examples of a low kidney reserve do not, I think, tend to show further manifestation of a like nature in subsequent pregnancies. The consideration of the cases under review bears out this conclusion.

The answer to the second question is in the affirmative. If the condition of chronic nephritis can definitely be established, it is, I think, certain that the kidney will show a progressive deterioration in subsequent possible pregnancy. As Gibberd says, "Pregnancy is the most delicate test of renal efficiency," and I think it is abundantly true that the kidney in this class of case is increasingly unable to stand this test.

It is the answer to the third question which is of most practical importance to us as obstetricians, and unfortunately here I must confess that I cannot give any dogmatic pronouncement. It is, however, abundantly clear that in about 30 per cent. of cases there is a tendency towards either recurrence of the actual condition in subsequent pregnancies or towards some other complication of that pregnancy, such as ante-partum haemorrhage, abortion, or intrauterine death of the foetus in the later weeks.

Certain clinical facts are to be noticed in studying my cases, which I think may be of help in anticipating the course which a subsequent pregnancy may take.

In the first place, there is the duration of the illness. These cases suggest to me that an attack of pre-eclampsia or eclampsia of short duration is less likely to be repeated than one which has been spread over many weeks. From this conclusion may be drawn the inference that these albuminuric cases should not, in the absence of signs denoting definite improvement, be subject to overlong treatment, but that termination of labour should be practised, say, after ten days.

Secondly, there appears to be no doubt that the blood pressure bears as important a relation to future events as it does to a present condition. In these cases which I have studied I find no case of recurrent albuminuria in which the systolic blood pressure during the initial attack was under 150 mm. The changes in blood pressure after delivery are also important, as I shall show in a moment; for the next clinical facet of the case of albuminuria which is important in view of its prognostic value is the reaction to treatment. One has found that most cases in which medical treatment is quickly followed by a general improvement and by a fall in blood pressure do not tend to recur should the patient become pregnant again. In considering the history of the convalescence, the following two points are abundantly clear. First, when the blood pressure remains constantly raised during this period we are dealing with a patient in whom we may reasonably expect symptoms during a subsequent pregnancy. It is also, I think, true that a persistence of albumin over more than two to three months is a sign that pregnancy may be complicated by a similar state of affairs should it occur again.

Perhaps I might digress a little from the actual consideration of the fate of albuminurics in regard to future pregnancies, and for one moment suggest to you that the experience of these cases which have been followed through succeeding pregnancies enables one to make suggestions which I think you will find justified. They are reflections on the prevention and management of these pre-eclamptic states. First, I would stress the importance of early recognition. Any patient should be encouraged to report any untoward symptom, and the attendant should be constantly on the watch for the early manifestations of this condition. Secondly, I would suggest the value of energetic and thorough treatment of the condition once it occurs. We are too apt to regard the early signs of an albuminuria as not sufficiently important, and I would recommend that all such patients should at once be placed under a strict regime of treatment. Thirdly, they should not be treated too long, as mentioned above. I have an idea that this prolonged treatment defeats its object and leaves the patient more subject to recurrent attacks. This leads me to the conclusion that when a time limit has been set, say of seven days, should recovery be not noted, radical treatment should be chosen. Though I cannot subscribe to the belief that eclampsia should be treated by Caesarean section, nevertheless I do believe

there is scope for this operation in the severe toxæmias of recent origin.

Turning from the consideration of the histories of these patients in recurring pregnancies, may I just draw your attention to the comparative commonness of mental symptoms after severe albuminuria occurring in pregnancy? My experience is that from 15 to 20 per cent. of known eclamptics do exhibit a confusional mental state, which state may even extend to mania. As a rule, their recovery is complete and generally fairly rapid, and I think any permanent mental instability is an expression of some pre-existing state, and not a result of the toxæmia of pregnancy, though it is probable that the toxæmia has contributed to making the condition a permanent one.

To the fourth question I can give no answer. I do not know the etiological value of an albuminuria of pregnancy in the causation of chronic nephritis, and for the elucidation of this point I think we must invoke the assistance of physicians.

THE INTESTINAL ORIGIN OF ECLAMPSIA.

BY

R. CHRISTIE BROWN, M.B., M.S., F.R.C.S.,

SURGEON TO OUT-PATIENTS, SAMARITAN HOSPITAL FOR WOMEN; ASSISTANT OBSTETRIC SURGEON, CITY OF LONDON MATERNITY HOSPITAL, AND JEWISH MATERNITY HOSPITAL.

THE purpose of this article is to offer an argument in favour of the intestinal origin of eclampsia of pregnancy.

Eclampsia has been well named "the disease of theories," and like many other diseases around which an enormous literature has accumulated, and for which many theories have been advanced, there is very little known about it. All the pathological changes met with in this disease can be best explained on the assumption that a condition of toxæmia exists. The composition and origin of the toxin are entirely unknown, but it seems logical—as eclampsia occurs only in pregnant women—to assume that it has its origin in the pregnant uterus, arising either from the foetus or the placenta, most probably the placenta.

For the present argument it is not necessary to deal minutely with the pathological changes; it is sufficient to state that similar changes occur in different organs—the kidneys, the liver, the brain, etc. The changes found in the liver appear to be of chief importance in eclampsia. Areas of haemorrhage and necrosis scattered throughout the liver are apparent to the naked eye, while the microscope reveals: (1) Degeneration of hepatic cells, beginning at the periphery of the lobule and gradually spreading towards the centre of it, so that in some cases the whole lobule is involved. (2) Interstitial haemorrhages and areas of necrosis. In nearly all cases of eclampsia the kidneys are similarly affected; small interstitial haemorrhages and areas of degeneration and necrosis are found in the cortex. There is also a degeneration of the cells lining the convoluted tubules.

It would appear that the toxin in the circulation affects various organs by producing areas of necrosis and small interstitial haemorrhages, with consequent alteration in their normal functions. Thus we find the kidney excreting albumin and no longer acting as an efficient barrier to the colloids of the blood. Analogously, the liver may also cease to act as a barrier between the portal and the systemic circulation, so that substances in the portal blood are allowed to pass unchanged into the systemic blood. If this is so, a condition exists in which a primary toxin of unknown origin damages the liver, with the result that substances from the portal blood are allowed to pass unchanged into the systemic circulation, producing a secondary toxæmia which may be the origin of the fits. In this connexion it is well to remember that it is the periphery of the liver lobule which is most affected, the primary toxin probably being brought there by the hepatic artery and taking effect where it is most concentrated. The portal venules are also around the periphery of the lobule, and thus convey their blood directly to a damaged area of the liver, which may be incapable of detoxicating its contents.

Of course, before any portal substances can penetrate the systemic stream, they have to pass normal cells in the centre of the lobule, but these cells represent only a small fraction of the whole, as it is obviously mathematically correct that the cells in the periphery form the majority of the cells in the lobule.

Among its many functions the liver acts as a detoxicator of poisonous substances absorbed from the intestinal canal via the portal vein. Indole and phenol are examples of noxious substances carried by the portal vein; they are products of protein decomposition and are formed in the large bowel by bacterial action on the amino-acids tryptophane and tyrosine respectively. These are detoxicated in the liver by oxidation, and conjugation with sulphuric acid, and pass on to the body, from which they are eliminated by normal kidneys most probably within twelve hours. Indole is conjugated to indican, and consequently the proportion of indican in the urine forms a rough guide to the amount of putrefaction occurring in the large bowel. Thus indican is present in large quantities in the urine of a patient suffering from intestinal obstruction, but apart from such a grave lesion it is found almost invariably in the urine of constipated persons and can be made to disappear therefrom by purgation. The amount of indican in the urine might serve as a guide to the functional capacity of the liver for dealing with portal toxins, especially in subjects of constipation—a condition present in practically all pre-eclamptics or eclamptics. In constipation we have every reason to believe that indole is passing via the portal vein to the liver, which, if functioning correctly, will convert it into indican, and the latter substance will be detected in the urine. If the liver fails to function, no indican should be present in the urine. The absence of indicanuria in a patient who is purged obviously has a different interpretation, and in eclampsia may be due to failure of the kidneys to excrete it.

An interesting experiment was suggested by a Russian surgeon, Eck, and successfully carried out by Pavlov. An artificial opening was made connecting the lumen of the portal vein with that of the vena cava in a dog. The portal vein was then ligated above the anastomosis, so that the blood passed directly into the systemic circulation without passing through the liver. In some of the animals operated on in this way it was found that so long as their diet consisted only of carbohydrates they could be maintained in fair health. If they were given a large meal of meat, many of them became ill and suffered from convulsions which ended in coma. At the same time there was a large increase in the ammonia output of the urine. This condition was supposed by Pavlov to be due to ammonaemia, the liver being regarded as protecting the body from ammonia produced in the intestine by converting it into urea. In this condition—Eck's fistula—the speed and amount of conjugation of bodies such as indole and phenol is greatly reduced.¹

Slight injury to the liver by chloroform and phosphorus has little effect upon the phenol conjugation, but extensive injury reduces it greatly. Pelkan and Whipple² suggest that the fatal result of the Eck fistula experiment or even of chloroform poisoning may be due to the lack of conjugation of phenols. It has been pointed out by Gibbon FitzGibbon²—and I have personally confirmed this in my own experience—that the eclamptic patient usually suffers from constipation and indulges in dietetic excesses. Gibbon FitzGibbon lays great stress upon the intestinal overload, and certainly the success of the Rotunda treatment (purges and high colonic washes) confirms this belief. It is also interesting to note that the body weight of patients developing eclampsia increases more than the average.² This abnormal increase would be expected in a patient who is overeating. The seasonal variation, being highest in spring, could be explained also in this way, for in the months immediately preceding more meat and more food as a whole are consumed. An eclamptic patient therefore appears to be in a suitable condition to suffer from intestinal toxæmia. She is constipated and overeats, and her detoxicator—the liver—is damaged, which, on analogy with the kidney, may allow noxious substances from the portal vein to pass unchanged into the general circulation,

causing a condition closely resembling that found in any animal upon which Eck's experiment has been performed. In such a patient purging and colonic washes will obviously not only eliminate the primary toxin, but cut off the supply of the secondary toxin at its source.

From what has been said above, it will be clear that one might expect eclamptic women, even though constipated at the time, to exhibit either very little or no indicanuria, and this I have almost always found to be the case in the few eclamptics whom I have investigated in this manner.

Summary.

In cases of toxæmia of pregnancy there is present in the circulation a toxin (or toxins) of unknown origin which affects the cells of many organs, interfering with their normal functions. The kidneys, if affected, no longer act as barriers to the passage of certain colloids from the blood into the urine. Should the liver be affected, it may no longer detoxicate portal poisons, but allow either all or some of them to pass into the general circulation, introducing a secondary toxæmia which may be the cause of the convulsions.

REFERENCES.

- ¹ Pelkan, K. F., and Whipple, G. H.: Studies of Liver Function—(III) Phenol Conjugation as Influenced by Liver Injury and Insufficiency, *Journ. Biol. Chem.*, 1922, 1, 513.
- ² Gibbon FitzGibbon: The Relations of Eclampsia to the other Toxæmias of Pregnancy, *Journ. Obstet. and Gynaecol. of the British Empire*, 1922, xxix, 402.

INCIDENCE OF THE SEROLOGICAL TYPES OF THE PNEUMOCOCCUS IN LOBAR PNEUMONIA.

BY

J. M. ALSTON, M.B., M.R.C.P.ED.,
LECTURER IN BACTERIOLOGY, EDINBURGH UNIVERSITY;

AND

DONALD STEWART, M.D., M.R.C.P.ED.,
ASSISTANT PHYSICIAN, LEITH HOSPITAL, EDINBURGH; DAVIDSON
RESEARCH FELLOW, EDINBURGH UNIVERSITY.

(From the Bacteriology Department, University of Edinburgh.)

THE incidence of the different serological types of the pneumococcus in lobar pneumonia has been studied extensively during the past seventeen years, and the original classification of Dochez, Avery, Gillespie, and others is now accepted by most bacteriologists. In the present article, in addition to a note of recent observations on the incidence of these types in Edinburgh, it is proposed to review briefly the findings of different observers during the past few years.

By protection tests and the agglutination reaction with antisera Dochez and Gillespie were able to divide strains of the pneumococcus into four groups, designated I, II, III, and IV. Groups I, II, and III were specifically differentiated in this way; Group IV comprised heterogeneous strains which could not be identified immunologically with the other three groups; Group III was also characterized by the possession of a thick mucoid capsule noticeable in the mucoid character of growths in culture media (*Pneumococcus mucosus*). More recently a number of constituent types referable to Group IV have also been identified by certain workers (Cooper, *et al.*), but, as will be shown, in this country such further serological subdivision seems unnecessary from a practical standpoint, though it may be of importance in other countries. The results of Dochez and Gillespie are noted in Table I.

TABLE I.—The Original Classification of *Pneumococci* by Dochez and Gillespie.

	Classification by Protection Tests.		Classification by Agglutination Tests.	
	No. of Cases.	Per cent.	No. of Cases.	Per cent.
Group I ...	28	45	22	41
Group II ...	12	20	11	20
Group III ...	9	14	9	17
Group IV ...	19	22	12	22