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DIABETES AND PREGNANCY, WITH THE RECORD OF SEVEN CASES.¹

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PART I.—CLINICAL INVESTIGATION.

DIABETES was looked upon as a very serious disease in the few cases where it was complicated by pregnancy. Since the discovery of insulin as a means of treatment the whole aspect of the condition has changed. Our views have, therefore, to be modified as to the dangers of pregnancy in this disease. The older literature gives records of a comparatively small number of cases of diabetes

associated with pregnancy and much confusion arose as to the accurate diagnosis of true diabetes of pancreatic origin. Sugar in the urine is not infrequently found in pregnant patients. In the majority of women this is a glycosuria due to alimentary or renal causes and usually clears up on dieting or soon after parturition is completed. Lactosuria is associated in late pregnancy with mammary function and is of little clinical importance. The use of insulin and also the investigation of cases of pregnancy by biochemical methods have definitely demarcated true pancreatic diabetes from benign glycosurias. Co-operation with the physician and biochemist has given the obstetrician a much better understanding of disease when complicated with pregnancy. Ante-natal supervision, in many cases, has been the means of ascertaining the presence of disease and of obtaining early and successful treatment.

Sterility.—The explanation of the rarity of cases of pregnancy in diabetes is given as due to the inhibitive influence of the disease upon the function of reproduction. Ovulation ceases and atrophic changes take place

¹Read at the Obstetrical Section of the Royal Society of Medicine, June 19, 1931.

in the ovaries and uterus. These changes lead to irregular menstruation and prolonged periods of amenorrhœa. Sterility is a marked consequence. Matthews Duncan in 1892 was the first to prove that pregnancy could take place in these cases. He collected the records of twenty-two pregnancies, but he pointed out the grave nature of the complication of pregnancy. Stander and Peckham state that only about 5 per cent. of diabetics become pregnant.

Obesity is associated with diabetes and impaired endocrine function. Malnutrition due to impaired carbohydrate metabolism is also associated with defective genital function. Lambie refers to obesity and the decline of sexual function in these patients. He considers that menstruation is absent in about 50 per cent. of diabetics. Treatment by insulin tends to restore reproductive function and to promote conception. Since the introduction of insulin, more cases of diabetes with pregnancy have been reported. Therefore, it is possible that in the future the problem of the cure of sterility in some patients may be solved by the biochemical investigation of their sugar curves and treatment by insulin.

Pregnancy.—For all practical purposes the literature before the discovery of insulin is now out of date. Since the discovery of insulin, the two most outstanding papers in this country are those of Lambie in 1926, and of Arnold Walker given to the Obstetrical Section in 1927. The latter has given a very valuable and comprehensive review of the literature. He found that in 10,000 recorded cases of maternity patients treated in the Middlesex Hospital, only one patient had diabetes. The City of London records showed no cases among 24,567 obstetrical patients. Arnold Walker found only three cases in Britain treated with insulin. He gave notes of a patient in the Middlesex Hospital under the care of Mr. Comyns Berkeley. Another case from the same hospital is described by Shirley Smith and Roques. The opinion expressed by these

writers is that diabetes is no longer a danger when associated with pregnancy if treated with insulin. In his 1930 edition, on p. 601, Whitridge Williams states that diabetes is rarely noted in pregnant women and when found is ominous for mother and child. In sixty-six cases which he collected from the literature in 1909, 27 per cent. women died at the time of labour or within two weeks. An additional 23 per cent. died within two years. One-eighth of the pregnancies resulted in abortion or premature labour, and one-third of the infants born at term were dead. He admits that the most serious cases were published and compares the favourable results of the present day in his Clinic as reported by Stander and Peckham.

The Mayo Clinic, in 1928, contrasts the doubtful results in patients before insulin and gives the successful issue in two cases. These late records all point to the fact that the association of diabetes and pregnancy occurs more frequently than formerly, and that the results are much more favourable when given appropriate treatment.

CLINICAL RECORD OF SEVEN PATIENTS WITH EIGHT PREGNANCIES IN OBSTETRICAL UNIT.

A large number of patients with glycosuria have been under observation in the Clinic.

All these patients have been carefully investigated, and only those who showed definite diabetic symptoms and blood-sugar findings have been included in the present communication. The record is for patients from the year 1927. The biochemical investigation has been carried out by one of us—E. C. P.-W.—in the Pathological Department of the Hospital. Many cases of potential diabetics were excluded after careful consideration as though their curves were definitely of the diabetic type, they had no symptoms. A case of diabetes in a congenital syphilitic was also excluded. Cases of doubtful endocrine origin were also excluded.

Age and Parity.—Age seems to have little influence. The patients' ages ranged from 26 to 40 years. Shields Warren holds the view that diabetes is more serious at puberty and at the menopause. Middle reproductive life may possibly be more favourable.

None of the cases were primiparæ. Five had had one previous pregnancy and the other two each three previous pregnancies. The condition had, however, developed and been diagnosed before the onset of the pregnancy under consideration in five of the cases. These cases had, therefore, received some treatment for their diabetic condition for varying periods up to two years before they became pregnant.

Symptoms.—As the majority of the patients had already been treated for their diabetic condition, few had marked symptoms. They all complained of loss of energy and of being easily tired and breathless on exertion. They, with one exception—a very obese patient—appeared to be poorly nourished, with flabby muscles. This patient, No. 7, had diabetes and peripheral neuritis before the onset of her last pregnancy and walking was difficult. She had become lazy in her habits, and this may account for her obesity. Thirst was a feature in the two untreated cases, and these cases were passing a high percentage of sugar in the urine. Headaches and occasional giddiness occurred in several cases. Vomiting was not a marked symptom in any of the patients. Hydramnios was not present in any of the patients, although it seems to be a symptom in those untreated cases recorded in the literature. Graefe describes five cases of hydramnios out of seven of diabetes. Sugar has been found by some investigators in the amniotic fluid, but not in the foetal urine. This shows that it is a maternal transudation. Marcel Labbé and Couvelaire report a case where hydramnios disappeared on treatment with insulin. In our cases treatment prevented its occurrence. Frequent estimations of the sugar curves and careful diet kept the

patients well controlled throughout pregnancy and during delivery.

Warren Shields draws attention to the condition of the heart as a complication in diabetic patients. One patient had slight cardiac enlargement with a presystolic thrill, but no clinical symptoms were present. The heart was normal in the other patients.

DIAGNOSIS.

Examination of the urine is carried out as a routine in all the patients attending the ante-natal clinic. Fehling's test is used for sugar. If sugar is present, the patient is sent to the biochemical laboratory for further investigation. As a rule, patients with benign glycosuria do not suffer from any symptoms. They feel well and do not complain of thirst or wasting. Diet regulation causes disappearance of the sugar in most cases. Increase occurs after a sugar meal. If renal in origin, sugar may persist in pregnancy and disappear after parturition. The diagnosis will be referred to in detail in Part II.

PROGNOSIS.

The prognosis is said to be worse in young primigravidæ, better in multiparæ in late reproductive life. It is better in the second half of pregnancy, and diabetes occurring during pregnancy is more favourable for treatment than when it begins before the onset of pregnancy, as there is less pancreatic loss of function. If diabetes is present and untreated in early pregnancy, abortion is more likely to take place. The prognosis depends upon the early recognition and treatment of the disease. The diabetes is probably mild in character when discovered for the first time on ante-natal examination. Its incidence may be due to the lowered renal threshold in pregnancy.

Pregnancy should be avoided in women who are suffering from diabetes. If pregnancy does take place, the general condition of the patient and the possibilities of carrying out appropriate treatment must be con-

sidered. Since the advent of insulin, induction of abortion is rarely advised. In none of the cases in the clinic was it considered. If treatment fails and the condition of the patient is serious, induction may be unavoidable. Sepsis is a very dangerous complication in a diabetic patient. Induction should be performed by tents and rubber tube and

glycerine, and not by a rapid method. The practice formerly was to induce almost every case of diabetes and, if possible, sterilize the patient. Now the patient is treated for her disease, and the pregnancy is, as a rule, allowed to go to term. Induction of labour may be necessary in cases where the foetus is unduly large, as sometimes takes place.

DIABETES DIAGNOSED DURING PREGNANCY.

No.	Age	Diagnosed	Pregnancies	Labour	Infant
Case 1	31	20th week	1 child. Weight 10 lb. Died of measles 1 year 9 months. Long labour	Spontaneous at term. Normal	8 lb. 5 oz. Satisfactory
Case 2	29	22nd week	1 child. 2 years ago. Stillborn. Forceps	Induced at term for small pelvis	6 lb. 15 oz. Satisfactory

PREGNANCY AFTER ONSET OF DIABETES.

No.	Age	History	Pregnancies	Labour	Infant
Case 2 2nd observed pregnancy	32	Reported only occasionally since last confinement	1st child 5 years ago. Stillborn 2nd, 3 years ago, in R.F.H. Well	Term. P.P.H. ...	7 lb. 12 oz. Stillborn. Tentorial tears. Precipitate labour
Case 5	26	Diabetes since birth of first child	1 child 1 year and 6 months ago. Died 8 hours after birth. Forceps	Term. Delivered in another hospital	9 lb. 8 oz. Satisfactory
Case 4	29	Diabetes diagnosed 2 months before onset of pregnancy	3 children— 1st—7 years. Stillborn. 2nd—4½ years. Weight 10 lb. 3rd—3½ years. Alive.	Term. Spontaneous. Some P.P.H.	7 lb. 4 oz. Satisfactory
Case 6	27	Diabetes for 1 year before pregnancy	Twins 3 years. 1 alive	Term. Spontaneous	7 lb. 12 oz. Satisfactory
Case 7	40	Not well for 6 years. 1 year intense thirst. Pruritus. Early peripheral neuritis	1 child 4 years ago. Stillborn. Forceps	Term	8 lb. 1½ oz. Nutrition unsatisfactory. Died in a few weeks. P.M. No abnormality found. Congenital mental deficient
Case 3	35	Under treatment for 2 years, from last pregnancy	3 children alive— 1st—9 years ago. Weight 5 lb. 2nd—4½ years. Weight 5 lb. 3rd—2 years. Weight 10 lb.	Term. Spontaneous. Slight P.P.H.	7 lb. 10½ oz. Satisfactory

Insulin seems to prevent excessive growth of the foetus.

LABOUR.

There were no outstanding features in the labours of the patients. The average duration was normal. In one case of small pelvis the labour was precipitate, the infant being stillborn. Tentorial tears were found at post-mortem examination. No prolongation of the third stage was observed. In two cases, P.P.H. was slight. Forceps were not applied in any patient, nor was Cæsarean section indicated. Sterilization was not performed on any of the patients.

Operative interference is to be avoided owing to the dangers of sepsis. Diabetic patients tolerate morphia well, it is a useful sedative for the first stage of labour. Gas and oxygen with ether if required were given for delivery. Chloroform is especially contra-indicated in diabetes.

The Puerperium.—Infection is frequent among dietetic patients. Shields Warren states that of 300 fatal cases of diabetes without pregnancy, 126 died of infection. He says on p. 154 "Once a diabetic is infected his diabetes becomes more severe . . . sepsis is the greatest foe of insulin." The puerperium was uneventful in all the cases. This is probably due to ante-natal treatment and to the fact that the majority of the deliveries were normal. It would seem, therefore, that insulin has a marked prophylactic effect upon sepsis. In surgical practice this is now recognized and treatment is carried out before operations are undertaken. In the ante-natal examination of diabetic patients, special examinations should be made of the teeth and tonsils and appropriate treatment advised.

There were no maternal deaths.

Infant Mortality.—The table shows the previous births as compared with those which took place after treatment. Abortion did not occur in any of the patients undergoing treatment. Five infants were born at term alive and well. One was induced near term for small pelvis, alive and well. One

was a precipitate labour, stillborn, with tentorial tears. One was born alive at term but was very difficult to feed. It seemed to be mentally deficient. It died a few weeks later of malnutrition. No lesion was found on the post-mortem examination. Before the introduction of insulin, the infants of diabetic mothers were sometimes found to be of excessive weight. All the infants were of average weight.

Feeding.—Diabetic mothers have a deficient milk supply. Some of the infants were partially breast-fed for a few days, but eventually had to be artificially fed on humanized milk and sugar and water. Breast-feeding was entirely given up in all the cases. It should not be undertaken if diabetes is present.

The patients as far as possible have been followed up since their confinements and sugar estimations made. These will be referred to in Part II. No patient has given any evidence of tuberculosis. One infant died of tuberculosis later, but infection was supposed to have been got from a particular cow.

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PART II.

BIOCHEMICAL FINDINGS.

By E. C. PILLMAN-WILLIAMS.

These seven cases (whose clinical side has been reported above by Professor McIlroy and Dr. G. Hill) from a biochemical view must be divided into two classes, severe and mild.

The three severe cases will be considered first. Case 1 and Case 2 were kept well

SEVERE CASES.

Case 1, Chart I.

This patient (multip. 1), aged 31, was referred to me from the North Islington Clinic for glycosuria. She complained of thirst and polyuria. She was four months pregnant. Her fasting blood-sugar was 0.197 gram. per cent., and the 24-hourly specimen of urine contained 6.4 gram. per cent. glucose. As she had arranged to go for a fortnight's holiday the next day, she

CHART I.

controlled during pregnancy except for small periods of infection such as colds. The third case was more difficult to control during the last month of pregnancy and her insulin had to be almost doubled. On the charts the blood-sugar findings during pregnancy are coloured red; the ringed values are fasting blood-sugars, whereas all other values were taken at 11-11.30 a.m. after insulin and breakfast.

was dieted and allowed to go. On return she was leaking 7.9 gram. per cent. sugar in her 24-hourly specimen, and her fasting blood-sugar was 0.295 gram. per cent. She was admitted to hospital and put on 25 units of insulin and diet containing about 100 gram. carbohydrate. This was later increased to 145 gram. of carbohydrate, on which diet she was practically acetone free. During pregnancy the blood-sugar level of the patient was

satisfactory except for the period at the end of December and the beginning of January, when she had a cough and cold (also Christmas dinner), but it was difficult to keep her sugar free, as the renal threshold for sugar was low. During the puerperium the insulin had to be reduced to 20 units, and on discharge from hospital her condition was satisfactory.

After delivery the diabetic condition definitely improved temporarily, but it was still necessary to give her 20 units of insulin a

She was passing urine loaded with sugar and had a resting blood-sugar of 0.187 gram. per cent. She was admitted and put on a balanced diet and insulin, first 15 units a day, which was later increased to 35 units. The diet contained over 100 gram. carbohydrate, which was later further increased.

As is seen by the chart, her blood-sugar was kept at a reasonable level and the urine sugar and acetone free. The patient was discharged on the tenth day in a satisfactory condition still on 35 units of insulin.

CHART II.

day to keep her controlled. The patient is, unfortunately, emotionally unstable, and any worry (see chart) sends her blood-sugar up. During the last three years her condition has deteriorated slightly, and she now needs 28 units of insulin per diem to keep her controlled on a diet containing about 100 gram. carbohydrate. The case is unquestionably one of a moderately severe diabetes.

Case 2, Chart II.

First seen by us when twenty-eight weeks pregnant (sent on from Mothers' Hospital).

She reported at intervals for six weeks and then ceased to attend.

A year later, when non-pregnant, the patient again reported, leaking 1.9 gram. per cent. sugar in her urine, not having taken any insulin for the year. The fasting blood-sugars were markedly raised (see chart), after 20 gram. of glucose the sugar curve was of a typical diabetic type, starting with a fasting level of 0.150 gram. per cent., rising at the hour to 0.315 gram. per cent., and at the second hour still being up at 0.217 gram. per cent. The patient was dieted but only

attended a few times and was not seen again until she was referred by the Mothers' Hospital when six months pregnant (i.e., two years eight months after first treatment). On this occasion she had a resting sugar of 0.196 gm. per cent., and was leaking 5 gm. per cent. sugar. She was admitted and put on 20 units of insulin and a diet containing 150 gm. carbohydrate and rather reduced fats, as it took some time to get her urine acetone free.

This patient was delivered and from a

pregnancy she was controlled with less insulin than during the first pregnancy, and that after confinement the insulin could be again reduced. Pregnancy, therefore, contrary to the normal experience, seems to have had no deteriorating effect on her diabetic condition, although in each case she was only treated during the latter months.

Case 3, Chart III.

This patient, aged 36, with three children, reported in November, 1928; she said she

diabetic point of view her condition kept very satisfactory. The level of her blood-sugar became lower and the insulin was reduced to 16 units per diem. After five months' interval the patient again returned quite out of balance, taking no insulin (see chart). Although this patient is very casual and does not see the necessity of keeping to a diet, she can be kept in a satisfactory condition when under observation, and it is interesting to note here that in the second

had not been well since birth of her last infant fourteen months previously. She complained of thirst, hunger, polyuria, and pruritus. Her fasting blood-sugar was 0.255 gm. per cent., and she was passing urine loaded with sugar and acetone. She was put on insulin and a balanced diet and on this was controlled. Eleven months later the patient complained of giddiness and amenorrhœa and she was found to be pregnant. From the second to fifth months of pregnancy she remained well on 35 units

of insulin, then she did not report for three months, and when she came she was passing much sugar and acetone in her urine, and her blood-sugar was 0.297 grm. per cent. She was admitted and it was found necessary to increase her insulin from 35 to 75 units before she was controlled (carbohydrate 136 grm.), and just before delivery this had to be raised to 81 units. Soon after delivery the insulin had to be reduced and her blood-sugar values fell very quickly, until on the fourteenth day she was having 45 units per

MILD CASES.

Case 4, Chart IV.

This patient was referred from Medical Out-patients to the diabetic clinic for glycosuria, November, 1927, and was put on a diet and insulin, 15 units, and became sugar and acetone free. There was then an interval of three months before she attended again, when she reported two and a half months pregnant.

During pregnancy this patient's blood-sugar remained low, but it was very difficult

CHART IV.

diem. This patient had to return home to look after three children. She was readmitted recently as her sugar values were unsatisfactory following an attack of influenza, and after treatment was discharged controlled with 45 units. This patient is very difficult to control as her blood-sugar values alternate rapidly after insulin and she is always fluctuating between hypo- and hyperglycæmia. This may partly be accounted for by the fact that this patient is slightly hyperthyroidic.

to keep her urine sugar and acetone free. Her carbohydrate was therefore increased and insulin put up to 16 units.

During the puerperium her blood-sugar remained at a satisfactory level, and she gradually became sugar and acetone free. At the end of three months the insulin was reduced to 9 units, and three months later to 3 units a day. She is now doing well, sugar and acetone free, with a balanced diet containing 100 grm. carbohydrate on 3 units of insulin daily.

Case 5, Chart V.

This patient, when five months pregnant, was brought up to me by her sister, Case 4, who diagnosed diabetes on account of thirst and the fact that her urine reduced Benedict's solution. She did not wish insulin, but as she continued to pass sugar she was admitted, and it was found necessary to give her 8 units of insulin a day before she was balanced. This patient, unfortunately, was confined at a hospital near her home, and so for this period we have no figures. She

Case 6, Chart VI.

This patient reported complaining of thirst and polyuria for one month. She was passing a large quantity of sugar and also a trace of acetone. Her blood-sugar three hours after breakfast was 0.297 gm. per cent. She was put on 10 units of insulin before mid-day meal. She was only under treatment a few weeks before pregnancy started, and six weeks later she complained of tremblings three hours after insulin (she was sugar free). Insulin was therefore re-

CHART V.

went through her confinement and puerperium normally. The infant was 9½ lb. She now attends hospital occasionally and is not being so strict with her diet, so that it is probable that her insulin will have to be increased. Although easily controlled, this patient is a definite diabetic. A sugar curve done this month (four months post-delivery and not breast-feeding) after 25 gm. of glucose, gave values up to 0.304 gm. per cent., and at the end of two hours her blood-sugar was as high as 0.240 gm. per cent.

duced to 7 units per diem. This dose was later altered to 4 units twice daily, which suited the patient, and on this dose she remained well. Delivery and puerperium were normal, and on the 8 units of insulin that she had been having before delivery, the patient's blood-sugar level became too low, so the diet was increased to balance the dose of insulin which was kept constant. She remained well until two weeks ago, when she was sent to a convalescent home for a holiday. There she developed quinsy,

CHART VI.

CHART VII.

and consequently returned quite unbalanced with a blood-sugar of 0.290 grm. per cent. and passing sugar in the urine.

This case, though mild, is definitely diabetic and illustrates well the injurious effect of sepsis on the condition.

Case 7, Chart VII.

This patient was in a medical ward for diabetes in July and August, 1929. She complained of thirst, pruritus, neuritis and loss of weight. Her resting blood-sugar was 0.286 grm. per cent., and her urine was loaded with sugar and some acetone. She was put on a balanced diet and 20 units of insulin a day.

Her condition and neuritis improved, and on discharge she could walk with very little difficulty. Fourteen months later she reported at the maternity department four months pregnant and was admitted. She was then found to be sugar and acetone free and to have a low blood-sugar on 125 grm. carbohydrate a day. The insulin was reduced and carbohydrate put up to 153 grm. Insulin had to be further reduced as the blood-sugar was consistently on the low side, and finally at the end of ten days it could be stopped altogether. She was sent home a week later balanced on no insulin and a diet containing 145 grm. carbohydrate.

This patient was admitted later for confinement, which went off normally, and she was finally sent out with urine acetone and sugar free, a normal blood-sugar and on no insulin.

Had this patient only been seen during pregnancy, without knowing the previous history the diagnosis of diabetes would have been in doubt; but in her medical record there can be no doubt that she was a true diabetic, the function of whose pancreas had improved under efficient insulin treatment.

DISCUSSION.

The cases recorded above show that with adequate treatment by a balanced diet and

suitable doses of insulin, women suffering from diabetes may pass through pregnancy with no injurious effects. The importance of a sufficient supply of carbohydrate in the diet must be stressed, as all pregnant women are liable to a mild ketosis, and these patients particularly so. In my opinion, 125 to 150 grm. of carbohydrate a day is necessary and the insulin must be adjusted to this intake.

The fact that these patients during pregnancy frequently pass small or large quantities of sugar in the urine, must not be taken as an indication of an increase in severity of the condition, as it is largely due to the lowering of the renal threshold for sugar which occurs in pregnancy.

In conclusion, it should be noted that in all the cases reported there was an increase in the sugar tolerance, several actually requiring less insulin than their pre-confinement value; a result, no doubt, of the more effective control during pregnancy due to the fact that the women were more willing to attend regularly during this period.

THE TREATMENT OF PNEUMONIA.

By H. V. MORLOCK,

M.C., M.D., M.R.C.P.

LOBAR pneumonia is a self-limited infection; that is to say, within a given time (five to eleven days) the infection has run its course, the patient has either overcome the infection and completely recovered, or the infection has overwhelmed the patient and death has taken place.

What then is the deciding factor in the production of one or other of these results? This deciding factor is the ability or the inability of the patient to build up sufficient antibodies to overcome the infecting organism and its toxins.

Therefore in the treatment of pneumonia,