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THE INFANT OF THE DIABETIC MOTHER: MEMORIES FROM 1960 – 1982*

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Between 1959-1963 and 1969-1982 I worked closely with the obstetricians caring for pregnant diabetic women, first in Birmingham and then in Bristol. This short account draws on that experience.

Prior to the discovery of insulin, many women with diabetes were sterile and half of those who were not, would die during pregnancy. With the coming of insulin, the maternal mortality had fallen by 1950 to about 1%. However, the perinatal mortality remained very high, around 40%.

The classic story of the infant of a diabetic mother was of a typically large-for-dates, obese, plethoric infant (Figure 1) who died suddenly during late fetal life or during labour. To circumvent this problem and the difficulties of controlling the maternal diabetes in late pregnancy, in the mid 1950s obstetricians introduced the strategy of delivering the mother by Caesarean Section at 35 to 36 weeks gestation. This practice combined with improved diabetic management succeeded in reducing the perinatal mortality to around 25%.

That was the situation when I was appointed to the Birmingham Maternity Hospital in

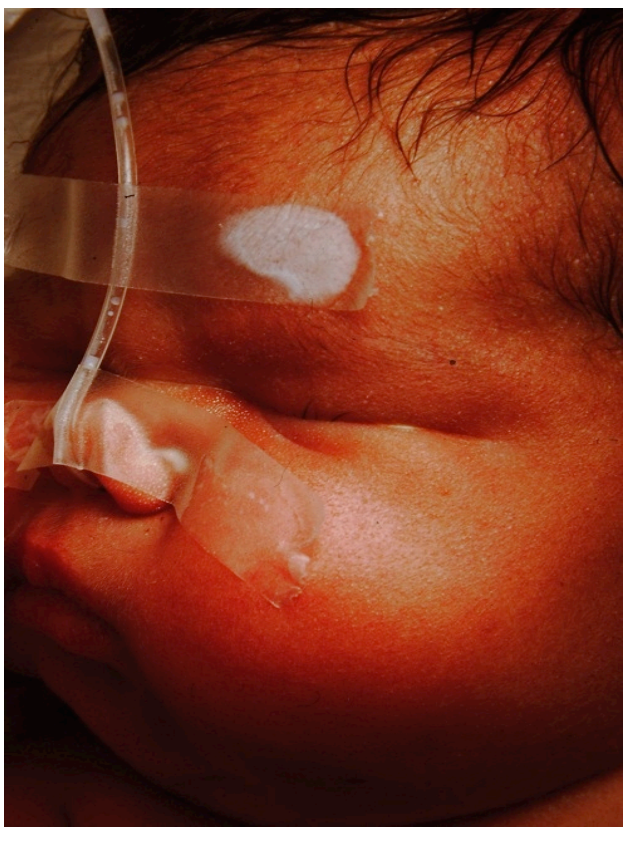

Figure1
Facies of a plethoric large-for-dates baby born to a mother with diabetes mellitus

1959, as the doctor responsible for newborn care. During the two years, 1960 and 1961, 84 mothers with insulin dependent diabetes

*Based on a presentation to the Portuguese Neonatal Society, Oporto meeting, September, 1997

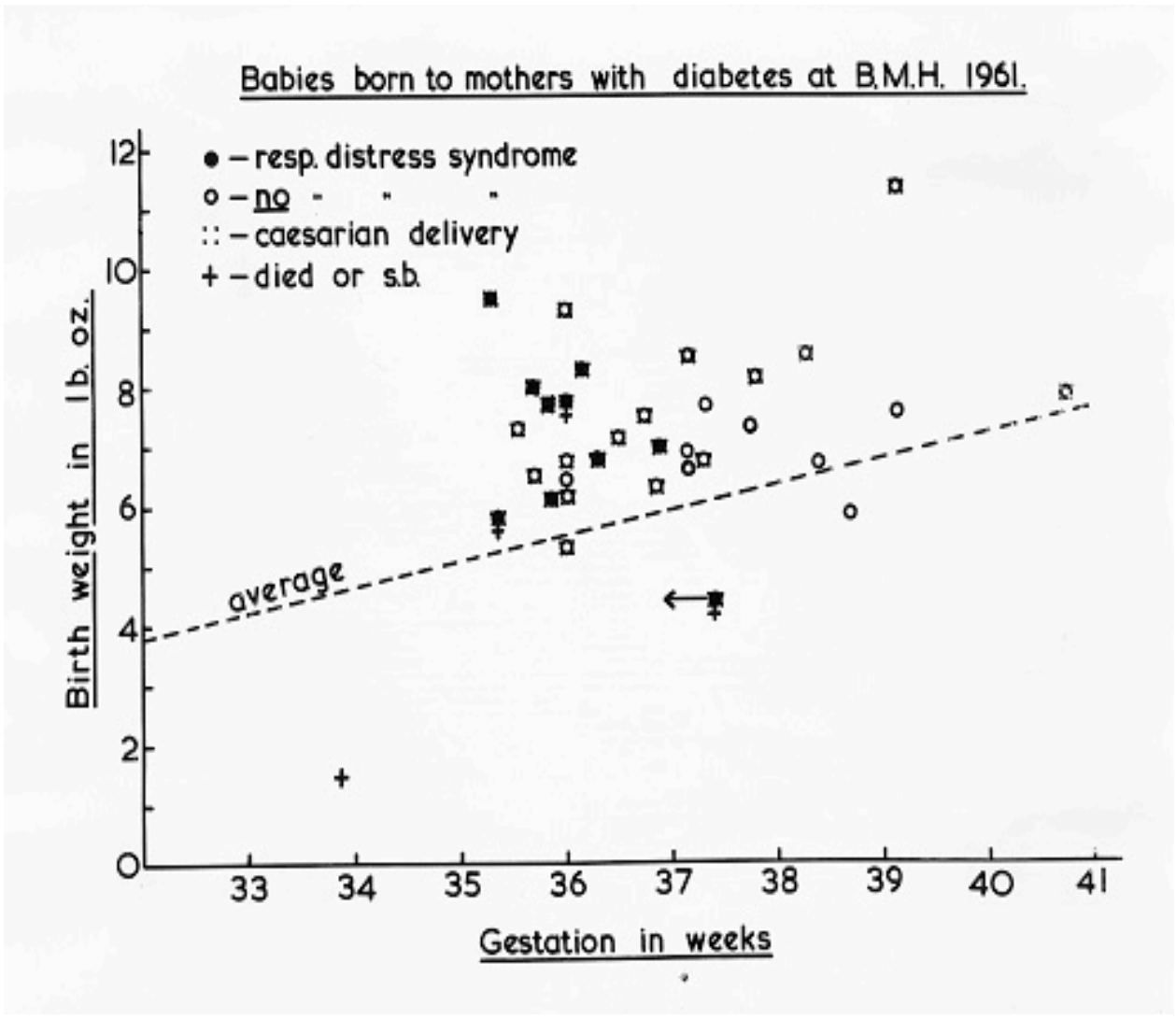

Figure 2 Birthweight-for-gestational age, method of delivery, incidence of RDS and mortality of babies born to diabetic mothers at the Birmingham Maternity Hospital in 1961.

were delivered in the hospital. There were no maternal deaths. The perinatal mortality was 15.5%. However, all the deaths, with the exception of one malformed infant, took place after birth from the respiratory distress syndrome. You have to remember that intensive care was non-existent at that time and even special care was fairly primitive. The birthweight for gestational age and outcome of the infants of diabetic mothers born during the year 1961 is shown in Figure 2. The following observations may be made. First, that the babies, as expected, were almost all large-for-dates. Second, that there were no neonatal deaths among the infants born after thirty-seven weeks gestation. Third, that all the cases of respiratory distress syndrome, including the three infants dying, were delivered by Caesarean section before the 37th week. Forth, the stillbirth rate, excluding one malformed baby, was zero.

At that time I had already shown that the incidence of respiratory distress syndrome and its mortality correlated closely with gestational age, being very rare after 37 weeks but rising sharply with lessening maturity[1] (Fig 3).

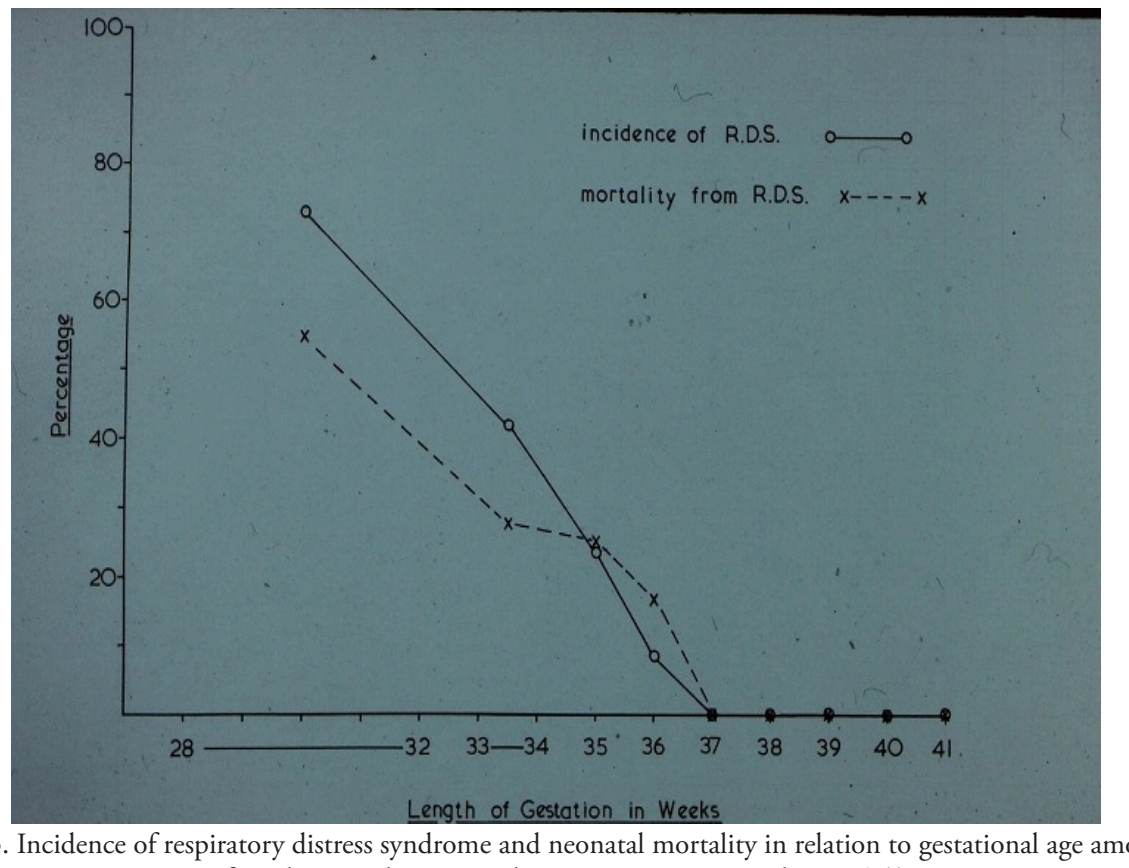

Fig 3. Incidence of respiratory distress syndrome and neonatal mortality in relation to gestational age among infants born at the Birmingham Maternity Hospital in 1961[1].

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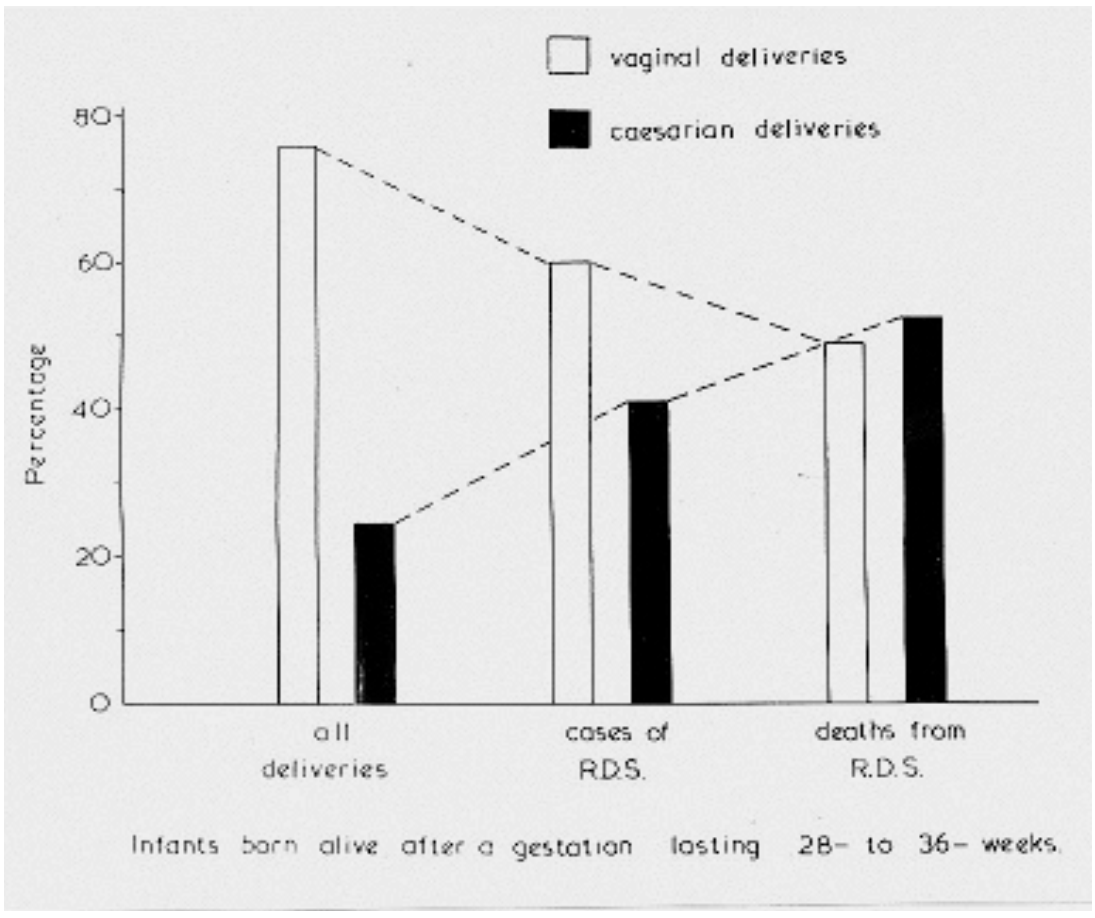

Fig 4. Incidence of respiratory distress syndrome and neonatal mortality among infants born alive with a gestation of 28 – 36 weeks at the Birmingham Maternity Hospital in 1961[2].

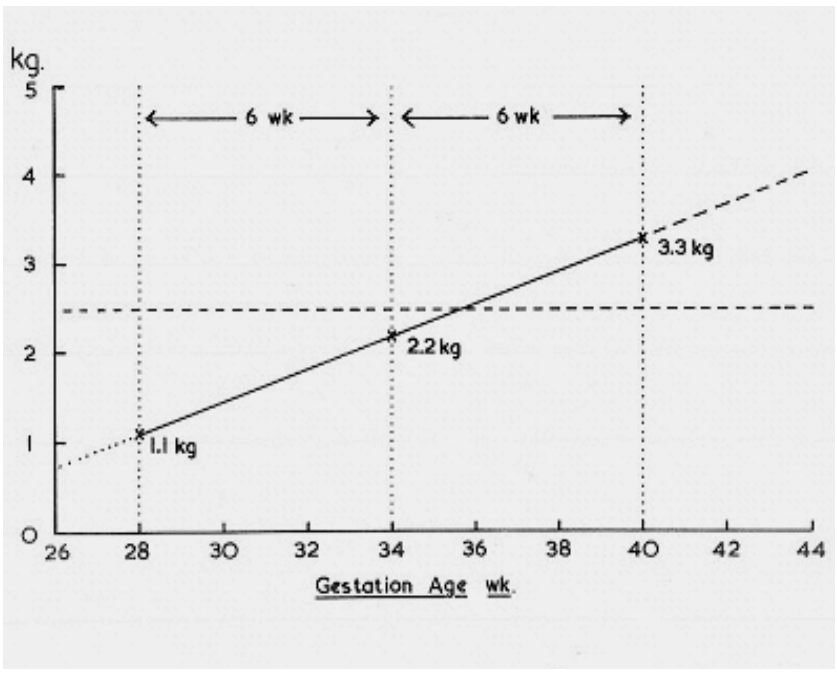

Figure 7.
Birthweight for gestation of the average fetus during the third trimester of pregnancy. Note that growth is twice as rapid during the first 6 weeks as in the second[4]

Likewise it had been possible to show that for babies born between thirty-three and thirty-six weeks gestational age, those delivered by Caesarean section were three times more likely to develop respiratory distress syndrome and three times more likely to die than those born per vaginam[2,3] (Fig 4).

Furthermore, I was able to show that the incidence of RDS and mortality among the Caesarean babies of mothers with diabetes was exactly the same as for similar babies born to mothers without diabetes. Armed with this information, I suggested to my senior obstetric colleague, Mr. Sam Davidson, that he should in future aim at delivering these babies two weeks later than usual, namely at 37-38 weeks, and then preferably by the vaginal route. At first he was unconvinced, but when Sir John Peel, the then President of the Royal College of Obstetricians and Gynaecologists, made the same recommendation a year later in 1963, he changed his practice with a greatly improved neonatal outcome.

Meanwhile, I had been reflecting on why a tiny 2kg malnourished infant (Fig 5) could survive with a cobweb-like placenta to be born alive post term, while the huge fat 5kg infant of a diabetic mother (Fig 6) with a large and apparently healthy placenta would often die in late pregnancy or during labour. I came up with a quite simple hypothesis[4]. It was based on the extraordinary rate of growth that occurs in fetal life. For example, on average a fetus doubles its weight over the six week period between 28 and 34 weeks gestation (Fig 7). This is a 52 times faster rate of growth than that of a child of 5 who takes 6 years to double its body weight. From 34 weeks onwards though, the rate of growth steadily falls and often comes temporally to a standstill at term as the fetal weight curve flattens out. But supposing that the rate of growth does not slow down but continues in an unrestrained fashion? This would impose enormous demands on the placental lifeline.

To test this possibility, I postulated the following hypotheses:

'That a fetus growing at a rate that enables it to double its bodyweight in 6 weeks, as is normal between 28 and 34 weeks, has a metabolic requirement for growth (M per Kg) equal or equivalent to that required to support basal metabolism'.

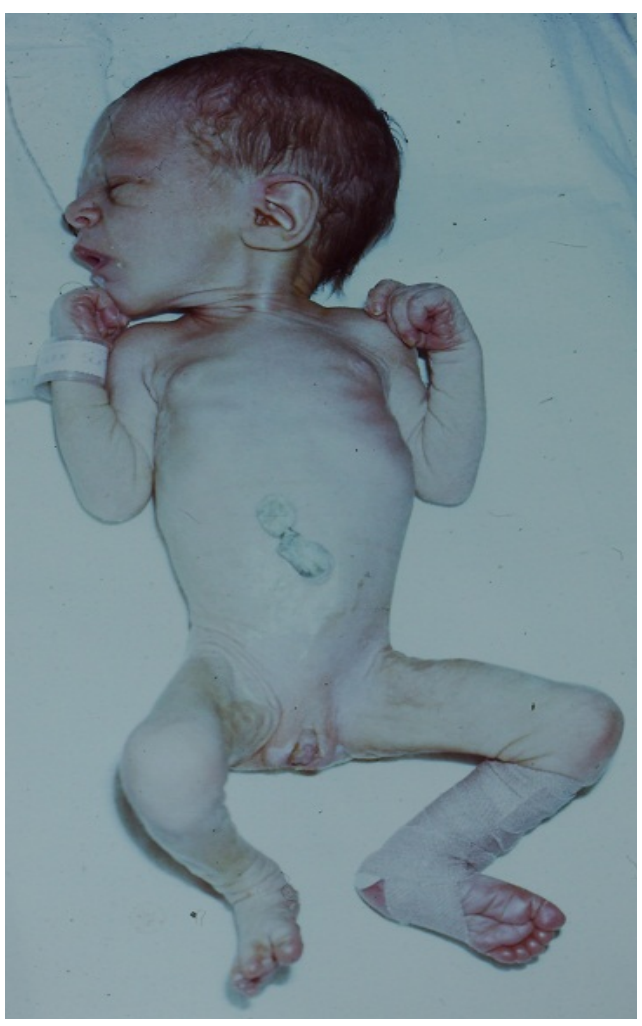

Figure 5.
Malnourished infant weighing just 4lb after a gestation of 44 weeks

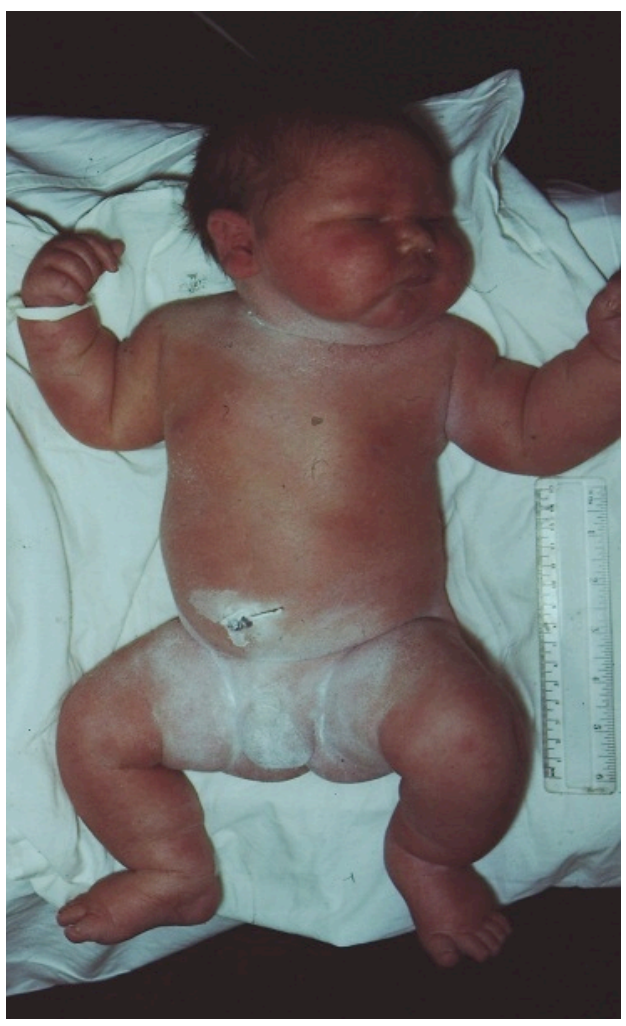

Fig 6.
Baby of a diabetic mother born weighing 11½ lbs after a gestation of 36 weeks

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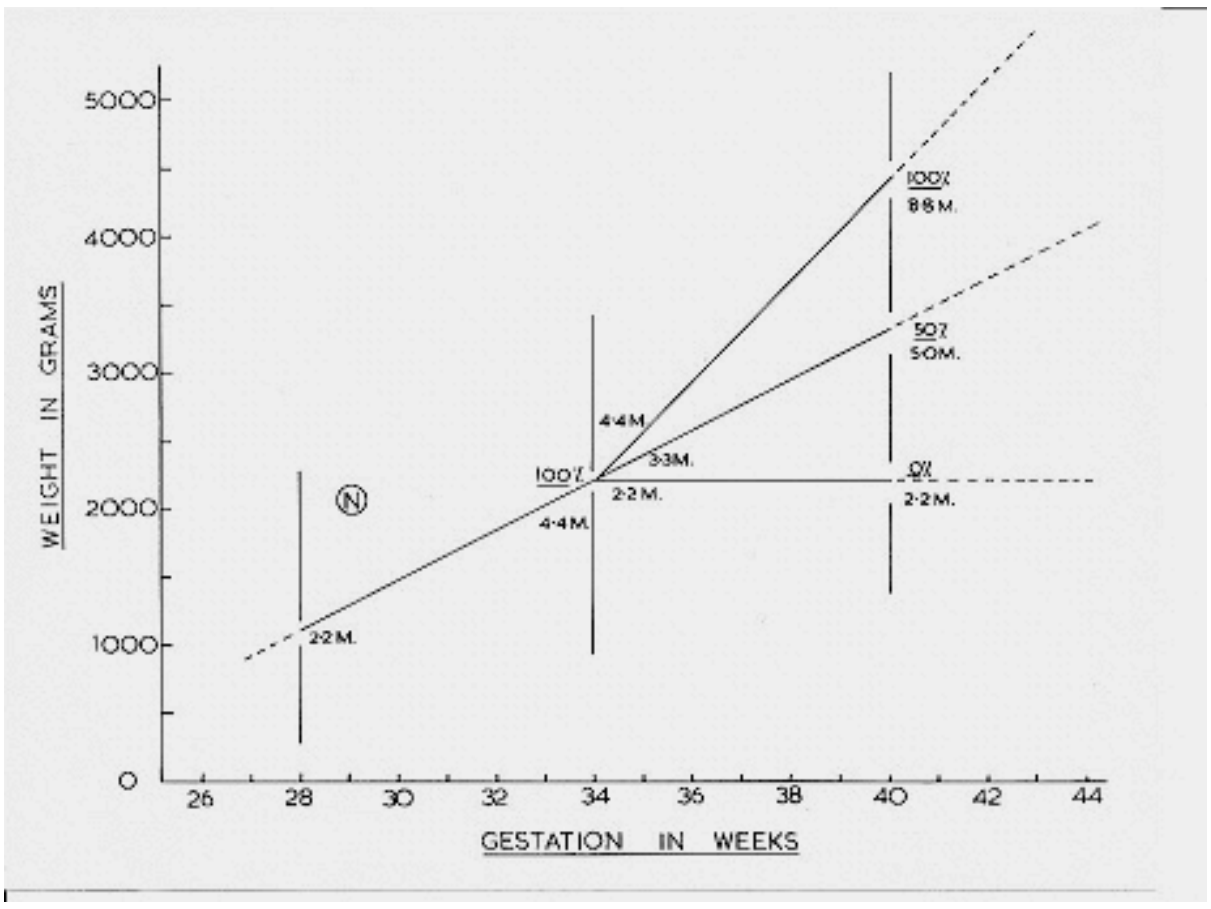

Figure 8.
The hypothetical metabolic requirements (M) of a fetus in relation to its rate of growth and size during the last trimester of pregnancy[4].

I then envisioned three growth curves in the last trimester – low, normal and high – giving fetal birthweights of 2.2, 3.3 or 4.4 kg at term (Fig 8). In the lower curve, growth would be switched off during the last 6 weeks, while in the upper curve growth would continue at the same rate as in the first half of the last trimester.

My next assumption was that the vasculature of the placenta had a finite effective life=span of, say, term plus 6 weeks or a total of 46 weeks, and that its ability to support the fetus thus steadily deteriorated in late pregnancy, especially post-term (Fig 9).

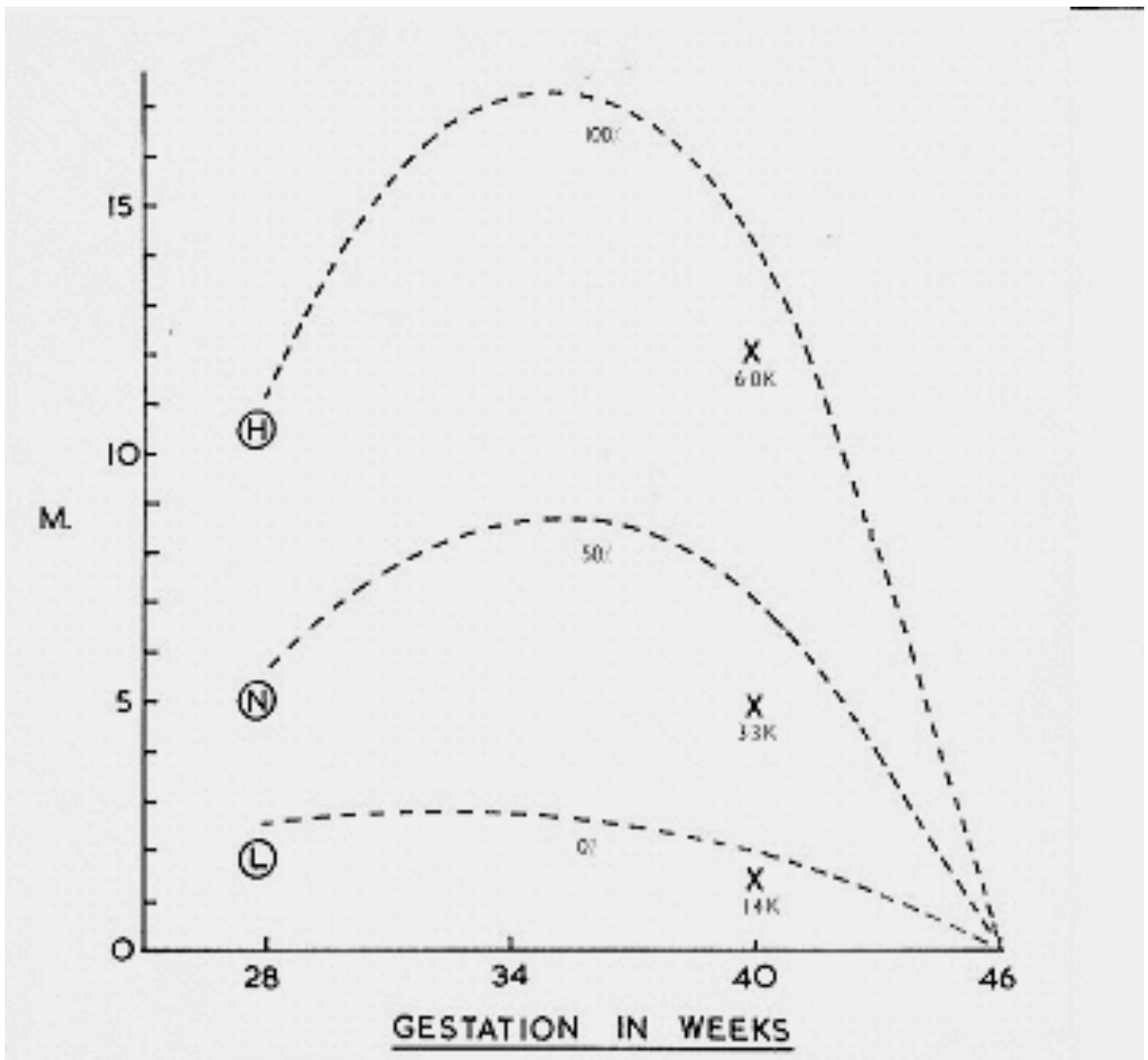

Fig 9.
The hypothetical potential of three types of utero-placental circulation with good, average, and poor function to transfer metabolic requirements to the fetus during the last trimester of pregnancy. The assumption has been made that, due to aging on the vasculature, utero-placental function would fall to zero at 46 weeks of gestation[4]

Putting these two postulates together, then one achieves the metabolic requirement curves of the fetus growing at low, normal or high rates shown in Fig 10 as the uninterrupted lines, and the placental ability to provide the metabolic needs of the fetus, shown as the interrupted lines. It will be seen at once that while the two curves for the slowly growing fetus approach each other, run parallel but do not cross; meanwhile the curves for the fetus growing at a high rate and its placenta come into direct and abrupt conflict at or after term. In other words, the rapidly growing large-for-dates fetus at term makes demands on its lifeline, the placenta, which may not be met by its aging vasculature. Sudden unexpected asphyxia and death during labour might be expected to be the outcome.

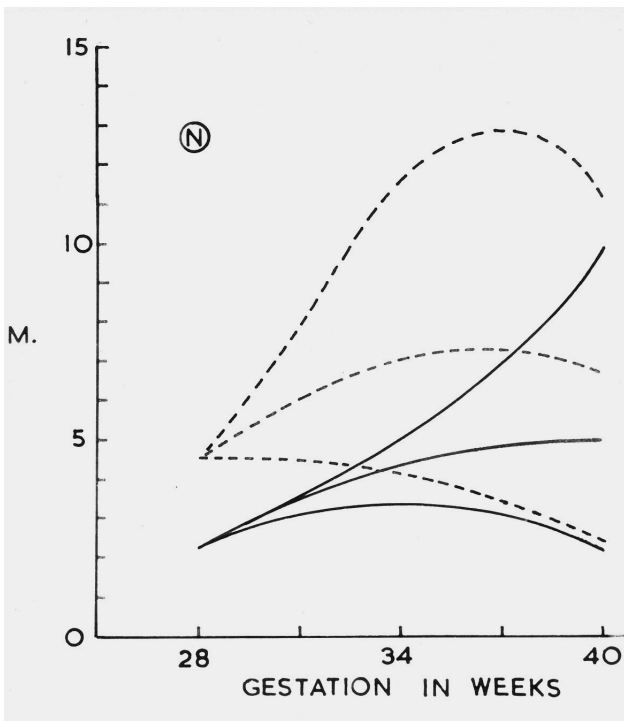

Figure 10.
The hypothetical dynamic interplay between the metabolic requirement (M) in relation to the rate of growth and size of the fetus (unbroken line, see Figure 8) and the ability of the utero-placental circulation to provide this metabolic requirement in relation to its functional capacity and age.
(interrupted line, see Figure 9)[4].

If excessive fetal growth in late pregnancy leads to a form of placental insufficiency in that fetal demands outpace placental support, we need to enquire what leads the infant of the diabetic mother to grow so fast. My own theory back in the early 1960s (and it was shared by others) was with maternal diabetes the fetus was on the receiving end of a maternal glucose drip, to which it responded by increasing its own output of insulin. This in turn would lead to the deposition of fat and glycogen, and to the stimulation of growth.

Certainly there is evidence of hypertrophy of the islets of Langerhans in the fetal pancreas of these babies (Fig 11), and also high levels of blood insulin. Therefore in order to control

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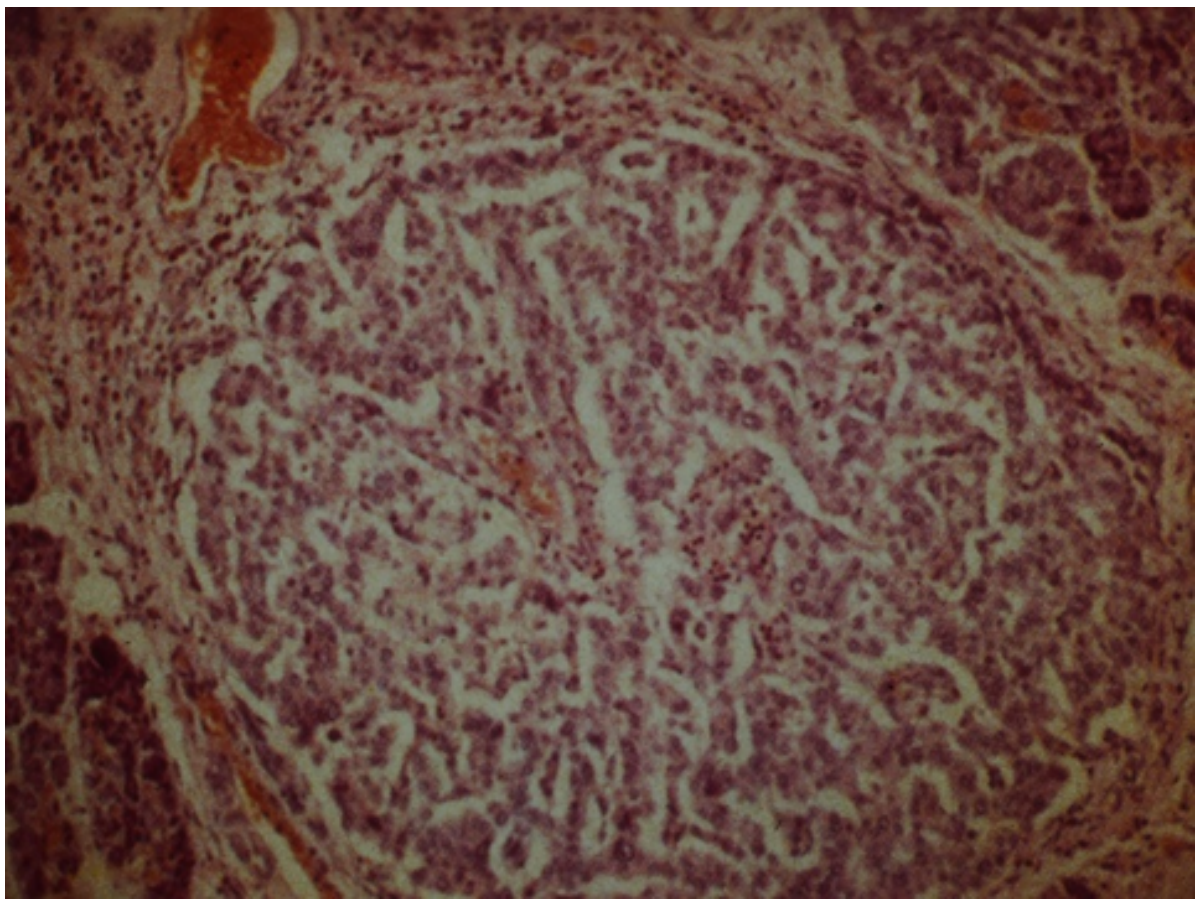

Figure 11.
Hyperplasia of an islet of Langerhans from an infant stillborn at term to a mother with diabetes mellitus

fetal growth, the logical approach should be to control the maternal diabetes.

In 1968 I was appointed to look after the babies in the University of Bristol Department of Obstetrics and Gynaecology, whose head was the late Professor Geoffrey Dixon (Fig 12). Maternal diabetes was one of his particular interests. He belived in very strict control of the mother's diabetes from early pregnancy or even better, before conception. His aim was to keep the mother's blood sugar below 4mmols/1 or 100mg%. He also believed, like me, in attempting vaginal delivery whenever possible at 38 weeks gestation, rather than

Figure 12
Professor Geoffrey Dixon, Head of the University of Bristol Department of Obstetrics, 1967-1980.

Caesarean section at 35-36 weeks. During the 13 years we worked together before Geoffrey's untimely death, we were able to reduce the perionatal mortality for babies of diabetic mothers receiving insulin to 4 percent, the lowest that had been reported anywhere in the world at that time. That was during the 1970s. Even more interestingly, but not surprisingly, the typical large-for-dates and cushinoid appearance so characteristic of these babies in the past, largely disappeared, except when the diabetes had been undiagnosed, was latent, or had only been detected late in pregnancy.

In this very brief talk I have tried to address the central problems facing the infant of the diabetic mother. However, these babies may have a number of other neonatal complications[5] which are listed in Fig 13.

INFANT OF DIABETIC MOTHER
Morbidity

- Birth trauma
- Birth asphyxia
- Hypoglycaemia
- Hypoglycaemia/magnesaemia
- Respiratory distress syndrome
- Polycythaemia
- Hyperbilirubinaemia
- Renal vein thrombosis
- Congenital anomalies

Figure 13. Some neonatal problems of an infant born to a diabetic mother.

The birth trauma and birth asphyxia may hopefully be avoided by careful control of the maternal diabetes and hence, of fetal growth. Likewise, the polycythemia which may give rise to hyperbilirubaemia and also in rare instances, to renal thrombosis, is much less in evidence when the diabetes is well controlled. If severe polycythemia is present, it is always possible to do a dilution exchange transfusion. The hypoglycaemia which is quite often encountered in the first hour after birth is usually due to the sudden cessation of placental transfer of glucose with cord ligation, in the presence of hyperinsulinaemia. It may be readily treated with glucogen and intravenous dextrose. Hypocalaemia, possibly due to transitory maternal hyperparathyroidism, has never in my experience proved to be a problem. There remains the increased incidence of congenital anomalies. In 1964 Pedersen and his colleagues in Copenhagen reported that babies born to mothers with diabetes were three times more likely to be malformed than other infants. They even suggested that this was an indication for pregnancy termination. I responded to the Lancet[6] to say that we and others had not shared his experience at that time, and that it was not improbable that the difference in experience was due to the method of management rather than the actual diabetes. The use of oral drugs such as tolbutamide to control the diabetes might, for example, be teratogenic. Having said this I too have noted an increase in congenital malformations since those early days, among which sacral agenesis (Fig 14) seems to be especially associated with the maternal diabetic state. This is a subject which requires further investigation.

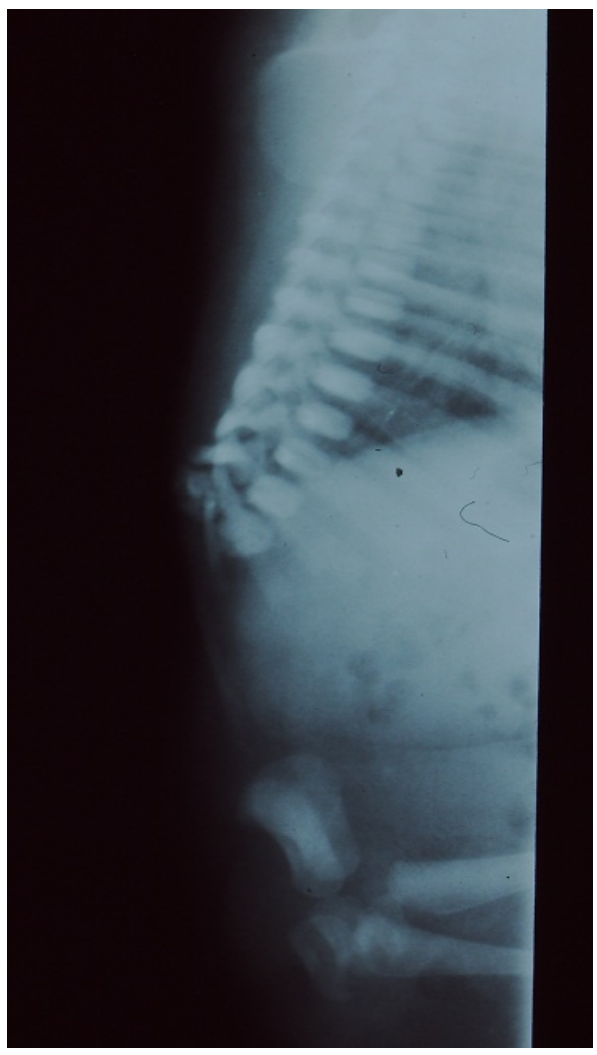

Figure 14.Lateral X-ray showing sacral agenesis in the lower spine of an infant born to a mother with diabetes

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CONCLUSION

In summary, I have addressed the aspects of the infant of the diabetic mother that have been of the most interest to me, namely, first strict control of the maternal diabetes to prevent excessive fetal growth and second, to favour safe delivery at or after thirty-eight weeks gestation, whenever possible by the vaginal route.

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