one convulsion to another, and which may terminate fatally, or when one sees the patient in the stupor or coma after an attack of epilepsy.

3. Uraemia may be the cause of some difficulty in making the diagnosis. It develops from a sudden suppression of urine, or when the kidney substance has been destroyed, and eclampsia develops in the same way when the pregnancy kidney has reached a certain stage of degeneration. But puerperal eclampsia may develop when the kidney is apparently normal, when the urine examination is consistent with health, and when there is no albumen present in the urine. Undoubtedly there are many points of resemblance between the two affections. It has been observed that the freezing-point depression (cryoscopic point) of the blood differs in the two conditions.² But, as in cholaemic convulsions, it may truly be said that only the *post-mortem* room can really decide when either occurs in the pregnant woman.

4. Coma, due to cerebral apoplexy, alcohol, or meningitis, which may come on during pregnancy, may be mentioned, as well as hysteria, acute poisoning from strychnine, phosphorus, or nitro-benzol,³ but when the whole of the antecedents of each case are considered there is not likely to be much difficulty in making a diagnosis from puerperal eclampsia.

PROGNOSIS.

This must always be serious, because the mortality of the mother is 20 to 25 per cent., and of the fetus 33 to 50 per cent. Stroganoff had a maternal mortality of 6.6 per cent. in a series of 400 cases, which is extraordinarily favourable and most unusual. But prognosis may be exceedingly difficult and uncertain, because where the convulsions may be slight and have ceased, where the secretion of urine has been re-established, and where the temperature is not high and the patient seems to be doing well, a convulsion occurs, ending in profound coma and death. Persistent high arterial tension is always unfavourable.

Speaking generally, if the temperature is not running up, the pulse is fairly good and not rapid or thready, the fits decreasing in frequency or have ceased, and the kidneys are acting well, all may go well. If convulsions commence after labour, the prognosis is, according to recent statistics, equally serious as in those cases where they commence before or during labour. According to Veit, the mortality is about 14 per cent. in primiparae and about 19 per cent. in multiparae. Olshausen considers that the mortality is about the same in both. According to Seitz, the prognosis is worse with each convulsion up to 20 or 30. The prognosis really seems to depend on the rapidity with which the attacks follow each other and the duration of the coma after the convulsion.

PATHOLOGY.

It may be briefly stated that all the organs of the body are in some manner affected, the main lesions being found in the liver, kidney, heart, and brain. In other words, it may be said that these organs are affected in puerperal eclampsia in the same manner as they are in many toxæmias. As I remarked under the head of diagnosis, the *post-mortem* room alone could decide in cases of cholaemic convulsions, with its more or less necrotic changes in the liver in its most marked degree, acute, yellow atrophy of the liver,⁴ or puerperal eclampsia, for they are really the result of profound poisoning. It was usually thought that the kidneys were the main source of trouble, considering that renal changes are constantly present in eclampsia, but in 1888 Pellet called attention to haemorrhagic lesions in the liver in eclampsia. Schmorl confirmed his observations and pointed out that eclampsia was distinguished by profound changes characteristic of no other disease, and that he had found in every case lesions of the liver which he considered were more characteristic than those observed in the kidneys. In 1893 he published the result of his examination of 73 fatal cases, and it may be interesting to mention more especially the changes in the kidney which took place in 99 per cent. of the cases, and which are of a degenerative nature. The macroscopic appearances are those of parenchymatous nephritis. Microscopically protoplasm of the epithelial cells of the convoluted tubes is found in various stages of degeneration, cloudy swelling, fatty degeneration,

and coagulative necrosis. Schmorl states, contrary to the opinion of Winter, that the glomeruli are not chiefly affected. In one case he found the kidneys healthy although the other organs had the usual changes. He found the liver affected in all but 27 of his cases, and says the condition consists of necrosis of cells, singly or in varying sized patches, which may be anaemic or haemorrhagic, and has met with fibrinous thrombi of the capillaries of the interlobular as well as the intralobular veins, and a fibrinous exudate between the liver cells. The macroscopical appearance of the liver shows minute haemorrhages under the capsule, as well as minute infarctions due to thrombosis of the smaller branches of the portal vein. The pathological conditions of the liver closely resemble those found in acute yellow atrophy, yellow fever, and phosphorus poisoning. There are metastatic thrombi of liver and placental cells, and fat emboli have been found in the lungs and glomeruli by Virchow and Winkel.⁵

In eclampsia there seems to be general thrombosis of capillaries. It is an affection of different organs at the same time which allows puerperal eclampsia to be diagnosed after death. It may be said of the blood that in the majority of cases the red corpuscles are greatly in excess, and that this is also true of the white corpuscles, which are much more numerous than in normal pregnancy.⁶

Dienst lays great stress on this excess of white corpuscles, as he considers that they are the origin of fibrinogen, which, according to him, is, by its increase, the actual cause of the disease, to which I shall presently refer.⁷

In the fetus minute haemorrhages have been found in the more important organs, as well as fatty degeneration or necrosis. This will show the severity of the poison, and as the changes are akin to those found in the mother, it is evident that the same kind of poison affects the circulation in both, leading to these pathological changes.

ETIOLOGY.

This part of the subject may be divided into (a) causes residing in the mother, (b) causes residing in the fetus.

Of the causes which reside in the mother, two great theories have been in vogue:

1. The pressure, or mechanical theory, due to increased intra-abdominal pressure, and the pressure of the enlarging uterus.

2. The toxæmic theory.

These, again, may be divided into predisposing and exciting causes. The predisposing causes may be said to include:

(a) Any disease of the kidney, or any condition which causes faulty elimination, because, of course, if elimination is interfered with, waste products must be retained in the circulation, and may damage the kidneys, as well as other organs.

(b) Pressure on the renal veins, or on the ureters, by an unusually large uterus, as in twin pregnancy, causing retention of urine.

(c) Abnormally large fetus or fetal head.

(d) Small pelvis.

Statistics show the occurrence of eclampsia in 11 per cent. of multiple pregnancy as compared with 1.1 per cent. of single pregnancy. Primiparae of extreme youth or extreme age are especially liable to eclampsia because of rigidity of muscles. The proportion of eclamptic primiparae to multiparae is as 3 to 1.⁸

The theory of pressure on the ureters or veins need not be discussed unless it can be shown that it in any way raises blood pressure. The secretion of urine is determined by pressure of blood in the glomeruli of the kidneys. Whatever causes contraction of the arterioles of the body generally raises pressure in the arteries, and will raise the pressure in the glomeruli also, leading to increased secretion. In certain circumstances the contraction of arterioles may be so great that the branches of the renal arteries are also constricted. Then, although the general pressure is so high, the pressure on the glomeruli falls so much that secretion of urine ceases and suppression of urine is established. This condition may explain the absence in some cases of changes in the kidney.

We know that abdominal tumours, even of enormous size, do not cause eclampsia. The exciting causes, supposing, of course, that the pathological factors are present,

may be sudden suppression of urine, partial or complete, constipation, painful contractions of the uterus, rigid os in primiparae, exhausting expulsive efforts, and emotion. After the first convulsion, the slightest shock or irritation may cause another one.

In the light of modern research it may be said that puerperal eclampsia is caused by a toxæmia—some poison circulating in the blood—and that as the poison must be derived from some changes in the body itself, it must be autogenetic, or an auto-intoxication. The whole condition is, in fact, due to defective chemistry of the body, and I may briefly lay before you the more recent views as to the causation of that toxæmia.

There can be, as far as we know at present, no "eclamptic toxin," but there must be some poison or poisons to begin the changes in the cells which lead to disorganization of the organs as a rule most affected—the liver and kidneys. Zangemeister's investigations⁹ have shown that the retention of nitrogenous substances is not to be regarded as a causal factor under any circumstances. I shall briefly relate the substance of most of the recent theories regarding the origin of the poison.

1. *The Circulation in the Mother's Blood of Fetal or Placental Elements.*

This was brought forward by Veit in 1902. It is founded on the knowledge that particles of fetal ectoderm, and even portions of chorionic villi, become separated from the placenta and gain access to the mother's blood. Veit believed that this gave rise to a poison termed syncytiotoxin, which is normally rendered harmless by an antibody syncytiolysin, which develops in the mother's serum. If the amount of poison is too great to be neutralized by the syncytiolysin, poisoning and eclampsia occur. He injected an emulsion of human placenta into the peritoneal cavities of rabbits, which led to albuminuria and sometimes death, but these results follow the injection of any animal matter. If an ovum gets into the peritoneal cavity by rupture of a tube, eclampsia does not develop. Dreyfuss says¹⁰ that there is no definite proof of the placental origin of eclampsia. Lavare has discovered a blood-coagulating ferment in the placenta, which is important when it is remembered how much thrombosis of the capillaries throughout the body takes place in eclampsia. Sievinski and others have shown that the fibrinogen content of the blood is raised in pregnancy, and is very high in eclampsia. It may be said, of course, that the cause of this disease lies in the failure of the so-called "organs of defence," including the thyroid, parathyroid, suprarenals, etc., to completely perform their functions, but we cannot speak positively concerning this point.

2. *Poisoning by Material Formed or Retained in the Placenta.*

Freund and others have attempted to prove that eclampsia is due to endotoxins contained in the chorionic villi, and particularly in the syncytium. Injections into animals of placental extracts were generally followed by death, and sometimes convulsions. The *post-mortem* examinations showed genuine thrombosis, with lesions of the liver and kidneys. Freund thought that the placenta contained poison made up of two constituents, one acting on the nervous system and the other causing thrombosis, but Lichtenstein in 1908 demonstrated that the results obtained could be produced by the injection of indifferent material.

3. *Derangement of the Metabolism of the Mother.*

With reference to this, it is important to briefly refer to the functions of the liver, and to remind you that, whilst it is the chief assimilative organ in the body, it is also the chief antitoxic and defensive organ. It must be remembered that it has to do with the disintegration of protein and the profound modification of the various products of protein metabolism (proteolytic functions). As the result of these combined processes, there occurs a remarkable degree of detoxication of the portal blood, which loses the highly toxic properties (for example, in respect of ammonia) it formerly possessed (detoxicating and defensive functions).¹¹ These processes are carried out largely by the aid of appropriate ferments (proteolytic, glycolytic) produced by the liver cells, and able to produce these effects even after death. Thus by a process of

self-digestion, or autolysis, the following products can be formed: Leucine, tyrosine, glycoll, xanthine bases, ammonia, resembling those resulting from tryptic digestion. These ferment activities differ from those exercised by other digestive glands, inasmuch as the proteolysis and glycolysis they effect take place within the liver cell. This peculiarity exposes the liver cell in a special degree to disturbance, to the extent even, in the case of severe toxic influences, of contributing to its autolysis when it is left exposed to the action of its intracellular proteolytic enzymes, unchecked by the influences which normally control their activity. The conditions presented by the liver in acute yellow atrophy, chloroform and phosphorus poisoning, exemplify the powerful destructive actions of the proteolytic enzymes present in the liver cells. Thus the liver cell becomes exposed to the destructive action of its own proteolytic ferments. A process of self-digestion or autolysis may set in, either in the parts of the liver affected or in the whole liver, as in acute yellow atrophy, and results in the complete disintegration of the liver cell, with suppression of all its functions, not only the proteolytic and glycogenetic, but still more of its nutritive functions. The disturbances then brought about are amongst the most severe, violent, and fatal known to the body (choleamia and hepatic toxæmias).

The influence of the nervous system must be considered in dealing with the functions of the liver. Belief in the possible effects of mental emotion on liver metabolism, based on clinical experience, receives some support from recent pathological observations regarding the part played by autolysis or self-digestion in liver disease. If the intracellular alkalinity in the liver cell fall to a low point as the result of acidosis, of inanition, or previous liver disease, the effect of severe mental depression or emotion accompanying liver disease may well be in particular cases to depress the functional activity of the liver cell beyond the point at which it can resist its own proteolytic ferments.¹²

Herman, Masson, and others found the relative amount of urea lessened in eclampsia, and Hérouin discovered that the relation of the amount of nitrogen contained in the urea to the total nitrogen was greatly altered. The normal ratio is reduced in pre-eclamptic toxæmia and eclampsia. Study of the "nitrogenous partition" by Zweifel, Ewing, Whitridge Williams, and others,¹³ shows a marked increase in amino-acids, as well as uric acid, creatinin, and the xanthine bases. Zweifel demonstrated large quantities of sarcosolactic acid in the urine, and this was also found in the cerebro-spinal fluid by Fith and Lockemann. But we have no proof, as yet, that lactic acid is the cause of eclampsia, because, as suggested by Whitridge Williams, it is probably only a result of the muscular work incident to the convulsions.

This theory of toxæmia has been much studied since Bouchard stated that our health depended on the even balance between the production and excretion of toxic substances. He considered that the urine would be a guide to the amount of toxin present. Much labour has been devoted to the analysis of the urine since then, in pregnant and non-pregnant women, with contradictory results. Tarnier and others considered the urine of the healthy pregnant woman less toxic than normal. Schumaker believed that the difference was due to the amount of concentration.¹⁴ In the urine of eclampsia, with convulsions, different observers found the urotoxic dose vary, so that the results were quite contradictory, and it was found that the more precautions were taken in collecting urine, the method of preparation, etc., the less toxic it became, and Stewart, who took care to inject only pure urine, free from bacteria, declared it was innocuous.

Owing to the influence of the thyroid gland on metabolism, Nicholson considered that eclampsia must be due to insufficiency of iodothylin, which is manufactured by the thyroid to aid the metabolism of nitrogenous substances.

Lange¹⁵ found that in 133 women during the last twelve weeks of pregnancy the thyroid gland enlarged in a little over 81.2 per cent. If iodothylin were administered, the thyroid became less in size, and enlarged when the drug was stopped. In 18.8 per cent. there was no enlargement, and of these 16 had albuminuria with casts, and 6 had eclampsia. If there is a deficient amount of iodothylin, the metabolism of nitrogenous substances

is not complete up to the stage of urea formation, and toxæmia follows. If the thyroid gland is completely removed, toxæmia may follow, causing convulsions.

Nicholson¹⁶ considers that iodothylin affects the kidneys—first, by exerting some specific action on them; secondly, if diminished, it allows the formation of toxins which damage the kidneys; thirdly, it prevents the formation of urea, and as urea is a powerful diuretic, it decreases this stimulus, for it is a marked vaso-dilator, and so maintains renal activity, since, if it is absent, it allows the secretion of the suprarenal, to which it is antagonistic, to come into action, leading to spasm of the renal arteries, which may arrest renal secretion.

The suppression of the thyroid function reduces the metabolism of cells in the same way as it does that of albumen, though the two processes do not proceed parallel with one another.¹⁷ The theory advanced by Baumann, Oswald, and others is based on the assumption that the specific activity of the colloid present in the thyroid secretion is directed to the neutralization of toxic substances, and that this neutralization takes place within the blood stream. Attempts to obtain this toxin from the blood of thyroidless animals have, however, met with no success.

4. Anaphylactic Reaction.

By anaphylaxis—a term coined by Richet in 1902—is meant the hypersensitiveness of the organism to a foreign protein. In 1908 it was suggested by Rosenau and Anderson that eclampsia might represent an anaphylactic reaction. Lockemann and others believed that the mother was sensitized during pregnancy by minute quantities of fetal protein, and would develop anaphylactic shock if any amount of fetal blood were suddenly introduced into the circulation. They identified this condition with eclampsia. Others have failed to support them. Schenk, Veit, Heynemann, and Dienst have agreed in rejecting this theory.

Budin has shown that the poison absorbed from the intestinal tract has been in close relation to the toxæmias of pregnancy. Comyns Berkeley considers that eclampsia might be primarily due to renal toxæmia, hepatic, thyroid, or intestinal toxæmia—a failure of any of these organs to perform their functions properly resulting in the accumulation of the particular waste products they customarily deal with, and consequent general poisoning of the body, so that all the organs are more or less affected, and eclampsia results. Délore and Rodet suggested the presence of bacteria in the blood, and Müller thought a bacillus of the uterus causing a general intoxication would account for eclampsia.

5. Mammary Toxæmia.

Sellheim¹⁸ advanced the theory that the poison of eclampsia was manufactured in the breast. This originated from what he had learnt of the birth palsy, and the calf disease of the cow, which in one of its developments singularly resembles eclampsia of the woman, and is considered by many veterinary surgeons to be exactly the same disease. It has been found that by the injection into guinea-pigs of small quantities of colostrum obtained from cows suffering from vitellus, the animals die with lesions of the same character as those found in eclampsia. Therefore it is suggested that eclampsia may be due to poison manufactured in the mammae.

6. The Theory of the Fetus as a Cause of Eclampsia.

Those who support this theory have in their favour the facts that eclampsia is more frequent with twins, and still more frequent with triplets; that convulsions usually cease after delivery, and have been known to cease on the death of the child *in utero*; that sometimes infants born of eclamptic mothers have convulsions after birth, and *post-mortem* evidences the same as those found in the mothers. Usually cases of eclampsia occur after the fifth month, so that waste material has had considerable time to accumulate.

Again, Dr. Drennan¹⁹ has advanced the hypothesis that the abstraction of calcium salts from the mother by the fetus is a cause of puerperal eclampsia. In that article it is stated: (1) That, although it is generally believed a certain amount of fatty infiltration of the liver cells around

the hepatic veins, the central zone of the lobule, is physiological in pregnancy and lactation; it is really pathological, and that it is due to the extraction of calcium salts from the mother's blood by the fetus, in such quantity as to deprive the mother of what should rightfully be hers, to unite with the fatty matter in her liver cells, to form lipoids—soluble fats—which would then be conveyed by her circulation, to be deposited in tissues normally the dépôts of free fat, and also as a source of fat to the fetus. (2) This fatty infiltration causes disturbed liver function, with the production of toxins from imperfect protein digestion. (3) Circulation of toxins causes fatty degeneration of liver cells, thereby increasing the liability of the liver to functionate, with resulting increased toxæmia. For those who believe in the theory of immunity, this means that the organism does not form a sufficient amount of antibodies to render harmless any excess of toxic material.

I have spent a considerable time in laying before you the more important theories of the causation of this disease because I believe that if we could ascertain the cause we should not only be able to treat the patient with more likelihood of success, but we should by prophylactic measures be made able to safeguard all pregnant women.

Sir Halliday Croom is of opinion that, as all *post-mortem* examinations show the liver and kidneys are primarily involved, an explanation may be furnished by the fact that these organs are at fault, and functionate badly. The fact that the kidneys are not perfectly sound would account for a sudden chill being the immediate cause of an attack, and a chill may be brought about in many ways, and in any weather. Nagel found, from the records of the Berlin Hospital,²⁰ that some periods of the year had practically no cases of eclampsia, and in other months they occurred in series. On referring to the Royal Meteorological Institute of Potsdam, he found that the months which were free, or almost free, from eclampsia, were those months of a high barometer and even temperature, a change bringing damp, wet, and raw weather, making existing nephritis worse, and as a consequence increasing the number of eclampsia cases. Against these views, however, it must be admitted that cases occur in which no changes in the kidney or urine are made out, although the kidneys are involved in about two-thirds of the cases of eclampsia, and albumen is found in the urine in about 84 per cent. of all cases.

TREATMENT.

It would be impossible for me here to discuss all the methods which have been advised or adopted by those who have had experience of this illness, but there are two points which ought to be borne in mind in approaching the study of treatment. First, that about 75 per cent. will recover, whatever may be done; and, secondly, the condition is so deceptive that, with reference to drugs, it is impossible to say that because a certain remedy has been successful in a few cases it will benefit all, or even the majority. Life is too short for any one man, however extensive his practice may be, to come across a sufficient number of cases in his own individual private work upon which to found rules applicable to all eclamptics. There are some practitioners who have attended many hundreds of confinements and yet have but rarely met with a case, and Croom mentions two²¹ who have had between two and three thousand cases of labour and have never had a single case of puerperal eclampsia. Therefore it is easy to conceive of a practitioner, having had a few cases treated in a certain manner, being so impressed by them, if followed by success, as to feel strongly that his treatment saved the patient. We are therefore compelled, in dealing with treatment, to draw our particulars from hospitals and large clinics where the opportunity is afforded of admitting considerable numbers. It is natural that, in dealing with an anxious case, such as one of eclampsia, the medical attendant, if within reach of any maternity or hospital, should be glad to send the patient—if suitable as a hospital patient—there, so that he may be relieved of the responsibility of her treatment, and in the full knowledge that everything possible will be done for her. Hence the facility of dealing with large numbers, and of drawing conclusions therefrom, for, as the average number of cases varies from 1 in 500 to 1 in 250, according to where the statistics are compiled, it is evident that

we must have a large number of confinements to give us data.

Prophylactic Treatment.

Although we do not know the exact cause of the disease, and therefore cannot prevent toxæmia, we do know that frequently there are signs and symptoms of pre-eclamptic toxæmia which occur, and which give us warning of the approaching storm. I shall therefore divide this subject into (a) preventive, and (b) curative treatment.

The most common signals of danger are headache, which may persist for some days without any other symptoms, or it may be accompanied or followed by nausea, epigastric pain, sickness, diarrhoea or constipation, increased arterial tension, rapid pulse, lessened excretion, dimness of vision, and disinclination to exertion, or sometimes restlessness and excitement, the urine, as a rule, containing albumen. These symptoms may or may not be accompanied by oedema of the extremities and face. In my own experience the most common symptom has been headache, which has been more or less persistent, and slight blurring of vision. Occasionally dimness of vision may come on quite suddenly, and may be marked in one or both eyes. I remember one patient at the seventh month who complained of headache in the morning, and next day had well-marked albuminuric retinitis, but no oedema of the face or extremities. In many cases, before any symptoms arise at all, if the urine should be examined, albumen may be found, and this is always a danger signal if present in any quantity. It must be said, however, that in some cases symptoms will develop and no albumen be present, and in others no symptoms appear until the first convulsion. In one case of a patient who appeared to be absolutely well about six weeks before the confinement was due, I found on examination of the urine about three-fourths of albumen. In spite of my strong opinion that premature labour should be immediately induced, six days were allowed to pass, and I was summoned to her in the country, to find her unconscious and in continued convulsions. A large amount of albumen is not, however, always followed or accompanied by eclampsia. I remember one patient whose extremities were oedematous, and whose urine was scanty and almost solid with albumen, who arrived in town, owing to unavoidable delay, only immediately before the expected date of her confinement, when she was seized with labour, through which she passed satisfactorily. Another, to whom I was summoned in the country, had a fair amount of albumen, with no pre-eclamptic symptoms, who went through labour well, and was seized with violent convulsions afterwards, from which she recovered perfectly.

When the foregoing symptoms occur, accompanied by a small amount of albumen, undoubtedly the best treatment is to put the patient to bed and feed her on milk, giving as much aperient saline medicine as may be necessary to keep up free relief. According to Nicholson, eclampsia is due to an insufficiency of iodothyron. Milk diet does not require so much iodothyron; but a meat diet yields too little iodothyron, and also yields too little iodine for the manufacture of a fresh supply. Therefore the patient may get well on this simple milk diet. Should the albumen increase in amount in spite of this treatment it will generally be found that the output of urea decreases in relation to the rise of albumen. It has been pointed out by Herman that there is a great diminution in the amount of urea in puerperal eclampsia, although we know from experiments that urea is not the reason of eclampsia. If the amount of albumen is rising—a sure indication that the woman is being increasingly poisoned—we have either to allow her to take her chance of continued rest and milk causing amelioration, or induce premature labour. The latter, in my opinion, is far the better course, because, as the affection is a disease of pregnancy, when that condition is over the results of the disease will most likely pass away. As I have already pointed out under the head of etiology, painful contractions of the uterus may be sufficient to cause a convulsion. The woman is in a state of unstable equilibrium, and the least irritation may turn the balance, so that the necessary manipulation to induce labour may be the means of bringing about the one thing we wish to avoid. Yet I still say that it is more prudent to induce labour and take this risk, because if there be a risk of induction it is hardly likely that the state of

irritability will be less by the time labour spontaneously starts, even if the patient continues free from convulsions for so long.

With reference to the method of inducing labour I shall only mention that, in my opinion, the safest and simplest, provided there is no reason for hurrying, is by passing one or two sterilized bougies into the uterus with every aseptic and antiseptic precaution. I have done this on many occasions, and up to the present have not met with any difficulty or haemorrhage from the bougie passing between the uterine wall and the placenta. Even if bleeding did take place in the special case under consideration it would probably do more good than harm.

Of course, the time at which the albumen occurs or is discovered, and the amount, will influence one's opinion, for if it be before the seventh month it is natural to give the woman every chance of continuing the pregnancy sufficiently long to bring forth a living child. If, however, rest in bed, combined with a milk diet, does not seem to lessen the amount of albumen, or if other symptoms do not seem to be improving, it is far better, in the interests of the mother, not to delay terminating pregnancy, at whatever date from conception it may be.

Although the foregoing treatment is the best to prevent the actual onset of eclampsia when any symptoms or signs develop, yet we know there are cases which occur where there are no signs or symptoms whatever, and the first indication of anything being abnormal is the sudden onset of convulsions. We know also that albuminuria in large quantity may occur quite suddenly, and therefore it is important to examine the urine from time to time, although this may not always be practicable, for the patient may not be seen at all until shortly before confinement, or only when taken with symptoms of illness.

Curative Treatment.

As the etiology is still obscure, it is not possible to prescribe a causal therapeutics, but as we believe the disease to depend on some toxin, our endeavour must be to eliminate that toxin as quickly as possible, while we take care of the patient during the convulsive stage. The treatment may therefore be divided into (a) surgical, and (b) medical.

Although it will not be possible to discuss all under the first heading it will be of interest to enumerate the methods suggested.

Emptying the uterus: (a) Abdominal; (b) vaginal.
Total extirpation of the uterus.
Decapsulation of one or both kidneys.
Amputation of both mammae.
Trepining of the cranium.
Lumbar puncture.
Bleeding.
Intravenous injection of hirudin.
Injection of air into mammae.

Emptying the Uterus.

In discussing the subject of emptying the uterus, which means active interference with a patient who is in such a state that the least irritation may lead to a fresh convulsion with risk of death, it would be rather a pleasant reflection with which to console one's self that the patient would be better untouched by operative interference, because some statistics prove that emptying the uterus does not stop fits, and therefore that it does not influence the disease. But as this is a disease of pregnancy, we know that when the child is born, the woman, should she survive, is at least nearer the end of her troubles. In fact, in my opinion, puerperal eclampsia may be looked upon as a disease having a definite course to run, like typhoid fever; in this case, if the poison in the system be sufficient to kill, then the patient will not outlast the ordinary course of the disease, but if the powers of resistance, or her "defensive forces" are strong enough, she will continue to the end, and recover. Now we know that, as a rule, in eclampsia, it does not run its course until the confinement is over, and therefore it is clearly good treatment to help terminate the pregnancy, providing that can be done without adding a greater danger, either immediate or remote, to the patient, always remembering that she is in a desperate condition, because, although we know the average of recoveries, we can never tell that the next convulsion will not kill the patient in whom we are interested. Therefore it is absolutely essential that each case should be treated on its own merits.

I do not wish to burden you with statistics, but with reference to the rapid termination of pregnancy there are some I must refer to, and I would remind you that such is the interest in puerperal eclampsia that every year which passes helps us, on account of accumulating experience, to take a different view regarding figures which were collected some years ago. In an admirable paper in 1902 by Herman, who collected from the reports of different clinics 2,142 cases of puerperal eclampsia, he states that of these the fits ceased in 850 after delivery. He considers that the comparison of the cases in which the uterus was rapidly emptied with those in which it was not interfered with was to show that there was no benefit in emptying the uterus, the fits were not stopped, neither was the death-rate apparently smaller. It is only right, however, to point out, and Herman thinks the objection a fair one, that the figures showing a very high mortality among the patients delivered by operation are taken from pre-antiseptic times, and do not apply to operative delivery under conditions of the present day.

Of course, in dealing either with operative means or spontaneous delivery, the most important point for consideration is the amount of time elapsing from the moment of the first convulsion to the emptying of the uterus. There can be no doubt about the increasing mortality with the multiplicity of the fits. In 571 cases collected by Seitz from Schauta, Schlesinger, Duhrssen, and others, this is clearly shown, and Reuben Peterson²² tabulated 615 cases showing the results of prompt delivery and the expectant plan of treatment of eclampsia, and the former give a mortality percentage of 15.9 as compared with 28.9, the mortality of Professor Bumm being 4.8 as compared with 31.1 by the expectant treatment. These figures are very striking as showing the advantages of prompt delivery. In this table Zweifel had a mortality of 32.6 by the expectant treatment, which fell to 15 per cent. when he changed to immediate delivery after the patients entered the clinic. This table is especially valuable, as it shows the reduction in mortality in the same clinic through a change in the methods of treatment, and I therefore hand it to you, with other tables, on a separate printed slip.

It is natural to inquire what effect prompt delivery has on the recurrence of convulsions. It was observed long ago that they were fewer in number and less severe after the birth of the child than before. It is evident that if convulsions continue after the termination of labour the patient is profoundly affected by the poison, and the danger to the kidneys, liver, etc., may be so great that the eliminative treatment is not of the least use, and the patient is fatally ill with the first convulsion.

In a table given by Peterson, modified from Seitz, out of 2,135, convulsions ceased in 52.7 per cent. after delivery, including operative and spontaneous, whereas in 453 cases of vaginal and Caesarean section the convulsions ceased in 62.6 per cent. In another table showing cases in which convulsions ceased after spontaneous delivery he gives 59.7 per cent. This is almost exactly the same percentage as that of 994 cases in which convulsions ceased after operative delivery.²³ Therefore, from the foregoing figures it may be said that convulsions cease after delivery in a little more than half of the cases, and that it seems to make but little difference as regards convulsions whether delivery be spontaneous or terminates by operation. Although convulsions cease after delivery, it is not certain that the patient will recover, for 18 per cent. die; but she will have a better chance, because where the convulsions continue after labour the mortality is 10 per cent. higher. An interesting table shows that the convulsions may be taken as an index to the extent of the poisoning of the mother, and that the fewer the number of convulsions before vaginal Caesarean section the better the percentage of safety to the mother. It varied from a mortality of 18.5 per cent. when the operation was performed after from one to five convulsions to 100 per cent. when undertaken after from sixty to sixty-four fits.

It is necessary to refer to the fetal mortality in general in eclampsia compared with that following vaginal Caesarean section. Peterson gives the fetal mortality after all kinds of treatment as 29.4 per cent., and after vaginal Caesarean section undertaken at varying periods after the first convulsion it is 21.2 per cent., which is

lower than in other series. Where only three convulsions occurred before the birth of the children by vaginal Caesarean section, the fetal mortality was only 11.8 per cent. Out of 139 cases of spontaneous delivery the mortality percentage of the fetus was 25.1. The fetal mortality is lower after spontaneous than after various operative means of delivery (25.1 and 30 per cent.), but it is not so low as after vaginal Caesarean section. The reason for this lower fetal mortality after Caesarean section is that the operation is quickly performed, and the child is subject to little traumatism, which is undoubtedly the cause of the death of many infants. In the anxiety to deliver quickly by the ordinary methods, the child is frequently apt to suffer. While eclampsia is nearly three and a half times more in primiparae than in multiparae, the mortality in the latter is higher (28.02 and 22 per cent.)

It is evident from the foregoing that prompt delivery gives the woman the best chance, and in seeing a case you will quickly have to decide upon the most expeditious manner of emptying the uterus. Much, of course, will depend upon the time when the first convulsion occurs, and whether the patient has actually begun labour. If she be a multipara, with a soft dilatable os, or a primipara where the cervix has been taken up and no difficulty offers against dilatation, then if this can be safely and fairly rapidly done, it is far better for the woman than anything else, provided there be no narrowing of the pelvis. The dilatation can be carried out with simple dilators—Bossi's dilators—or manually. On the occasions when I have used Bossi's dilators I have had no difficulty, but I am certain that it requires great care not to cause laceration of the cervix. When the cervix is fully dilated, and not before, the membranes can be ruptured, and version performed, or forceps applied. As a point of great practical importance, I am sure that thorough dilatation of the cervix is essential before version or the application of forceps if you are to feel safe in avoiding lacerations in delivering the child. Of course all this takes time, however favourable the condition of the cervix, but in spite of the comparative delay it is far more satisfactory to deliver in this manner than to perform Caesarean section. But supposing the cervix is rigid, and quite undilatable (a word which must only be used with reference to the time likely to be spent upon dilating a hard and rigid cervix), the fits are recurring, and you consider rapid delivery will give the best chance to the woman, you must decide between vaginal Caesarean section or abdominal Caesarean section, and remember that the woman will have a better chance from either operation if she has not been subjected to manipulation by other operative procedures prior to Caesarean section.

Supposing the surroundings and arrangements for the abdominal operation are satisfactory, and the patient is at term, or approaching that time, abdominal Caesarean section is easier, and provides a clear exit for the child, especially if there be the least contraction of the pelvis. In vaginal Caesarean section the difficulties which may be met with are principally connected with the injury to the bladder, the difficulty in drawing down the cervix and in suturing it, and in tearing the cervix. But out of 530 cases collected by Peterson there was no difficulty with the operation as originally recommended by Dührssen in 1896 in 214 cases, and he concludes that the anterior incision ordinarily serves all purposes, and that the additional incision in the posterior cervical lip can be dispensed with. In using both incisions the percentage of tears of the uterus and soft parts was rather higher than when only one was used.

Taking into consideration that in Dührssen's operation the parts operated on are high up, that often one must trust to touch, because everything is not in sight, that haemorrhage may also tend to obscure the field of operation, and that when finally version or forceps are used, with the knowledge that injury may be done to the bladder or uterus, I think that most will prefer the abdominal route. This is probably more true to-day than when Dührssen's operation was originally introduced, because the field of Caesarean section has become more extended. The earlier methods of operation have been improved upon. There are modifications of the uterine incision, and, of course, the most important development is the extraperitoneal Caesarean section introduced by

Frank, of Cologae, in 1907. In this operation the peritoneum can be stripped from the bladder and uterus, so that the risk of infection becomes lessened.

Freund states that the methods in use in the Charité in cases of eclampsia are early delivery in order to diminish the severity of labour, venesection, and isolation. In 551 cases which were delivered in the first hour the mortality was 0 per cent. The mortality rapidly deteriorated with the duration of the disease at time of operation.

Decapsulation of the Kidneys.

According to Kermauner,²⁴ decapsulation carried on before delivery is of no value. Unilateral decapsulation only is irrelevant, and has had to be given up. Bilateral decapsulation carried out some hours after delivery yielded, according to Balser's collection of cases, thirty-seven deaths out of a total of ninety-one—that is, 40 per cent. As it is possible that favourable rather than unfavourable cases are published, the results must be regarded as of small value.

Total Extirpation of the Uterus.

This has been carried out on the assumption that the poison, or part of the poison, causing eclampsia was manufactured in the uterus.

Amputation of the Mammary Gland.

Sellheim²⁵ records a severe case of *post-partum* eclampsia recovering after amputation of the mammae, and Martin, who has published a case of severe eclampsia recovering after the same operation, believed that the fall of blood pressure caused by the operation had a great deal to do with its success.

Lumbar Puncture.

Bataski²⁶ published cases treated by lumbar puncture. When the arterial tension denotes a permanent state of hypertension, he considers it more rational than venesection. He withdrew 20 to 35 c.cm. of cerebro-spinal fluid, which was followed by relief in each case.

Medical Treatment.

I may enumerate some of the many remedies suggested in this affection, and then indicate what seems to be the most satisfactory means of treatment. Anaesthetics, morphine, chloral, veratrum viride, adrenalin, thyroidin, parathyroidin, hirudin, nitroglycerine, to act on the peripheral system; erythrotetranitral, calcium chloride, potassium chloride, serum treatment, removal of colostrum, hot packs and hot-air bath, oxygen, the injection of air or oxygen and potassium iodide into the mammae, lumbar anaesthesia.

As the treatment should be eliminative, based on the knowledge of a toxæmia, our object is to get rid of the poison as quickly as possible, or dilute it. A good dose of magnesium sulphate or some other saline may be given at once, or some prefer croton or castor oil, so that rapid aperient action may be secured. If there are reasons against rapidly emptying the uterus, one of the best means of diminishing the poison is to bleed freely and to use saline injection, or transfusion directly into the circulation by a vein. Bleeding is one of the oldest remedies, and in former days very free bleeding was practised. Ramsbotham²⁷ used to take "from 40 to 60 oz. and even more in the course of a very few hours." Of course, each patient will not stand the same amount of loss, but about 500 c.cm. or 600 c.cm. may be withdrawn at first, or an amount until the pulse becomes affected or the patient turns pale. There is no better means of diluting the poison than by these two simple methods, for, if no transfusion apparatus is at hand, continuous proctoclysis can be kept up by a small catheter in the rectum with normal saline solution.

Theoretically, hot packs and hot-air baths, by drawing off perspiration and tending to increase the thickness of the blood, ought to be harmful, but practically they seem to do good in some cases. Little²⁸ has had great success with the use of hot-air baths.

Döderlein²⁹ and Leopold advised against sweating, but if the patient can drink plenty of fluid, and if the saline solution be flowing freely into the intestine, rectum, or vein, then dilution of the poison is taking place and no harm can come of it. You must, however, remember that

such treatment is of no good if the patient is already oedematous, and if the kidneys are not acting at all.

Some prefer to give at once a large dose of morphine or chloral hydrate. If the patient is very restless, I prefer chloral. Of course, if there is high blood pressure the morphine reduces it, for it is a powerful vaso-dilator, but, if possible, it is better to do without it, because it undoubtedly adds risk to the child, and it is not without danger to the mother, with kidneys insufficiently acting. If the tension is high, veratrum viride will certainly lower it, and has long enjoyed a reputation in this affection. If the uterus has been emptied, and the convulsions should continue, with high tension of the pulse, this drug is well worth trying, but it must be used with care, for it is very powerful.

The patient may be kept soothed with some anaesthetic; and although chloroform is certainly more convenient, yet, if it is to be administered for a considerable time, it must be remembered that chloroform poisoning produces changes in the liver which are practically the same as those caused by the disease. Ether may be substituted for it, for Mr. Bellamy Gardner informs me that it does not attack and disintegrate the cells of the liver as does chloroform. For the actual convulsions, the inhalation of oxygen may be used when the surface of the skin becomes dusky.

According to Zweifel,³⁰ between 1887 and 1892, when chloroform and sweating but no venesection were employed, the mortality amounted to 32 per cent. In the years 1892 to 1895, when operation was done without chloroform and morphine and without sweating, the mortality sank to 15 per cent. He advised against sweating, because it thickens the blood, and is in favour of artificial dilution of the blood, and the excess of acid in the blood to be combated by the administration of vegetable acids.

Lichtenstein³¹ recommends venesection, usually withdrawing 500 c.cm. of blood, and states that his recoveries amounted to about 24½ per cent.

There are two methods of treatment which deserve to be mentioned, because in the hands of some they seem to have been efficacious. One is the therapeutic employment of normal serum from pregnant women, as carried out by Mayer (Tübingen) and the other is the use of large doses of thyroid gland. I have already said that I have no intention of mentioning nearly all the many remedies which have been suggested, but anything which is likely to act as a direct antidote to the poison is worthy of consideration, and thus may act in this manner. Nicholson³² considers that thyroid extract is the ideal vaso-dilator in cases of eclampsia, but that it is necessary to use large doses; 30 or 40 grains are given at first, and a second dose of 20 or 30 grains in six or eight hours if there should be no improvement. He considers that the noteworthy points in relation to this treatment are the unusually early re-establishment of the renal functions and the rapid and complete disappearance of symptoms. He believes that normally thyroid secretion is the opposing influence which safeguards renal circulation from a dangerous over-action of the internal secretion of the suprarenals, which acts as a constrictor of the arteries and capillaries. Englemann has injected hirudin (leech extract) intravenously with the object of inhibiting the coagulation of the blood and preventing thrombosis, and recently Licht³³ has published cases of intramammary injections of air.

I need not weary you by detailing other remedies, but I feel sure that the best results will come to those who regard this, in the light of our present knowledge, as a poison in the blood acting on the nerve centres; and as our treatment of all poisons is by an antidote when the poison is known, and by elimination, and, failing this, dilution when the poison is unknown, so the simplest way of regarding a patient suffering from puerperal eclampsia is as one suddenly poisoned, and treat her accordingly. Therefore anything which will, in any degree whatever, strengthen the defensive forces of the body, will do good. My belief is that venesection, combined with the endeavour to eliminate the poison, and dilution with saline transfusion will be of most service.

There are many cases in which no treatment is of any avail, and which are mortally ill from the moment of the first convulsion. There are others, again, which are not so seriously affected, although this can never be known

at first, and therefore they are the ones which may recover under any treatment whatever, and are the cases where one is apt to have an exaggerated idea of the importance of any special line of treatment if it happens to be successful.

If the temperature be steadily rising, the patient comatose, with a rapid pulse, tending to be more frequent and thready, a tepid bath may be given if this be possible. The patient may be put into a warm bath, which is gradually cooled down to 80° F. or lower, and allowed to remain in for twenty minutes. This doubtless acts in the same way as it does in serious cases of typhoid fever or acute rheumatism.

Conclusions.

From the foregoing it may be concluded:

First, that in spite of all the labour which has been spent upon investigation, we know of nothing which we can definitely state gives rise to the disease, although everything seems to point to poison circulating in the blood as being the cause.

Secondly, that without any doubt recent statistics show that the best treatment is that of rapidly emptying the uterus—by whatever means this may be most safely accomplished—after the first few convulsions; that is to say, without indefinite delay. The woman and the child are thereby given the best chance of life, and, as already stated, the maternal mortality has been lowered in the hands of some to under 5 per cent.

Thirdly, that the greater the delay in carrying out this treatment after the onset of the first convulsion, the greater will be the danger.

We must hope that the time is not far distant when, by continued research, the knowledge of the actual cause will provide us with a weapon to surely prevent the onset of this disease, and relieve the accoucheur of the future of one of the most terrible complications of the lying-in room.

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FROM statistics of the number of women pursuing higher studies in Prussia which have recently been published it appears that in the last winter session the total number was 2,980, as against 2,892 in the previous year. Of these, 361 were students of medicine, as against 329 in the corresponding session of 1911-12.

A MEETING of the committee of the German Society for the Repression of Quackery was held at Dresden on March 9th, when the following officers were chosen for the ensuing year: President, Professor Beythien; Vice-President, Professor Schmori; Secretary, Dr. Neustatter; Assistant Secretaries, Drs. Decker and H. Weber; Treasurer, Dr. Eger.