A Lecture ON THE TOXAEMIAS OF PREGNANCY.*

BY
ALECK W. BOURNE, M.B., B.CH., F.R.C.S. ENG.,
OBSTETRIC SURGEON TO OUT-PATIENTS, ST. MARY'S AND
QUEEN CHARLOTTE'S HOSPITALS.

THE exact relation of the mother to her unborn child has been debated since Bar¹ first suggested that both lived for the mutual advantage of each other. He believed that in return for the protection and nourishment of the growing fetus afforded by the mother, the fetus conferred certain nutritional advantages, as shown by an accelerated and intensified metabolism, which make for her improved general health, lasting not only during pregnancy but for long after the birth of the child.

But welcome as such a theory may be to our sentiment, the recent immunological investigations on pregnant women, notably by Leith Murray,² afford strong evidence that the fetus *in utero* is not only not a symbiotic partner but rather a foreign element, always a source of potential danger to its host. Such laboratory findings only support common clinical evidence. Though the pregnant woman may be in what she calls good health from the beginning to the end of gestation, yet we know that departures from the normal, sometimes very serious, are only too common, and in general it is undeniable that pregnant women are in a less stable and robust condition than when not carrying.

It is necessary to realize that a state of poisoning exists throughout pregnancy, the toxin produced almost certainly by the growing ovum being absorbed by the maternal circulation. Whether the pregnant woman be well or ill depends not upon the formation and absorption of some unusual poison, but on the capacity or failure on the part of the mother to develop an adequate antipoison, by which she is rendered immune. We may almost say that the ovum is always poisoning its mother, but that in all healthy women, fortunately the majority, the poison is effectively countered by her own immunizing efforts. Where these fail, then can the toxin effect its work unhindered.

The actual source and nature of the toxin of pregnancy have been the reason of years of search and controversy, but it would be unprofitable to day to devote any time to discussion of all the various theories. I will simply consider the later views in so far as they may help us in understanding more fully the clinical features of the toxæmia of pregnancy and act as a guide to its rational treatment.

The most recent and important work bearing on this question began with Schmorl's discovery that small pieces of syncytial protoplasm could be found in the maternal circulation. The importance of this observation was the definite proof it affords that the foreign fetal protoplasm is conveyed into the maternal circulation. The next question which naturally arose was whether there was any biochemical defence against this invasion, set up by the mother's tissues, comparable with that which the organism makes against invasion by any other foreign protein or bacterial products. The answer was probably given by Abderhalden in 1911, when he demonstrated that the maternal blood during nearly the whole of pregnancy and for ten days afterwards contains a specific ferment capable of digesting placental protein. An enormous amount of experimental work has been done in order to confirm or disprove Abderhalden's claim, and, though there is still some controversy as to the exact meaning of the reaction, the general thesis that the mother's blood contains an anti-enzyme (or other form of antibody) capable of rendering innocuous the foreign proteins from the placenta, is probably true.

Further evidence of a biochemical response on the part of the mother was furnished by Theis and Lockemann,³ who showed clearly that the maternal serum is sensitized to some bodies in the fetal serum and placenta; by Murray⁴ and Fieux and Mauriac,⁵ who showed by the complement-fixation reaction a definite antibody for an antigen existing specially in young chorionic villi; and by many others.

A modification of this theory has been put forward by Young,⁶ who suggests that the poisoning is due to the absorption of auto-digestion products from a portion of prematurely separated—and presumably necrosing—placenta. But his view is apparently not applicable to all cases of toxæmia, though it goes far to explain the association of eclampsia with accidental haemorrhage.

Finally, I may refer to the view of Tweedy, who believes that the toxins arise from the maternal gut. He argues that in the non-pregnant condition the neutralizing and excretory mechanism of the body is capable of dealing with any noxious products absorbed from the bowel, but that in pregnancy this mechanism can be overwhelmed by the strain due to the excess of such products caused by the metabolism of the fetus *in utero*. His conclusions are based largely on the good results he has observed after starvation and purgation, with thorough lavage of the stomach and colon. But in spite of this observation a general survey of clinical and laboratory knowledge leads irresistibly to the view that the toxin is supplied by the placenta, that ordinarily this toxin is neutralized by maternal antibodies, and that failure to develop these in sufficient quantity causes symptoms of pregnancy toxæmia.

Biochemical Examination.

Turning now from theories, we find that the investigations of laboratory workers have been chiefly in the direction of blood and urine analysis, immunological reactions of the serum, and experimental attempts to isolate a toxin and cause the disease of eclampsia by injecting it into animals. In 1914 Young⁶ described experimental toxæmia in animals caused by the injection of placental extracts. In many respects the animals showed symptoms almost indistinguishable from eclampsia, and, still more significant, the *post-mortem* appearances were almost identical with those in patients dead of eclampsia.

The broad results of urine analysis are the finding of albumin, a tendency for the urea output to be diminished, a variable increase in the percentage of nitrogen excreted as ammonia, and the presence of acetone. Further, the amount of urine may be diminished even to complete suppression, and a deposit of renal casts and red blood cells is frequently observed. The general results of urine analysis point to (1) degeneration or necrosis of the specific excretory cells of the kidney, shown by diminished quantity and the presence of albumin and casts; (2) degeneration or necrosis of the liver cells, causing the disturbance of the urea and ammonia coefficients.

Let us consider the hepatic derangement and its consequences first.

We know that in health the amino-acid cleavage products of the digested proteins are absorbed and transported to the liver, where they are largely transformed, the nitrogenous moiety being converted chiefly into urea. In experimental occlusion of the hepatic portal circulation no urea is produced, and if ammonium carbonate or amino-acids are perfused through the living isolated liver, urea is formed. An intermediate product, however, in the formation of urea is ammonia (or ammonium carbonate).

It follows, therefore, that a diminished urea output indicates some degree of hepatic insufficiency; an increased ammonia coefficient in the urine may similarly indicate a stage of hepatic degeneration, short of a complete functional breakdown, but enough to prevent the final stage of urea formation from the ammonia.

One indication, then, of high ammonia and low urea excretion is hepatic degeneration, short of massive necrosis, for in this condition neither ammonia nor urea could be formed. But, as Leith Murray⁷ points out, a high ammonia output has a second significance in pregnancy toxæmia, as in other conditions. It may indicate an excessive acid formation in the system, for ammonia production is the body's natural mechanism for the neutralization of that amount of acid formed above the quantity which can be neutralized by the fixed bases (sodium, etc.).

The ammonia of the urine may therefore be divisible into two moieties, the first being an intermediate product of the liver in the course of a conversion of the amino acid into urea, and the second being that which is purposely produced by the liver, as such, for the work of neutralizing fatty acids due to an abnormal fat metabolism. The first indicates partial hepatic insufficiency in that the final urea

* Delivered to the Hamstead Division of the British Medical Association, April 15th, 1922.

stage is not reached; the second that the patient is in a condition of acidosis—of which more anon.

These different fractions of ammonia may be separated by giving large doses of sodium bicarbonate, for should the body be producing ammonia in order to neutralize excess of acid, it will be relieved of this work if the required alkali be supplied by the mouth, and the ammonia excretion in the urine will fall. In short, the fall of the ammonia, after giving sodium bicarbonate, will be a measure of the acidosis present.

The ammonia remaining, if much above the normal in pregnancy (and it tends ordinarily to be higher in pregnancy), will be a measure of how far the liver is failing to convert its nitrogen to the final stage of urea, and therefore of hepatic degeneration, but not of massive hepatic necrosis.

In spite, however, of the importance of the liver changes, it is obvious that the results of analysis of the urine may depend very greatly on the condition of the kidneys. The liver may be working well, and yet the waste products it has produced may be unable to pass through the damaged renal epithelium. How, therefore, may we obtain an index of the efficiency of the kidney? First, the quantity of urine excreted. If with an ordinary or excessive fluid intake the urine is scanty, it is reasonable to suppose that the kidney is either damaged or that, owing to congestion, the urine is unable to escape. White⁸ has shown that the kidney in eclampsia may be so intensely congested that the urine cannot flow down its collecting tubules.

Secondly, the microscopical examination of the deposit will give valuable information. Few or no casts or red blood cells with a fair secretion will indicate only slight kidney changes, while a heavy deposit of casts with much blood will be a sign of more extensive damage.

Unfortunately, the quantity of albumin gives very little information, for we find some cases of serious toxæmia with little albumin, and the contrary condition is often present.

Acetone is found in the urine in some cases. It is derived from a disordered fat metabolism, and indicates an abnormal production of acid in the system. It is commonly seen in starvation and is constantly present in those cases of toxæmia associated with intractable vomiting. In eclampsia it may indicate acidosis, and its presence is of great diagnostic value.

Symptoms in the Prodromal Stage.

During the prodromal stage the patient usually comes to her doctor on account of headache and malaise or oedema of legs and face, less commonly for a failing of sight, and more rarely still for epigastric pain and vomiting.

A headache in late pregnancy is common, not always due to toxæmia; frequently it is a symptom of a low tension debility, often complained of by multiparae. By itself, without changes in the urine, or a high blood pressure, it usually means nothing; but it is a fairly constant warning symptom, which is of value in showing the need for a complete examination of the patient. Similarly, oedema of the legs is often non-specific in its indication, but if combined with oedema of the face and other parts its presence should call for full investigation. Failing or altered vision is an important and dangerous symptom, and warrants an immediate ophthalmoscopic examination of the fundus oculi. Miller¹⁰ states in a recent paper that early eye changes are usually significant of chronic nephritis rather than of pregnancy toxæmia. The differentiation is important for prognosis and for treatment. Of itself, retinitis is one of the more serious symptoms of albuminuria, and if, as has been pointed out, this condition indicates a pre-existing kidney disease rather than an albuminuria of pregnancy origin, then the safest course is to end pregnancy as soon as possible. If treated expectantly such patients may develop uræmia or permanent increased damage to the kidney and lasting changes in the retina.

Epigastric pain and vomiting coming on in late pregnancy, when simple dyspeptic causes can be safely excluded, may be for a few days the only symptoms of impending eclampsia. In fact it is not uncommon for a patient's friends to state that the attack of eclampsia was preceded by a few hours or days by vomiting. As a pregnant woman has probably suffered vomiting during the early weeks,

the recurrence of the symptoms does not excite her apprehension, and therein, perhaps, lies danger. Vomiting and pain coming on suddenly in late pregnancy should always be regarded very seriously, and an exhaustive examination made. In a minority of cases, as already stated, little or nothing else can be found, and the absence of albuminuria fortifies one in the belief that whatever may be the cause it is not toxæmia. Should the cause be simple, sickness rapidly yields to simple treatment, such as rest and starvation, but if in spite of careful dieting or starvation, combined with enemata and diaphoresis, the patient continues to vomit, then she is in the gravest danger, and pregnancy should be terminated with all speed. But most patients suffering from toxæmia who begin with vomiting as the first and only symptom, rapidly develop the other familiar signs, and the diagnosis is easy.

Perhaps of greater value than the symptoms are the signs discovered by examination, and of these I regard an elevated blood pressure as the most important single sign. It is the most important because it is one of the earliest and also most constant. Albuminuria may vary from 3 per cent. to the slightest trace, which is often found in normal pregnancy, but the blood pressure is nearly, if not always, definitely raised early in the prodromal stage.

Further, unlike albuminuria, the height of the blood pressure is some measure of the gravity of the toxæmia, and an indication of the likelihood of fits supervening; for instance, Irving⁹ has shown that with blood pressure—

Between 130 and 140 mm. Hg	...	1 in 32	developed toxæmia
" 140 and 150 "	...	1 in 11	" "
" 150 and 160 "	...	1 in 3	" "
" 160 and 170 "	...	1 in 2	" "

Above 180 all developed toxæmia.

Therefore, in any patient complaining of any one of the prodromal symptoms, or during the routine ante-natal examination of pregnant patients, the blood pressure should invariably be taken and noted. During antitoxæmic treatment the blood pressure movements are amongst the best indications of the reaction of the patient. In bed, on a low or starvation diet, and freely purged and sweated, the blood pressure should be low—in the region of 100 to 110—and if it quickly falls from its original high figure to this low level the other symptoms usually clear up with it, and an expectant attitude may be continued. But if, in spite of depletion, the tension maintains its height, as it not uncommonly does, then eclampsia is still just as likely to develop, and further expectant treatment is dangerous. During pre-eclampsia the blood pressure should be determined at least twice a day, and the results plotted on the chart.

The second sign in the early stage is the quantity of urine excreted. The total for the twenty-four hours on an ordinary diet should be collected and measured. A definite diminution is significant, and the urine always shows other signs of abnormal renal activity in the shape of casts, albumin, or diminished urea output. Diminution in quantity is not an early sign, however, and therefore its chief value is as an indication of the progress of the case under treatment. The most reliable method of obtaining the quantity is by regular catheterization, as otherwise some urine may be lost during a movement of the bowels. But inasmuch as the total quantity of urine is variable in normal health, depending upon the amount of fluid taken, diarrhoea and sweating, it will be readily understood that figures of the total quantity of urine have not the quality of exactness, as an indication of progress, that is possessed, for example, by the blood pressure determinations. However, gross variations from the normal are easily observed, and are indications of serious renal insufficiency.

The third sign is albuminuria. In the great majority of all cases of toxæmia in pregnancy there is some albumin, and therefore its presence has definite value for diagnosis. Only in a small minority is albumin absent until fits occur, when it may suddenly appear in large amount. The percentage of albumin (Esbach) is very variable and cannot be taken as a guide to the severity of the case, nor is it of much value in prognosis. Some patients may suffer many fits with little more than a trace of albumin, while others with as much as 3 per cent. or 4 per cent. may never develop fits or other serious symptoms.

The chief value of albuminuria as a sign may be summarized as follows:

1. Its mere presence, very easily tested for, is the strongest evidence of some degree of toxæmia.

2. If there is a sudden increase in the amount while the patient is under treatment during the prodromal period, we have a definite sign that the patient is not under control, and is passing into a dangerous condition.

3. After an attack of eclampsia the rapidity or slowness of its disappearance has some significance. Broadly speaking, if it disappears rapidly and completely the disease has been due purely to pregnancy toxæmia and the prognosis is good, both immediately and for future pregnancies, while if the amount of albumin remains high and persists for some weeks during the puerperium there is evidence either that the disease was really chronic nephritis, and not true pregnancy toxæmia, or that if it were really toxæmia the kidney has suffered some permanent damage. The prognosis for the next pregnancy is not so good. It is therefore important to have the amount of albumin determined each day by the Esbach tube.

The Convulsive Stage.

Eclampsia proper differs from the prodromal stage in that there is added a fresh symptom—convulsions and often coma—while the other conditions, such as oedema and urine changes, may be more marked.

The fits vary in onset, number, and degree, and are of the utmost importance in their effect on the patient's chances of recovery. In general, a few slight fits without coma are associated with recovery, while the prognostic outlook worsens as the fits increase in number or severity, or if coma be superadded. To this there are exceptions—for example, a patient who has only had one fit may die, while occasionally another, who has had forty or more fits, recovers; but such cases are unusual, and it remains true that the patient's life is gravely prejudiced by a large number of fits. Every fit is a fresh threat to the patient, especially because of the great danger of cerebral hæmorrhage, which is often the cause of death; moreover, every fit renders a living child still more doubtful.

The time of onset of fits is also of importance, inasmuch as the earlier in pregnancy they occur the more severe is the disease, and, further, ante-partum fits are more dangerous than intra-partum or post-partum fits.

While it is difficult to be sure as to other factors, the occurrence of convulsions has a definite relation to three conditions—the blood pressure, delivery, and external stimuli. First, the blood pressure usually mounts after fits have been established, and, in the absence of treatment, remains high. So long as it is elevated, especially while the patient is undelivered, fits are so liable to occur that a sequence of them may be expected. They may also occur in the later moribund stages, when the blood pressure is falling from exhaustion and cardiac failure, but should the tension be reduced by means of treatment there is every prospect of a diminution or cessation of fits. Further, if during treatment the blood pressure again rises to a dangerous height, fits will be likely to reappear.

Delivery of the child has such a marked influence in stopping fits that it has led many to believe that the only rational treatment of the disease is the earliest possible delivery. In about 8 or 10 per cent. of cases, however, the fits first occur after delivery, within the first twelve hours, so that though delivery is one of the surest methods of stopping fits it is not quite certain.

It is important to remember that, apart from the severity of the toxæmia, the number of convulsions may be increased by external stimuli, such as light, noise, manipulation, and passing a catheter; in fact, almost any interference with the patient may start a fit.

A second sign of fundamental importance is suppression of urine. For this reason a close watch should be kept on the amount of urine in the bladder at definite intervals. With the large amounts of fluid usually administered in the treatment of eclampsia, scanty urine or its suppression is a serious sign; on the other hand, an increase in the amount is of favourable import. Complete suppression of urine is so dangerous a symptom that it demands active and rapid surgical interference—nephrotomy or capsulotomy—as almost the only chance of saving the patient.

The qualitative examination of the urine in ordinary clinical work should be chiefly directed towards the search for casts and red blood cells in the deposit, as a large number of cellular casts is strong evidence of serious kidney mischief, and thus influences the prognosis. Further,

the amount of albumin should be estimated in each specimen of urine obtained. The determination of urea and ammonia, though of great scientific interest, has probably not the same clinical importance as the other estimations.

A third point, sometimes overlooked, is the condition of the heart. Throughout the whole of the first or prodromal stage while the tension has been high, and particularly during the convulsive stage, the heart has been subjected to a great strain; not uncommonly dangerous dilatation, leading to sudden heart failure and death, occur. Further, I have recently seen a case which furnished strong evidence that the toxins of pregnancy exercise a specially deleterious action on the heart muscle, apart from the extra strain imposed upon it by the occurrence of fits. It is no uncommon result for a patient who has been successfully shepherded through the actual attack of eclampsia to die suddenly during following days from heart failure. Where there has been pre-existing chronic nephritis compensatory hypertrophy of the left ventricle will probably have developed, but in pregnancy toxæmia there is a sudden very great effort required of a heart which is already suffering from the additional handicap of a specific myocardial poisoning. A study of the cardiac condition is of importance when deciding upon the various measures of treatment, such as massive saline injections, or doses of veratrine, or venesection, and we should be guided in the adoption of such measures by a knowledge of the state of the heart. After delivery also the heart should be carefully watched and treated if it has suffered dilatation.

Treatment.

It is not here possible to do justice to the very numerous methods of treatment which have been advocated for eclampsia. There has been endless controversy around the most fundamental principles of treatment. Broadly, there are two main schools—the "active" and the "conservative." The first maintains that as the child or placenta are the source of the poison, the sooner they are removed the better, and to this end it is prepared to deliver as soon as possible by Caesarean section or accouchement forcé; while the second group holds that the main line of attack should be towards elimination of toxin already in the system and prevention of the fits, combined with a more deliberate obstetric treatment.

Each side upholds its method by statistics more or less favourable, but the subject is still *sub judice*. Examples of such statistics are as follows:

Brandt¹¹ reports:

		Maternal Mortality.	Fetal Mortality.
1889-1905.	Entirely expectant ...	23.6 %	31.3 %
1909-1912.	Entirely "active" ...	18.4 %	23.4 %
1913-1915.	"Active" plus narcotics...	15.0 %	34.4 %
Total 431 cases.			

Esseen-Møller¹² reports 64 cases:

Spontaneous delivery (12 cases) ...	14.2 %	—
Active treatment (52 cases) ...	13.4 %	—

Forssner¹³ reports:

1912-1915. 51 cases entirely expectant	9.8 %	—
--	-------	---

Whatever statistics are examined, the wide variations in mortality under either method of treatment are striking. The difficulty lies in the undoubted variation in severity that seems to occur in different towns and at different seasons.

Those who advocate active interference involving the most rapid delivery hold that as the ovum is the source of the toxin the sooner the child is delivered the better. To this the answer of the conservatives is that while it is true that the ovum is the origin of the toxin, yet the insult and shock to the organism involved by rapid delivery is so evil in its effects that it more than counterbalances the benefit derived from an immediate arrest of the production of the poison; that sedative treatment in controlling the fits robs the disease of its chief dangers though not immediately curing it; and, finally, that while the fits are controlled the elimination of the toxin already present is the rational procedure.

Now, for the treatment of a protean disease like eclampsia, it appears to me futile to lay down a rigid set of rules. If ever a case should be treated on its own merits it should be eclampsia, for scarcely two cases present the same clinical condition. We should approach these cases in a flexible attitude of mind, prepared to do

anything, from the simple injection of veratrine or morphine to the performance of Caesarean section and nephrotomy.

The greatest success will follow the path of the *via media*, each patient being treated on her merits. For example, a primigravida at term, developing frequent severe fits before labour, with the os closed and cervix not "taken up," and passing no urine, will probably do better if the child is removed by abdominal Caesarean section, combined with sedative and eliminative measures, than if labour is waited for or slowly induced, and allowed to drag on through many hours of fit-provoking pains.

But a multipara overtaken by fits, after premature labour has begun, with the prospect of a quick delivery, will certainly have a poorer chance if she is subjected to a forcible dilatation of the os, or cervical incisions, or vaginal Caesarean section. Broadly speaking, labour should be induced by a bag if it has not already started, but if it is established when the patient is first seen, it should only be interfered with if delayed, which is not common in eclampsia.

For the moderate cases I think the best is to employ the first few hours by sedative and eliminative treatment, which will diminish the degree of toxæmia, and put the patient in a better condition for the forthcoming labour. Of all the drugs veratrine appears the most satisfactory for the prevention of the fits and the reduction of albumin. Its chief physiological effect is the reduction of the blood pressure and pulse rate when they are high, a heavy fall occurring within half an hour after injection. It is not uncommon for no more fits to occur while the blood pressure is kept low by judiciously repeated injections of veratrine. The dose and time of injection are entirely conditioned by the state of the blood pressure and pulse—in fact, a dose should not be given unless both figures have just been determined.

The higher the tension and pulse the greater is the absolute fall after veratrine injections. The drug is potent, and liable to cause dangerous prostration if administered without due care. The general method of its use is to give an initial dose of 1 c.cm. where the tension is at 170 or above, with a correspondingly rapid pulse. For less high pressures a smaller dose, such as 0.75 or 0.5 c.cm., may be given. The first dose causes a rapid fall within half or three-quarters of an hour from 180 to perhaps 130, or less, usually with complete cessation of the fits, but it shows a tendency to rise again, sometimes within two hours, the pulse rate following suit. By repeated estimations of blood pressure every hour it is easy to arrive at the time for the next injection, usually of 0.5 or even 0.25 c.cm., according to the level of the tension. Veratrine does not stop restlessness in all cases, and for this troublesome and exhausting condition small doses of morphine are useful and without danger.

Having reduced the tension and pulse rate, and with this the liability to fits, say, after the first hour of treatment, it is necessary to have the colon washed out thoroughly until the washings are clear, as much as five or six pints being used if necessary. Gastric lavage is strongly advocated by many, but it is very disturbing to the patient, and may easily provoke a convulsion.

Every encouragement is to be given to free sweating by hot packs, electric lamps, or hot bottles, and after the colon has been washed out it is well to give saline rectal injections, containing glucose and sodium bicarbonate, up to a maximum of two pints within the first four hours. Further injections of saline are beneficial if there is good sweating and an increasing output of urine, but should there be a serious deficiency of the excretory activity too much saline injected is liable to embarrass the heart and cause pulmonary oedema, two not uncommon causes of death. Venesection is not so commonly employed as formerly, but is distinctly indicated if there is cyanosis and embarrassment of the right heart. It should always be considered in relation to the proximity of delivery, when a sufficient amount of blood may be lost from the uterus.

After twelve or more hours of this treatment the patient is usually in a much better condition and ready for the induction of labour or any other obstetric operation. The fits have ceased, the mental condition is less confused, the pulse slower and stronger, the blood pressure between 110 and 140, the skin acting freely, and the bladder containing more urine.

Where these conditions obtain in a multipara and labour

pains have not begun, I think the quickest and safest obstetric procedure is the insertion of a Champetier de Ribes bag. Labour is rapidly induced, and there is a minimum of shock. Should the presentation be a breech, an alternative is the bringing down of a leg. Observation of the blood pressure and pulse rate, with the administration of veratrine when necessary, should be continued for at least twelve hours after delivery, even when no further fits have occurred.

This is, of necessity, only the briefest account of the treatment of eclampsia—time forbids discussion of variations and elaborations of method. Suffice it to say that for cases of moderate severity I am a firm believer in the preliminary employment of conservative sedative and depletive treatment, followed later, and only if necessary, by obstetrical assistance. This should never be a violent interference, such as accouchement forcé by the vaginal route, but rather of the nature of the use of forceps, version, Champetier de Ribes's bag, and bringing down a leg, or, as an operative measure, abdominal Caesarean section. Few diseases show a greater variation in mortality. We find the same principles of treatment producing widely differing results in different towns and countries, rendering a comparison of statistics very difficult.

Some cases will die—must die—whatever is done for them. No patient can survive if the liver is almost totally destroyed by massive necrosis. But it is in the pregnancy toxæmias that preventive medicine has one of its greatest opportunities. Eclampsia is almost an entirely preventable disease, for its premonitory signs are plain for any who take the trouble to watch for them.

REFERENCES.

- ¹ Paul Bar: *Leçons de Pathologie Obstétrique*, 2, 1907. ² Leith Murray: *Journ. of Obstet. and Gynaec.*, February, 1913. ³ Theis and Lockemann, quoted by L. Murray, loc. cit. ⁴ L. Murray: Loc. cit. ⁵ Fieuz and Mauriac: *Compt. Rend. Soc. Biol.*, 1910, T. 68, No. 17. ⁶ Young: *Proc. Roy. Soc. Med.*, June, 1914. ⁷ L. Murray: *BRITISH MEDICAL JOURNAL*, 1915, vol. i. ⁸ C. White: *Proc. Roy. Soc. Med.*, 1919, vol. 12. ⁹ Irving: quoted by Dice, *Amer. Journ. Obstet.*, 1918, lxxvii. ¹⁰ Miller: *Amer. Journ. Obstet.*, August, 1915. ¹¹ Brandt: *Arch. Mens. d'Obstet. et de Gyn.*, July-September, 1916. ¹² Essen-Møller: *Ibid.* ¹³ Forssner: *Ibid.*

A Collective Investigation

OF

TEN THOUSAND RECRUITS WITH DOUBTFUL HEART CONDITIONS.

Conducted at the National Hospital for Diseases of the Heart by C. CHAPMAN GIBBES, R. O. MOON, S. RUSSELL WELLS, P. HAMILL, FREDERICK W. PRICE, and J. STRICKLAND GOODALL.

REPORT IV.*

COMPILED BY

S. RUSSELL WELLS, M.D., B.Sc.

THE ETIOLOGY OF MITRAL STENOSIS.

In dealing with the etiology of mitral stenosis we thought it wise only to take into consideration those cases where this lesion could be diagnosed with practical certainty. Excluding those cases where there was reason to believe that the murmur was really the so-called Flint, or was due to pericardial friction, we have taken as signs of mitral stenosis an apical presystolic murmur or a definitely apical murmur in diastole. This gave us an assemblage of 306 cases where the diagnosis of mitral stenosis depended mainly on the presence of a presystolic murmur, and an assemblage of 36 where either an early diastolic, a mid-diastolic, or a diastolic extending through the whole of diastole occurred at the apex. That is to say, in 342 of our 10,000 cases mitral stenosis was thought to be certainly present. There were, however, 48 cases in which mitral stenosis was strongly suspected, though no presystolic murmur nor definite diastolic could be heard. The reason for this opinion varied in the different cases, but it is needless to enter into the details here. Of these 48 cases 18 gave a history of rheumatic fever, and 30 no history of this affection. After careful consideration we thought it wiser to exclude these 48 cases entirely from our universe of discourse, which reduces the number of

* The earlier reports were published in the *BRITISH MEDICAL JOURNAL*, 1918, vol. i, p. 553; vol. ii, p. 248; 1919, vol. i, pp. 510 and 544.