unaffected by atropine, like chorda tympani vaso-dilatation in the submaxillary gland. This observation suggested that it was due to stimulation of sympathetic fibres. Sympathetic paralysants annulled the response, the hypertensive phase being the more resistant. The action of ergot preparations on the sympathetic is generally said to be a paralysis of motor or vaso-constrictor elements, leaving depressor or dilator fibres intact, but some observers take a different view. Rothlin, Hamet and Rothlin, and Hamet state that motor and inhibitor sympathetic elements are paralysed by ergotamine and yohimbine. In the present experiments the vaso-dilator part of the response was more definitely abolished than the pressor phase by these agents. The thoracic vagus trunk in the dog accordingly contains fibres which regulate vascular tone and which give the reactions of sympathetic elements. The effects of splanchnic section suggest that they are transferred to this system, and there are two possibilities as to how it may happen. It may be that we are stimulating pre-ganglionic fibres in the vagus and that these join up with the splanchnic through an intervening ganglion—thoracic or other ganglionic group. The second possibility is that post-ganglionic fibres in the vagus are merely borrowed from the sympathetic chain to be restored to sympathetic groups in the splanchnic nerve. Certainly the vagal reactions are greatly modified by splanchnic section, and it looks as if at least some of the fibres concerned are cut in the process. The result is not to be explained by injury to vagal fibres in dissecting the splanchnic, for the reaction was frequently observed to exist after this procedure and before rupture. Possibly rupture injures vagal fibres to the coeliac ganglion. The abolition was best marked in case of the right vagus.

Concerning the seat of the vaso-dilatation, the work of McMichael and of Griffith and Emery is of interest. The former is satisfied, from the results of injecting acetylcholine, that there are no vaso-dilator fibres of parasympathetic nature in the liver. He does not seem to have stimulated the vagus nerve electrically to observe if a fall of blood pressure ensues. It may be quite true to state that there are no parasympathetic vaso-dilator fibres in the liver, yet the left vagus nerve may bring vaso-dilator fibres to this organ, fibres of sympathetic origin. Only in case of pneumogastric excitation producing hypotension with no increase of liver volume should it be said that the liver is not the seat of vaso-dilatation. McMichael further concludes from the effects of ergot that there are no sympathetic fibres in the liver. Griffith and Emery also are opposed to the view of Hallion and François-Franck that vagal dilatation of hepatic vessels does occur. Griffith and Emery stimulated hepatic nerves on visceral arteries. By this means it may be supposed that antagonistic fibres were simultaneously stimulated. Records of portal venous pressure showed a fall of this when the vagus was stimulated, but it is not possible to state if this was due to diminished resistance from the hepatic dilatation or to other change. Carnot, Gayet, and Merklen observed a similar fall of portal pressure from excitation of the pneumogastric nerve. They say that acetylcholine is of uncertain action on this pressure.

With regard to the changes of renal volume a feature was their variability in different animals. Ergot preparations diminished the shrinkage of the kidney. This observation of the failure of atropine to affect the reaction points to sympathetic elements as producing it. Kuré says that parasympathetic fibres are vaso-constrictor to the pulmonary vessels and dilator to the kidney and intestine. Tournade described a vaso-constriction of the kidney from vagal excitation, which causes increased secretion of adrenaline and thus adds to the direct nervous constriction. In the present experiments there was no clear effect either on blood vessels or intestine which

could be ascribed to any marked secretion of adrenaline resulting from stimulation of the pneumogastric. But injection of acetylcholine when this nerve was paralysed by atropine had effects which could be best explained by increased secretion of adrenaline.

SUMMARY

The vagus nerves were stimulated peripherally below the origin of the cardio-inhibitor fibres. Motor effects on the intestine were obtained which were abolished by atropine and not affected by sympathetic paralysants. They are occasioned by parasympathetic fibres which really exist as myelinated units separate from the sympathetic. Inhibitory vagal fibres to stomach and intestine may be sympathetic in type. Vascular fibres exist in the vagus which on excitation yield hypertension and hypotension. These are unaffected by atropine, and are paralysed by ergot and yohimbine. They seem to be sympathetic elements. It is not possible to say if these occur in the vagus as pre- or post-ganglionic fibres. Stimulation of the vagus causes constriction of the kidney, but the reaction is well marked only in a certain proportion of animals. The nervous units responsible for this reaction behave like sympathetic elements.

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THE AETIOLOGY AND PREVENTION OF THE TOXAEMIAS OF PREGNANCY

BY

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There are distinct signs that individual observers are beginning to recognize that ante-natal clinics, as they are at present organized, have not served to lower the maternal mortality rate, and that even efficient ante-natal supervision cannot be substituted for sound midwifery. It is not, however, realized that the death rate per thousand live births from puerperal albuminuria and convulsions and the other toxæmias of pregnancy in England and Wales during 1931 was slightly higher than it was in 1921. The investigation into the causation of these toxæmias is therefore not merely a question of absorbing academic interest, but one of real importance, for until radical changes have been effected in our maternity services it seems probable that the only hope of

lowering the maternal mortality rate lies in preventing their occurrence.

THE "TOXINS" OF PREGNANCY TOXAEMIAS

The term "toxaemias of pregnancy" embraces many symptoms, syndromes, or diseases, and includes hyperemesis gravidarum, excessive salivation, chorea, neuralgia, peripheral neuritis, tetany, impetigo herpetiformis and dermatitis herpetiformis, accidental haemorrhage, acute yellow atrophy of the liver, severe anaemia of the pernicious type, the kidney of pregnancy, and eclampsia. There are, moreover, a considerable number of aberrant forms of toxaemia which are difficult to classify. A woman may die in coma in the absence of any other sign or symptom, and I attended one patient, diagnosed by a very competent neurologist as suffering from tuberculous meningitis, who commenced to make a complete and rapid recovery so soon as the uterus had been emptied. Each and every one of this imposing array of syndromes, manifesting symptoms differing from each other as widely as the poles of medicine and affecting every system of the body, is causally associated with pregnancy, for so soon as it is terminated the symptoms begin to disappear. Some of them—such as eclampsia, the kidney of pregnancy, and hyperemesis gravidarum—are peculiar to pregnancy, but by far the greater number are not. There is no analogy for the assumption that any one toxin could cause such a variety of symptoms, and if "toxins" are to be postulated the minimal number could hardly be small. Most writers on this subject have confined their attention to what they call the nephropathy of pregnancy and eclampsia, and with a fine disregard of clinical facts and of geographical and economic influences on the incidence of these diseases have formulated hypotheses of merely parochial application.

It is because the hepatic lesions which are frequently associated with eclampsia are so striking and occur in no other disease that the majority of authors have maintained that they can only be explained on the assumption that some peculiar toxin is elaborated in the products of conception. I have shown that in dogs similar lesions may be caused in the liver either by feeding the animals on a lean meat diet or by raising the intra-abdominal pressure. It was suggested that not only eclamptic convulsions but the pains associated with obstructed labour, and possibly even with normal labour, might cause haemorrhagic necroses in the periphery of the lobules of the liver.¹ Dr. R. M. Fry, assistant director of the Bernhard Baron Memorial Research Laboratories, Queen Charlotte's Hospital, was good enough to invite me to examine sections from the livers of several patients, which support this contention. The history of one of these cases is as follows:

Labour was induced in a primipara because of a flat pelvis. Four days later definite labour pains commenced, but it was not until after a lapse of a further forty-eight hours that delivery was effected with the forceps. There was no albumin in the urine, the blood pressure was not elevated, nor were symptoms of toxaemia present. Vomiting commenced the day following delivery, and was associated with a slight degree of jaundice. Death occurred sixty hours after the child was born. There was no evidence of puerperal sepsis. Sections from the liver show widespread haemorrhagic necrosis, especially affecting the periphery of the lobules, although a single layer of liver cells often separates Glisson's capsule from the area of necrosis. Glisson's capsule in many areas shows severe degenerative changes, while the centres of the lobules are loaded with fat. The sections show the classical lesions which have been described as being peculiar to eclampsia. The patient did not suffer from any toxaemia of pregnancy, and was thought to have died from delayed chloroform poisoning.

In view of the experimental work to which reference has been made there can be little doubt that these hepatic lesions were caused mechanically by the labour pains, and if this view be accepted the strongest argument in favour of an elusive toxin peculiar to pregnancy falls to the ground.

PREGNANCY TOXAEMIA AND DIETETIC DEFICIENCY

The hypothesis² I have advanced is that there is no such thing as a toxaemia of pregnancy, if by this term a toxin or toxins peculiar to pregnancy be postulated, and that all the manifestations enumerated above as well as the ordinary morning sickness and the proneness of the pregnant woman to suffer from decayed teeth, falling out of the hair, brittle nails, and, less often, bleeding of the gums, are expressions of dietetic deficiency or deficiency diseases. Normally, deficiency diseases are due to the fact that the food absorbed, and usually the food ingested, is deficient in one or more essential substances. During pregnancy an additional, and usually the most important, factor is that the foetus robs the mother of essential substances, and renders a diet, barely sufficient for the mother, deficient for the mother and foetus. It is imperative to realize that of a thousand men fed on an identical diet deficient in vitamin B only a small percentage will suffer from beri-beri. The explanation of this is not clear, but the fact is beyond doubt. Beri-beri is frequently associated with pregnancy, and it is my belief that some of the cases of peripheral neuritis associated with pregnancy in this country are suffering from that disease. Deficiency in key substances during pregnancy disturbs "*la fixité du milieu intérieur*," and this physiological breakdown renders impossible "*la vie libre*."

I would restate my hypothesis in the following terms. All the ailments and "toxaemias" associated with pregnancy are caused by an absolute or relative insufficiency of some substance or substances in the diet, the most important of which is calcium, which leads to an inharmonious working of the various physiological processes in the body and ultimately to hepatic dysfunction. The variety of ways in which hepatic dysfunction may be revealed is only limited by the number of physiological processes in which the liver is concerned. Similarly, the variety of ways in which calcium deficiency may be revealed is only limited by the number of functions dependent on calcium ions. The final breakdown may be sudden as in some cases of eclampsia, or be preceded for weeks or even months by "toxaemic" manifestations. Albuminuria, cases of chronic nephritis excepted, is caused by mechanical dietetic factors, and is, in some cases, inevitable. If the liver is unable to detoxicate the toxins from the bowel they will gain entrance into the blood stream and damage the whole body, including the kidneys. If this hypothesis be true, it is clear that the toxaemias of pregnancy can only be prevented if an adequate diet be given throughout the period of gestation. Absence of water in the radiator or oil in the engine causes the pistons of a motor car to seize. Prevention is simple right up to the moment of the occurrence of the tragedy, which may or may not be heralded by warning symptoms, but once the seizure has occurred an expensive repair becomes necessary. In like manner the proof of this hypothesis cannot lie in the dietetic treatment of eclampsia, but in the prevention of the onset of the disease. The Dublin school has taught that eclampsia is due to an excess of food—an entirely different conception—and in this connexion it is interesting to recall the fact that the first patient in the series of cases of eclampsia published by Lever³ in 1843 was a starving woman, who had lived for some considerable time on nothing but a daily meal of bread and tea. The object of this paper is to offer a few observations on an adequate

diet, with special reference to iron, iodine, and calcium ; to discuss a few symptoms ; and to report some results obtained by calcium therapy.

THE DIET

The diet should be well balanced and should provide a sufficient number of calories. The pregnant woman, even when showing toxæmic symptoms, is perfectly well able to assimilate proteins as provided in eggs (lightly boiled or raw), milk, and cheese. Vegetables, parboiled for preference, salads, and fruit should form an important part of the dietary, for these foods not only contain important vitamins and essential mineral substances, but promote peristalsis. It would be ideal if every woman during the latter half of her pregnancy could be assured of an adequate supply of vitamins A, B, C, and D, and the question resolves itself largely into one of economics. Towards the end of pregnancy it is often advisable, for mechanical reasons, to allow four small meals daily rather than three large ones. Heartburn may be relieved by almost any alkali, but a teaspoonful of sodium bicarbonate in a little warm water taken a quarter of an hour after meals is satisfactory, cheap, and easily obtained.

There is little doubt that in some cases meat is definitely harmful to a patient suffering from an elevated blood pressure and albuminuria. The evidence that lean meat can cause severe damage to the liver is conclusive, but that this damage is caused merely by its high protein content is almost as conclusively disproved. It is probable that meat is harmful because of some other substance it contains, possibly guanidine or guanidine-like bodies ; but of this there is at present no satisfactory evidence. In most cases fish may be substituted for meat with absolute safety. It is therefore advisable to limit meat to the midday meal after the twenty-fourth week of pregnancy, and to substitute fish if the slightest evidence of " toxæmia " be noted.

Iron

There are about three grams of iron in the body, of which three-quarters are combined as haemoglobin in the red blood corpuscles. The daily loss of this metal is small, but is not greatly exceeded by the amount ingested. Woman bleeds physiologically, man does not ; it follows that she is the more likely, other things being equal, to suffer from anaemia. The demands of the foetus for iron are relatively high, and if the mother's reserves of the metal are low she will suffer from anaemia, which is much more common during pregnancy than is generally recognized. Blood counts should be made more frequently at ante-natal clinics, for apart from the possible harm done to the foetus and the dangers inherent in the severer forms of anaemia an anaemic woman is very liable to develop puerperal sepsis. Spinach contains more iron than any other article of diet, while eggs contain a fair amount in a form which is readily assimilated. If the woman appears to be anaemic Bland's pills should be prescribed, and generously.

Iodine

Thyroxine exerts a very powerful influence on metabolism, and acts on the ovaries, the hypophysis, the adrenal glands, and the kidneys. The intake of iodine in the food is so small that most pregnant women in England come very near to suffering from iodine deficiency. In goitre belts it has been found possible to stamp out endemic goitre by giving pregnant women iodine. Although the importance of giving the expectant mother iodine for the sake of her unborn child has been appreciated, it has not been recognized that it should be given

to her for the sake of her own metabolism. There is a fair amount of iodine in watercress, but it is not easily absorbed from this green food. It is therefore essential to advise her to take fish, especially herrings, and to use iodized table salt on the table and in the kitchen. Cod-liver oil may also be recommended, for not only is it rich in vitamins A and D, but it contains a considerable amount of iodine.

SIGNIFICANCE OF CALCIUM IN PREGNANCY

Lime salts are present in nearly every tissue of the body, and form the great mass of the inorganic constituents of the bones and teeth. They are not only essential to life but to many of the physiological processes and ferments of the body, and in their absence the heart ceases to beat and the blood to clot. The amount of calcium circulating in the blood remains remarkably constant at about 10 mg. per 100 c.cm. of serum, but of this amount probably only 2 mg. exist as calcium ions, while 4 mg. are in some form of combination with protein or possibly lipoids. Calcium is not easily absorbed from the alimentary tract, and in an adult the amount absorbed is roughly equal to the amounts eliminated in the urine and faeces. Any excess of intake over output is stored in the bones, and that last laid down is first requisitioned when need arises. This calcium may be referred to as the deposit account, whereas that in the blood and soft tissues represents the current account, the amount in an organ like the liver varying within wide limits. It is evident that there must be a very delicate mechanism which maintains a balance between absorption, deposition, and elimination, and there is a very intimate relation between the calcium and the phosphorus in the blood.

It has been estimated that a woman during the latter half of pregnancy requires as much as 1.6 grams of calcium daily, and that the foetus itself retains 8 grams of this mineral during the last four weeks of its intra-uterine existence. The diet of very few women in England contains that amount of calcium, and of the amount ingested only a proportion is absorbed. It follows that the pregnant woman must, in the majority of cases, call upon her deposit account, as neither income nor current account is sufficient to meet the demands. Vitamin D controls absorption, but the exact relation between the parathyroids and vitamin D in regulating the serum calcium is not fully understood. Seeing that the skeleton contains more than a kilogram of calcium there is obviously always sufficient calcium in the bones to meet the demands of the body, but it does not follow that it is either readily available or easily converted into a suitable form, as free ions are believed to be necessary for many physiological processes. The great demands of the foetus on the maternal calcium have led various observers to suggest that eclampsia was caused by a deficiency of calcium in the maternal blood, and they have regarded the convulsions of this disease as a manifestation akin to the tetany which follows removal of the parathyroids. The serum calcium is definitely lowered during pregnancy, but not sufficiently to render any such hypothesis plausible. In 1928 a paper by Lamson, Minot, and Robbins⁴ appeared which showed that the addition of calcium to the diet caused dogs, previously susceptible, to become tolerant to carbon tetrachloride poisoning, and this discovery was all the more important as it was accidentally made. As I had for some time been treating eclamptic patients with intramuscular injections of calcium chloride I at once wrote to Professor Lamson, expressing the opinion that these results were extremely significant from the point of view of the aetiology of eclampsia. In a letter to me he stated that

there was no significant difference in the blood calcium figures of the dogs which were susceptible and those which were tolerant to the drug. It follows, if these results are confirmed, that calcium can protect the body against at least one poison, and that measurements of the serum calcium afford no indication of the amount of calcium which can be so used. It is probable that, until it is possible to measure the amount of calcium in the form of free ions, estimations of serum calcium will only possess a very limited value. In the following year, Minot and Cutler,⁵ working under the direction of Professor Lamson, published a short paper reporting the results of treating pre-eclampsia and eclampsia with calcium gluconate.

It is clear that during pregnancy it is essential to prescribe a diet rich in calcium and in vitamin D. Milk, cheese, and butter contain calcium in abundance in a form which is fairly readily absorbed, and every pregnant woman should take a pint or more of milk daily. The amount of vitamin D in milk varies enormously, and during winter may sink to a very low level, but this problem will be solved when irradiated milk is put on the market. It is extremely difficult to administer calcium by mouth. Calcium chloride is easily absorbed, but is irritant and increases the acidity of the urine, which consequently contains a larger amount of calcium. Calcium gluconate is converted in the stomach into the chloride, and so merely provides an expensive, if convenient, way of exhibiting the chloride. The ideal method of increasing the available amount of this mineral in the body is by injecting 10 c.cm. of a 10 per cent. solution of calcium gluconate (Sandoz) intramuscularly. The gram of calcium gluconate injected contains 0.093 gram of calcium element in a form which is readily ionized. Seeing that the total amount of calcium in the woman's serum does not exceed 0.3 gram, of which probably not more than 0.06 gram exists as free ions, it is obvious that one injection may double the amount of calcium ions in the blood. The injection is absolutely painless, and may be repeated at frequent intervals. Calcium levinulate is now on the market, and should be as good as, if not better than, the gluconate, but I have had no experience of this preparation.

RESULTS OF CALCIUM THERAPY

It may be confidently asserted that it is possible to prevent teeth from decaying, hair from losing its glossiness and falling out, and nails from becoming brittle by ensuring that the diet during pregnancy is adequate in its content of vitamin D and calcium.

Excessive Salivation.—This symptom is exceedingly uncommon. The wife of a doctor commenced to suffer from a severe degree of this affliction, associated with a foul taste in her mouth, during the early weeks of her first pregnancy. She was kept for several weeks in a nursing home, but in spite of the most skilled treatment the symptom persisted unabated until after the delivery of the child. The symptom recurred early in her second pregnancy, and again all attempts at its alleviation proved unavailing. The husband consulted me several weeks after the symptom, as bad as ever, had manifested itself in the third pregnancy. I advised the intravenous injection of 10 c.cm. of calcium gluconate and certain additions to the diet. The symptom practically cleared up immediately, and the doctor described the result as "almost miraculous." As I did not see the patient herself psychological factors can hardly have influenced the result.

Vomiting of Pregnancy.—There is not, in my opinion, the slightest justification for assuming that any case of hyperemesis gravidarum can be labelled neurotic. It is my belief that the threshold of vomiting is lowered during

pregnancy and that there is no difference in kind, but only in degree, between ordinary morning sickness and a fatal case of hyperemesis gravidarum. Those who have maintained that it is never necessary to empty the uterus for this condition and that all such patients may be cured by suggestion either have had a very limited experience or possess short memories. I have seen several cases in which the vomiting has been completely checked, although the patient has subsequently died or suffered from a severe attack of peripheral neuritis lasting for several months. In the last year or two quite a number of patients have been referred to me because of vomiting, some being in the early months, but the majority in the last few weeks of pregnancy. This is the type of note the patient brought from the ante-natal clinic:

"Slight trace of albumin. General condition poor. Poor colour and looks ill. Headaches occasionally. Blood pressure has varied from 134/68 mm. to 144/72 mm. Hg. She is vomiting a good deal and has much heartburn. No medicine seems to help."

In each and every case the intramuscular injection of calcium gluconate cleared up the symptom almost immediately and the change in the patient was remarkable.

Cramps.—A number of patients in the last weeks of pregnancy have been referred to me because of cramps, usually of the muscles of the calves but sometimes involving the gluteal groups as well. The symptom is generally worse at night, and causes the woman to get out of bed and walk round the room. Besides being painful these cramps, by interfering with sleep, reduce the sufferer to a low state of health. In every case it has been found possible to clear up the symptom completely and in most cases immediately by the intramuscular injection of calcium.

Oedema.—There are three main causes of oedema which operate during pregnancy: (1) pressure, (2) excess of fluid intake over fluid output, and (3) altered permeability of the tissues.

1. There is no need to lay emphasis on the factor of pressure, except to point out that the widening of the intercostal arch and the elevation of the diaphragm by the bulk of the uterus raise the venous pressure in the thorax and so tend to cause oedema of the upper as well as of the lower extremities. The most severe degree of oedema may be due to mechanical factors and, in particular, to acute hydramnios.

2. The normal pregnant woman can excrete the usual amount of urine in the twenty-four hours, but during the latter months, owing to mechanical factors, the proportion of urine passed by night increases until the night/day urine ratio often exceeds unity. Although she can excrete the average daily amount of urine her response to water diuresis is frequently, if not usually, impaired, and this impairment is more marked in cases of the nephropathy of pregnancy. It is obvious that if more water is ingested than can be excreted oedema is inevitable. For this reason the indiscriminate water elimination treatment of the toxæmias of pregnancy is fundamentally unsound, and must lead to water intoxication and possibly death from either oedema or convulsions. Ardent exponents of this treatment can only save the woman from "drowning" either by cruel and otherwise useless purgation or by the timely induction of labour.

3. From time to time patients are encountered who for no very apparent reason exhibit oedema. In one such patient the oedema chiefly affected the face and upper extremities, and disappeared after one injection of calcium, although delivery did not take place until some weeks later. Another was sent from the ante-natal clinic to be admitted because of marked swelling of the feet, ankles, and over the shins; but no treatment was considered

necessary. When she was permitted to get up during the puerperium the oedema returned and was as bad as ever on the morning of her discharge, fourteen days after delivery, although she had been in bed for the previous twenty-four hours. She was given an intramuscular injection of calcium and told to return in two or three days, when she reported that the swelling had gone down shortly after she "was poked with the needle." There can be little doubt that oedema may, in some cases, depend on the permeability of the tissues, which may be altered by calcium.

Dermatitis Herpetiformis.—A patient thirty-seven weeks pregnant was referred with dermatitis herpetiformis, which she had had for over five weeks. After one intramuscular injection of calcium the rash commenced to clear up, and had disappeared before her confinement. The improvement in her health was remarkable, and she declares that she felt a "different woman" the day following the injection. Another patient with this condition only presented herself a fortnight before her confinement complaining of sleeplessness. An injection of calcium caused her to sleep naturally and led to a very great improvement in the rash, which she had had for several months.

Chorea.—Last year I saw one patient early in pregnancy with marked choreiform movements and severe peripheral neuritis, particularly affecting one side. She was put on a complete diet with the addition of calcium and vitamins A, B, and D, and improved astonishingly. When she came to be confined she appeared to be normal, and gave birth to a healthy child.

Blood Pressure.—The systolic blood pressure is not usually raised during pregnancy, while during the early months it may measure less than 90 mm. Hg. In those cases in which the blood pressure is markedly elevated the systolic blood pressure varies within a few minutes, sometimes by as much as 50 mm. Hg, and this, in my experience, is a constant phenomenon. Adrenaline is the one known physiological substance which could cause such a sudden, considerable, and transitory rise of blood pressure, and it would appear most probable that these patients suffer from "jumpy adrenals." Everybody is agreed that the diastolic blood pressure increases by about 5 mm. Hg during the latter months of pregnancy. Seeing that it is possible by constricting the chest with a rubber band to a degree which causes no inconvenience to raise the diastolic blood pressure by as much as 10 mm. Hg, it would appear logical to assume that the partial fixation of the chest effected by the bulk of the uterus operates in a similar manner. It is easy to raise the diastolic and to lower the systolic blood pressure directly by mechanical means, but it is probable that the rise in the systolic blood pressure which sometimes occurs as a result of these manœuvres is indirect, for it cannot be obtained in anaesthetized animals. The varying effects on the systolic pressure caused by constricting the chest depend on the degree of constriction effected. It has been found possible to lower the systolic blood pressure to its normal level in nearly every case by the injection of calcium gluconate and without rest in bed, providing treatment is instituted before the pressure has significantly exceeded 140 mm. Hg. Once the blood pressure has exceeded 150 mm. Hg it is usually impossible to bring it down to the normal level, and the degree of improvement obtained may be in large part due to the rest in bed.

ALBUMINURIA

1. Albuminuria is common in girls and young women, the incidence decreasing after the twenty-sixth year.* The incidence of the albuminuria of pregnancy might therefore be expected to be highest in women below that age.

2. The 1,000 ante-natal clinics in England and Wales have merely served to lower the incidence rate of the albuminuria of pregnancy, but not that of eclampsia.

3. Women suffering from non-nephritic albuminuria usually pass an albumin-free urine during the early months of pregnancy.*

4. The most severe degree of albuminuria (and of oedema) may be associated with acute hydramnios, and may be cleared up by the Queen Charlotte Hospital method of tapping the amniotic sac without disturbing the pregnancy.

5. A slight increase of pressure in the renal veins causes albuminuria, and the mechanical-dietetic hypothesis is a simple and adequate explanation of the albuminuria of pregnancy.*

6. During pregnancy the amount of urine passed in the twenty-four hours is of much greater significance than the amount of albumin it contains. The routine measurement of the blood pressure and testing of the urine for albumin at fortnightly intervals during the latter weeks of pregnancy are nevertheless of the utmost importance, and often make it possible to detect the early stages of impending "toxaemia."

7. There is no reliable evidence that the "kidney of pregnancy" is liable to undergo nephritic changes.*

TREATMENT OF "TOXAEMIC" PATIENTS

Seeing that the whole thesis of this paper is that the sole satisfactory method of treating the toxaemias of pregnancy is to prevent them, only a short account will be given of these cases. Dr. Bethel Solomons was kind enough to try the calcium and vitamin treatment on his toxaemic patients at the Rotunda Hospital, and obtained very unsatisfactory results. This was possibly to be expected, seeing that many of his cases were pre-eclamptic, and that he combined water elimination treatment with the calcium therapy.

The present report deals with twenty-three patients, of whom nineteen were primigravidae. Most of the patients were admitted with a raised systolic blood pressure (in more than half the cases it was 160 mm. Hg or higher) and albuminuria, while some further complained of headache and vomiting.

All the patients were put on a full diet with the exception of meat, and most of them were allowed fish. They were neither violently purged nor persuaded to drink large quantities of water, and in no case was sodium chloride withheld. They got up each evening, walked about the ward, and bathed themselves. In addition to the diet they were given radiostoleum (B.D.H.) one drachm three times daily, marmite, potassium iodide, and frequent intramuscular injections of calcium gluconate. Both parathormone and thyroid extract were tried, but did not appear to be beneficial. Liver extract proved definitely harmful in one case, the systolic blood pressure rising sharply from 145 to 190 mm. Hg, and its use was therefore discontinued. The daily output of urine, the amount of albumin in the morning specimen, and the morning and evening measurements of the blood pressure were charted. Water diuresis tests were made when possible.

RESULTS

Oedema was conspicuous by its absence, and only persisted in two cases of twin pregnancy complicated by hydramnios. Five patients went into labour shortly after they were admitted, and one was admitted for induction of labour because of a dead foetus. In ten patients there was very definite improvement; the symptoms in some cases cleared up completely. One of this number was admitted at the thirty-seventh week of her pregnancy with a blood pressure of 160/120 mm. Hg, and a catheter specimen of her urine contained albumin ++. The urine became albumin-free, and the blood pressure dropped within five days to 128/90 mm. Hg. In the case of five patients it was found impossible to lower the blood pressure significantly. One patient had a fit two days after her admission, and was delivered normally of a healthy child fifteen days later. Labour was induced in only two cases: once because the patient was believed to be

overdue, and once because of hydramnios. Five babies were born dead, two being twins and three being macerated; and two premature babies died. It is interesting to note that although there were only four multiparae in this series, two of them gave birth to dead babies. Both had high blood pressures, but their urines were protein-free. The mother who gave birth to dead twins had been ill in hospital elsewhere for over a month before she was admitted to the ward. On admission her systolic blood pressure exceeded 170 mm. Hg; her urine contained albumin; the red cells were under 2,000,000 per c.mm., the colour index being 0.5; and she was jaundiced. She was in the ward for five weeks before delivery. The first foetus was macerated and the second was born dead, probably because too long an interval was allowed between the birth of the first and second twins.

All the mothers are well, and in no case could a diagnosis of chronic nephritis be made. The systolic blood pressure has remained high in two cases, and well above the average in two more, but there is no reason to believe that this elevated blood pressure did not in each case antedate the pregnancy.

CONCLUSION

It is inherently improbable either that any one toxin could cause the widely varying symptoms associated with the toxæmias of pregnancy, or that a number of separate toxins should originate in the products of conception. The fact that the hepatic lesions peculiar to eclampsia may be caused by dietetic or mechanical factors, or a combination of both, disposes finally of the strongest argument in favour of a pregnancy toxin. It is suggested that the foetus affects "*la fixité du milieu intérieur*," and that all the toxæmic disorders may be regarded as deficiency diseases. It follows that there is no fundamental causal difference between ordinary morning sickness and eclampsia. This hypothesis is not contradicted by any known fact, and is supported by the results of calcium therapy reported above. If excessive salivation, vomiting, cramps, dermatitis herpetiformis, oedema, and other symptoms can be cured by the injection of calcium, it is logical to suppose that they are caused by its deficiency. The number of patients who have been treated is small, but the success which has attended calcium therapy in such a variety of conditions warrants its extended trial. A great disservice has been done to the science of dietetics by those enthusiasts who stress this or that vitamin without considering the diet as a whole or the importance of personal hygiene. It is claimed that a complete, well-balanced, appetizing and easily digested diet, rich in the vitamins and in calcium, iron, and iodine, if given early in pregnancy, will prevent the onset of the toxæmias of pregnancy (but not always of albuminuria), although it may be necessary to increase the available amount of calcium by the injection of calcium gluconate: indeed, it might be expedient, and in the end economical, to give routine injections of this mineral at the thirty-second and thirty-sixth weeks of pregnancy. It is further believed that such a diet would increase the resistance of the woman to puerperal infection. The one advantage of this hypothesis, which is possessed by no other, is that it can be put to the test, and even under "field" conditions.

This work was done at the Hammersmith Hospital, and I should like to take this opportunity of thanking my assistant Dr. B. Williams, until lately resident medical officer, and Miss V. Page, sister in charge of the maternity wards, for their loyal co-operation.

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Memoranda

MEDICAL, SURGICAL, OBSTETRICAL

PRIMARY CALCULUS OF THE URETHRA

The following case seems of sufficient interest to be recorded.

A. B., aged 55, was admitted to the County Hospital, Wakefield, on March 4th, 1933, suffering from extravasation of urine. He stated that for ten years or more he had suffered periodically from gravel, with some pain in passing urine, and frequency. He very rarely consulted his doctor, but took copious draughts of barley-water. He worked in a coal mine and on the land. He had seldom had to cease work on account of the symptoms. Alert otherwise, he seemed, with regard to his genito-urinary tract, to be endowed with, in the circumstances, the priceless gift of mental torpor. He had never noticed any swelling in the perineum. A fortnight before admission he fell astride, but disregarded the injury. However, in an hour or two he had violent pain in the perineum, and blood was passed by the urethra. A sinus eventually formed in the scrotum, which gave him relief. On admission the scrotum was gangrenous, and cellulitis extended

The calculus, which measured $2\frac{1}{2}$ in. by $1\frac{1}{2}$ in. at its widest part.

on the left side of the abdomen in a slanting manner towards, and just beyond, the level of the anterior superior spine of the ilium. The right testicle was absent; penis and right abdominal wall were not affected. There was a sinus in the scrotum, from which issued a foul-smelling discharge. A catheter was passed beyond the injured part without difficulty.

At operation the scrotum was incised in the middle line, and the knife impinged on a hard substance. A calculus, or fragment of a calculus, lying loose in the sloughing, foul-smelling tissues, was removed. The finger was again introduced into the wound, and what appeared to be a smaller calculus, gripped tightly by the surrounding tissues, was discovered and removed by further incision. The anterior extremity of this was at the peno-scrotal junction. The left abdominal wall was incised. The gangrene had invaded the tunica vaginalis. Minute inquiry into the actual state of affairs was impracticable owing to the local and general condition of the patient. A rapid improvement followed the operation. Secondary suture was performed on April 1st, 1933, in the lithotomy position. In the left lateral wall of the urethra was an opening half an inch long. This led to a pouch roughly three inches by two, from which the calculus had been removed. The proximal wall of this diverticulum had disappeared in the sloughing process, except at its upper and lower extremities. The distal wall was intact, and was lined with what appeared to be mucous membrane—pale, smooth, and thickened. The distal wall was incised, and a flap was raised from it to repair the defect in the left lateral wall of the urethra. The rest of the sac was excised. The testicle was replaced in the remains of the scrotum, and a catheter was tied in. The insertion of the