called "non-tropical sprue," the administration of parathyroid extract, with or without an abnormal increase of calcium in the diet, relieves the symptoms of tetany by raising the level of the blood calcium. There are, however, other means whereby this may be accomplished in rickets, although in non-tropical sprue the most efficient method of treatment is undoubtedly the use of parathyroid extract, not only in controlling the paroxysms of tetany, but also in ameliorating the intensity of the gastro-intestinal signs and symptoms. In fact, cases have been reported in which it would appear that a permanent cure had been effected by this means. In osteomalacia the effect of parathyroid therapy has not as yet been determined, but its close relationship to infantile rickets would appear to indicate that this form of therapy might be fruitful of beneficial results.

In the last five years a considerable interest has been aroused in the relationship of parathyroid tumours to diseases of the bone. In 1891 Recklinghausen described a generalized osteitis fibrosa, a disease which now bears his name. This pathological condition was more intensely studied by Askanazy in 1904. The first to draw attention to the association of parathyroid tumours and bone disease was Erdheim in 1907, in which connexion he described a parathyroid tumour associated with osteomalacia. Hoffheinz in 1925, in a series of 45 cases with parathyroid tumours either hyperplasia or adenoma, found 27 with diseases of the bone, 17 of which were classified as generalized osteitis fibrosa, 8 so-called osteomalacia, and 2 rickets. In the same year Mandl reported a similar case, and in 1927 Gold reported another. Mandl found a great increase in the calcium excretion, while Gold described an increase in the blood calcium. This subject has recently been reviewed by Hunter in his second Goulstonian Lecture. He here records that 14 carefully studied cases have been published up to date giving the clinical characteristics of hyperparathyroidism. These characteristics are briefly as follows. Whether the disease be due to a tumour, a hyperplasia of the parathyroids, or whether these glands be found normal histologically, the condition occurs twice as commonly in women as in men, and generally between the ages of 30 and 55. The patients complain of pains in the bones, and spontaneous fractures are common. Hypotonicity of the muscles is sometimes present, and radiograms show a greatly diminished density of the bone shadows, at times with evidence of cystic formation. There is an increased serum calcium, varying from 13 to 23 mg. per 100 c.cm., a reduction in the plasma phosphorus to between 1 and 2.7 mg., and in all cases there is an increase of the calcium output which may vary from a moderate degree to eight times the normal figure. It would appear, therefore, as if this condition were the opposite to that found in parathyroid tetany, except that there is the additional anatomical finding of pronounced bone destruction.

The superficial similarity of generalized osteitis fibrosa and osteomalacia has led to considerable confusion in the study of this subject. Hunter brings forward arguments which would seem conclusive to warrant the opinion that these are entirely different diseases. Furthermore, the general course and accessory clinical manifestations such as tetany, which occurs in osteomalacia, would make it much more likely that it is a disease more closely allied to infantile rickets than it is to the hyperparathyroid condition so intimately connected with generalized osteitis fibrosa.

Nephrosis is an interesting condition which would appear, in part at least, to be a disturbance of the permeability of the capillaries. This is manifested by an intense degree of albuminuria and generalized oedema. There are, in addition, two interesting disturbances of metabolism, one or other of which is usually present—namely, decreased basal oxygen consumption and/or a lowered blood calcium. The chief interest in this disease, which shows such pronounced renal factors, rests in the fact that a marked lowering of the blood calcium is present in a considerable number of cases, and that some of them respond most favourably to the use of parathyroid extract, not only in so far as the restitution of the blood calcium is concerned, but

also in promoting a rapid disappearance of the generalized anasarca. As has been said concerning numbers 3, 4, and 5 in the table, so it may be said in regard to this disease, that although there be a disturbance of the calcium metabolism which may be rectified by parathyroid extract, there is no concrete evidence that the disease is primarily due to a deficiency of the parathyroid function. It is interesting to note in this instance that, although the serum calcium is reduced, there is never in these cases any suggestion of neuro-muscular hyperexcitability or tetany. The explanation is probably to be found in the tendency in these cases of the reaction of the blood to be towards a decreased pH.

In conclusion, we may state that, clinically, two conditions are identifiable with disturbed parathyroid function, the first being parathyroid tetany due to a hypoparathyroidism characterized by a low serum calcium, a positive calcium balance, and great hypertonicity and excitability of the neuro-muscular system. On the contrary, there is generalized osteitis fibrosa, a condition of hyperparathyroidism in which there is a high serum calcium, a negative calcium balance, and a tendency to hypertonicity and hypo-excitability of the neuro-muscular system, a pronounced rarefaction of the bones, and a resorption of the corticalis and original spongiosa, this being in striking distinction to the cessation of calcification characteristic of osteomalacia and rickets.

ALBUMINURIA OF PREGNANCY AND ITS LATE RESULTS.*

BY

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THE presence of albumin in the urine during pregnancy and labour may be fairly regarded as the commonest abnormality during these states. On reviewing some 6,000 cases in which there has been a complete routine examination, it is found that about 30 per cent. of all patients exhibit this abnormal urinary constituent. About seven-eighths of these only show albumin in the urine during the labour itself, and its presence may be regarded simply as the expression of severe muscular effort; therefore for clinical purposes this type of case may be disregarded. The remaining examples of the phenomenon mainly occur during pregnancy, and it has been my endeavour to ascertain as to what extent this abnormal condition influences the subsequent history of an individual.

It is necessary to say at the outset that when we try to formulate an answer to this question we soon become impressed by the futility of the effort. In the first place, we are struck by the absence of statistics bearing upon this point. It is only during the past few years that, at any rate in England, any attempt has been made to learn the subsequent history of patients who have suffered from this complication. As an example of the paucity of records, it is only necessary for me to say that, in answer to my requests for help, I have received from one hospital a statement that their records are in a condition of complete chaos, and from another that there are no records whatever bearing on this point. I think this sufficient to suggest that there is great need for more careful compilation of statistics in maternity institutions. The move for a unification of method in preparing clinical reports of maternity institutions should be productive of much good in this direction, especially if attention be focused on this class of case. It would, of course, be necessary to collate all details of the subsequent histories of albuminurics, both as regards the course of future pregnancy and the general health. Moreover, such investigations to be of material assistance should be extended over a period of at least five years from the date of the initial illness. We must also remember that the statistics

* Read in opening a discussion in the Section of Obstetrics and Gynaecology at the Annual Meeting of the British Medical Association, Winnipeg, 1930.

of maternity institutions do not represent the true state of affairs, as they only take account of those cases which return to the same hospital for subsequent pregnancies. There may be a considerable number of patients who show, for example, a recurrent albuminuria, and who are looked after by some other institution during their later illnesses. There is no way of checking this save by meticulous care in collecting facts from the patients and by the collaboration of hospitals in verifying these facts. Lastly, any attempt to answer or consider this subject accurately ought to be carried out in consort with the medical departments of general hospitals. We, as obstetricians, too often lose sight of our patients, and it is the general physician who will undoubtedly be able to give us valuable help in trying to discover what may happen to an albuminuric in after-life. An analysis of the medical records of general hospitals would also help these investigations by providing evidence as to the role of albuminuria of pregnancy in the etiology of established nephritis as seen in the medical practice of those hospitals.

Any consideration of the late results of albuminuria of pregnancy must necessarily take into consideration the general condition of which that albuminuria is a symptom, and here we find another considerable difficulty—namely, that of classifying the various states in which this symptom occurs. Hospital records differ largely in their attention to this point, and, indeed, I wonder whether any satisfactory classification can be made in the present state of our knowledge. In most records, the condition is regarded either as a transitory one, or as one of the signs of pre-eclampsia or eclampsia, or as an earnest of a chronic nephritic change. There is, of course, no doubt that the matter is not as simple as this. It is, I think, universally recognized that these clinical types do not always exist pure, and there is quite often a mixture of one or two in the same case. One might suggest with Dr. Stander, to whom is the credit of very helpful and careful work regarding all these conditions, that we might make the classification as follows:

1. Albumin present in cases of vomiting in pregnancy.
2. A clinical class of cases with "a low kidney reserve."
3. Frank nephritis complicating pregnancy.
4. That clinical condition which we know as "pre-eclampsia."
5. Eclampsia.

For the purposes of this discussion I propose to omit the vomiting of pregnancy entirely, and to confine my efforts to formulating some idea as to the subsequent history of the four remaining groups. In deciding to which group a given case belongs I have had to rely upon the information obtained by reading the clinical history, and it is but seldom that I have found the condition proved by any biochemical or any other more elaborate means of investigation. I have known of cases in which the clinical condition is very widely different from that which has been foreshadowed by the laboratory investigations, and I am not very sure that this method is of any considerable help. The idea was widely held up to the last few years that an attack during pregnancy of a purely toxic nature (I use the word in full consciousness that we are as yet ignorant whether it be a toxæmia or not) tended to make the patient less subject to the condition in succeeding pregnancies. When we read the textbooks of obstetrics we find that it is usually stated that an attack of severe albuminuria confers immunity upon the sufferer, and that subsequent pregnancies will take place without any untoward symptoms.

The painstaking work of Stander, James Young, Gibberd, and others has given us furiously to think. Young, for example, states that out of forty-seven cases of eclampsia there were six—that is, 12.8 per cent.—in which signs occurred in a previous pregnancy, and in nine cases there was a toxic condition in a subsequent pregnancy which did not reach the convulsive stage. This gives a recurrence of 31.9 per cent. These findings have been corroborated in the work which he has carried out since the paper in which these figures are quoted. Gibberd finds a recurrence rate of nearly 40 per cent., and much

the same conclusions have been reached by Harris of the Johns Hopkins Hospital. I have tried to investigate as many cases as possible in order to be able to formulate some ideas in this respect, but as I said at the outset, the matter is one of very considerable difficulty.

We have to answer, if possible, the following questions:

1. When a patient develops a mild albuminuria in pregnancy, with perhaps a slight oedema, with no marked rise of blood pressure, and a generally unimpaired state of health, is she likely to show in future years or in future pregnancies, any evidence that her kidney has been permanently damaged?
2. Is a patient who suffers from chronic nephritis likely to display a progressive deterioration of kidney function in future pregnancies?
3. Is a patient who has been the subject of a true eclampsia or a pre-eclampsia likely to suffer in a similar manner should she become pregnant again?
4. Does the toxic albuminuria of pregnancy play an important part in the etiology of chronic nephritis?

My own experience is confined to some 60,000 cases of labour. It is large enough to know that anything may happen to these patients, but it is far too small to be able to forecast what is most likely to happen. I have therefore endeavoured to obtain help from various other sources, and this I have received from Professor Louise McIlroy, who has given me the results of the recent experiences of the Royal Free Hospital Obstetrical Unit, and I have also to acknowledge the great assistance I have received from my registrar at Charing Cross Hospital, Dr. Dodds, who has very kindly examined the clinical records of the City of London Maternity Hospital in order to try to find some data bearing on the subject of this discussion. I must here express my gratitude to both these doctors, and also to the staff of the City of London Maternity Hospital in allowing my registrar to use their records.

In all, nearly 30,000 cases of labour have been examined, and of that number 1,700 exhibited a condition of albuminuria which necessitated treatment during pregnancy.

There are among this number eighty-six cases in which the albuminuria has recurred more or less severely in subsequent pregnancies. This is a much lower percentage of recurrence than that found by previous observers, but I imagine that, were the histories more complete, we should find a greater number of recurrent cases.

In going over the histories of these eighty odd patients one cannot help being struck by their extraordinary diversity. For example, out of my own practice I have notes of two patients, one of whom had a very severe eclampsia with her first baby, and showed the presence of albumin for eighteen months afterwards. She then became pregnant again, and at the third month this albumin completely disappeared, and has not been found again throughout her two subsequent pregnancies and labours. Another, who had a very severe eclampsia, for which I did a Caesarean section (this was some years ago) has never from the time that the baby was 1 week old had a trace of albumin in the urine, although she has had three other children. On the other hand, I have notes of a patient who had an eclampsia in her first pregnancy, became pregnant again after two years, and albumin appeared in the urine at the second month, accompanied by a rather high systolic blood pressure (190). She was treated for some time according to the ideas prevailing at the moment, but she died in what I have no doubt was an attack of uraemic coma in the fifth month of this second pregnancy. There are also notes of patients who had had a pre-eclampsia for the first and third pregnancies, while the second was entirely normal, and there are records of albuminuria in succeeding pregnancies as far as the seventh, and then the eighth and ninth are recorded as being normal. Such instances, taken haphazard from these collected cases, are sufficient to demonstrate to you that I am unable to give any precise answer to the questions I have set. All I can give you are certain general conclusions based on the analysis of these eighty-six cases.

The first question is, from my experience, to be answered in the negative. Those cases which may be accounted

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

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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.