(Sam G.P. Moses Oration)

SIGNTFICANCE OF GESTATIONAL DIABETES

Professor J.M. Stowers

After paying a tribute to Professor G.P. Moses, in whose honour the lecture was given, Professor Stowers reminded his audience of the definitions of gestational diabetes given by the National Diabetes Data Group in the U S.A. and by the World Health Organisation in Geneva. Neither definition requires that a post partum glucose tolerance test should be done in contrast to widely accepted older definitions which demanded that a test after pregnancy must be normal. Thus no diagnosis of gestational diabetes could be made during pregnancy. In Aberdeen an intravenous glucose tolerance test has been used for the last 23 years, expressing the results as “increment indices” and the relative advantages were stated. Gestational diabetes (GDM) has been found to be 4 to 10 times more frequent than insulin-dependent diabetes during pregnancy. GDM should be treated by diet and, some would say, only additionally by insulin, if needed, but in Aberdeen Chlorpropamide (not more than 100 mg/day) has been used for diet failures in over 120 patients and with no evidence of harmful effect on the fetus. In 9 of 13 women treated with Chlorpropamide for GDM this reverted to normal when they were retested later in pregnancy at least ten days after stopping their Chlorpropamide. A few patients who were more than 20 % overweight and refractory to diet alone have been treated with Metformin up to 500 mg twice daily.

GDM is important for the future health of the mother, the success of the pregnancy and the future of the progeny. O'Sullivan's longterm follow-up of women with GDM was was reviewed. He showed over a period of 22-28 years that 24.7% developed "decompensated diabetes" and only 3.4% of his negative control women. The features predictive of future diabetes were obesity, family history of diabetes, the height of the 2 hour blood glucose in the oral glucose tolerance test and the maternal age. The mortality of over 300 women with untreated GDM was 10.7°/ in 1.7-23 years and only 5.5% in a similar number treated with insulin in pregnancy. This was about the same as in the negative control women. The morbidity of untreated GDM was also worse than that of the negative controls in respect of hypertension, hyperlipidaemia, proteinuria and resting and stress ECG's. The future prognosis of the carbohydrate tolerance of GDM followed up in Aberdeen seemed rather better than O'Sullivan's experience in Boston. All 70 in the Aberdeen series had abnormal intravenous glucose tolerance tests (IVGTT's) at about six weeks post partum. as well as in pregnancy, whereas the oral glucose tolerance test (OGTT's) in O'Sullivan's series of 615 patients were abnormal post partum in only 1.8%. After an average of 11.4 years of follow-up 20% of the Aberdeen series still had an abnormal IVGTT and 6% were then being treated by insulin. At the same period of follow-up 33°/ of O'Sullivan's series had normal OGTT's by the 100 gram test and 45% by the WHO criteria. Groups in this series had treatment only during pregnancy whereas in Aberdeen the patients had follow-up treatment, mainly with diet but 27 with the addition of Chlorpropamide and 7 with the addition of Metformin, because diet alone was not proving effective. In another group of 72 subjects in Aberdeen treated with diet and placebo for impaired glucose tolerance 2.2°o developed overt diabetes each year, whereas only 1.3% did so of 131 treated with diet and a small dose of Chlorpropamide. The placebo-treated group were followed up for a mean period of 10 years and the Chlorpropamide series for 6 years, each follow-up test being done three weeks after temporary discontinuation of the Chlorpropamide. The more

favourable results in the Aberdeen series were probably due to the continuing treatment, but the diagnostic criteria were different and so of course were the populations studied. A study of impaired glucose tolerance (IGT), not diagnosed in pregnancy, published by Sartor and his colleagues in Sweden, showed that the mere disclosure of a finding of IGT to the subjects decreased the 10 year conversion to overt diabetes from 29 to 13% but none of the 23 subjects treated with diet and Tolbutamide became overtly diabetic in this time. The results of the 5 year follow-up of GDM by Meston in Los Angeles and the 4-8 year follow-up of the Pima Indians with GDM by Pettit and his colleagues were also mentioned.

In relation to the significance of GDM for the baby, there is fortunately *little or no increased tendency to congenital malformations*, probably because GDM seldom appears until the second half of pregnancy and so after the formation of the main fetal organs. Two studies, however, have related the risk of congenital anomalies directly to the degree of the maternal carbohydrate intolerance. In assessing the effects on perinatal mortality and morbidity it is essential to look at published series where women have not been selected for testing because of failure in previous pregnancies, for these are likely to recur. The best data are from the screening of unselected populations, such as was done by O'Sullivan in Boston and by Abell and Beischer in Melbourne. *O'Sullivan found a perinatal mortality of 64 per 1,000 in 187 GDM's, as compared with 15 per 1,000 in 259 control nondiabetic mothers. Obesity and increasing age* were adverse maternal factors. Abell and Beischer gave 2,000 unselected pregnant women a 50 g 3 hour OGTT at 32-34 weeks gestation. Those in the top 5 percentile of blood glucose response had a perinatal mortality of 32 per 1,000 compared with 6 per 1,000 in the normoglycaemic group, but they did not look at the effect of maternal age and obesity. In Aberdeen where pregnant patients are selected for glucose tolerance testing we looked at the results only for 212 GDM's diagnosed in their first pregnancy and compared them with those of 1373 women who had normal IVGTT's in pregnancy. The perinatal mortality was 23.4 per 1,000 in the GDM and 12.4 per 1,000 in the negative controls. These figures are not statistically significantly different, but this was probably because the GDM's were treated actively. In support of this, Muck and Christ (1973) in Erlangen found a significantly smaller perinatal mortality of 19 per 1,000 in 106 GDM's who were treated, compared with 54 per 1,000 in 56 who were untreated. Another way of assessing the effect of GDM on perinatal mortality has been used by Sutherland and Fisher in. Aberdeen. They tested the intravenous glucose tolerance post partum of 97 women who had an unexplained stillbirth and found that 26% of the tests were abnormal.

It is difficult to study the effect of GDM on perinatal morbidity, as this is now so low in Western countries that the improved care will also have improved the results for the infants of GDM's. More sensitive indices of fetal well-being are needed and these should include bodyweight and fatfold thickness, adjusted for fetal maturity, head/trunk ratios, blood glucose 2 hours after birth, serum bilirubin, serum calcium, etc.

Many of the effects on the fetus are attributable to the mild maternal hyperglycaemia but other factors may be the increased transplacental transfer of some aminoacids and triglycerides, as shown by Freinkel.